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CLINICAL CHARACTERISTICS, GENOTYPING AND MOLECULAR DETECTION OF *BURKHOLDERIA PSEUDOMALLEI*

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Doctor of Philosophy

Burkholderia pseudomallei is a saprophytic Gram-negative bacterium that infects human body through inhalation, ingestion or percutaneous inoculation and causes melioidosis. The pathophysiology and clinical presentations of melioidosis are influenced by *B. pseudomallei* load on exposure, route of infection and human risk factors. Laboratory methods for *B. pseudomallei* include various procedures applied for diagnosis, molecular epidemiology and pathogenicity studies using conventional, immunological and molecular techniques.

In this study, the clinical characteristics and risk factors of melioidosis were explored. Genotyping using multilocus sequence typing (MLST) was performed on clinical *B. pseudomallei* isolates to explore the degree of their genotypic diversity in the area of the study and to correlate the identified genotypes with clinical presentations and outcomes. In order to improve the laboratory detection of *B. pseudomallei*, a PCR-based assay targeting *sctQ* gene of the TTS1 cluster has been developed.

In this study, which involved 158 cases, the principal clinical presentations reported were lung infection in 65 (41.1%), skin infection in 44 (27.8%), septic arthritis/osteomyelitis in 20 (12.7%) and liver infection in 19 (12.0%). Bacteremic melioidosis was seen in most cases ($n = 121$, 76.6%). Focal melioidosis was seen in 124 (78.5%) of patients and multi-focal melioidosis was reported in 45 (28.5%) cases, while melioidosis with no evident focus was reported in 34 (21.5%) patients. Internal organ abscesses and secondary foci in lungs and/or soft tissue were common in this study. Sixty seven (41%) patients were admitted during the monsoonal wet season. Death due to melioidosis was reported in 52 (32.9%) of patients, while recurrent infections occurred in 4 (2.5%) patients. Twelve fatal melioidosis cases directly attributed to the absence of prompt acute-phase treatment were seen in this study. Pre-disposing risk factors were reported in 133 (84.2%) patients, which included diabetes (74.7%), immune disturbances (9.5%), cancer (4.4%) and chronic kidney disease (11.4%). On multivariate analysis, the independent predictors of mortality were the presence of at least one co-morbid factor (OR 3.0; 95% CI 1.1–8.4), the occurrence of septic shock (OR 16.5; 95% CI 6.1–44.9) and age > 40 years (OR 6.47; 95% CI 1.7–23.8).

Multilocus sequence typing of 83 *B. pseudomallei* isolates has revealed 32 different sequence types, of which 13 (40%) were novel, namely: ST1317, ST1318, ST1319, ST1320, ST1321,

ST1322, ST1323, ST1324, ST1325, ST1326, ST1327, ST1358 and ST1359. All retrieved sequence types were deposited in MLST database. The frequencies of sequence types among the 83 isolates ranged from 1–12 observations with predomination of ST54, ST371 and ST289. All non-novel sequence types identified in this study were not exclusive for Malaysia; they were identified in other regional countries with different frequencies. However, some of these sequence types were firstly identified in Malaysia such as ST371, ST164, ST47, ST306, ST55, ST376, ST402, ST507, ST368, ST369, ST10 and ST168.

Based on MLST data analysis, the constructed phylogenetic tree revealed more than half of the sequence types clustering with each other, as well as with the sequence types from Malaysia, Thailand, Singapore, Cambodia, Vietnam, Laos and China. Majority of novel sequence types were clustered with each other along the phylogenetic tree. The only novel and singleton sequence type in this study was ST1326. The present study has expanded the former Malaysian database for *B. pseudomallei* population genetics by adding more branching sequence types and the creation of new cluster after predicted clonal expansion emerged from ST84.

There was no evidence of associations for *B. pseudomallei* sequence types with clinical melioidosis presentations on the evolution tree. No clustering of particular sequence types with a given clinical outcome was noted. In addition, there was no evidence of differential virulence or strain tropism. Severe sepsis ($n = 11$) was caused by strains of 7 different sequence types, while both septic shock ($n = 29$) and abscesses ($n=30$) were caused by strains of 17 and 18 different sequence types, respectively. Presentations with sepsis, pneumonia, different melioidosis types, septic encephalopathy and other organ infections and disease outcome were caused by strains of several different sequence types. Finally, two-way tables for all bacterial genotype clusters in relation with each clinical outcome were statistically insignificant and no risk estimate was reported for every genotype cluster for developing any of clinical outcomes.

PCR was optimised to achieve the maximal discrimination between *B. pseudomallei* and its genetic relatives and to enhance the best detection limit. The in-silico specificity test showed complete match with a reference sequence for the target gene. *sctQ*-PCR showed 100% specificity once tested against *B. thailandensis* and *B. cecapacia* and a panel of genetically related and non-related microorganisms DNA. The sensitivity was 100% after successful amplification of isolates of different MLST strains and genotypes. The lower concentration of purified *B. pseudomallei* DNA that was amplified by *sctQ*-PCR was 100 fg/ μ L, whereas the lowest number of bacterial cells detected in spiked blood specimens was 18.2×10^5 CFU/mL. The developed PCR assay was capable of specific identification of suspected *B. pseudomallei* from cultured plate or directly from clinical specimens.

This study has provided major review for melioidosis and its causative agent, *Burkholderia pseudomallei* among selected population clusters residing in the Northeastern part of Peninsular Malaysia. Clinical presentations and risk factors of melioidosis were not unique for Malaysia and *B. pseudomallei* genotypes showed wide diversity that was correlated with the distribution of different strains in the environment. Novel sequence types indicated the genetic activity and instability of the bacteria which predicted the emergence of new strains that may harbor different virulence effect. This work kept on previous assumption that host and environmental factors were behind the diversity for clinical presentation of the disease. For molecular diagnosis, further upgrading and evaluation are needed to improve the performance of the assay.

Supervisor:

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OPTIMISING PHYSIOLOGICAL, PSYCHOLOGICAL AND PERFORMANCE OUTCOMES USING TAPERING TECHNIQUES AMONG JUNIOR CYCLISTS

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Doctor of Philosophy

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Introduction: Tapering involving a planned increase of training load during the final three days prior to competition may be particularly beneficial for athletes to improve performance. However, this suggestion has been based solely on theoretical predictions. Thus, there is a crucial need to confirm or reject this speculation on the basis of an experimental study. Therefore, the primary aim of this study is to investigate the effects increase in training load during final three days of taper using modified exponential taper on physiological, psychological and performance outcomes among junior cyclists.

Objectives: The aim of this study was to investigate the effects of increased training loads during the final three days of taper using modified exponential taper on physiological, psychological and performance outcomes among junior cyclists.

Methods: This study involved a pre- and post-experimental design with a control group and two experimental groups (modified exponential taper and normal exponential taper). Twenty one junior male cyclists were recruited and 19 subjects (Mean age = 16.95 ± 0.8 years) completed the whole study protocol. Participants were matched according to a baseline VO_{2max} value and they were assigned into either normal exponential taper (NET), modified exponential taper (MET) and control groups (CON). Both experimental groups underwent three months of progressive endurance training followed by two weeks of taper, while the control group continued their endurance training until the end of the study period. All parameters (physiological, psychological and

cycling performance) were measured at baseline, pre-taper and post taper.

Results: The results of the Mixed Factorial Analysis of Variance (ANOVA) revealed significant interactions between experimental groups across the measurement sessions for maximum oxygen consumption (VO_{2max}), maximum power output (W_{max}), maximum heart rate (HR_{max}), rating perceive of exertion (RPE), hemoglobin (Hg), hematocrit (Hct), lactate (Lac), creatine kinase (CK), lactate dehydrogenase (LDH), cortisol, fatigue and vigor. No significant interactions were observed for ferritin concentration value, anger, tension, depression and confusion scores. The results of post-hoc analysis revealed that both experimental groups (NET and MET) showed significantly higher values in VO_{2max} , W_{max} , RPE scores, Hg concentration values, Hct concentration value and Lac concentration value and vigor scores compared to the control group. Furthermore, the results of post-hoc analysis showed that the experimental groups (NET and MET) had significantly lower HR_{max} , CK, LDH, cortisol concentration values and fatigue scores compared to the control group. The result also revealed that the experimental groups had significantly faster time in the 20 km time trial compared to control group at post taper. However, no significant differences were observed between the MET and NET groups.

Conclusions: It is concluded that the MET and NET are equally effective in optimising the physiological, psychological and performance outcomes among junior cyclists.

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EFFECTS OF COMBINED SAGO-SOY SUPPLEMENTATION ON CYCLING TIME TRIAL PERFORMANCE IN THE HEAT

Daniel Tarmast
Doctor of Philosophy

The effects of carbohydrate intake and a combination of carbohydrate and protein intake on endurance performance have been studied by many researchers with equivocal findings. In this study, local food products such as sago starch (containing 88% carbohydrate) and a soy-protein isolate (containing amino acids) has been used. The purpose of the current study was to examine the effects of sago, soy, and iso-caloric combination of sago + soy supplementations during 90 minutes steady-state cycling at 60% VO_{2max} , on a subsequent 20 km cycling time trial performance in the heat (~ 31 °C; 70% relative humidity). Twelve well-trained male cyclists (age: 19.0 ± 5.6 years, body weight: 60.1 ± 11.2 kg, height: 170.8 ± 7.6 cm, and VO_{2max} : 56.5 ± 6.5 mL.kg⁻¹.min⁻¹) representing Kelantan (state level) cycling team were recruited for this randomised single-blind placebo-controlled crossover study. Following preliminary trials, to investigate the VO_{2max} and to determine workload of the steady-state cycling, participants performed four experimental trials. The experimental trials consisted of a 90-minute steady-state

pedalling at 60 % of VO₂max, followed by a 20 km cycling time trial. From the beginning of the experimental trials and at 20 minute intervals during the steady-state cycling (0, 20, 40, 60, and 80 minutes), participants consumed 200 mL of either: 7.5 % Sago, 7.5 % Soy, 6.0 % Sago + 1.5 % Soy, or placebo.

No significant differences were found in time-to-complete the 20 km time trial regardless of the drink ingested ($P > 0.05$). Metabolic responses including plasma concentrations of glucose and insulin were increased during the steady-state cycling in the sago and sago + soy trials compared with soy and placebo trials. At the end of the 20 km cycling time trial, the plasma lactate concentration was increased significantly in all trials ($P < 0.001$), and the plasma free fatty acids concentration was significantly higher in the placebo and soy trials than the sago and sago + soy trials ($P < 0.001$). There were no significant differences between the trials in plasma concentrations of creatine kinase and F₂-Isoprostanes after the experimental trials ($P > 0.05$). The present study demonstrated that ingestion of sago, soy, and isoc-aloric sago + soy combined supplementation did not improve the 20 km cycling time trial performance in the heat despite the availability of a higher level of plasma glucose and insulin. Hence, carbohydrate alone or a carbohydrate + protein combined supplementation may not be beneficial in exercise performance, specifically in the heat.

Supervisor:

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RECOMMENDATION STRATEGIES FOR THE PREVENTION AND CONTROL OF HIGH MORBIDITY OF DENGUE HEMORRHAGIC FEVER IN NORTH SUMATERA PROVINCE

Fazidah Aguslina Siregar
Doctor of Philosophy

Background: The incidence of dengue hemorrhagic fever (DHF) in North Sumatera Province remains high despite effort to control it.

Objectives: This study aimed to document information about the adequacy of the current Indonesia surveillance system for DHF and factors responsible for high DHF transmission. These will be used for recommending strategies for the prevention and control for DHF in North Sumatera Province.

Material and Methods: Five study designs were adopted in this study. In the exploratory study, all key personnels involved in the surveillance system for DHF at the district and health facility levels in the selected six districts were interviewed to determine the function and performance of the surveillance system. The case cohort study recruited a total of 682 respondents with case: subcohort ratio 1:1. ‘Simple and Multiple logistic regression’ were applied to determine the factors associated with DHF. For the comparative cross sectional study, 688 households both in high and low incidence district were selected using multistage sampling.

‘Simple and Multiple logistic regression’ were again applied to determine the factors associated with DHF among the households in districts with high incidence. In the entomology study, Independent *t*-test and Two Way Anova were used to determine the effect of larvae positive containers on DHF transmission, whereas for larvae and adult indices ‘Simple and Multiple logistic regression’ were applied. The climatic study utilises monthly a year’s climatic (2003–2011) secondary data. The relationship between climatic and dengue hemorrhagic fever incidence was determined by Pearson correlation and the impact of climates on DHF incidence by Time series regression. Seasonal Autoregressive Integrated Moving Average (SARIMA) model was then developed to predict the occurrence of DHF.

Results: The structure of DHF surveillance system was good but suboptimum with major deficiencies that include unavailability of guidelines, insufficient resources and poor core and supportive functions. Socio-cultural and environmental factors associated with DHF incidence were investigated through case-cohort and comparative cross sectional studies. Significant factors include experience with DHF in family, travelling history, length of stay, frequency of cleaning water container, frequency of cleaning garbage disposal, education, knowledge, practices in preventive measure, source of drinking water, house style and house with gutter. *Aedes* larvae and adult indices were above the critical level especially in the high incidence districts with house indices as the predictor for dengue transmission. Climatic factors that include rainfall, rainy days, temperature and relative humidity were significantly associated with DHF incidence. SARIMA model (0,1,1)(0,1,1)¹² was able to predict DHF occurrence.

Conclusion: The existing surveillance system for DHF need to be strengthened in every aspect. Socio-cultural and environmental factors associated with DHF should be addressed and controlled. Measures should be taken to eliminate or being down the density of *Aedes* vectors. Climatic factors should be integrated in the national prevention and control program for DHF.

Supervisor:

Professor Dr Mohamed Rusli Abdullah

FABRICATION OF A REUSEABLE PLASTIC BASED X-RAY DOSIMETER FOR RADIOTHERAPY

Iqbal Tariq
Doctor of Philosophy

The aim of this study was to fabricate a plastic composite dosimeter for the measurement of radiation doses of X-ray photons used in radiotherapy. The criteria for the proposed dosimeter were low cost, ease of use, non-toxic, and reusable.

As a dosimeter, it should have acceptable sensitivity and reliability in the dose measurements range of interest in radiotherapy. In making plastics based dosimeters, radiation sensitive material grains were uniformly embedded in transparent plastic host where they are kept spatially fixed. Changes in optical transmission spectra of the materials

was used as readout method, using Shimadzu UV 1800 spectrophotometer. These changes were then calibrated to get the absorbed doses. Optical bleaching of the irradiated samples were performed with two 100 watts ordinary bulbs for 18 hours. Among the thirteen materials that were selected for the study of their suitability as the embedding material, research grade pure sodium chloride was found to be the most suitable material. Other materials studied were beryllium oxide, seven different types of edible salts available in local markets, undoped aluminium oxide, potash alum (*tawas*), ammonium chloride (Noshadar) and bamboo salt. PMMA (polymethyl methacrylate) was chosen as the host material. The final plastic sample was produced using Haake poly drive internal mixer and hot press machine, as 2 mm thick plastic sheet, with uniformly embedded grounded (125 μm) pure sodium chloride grains in 40/60 sodium chloride to PMMA wt/wt ratio. All the evaluations of embedding materials were carried out with their samples placed inside a transparent plastic vial containing optically clear oil. This plastic vial was found to have optical properties very close to the final, material free, PMMA sample. It was observed that treatment of samples using 9 MeV electron doses of up to 2800 Gy does not change their sensitivity. The aforementioned final plastic sample, containing sodium chloride labelled as N1, have shown response to 6 MV photons with a linear dose response from 3 Gy to 10 Gy. The sensitivity appeared to be decreased between 10 Gy to 15 Gy, after which appeared to recover for the last observed dose of 20 Gy. The decrease in 15 Gy response is postulated to be due to the depletion of the trapped electrons of interest, supposed to produce optical absorption at 395 to 550nm, due to fluorescence up-conversion resulting from 570 to 625 nm absorption during measurements. The Z_{eff} of the PMMA plastic based dosimeter containing 40% N1 by weight was calculated to be 10.51 amu. The N1 samples irradiated with 5 Gy 6MV photons has shown fading of 16.92% and 48.06% for one week and one month respectively. The dose reproducibility was estimated with the average response of three fresh samples to 5 Gy 6 MV photons. The doses were delivered for alternate 4 days post optical bleaching of 18 hours. The area of dip in the percentage transmission curve corresponding the absorbed dose was found to have an average value of 96.4 arbitrary area units with standard deviation of 4.85%. The peak values of the dips were found to be between 460 nm to 472 nm. The fabricated plastic based dosimeter was found to be robust, cheap, easy to use and reusable and suitable for measuring doses of X-ray photons, in the dose ranges of linear responses, 3 Gy to 10 Gy and for observed higher doses, 15 Gy and 20 Gy.

IN-VITRO CELL BASED STUDY OF SMN2 EXPRESSION UPON EXPOSURE WITH HISTONE DEACETYLASE INHIBITORS AND POLYPHENOLS AS A POTENTIAL THERAPY FOR SPINAL MUSCULAR ATROPHY

Jafar Mohseni
Doctor of Philosophy

Autosomal recessive of spinal muscular atrophy (SMA) is the second most common inherited disease, leading to early infancy death. The SMN1 mutations are leading cause

of SMA. However, increasing expression of SMN2 has been exploited as therapeutic target for Spinal Muscular Atrophy (SMA). Several Histone Deacetylase Inhibitors (HDACIs) are known to increase SMN2 expression level. This study aimed to elucidate the effects of two hydroxamate-based HDACIs, SAHA and Dacinostat, and one SIRT1 activator, SRT1720, on the SMN2 expression, CpG Islands (CGI) methylation and SMN protein levels in fibroblasts taken from SMA Type I and Type II patients.

Toxicity assay/dosage determination was carried out using trypan blue exclusion technique. Each cell type was treated with serial concentrations of Dacinostat, SRT1720 and SAHA and their combinations for 48 hr. Quantification of Overall-SMN2 expression (Overall-SMN2) and SMN2 exon 7 inclusion (E7-SMN2) was subsequently done using QuantiGene® 2.0 Plex assay (Affymetrix). SMN2 CGIs methylation level was investigated using MS-HRM (Methylation-Specific High Resolution Melting) on bisulfite treated DNA. SMN protein was quantified using ELISA method using SMN protein assay kit (Enzo Life Science, USA). Methodologically, exclusive increase in E7-SMN2 (without increase in Overall-SMN2) should result in the decrease of SMN2 transcripts that lack exon 7 ($\Delta 7$ -SMN2). $\Delta 7$ -SMN2 quantification in this study was inferred from the difference between Overall-SMN2 and E7-SMN2. The p-values were considered statistically significant if they are less than 0.05 for comparison between untreated and treated cells.

It was found that the levels of SMN2 gene expression (Overall-SMN2 and E7-SMN2) and SMN protein level were significantly increased in 10 μM SAHA-treated Type I and Type II cells compared to untreated cells (Mock). The mean methylation levels in CGIs of SMN2 CpG Islands region showed significantly lower levels of methylation as well. Accordingly, the level of Overall-SMN2 and E7-SMN2 transcript increase were also significant in 32 nM Dacinostat-treated fibroblasts type I and type II cells as compared to untreated fibroblasts (Mock). The transcript increase induced by Dacinostat led to more increase of SMN protein compared to SAHA in Type I cells (2.54 + 1.57 fold). The $\Delta 7$ -SMN2 transcript in type I and type II cells were noted to be decreased, although not significant. Moreover, methylation levels in CGIs of SMN2 CpG Islands region showed statistically lower percentage in at 5% level of significance.

SMN2 gene expression (Overall-SMN2 and E7-SMN2) was remarkably increased upon exposure to SRT1720. While, the mean CGIs methylation percentage and SMN protein level alteration were decreased modestly. SAHA-Dacinostat combination increased SMN2 expression in Type I, but not Type II cells. SRT1720-Dacinostat combination increase Overall-SMN2 and E7-SMN2 transcripts nearly double the increase induced by individual compounds. SRT1720-SAHA combination resulted in lower increase than that induced by SAHA alone but higher increase than that induced by SRT1720 alone. Furthermore, SMN protein was noted to be increased and CGIs was more demethylated in treated cells.

In conclusion, SMN2 expression (Overall-SMN2 and E7-SMN2), SMN protein level and methylation level of CGIs were significantly altered upon exposure to SAHA, Dacinostat and SRT1720-Dacinostat combination in SMA fibroblast Type I and Type II. This is the first report about Dacinostat and SRT1720 effect on SMN2 modulation.

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EFFECTS OF TUALANG HONEY ON MEMORY PERFORMANCE, DEPRESSIVE-LIKE BEHAVIOUR, HISTOLOGICAL AND BIOCHEMICAL CHANGES IN YOUNG AND OLD MALE RATS EXPOSED TO LOUD NOISE STRESS

Khairunnuur Fairuz Azman
Doctor of Philosophy

Ageing and stress exposure may lead to memory impairment and depression while oxidative stress is thought to be one of the underlying mechanisms involved. The search for cognitive enhancers from natural products derivatives possessing antioxidants has gained much attention. Thus, this study aimed to examine the effects of ageing and stress on memory performance and depressive-like behaviour, and to elucidate the possible mechanisms underlying therapeutic efficacy of Tualang honey in improving memory performance and depressive symptoms in young and old male rats exposed to loud noise stress. Ninety six male Sprague Dawley rats were divided into eight groups: i) unstressed young with placebo, ii) unstressed young with honey, iii) stressed young with placebo, iv) stressed young with honey, v) unstressed old with placebo, vi) unstressed old with honey, vii) stressed old with placebo and viii) stressed old with honey. The honey supplementation was given orally, 200 mg/kg body weight for 35 days. All animals were subjected to novel object recognition test (NORT) and forced swim test (FST) prior to honey supplementation as well as before and after the noise stress procedure. Upon completion of the experiment, rats were lightly anaesthetised with ether and immediately killed by decapitation, and their blood and brain samples were collected. The right brain hemisphere was homogenised and used to measure levels/activities of antioxidant enzymes, oxidative markers, total antioxidant capacity (TAC), brain-derived neurotrophic factor (BDNF) and acetylcholinesterase (AChE) using commercially available assay kits. The left brain hemisphere was fixed in 10% formalin for histological study of medial prefrontal cortex (mPFC) and hippocampus. Serum corticosterone, adrenocorticotrophic hormone (ACTH) and testosterone levels were also measured using commercially available assay kits. The present study demonstrated that there were significant main effects of age on depressive-like behaviour, levels/activities of corticosterone, ACTH, testosterone, TAC, SOD, GPx, GR, CAT, MDA, PCO, BDNF, AChE and number of Nissl-positive cells in the mPFC and all the hippocampal regions. There were significant main effects of stress on memory performance, depressive-like behaviour, levels/activities of corticosterone, ACTH, testosterone, TAC, SOD, GPx, GR, CAT, MDA, PCO, BDNF and number of Nissl-positive cells in the mPFC and hippocampal CA2 and CA3 regions. Tualang honey supplementation was able to improve memory performance and depressive-like behaviour, increase the levels/activities of

TAC, SOD, GR, BDNF, testosterone and enhance the neuronal proliferation in the mPFC and hippocampus, and decrease the levels/activities of MDA, PCO, corticosterone, ACTH and AChE. In conclusion, Tualang honey has the potential to be used as an alternative therapy to protect against memory decline and depressive symptoms due to stress exposure and/or ageing.

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DEVELOPMENT OF SYNTHETIC MULTIEPITOPE PEPTIDE (rMEP) AS POTENTIAL SERODIAGNOSTIC MARKER AND VACCINE CANDIDATE FOR *Toxoplasma gondii* INFECTION

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Introduction: Infection with the intracellular parasite *Toxoplasma gondii* exhibits a worldwide distribution. Such disease is known to cause abortions and serious clinical complications on the fetus, neonate, and immunocompromised individuals, resulting in considerable clinical and economic effects. The most effective measure for controlling toxoplasmosis and minimizing the harms caused by the parasite is prompt diagnosis and treatment. Meanwhile, vaccination is an efficient tool for preventing the occurrence of the infection. Therefore, development of a novel antigen for diagnostic or vaccination purposes is important.

Significant efforts have been made to acquire such antigen. As a result, developing multi-epitope-based antigens using software-based prediction tools and molecular techniques may provide a novel and alternative means for acquiring less expensive and more accurate diagnostic kits or potential vaccine candidates. The advantage of the multi-epitope antigen lies in the capacity to combine epitopes from different stages of the parasite. Thereby, this approach would serve as a promising and valuable strategy to overcome the antigen complexity of the *T. gondii* life cycle.

Results: In this study, a single synthetic gene of approximately 456 bp in size, which encodes potential epitopes of *T. gondii* antigens, was successfully constructed using gene assembly PCR. The constructed gene, designated as *USM.TOXO1*, was then cloned into a pET32a(+) expression vector and transformed into BL21 (DE3) pLysS *E. coli* Competent cells. The entire protein was successfully expressed and purified. Subsequently, the immunoreactivity of this antigen was evaluated by developing immunoglobulin G (IgG) enzyme-linked immunosorbent assay (ELISA) and Western blot

analysis using human sera. Meanwhile, the immunogenicity was tested in BALB/c mice.

The usefulness of USM.TOXO1 for the diagnosis of toxoplasmosis through ELISA was tested on 151 sera from positive *T. gondii* patients and 96 sera from negative patients for the detection of specific anti-*T. gondii* IgG. The USM.TOXO1 ELISA presented an 85.43% sensitivity, 81.25% specificity, 87.76% positive predictive value, and 78% negative predictive value.

Immunisation of the BALB/c mice with USM.TOXO1 generated a strong mixed Th1/Th2 response polarised toward the IgG1 antibody isotype. Additionally, analysis of cytokine profiles following in vitro stimulation revealed the significant synthesis of IFN- γ cytokines, but not IL-4, in the immunised mice compared with the control group.

Conclusion: USM.TOXO1 is a potential serodiagnostic marker for the detection of *T. gondii* infection in humans, as well as a promising vaccine candidate that elicits protective immunity in BALB/c mice. The proven immunoreactivity and immunogenicity of USM.TOXO1 can serve as a premise for the further use of epitope-based antigens in the routine diagnosis and immunoprevention of human and animal toxoplasmosis.

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EFFECTIVE OF HEALTH EDUCATION MODULE IN IMPROVING LIFE SATISFACTION AMONG FAMILY CAREGIVERS' CARING FOR FIRST- EVER STROKE SURVIVORS AT HOME

Noor Aini binti Hussain
Doctor of Philosophy

The involvement of family member as “unpaid caregivers” negatively affected the caregivers’ psychological, physical and social health either while the stroke survivors are in hospitals or at home. The objective of this study was to determine the effect of the health education module on life satisfaction among family caregivers of first ever stroke survivors at home, health progress of first ever stroke patient and predictors of life satisfaction among family caregiver.

A quasi-experimental pre and post intervention design with purposive sampling was used in this study. Life satisfaction of family caregivers was measured using the Bakas Caregiving Outcome Scale (BCOS), whereas the health status perception of stroke patients was measured by Barthel’s Index (BI) and EQ-5D. A repeated measures Split Plot two-way ANOVA and multiple linear regression test was used to test the hypothesis. The assumption of SPANOVA test was met when the Levene’s and Box test are not significant ($P > 0.05$). Huynh-Feldt Epsilon value was used when Mauchly Sphericity test is significant ($P < 0.05$).

This research involved 52 family caregivers of intervention group, while 50 family caregivers were in the non-intervention group of hospitalised first ever stroke patients from two

tertiary hospitals in Kelantan. Data collection was at pre-intervention visit (hospital) and post-intervention home visits (1 month, 3 months and 6 months).

The findings showed that majority of the family caregivers are among the aged of 20 to 60 years old, female, unemployed and wife or children of the first-ever stroke patient. The SPANOVA findings showed that there was a significant interaction between repeated measure time and family caregiver groups [$F(2.45, 245.73) = 25.76, P < .001, \eta^2 = 0.21$] and main effect between the groups of family caregivers [$F(1, 100) = 65.980, P < 0.001, \eta^2 = 0.39$] on the family caregivers life satisfaction score. The findings also showed that there was a significant interaction between repeated measure time and first ever stroke patient groups [$F(2.09, 209.58) = 9.29, P < 0.000, \eta^2 = 0.85$] and main effect between groups of first ever stroke patient [$F(1, 100) = 23.20, P < 0.000, \eta^2 = 0.19$] on the score of health perception status of stroke patient. A large effect size was evident. Significant predictors of life satisfaction of family caregivers were combination of caregiver’s health and presence of chronic diseases [$F(2, 49) = 34.807, P < 0.001$], stroke patient’s age (> 61 years) [$F(1, 50) = 9.436, P < 0.05$] and physical function ability [$F(1, 50) = 9.363, P < 0.05$].

Families are responsible for their disabled sick family members in hospital or at home because of the social values and religion. A structured health educational module with skills manual developed in this study has proven to improve life satisfaction of the family caregivers and health status perception of the first-ever stroke patients. This health educational module is suggested to be a guidance for nurses and become a tool in the improvement of existing health education modules for the benefit of the family caregivers, stroke patients, and rehabilitation centers.

A MULTIDIMENSIONAL ASSESSMENT ON SEVERE MATERNAL MORBIDITY AND NEAR MISSES IN KELANTAN

Norhayati binti Mohd Noor
Doctor of Philosophy

Introduction: Increasingly, severe maternal conditions are used as alternative measurements of the quality of maternal care and as alternative strategies to reduce maternal mortality. Since maternal morbidity is more common than maternal death, the former provides superior information on the burden of disease and quality of care.

Objectives: To evaluate the prevalence and factors associated with severe maternal morbidity, to compare the quality of life, maternal functional status and postpartum depression between women with and without severe morbidity at one month and six months postpartum. To explore the experiences of women with maternal near miss and their perceptions of the quality of care and social support they received.

Methodology: This study consists of three phases. Phase I and II was a one-year cross-sectional study and a six-month prospective double cohort study, respectively. Phase III was a qualitative study using a phenomenological strategy. (i) In Phase Ia, all eligible postpartum women with severe maternal morbidity who were admitted to Raja Perempuan

Zainab II Hospital and Universiti Sains Malaysia Hospital in 2014 were recruited. Descriptive analyses were performed. (ii) In Phase Ib, consecutive sampling was applied for the selection of cases and for each case identified, one unmatched control from the same hospital was selected. Simple and multiple logistic regression analyses were performed. (iii) In Phase II, postpartum women with and without severe maternal morbidity were selected as the exposed and non-exposed groups, respectively. For each exposed woman identified, a non-exposed woman with a similar mode of delivery was selected. The outcomes were measured at one month and six months postpartum using Short Form-12 Health Survey, Inventory of Functional Status after Childbirth and Edinburgh Postnatal Depression Scale. Repeated measure analysis of variance and analysis of covariance were performed. (iv) In Phase III, all eligible women with maternal near miss were invited. Purposive sampling and in-depth interview method were applied. A semi-structured interview guide was used. Thematic data analysis was performed. Women with severe maternal morbidity and maternal near miss were defined and classified using the World Health Organisation criteria. Data management and analyses were performed using Stata Intercooled version 11.0, IBM SPSS Statistics version 22.0 and NVIVO version 10.0.

Results: In total, 21,579 live births, 395 women with severe maternal morbidity, 47 women with maternal near miss and two maternal deaths were analysed. The severe maternal morbidity incidence ratio was 18.3 per 1,000 live births and the maternal near miss incidence ratio was 2.2 per 1,000 live births. Haemorrhagic disorders were the most common event for severe maternal morbidity (68.6%) and maternal near miss (80.9%). Factors significantly associated with severe maternal morbidity were age of 35 or more years old [adj. OR (95% CI): 2.6 (1.67, 4.07)], women with past pregnancy complications [adj. OR (95% CI): 1.7 (1.00, 2.79)], underwent caesarean section deliveries [adj. OR (95% CI): 6.8 (4.68, 10.01)], preterm delivery [adj. OR (95% CI): 3.4 (1.87, 6.32)] and referral to tertiary centres [adj. OR (95% CI): 2.7 (1.87, 3.97)]. Immediate and long-term consequences of severe maternal morbidity showed that there were significant differences in the functional status score changes ($P < 0.001$) between women with and without severe maternal morbidity at one month and six months. Functional status of women with severe maternal morbidity was 0.1 score lower at one month postpartum ($P = 0.001$). However, there were no differences in physical component quality of life scores ($P = 0.848$) and mental component quality of life scores ($P = 0.769$) as well as postpartum depression scores ($P = 0.441$) between women with and without severe maternal morbidity. Thirty women were interviewed and four themes were identified: (i) self-appraisal of maternal near miss events, (ii) their perception of the quality of care, (iii) their predisposition to seek healthcare and (iv) the social support they received.

Conclusions: Comprehensive emergency care and intensive care as well as overall improvements in the quality of maternal health care need to be achieved to substantially reduce maternal death. This study suggests for enhanced screening and monitoring of women of advanced maternal age, women with past pregnancy complications, those who underwent caesarean section deliveries, those who delivered preterm and the mothers referred to tertiary centres as they are at increased risk of severe maternal morbidity. Identifying these factors

may contribute to specific and targeted strategies aimed at tackling the issues related to maternal morbidity. Healthcare providers are recommended to assess the functional status of severe morbid mother in addition to existing routine physical examination. Provision of support from spouse and family on the high-risk mothers particularly on infant care during their early postpartum period is crucial to optimise health and minimise the negative health outcomes. The women with maternal near miss viewed their experiences as frightening and that they experienced other negative emotions and a sense of imminent death. Their perceptions of the quality of their care were influenced by the competency and promptness in the provision of care, interpersonal communication, information-sharing and the quality of physical resources. These factors should be of concern to those seeking to improve services at healthcare facilities. The predisposition to seek healthcare was influenced by costs, self-attitude and beliefs. Religious faith formed the basis for adaptation and appeared to have had protective effects on the women's well-being.

Supervisor:

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DEVELOPMENT OF AN ELECTROCHEMICAL IMMUNOSENSOR ON SCREEN PRINTED CARBON ELECTRODES FOR THE DETECTION OF DENGUE NS1 ANTIGEN AND IGM ANTIBODY

Om Parkash
Doctor of Philosophy

Dengue is a major public serious health issue in the tropical and subtropical regions and about 2.5 billion lives are at risk in more than 112 countries. Due to the unavailability of effective antiviral drugs, early diagnosis is very crucial for patient management and vector control. However, laboratory diagnosis of dengue still remains a problem, as conventional diagnosis methods have their own pitfalls. Herein, an electrochemical immunosensor exploiting the screen printed carbon electrodes (SPCEs) as biosensing surface and enzyme labelled detection antibody as electrochemical signal amplifier developed to detect dengue non-structural 1 (NS1) protein and immunoglobulin M (IgM) as markers for the acute and late infection phase, respectively. Initially, the SPCEs were electrochemically characterised for their reproducibility, stability and conductivity. Subsequently, recombinant dengue NS1 antigen was sandwich hybridised between anti-NS1 capture antibody and anti-NS1 detection antibody to develop dengue NS1 electrochemical immunosensor assay, whereas dengue IgM electrochemical immunosensor assay was developed based on IgM antibody capture enzyme-linked immunosorbent assay (MAC-ELISA) principle. Chronoamperometric responses resulting from the catalysis 3,5,3',5'-tetramethylbenzidine (TMB)/hydrogen peroxide

(H₂O₂) were generated at -200 mV by horseradish peroxidase (HRP) labelled detection antibody. To enhance the sensitivity of the electrochemical immunosensor assay, various immobilisation techniques were investigated. In addition, various parameters were also optimised such as immunoreagents, concentration, incubation time, washing frequency; suitable blocking agent and washing buffer were also investigated. Analytical sensitivity and specificity, diagnostic capability and stability of the electrochemical immunosensor assay were evaluated to use the immunosensor empirically.

The SPCEs used in this study demonstrated good electrochemical properties with good stability, conductivity and reproducibility. Protein A based immobilisation technique for anti-NS1 capture antibody technique found to be the best in dengue NS1 electrochemical immunosensor assay. Dengue NS1 electrochemical sensor showed excellent sensitivity using recombinant NS1 with a limit of detection of 0.03 µg/mL, suggesting that the developed immunosensor could detect NS1 in real serum samples. Development of a matrix buffer made it possible to detect NS1 in spiked and real serum samples. Similarly, the developed immunosensor showed excellent sensitivity using NS1 spiked serum samples with a limit of detection of 0.03 µg/mL, which was lower than 0.12 µg/mL detected by ELISA while analytical sensitivity using real serum samples was found to be 1:256 serum dilution. For dengue IgM electrochemical immunosensor assay, streptavidin/biotin based immobilisation technique was the best immobilisation technique for goat anti-human IgM antibody. The dengue IgM electrochemical immunosensor also showed excellent sensitivity with a limit of detection 106 serum dilution which was lower than 105 serum dilution detected by ELISA, suggesting that the developed immunosensor was highly sensitive. Cross-reactivity analysis showed that both dengue NS1 and IgM electrochemical immunosensor could discriminate dengue from non-dengue samples. Dengue NS1 and IgM electrochemical immunosensor also successfully discriminated the 150 dengue NS1 and dengue IgM real serum samples, respectively. The overall diagnostic performance of the dengue NS1 and IgM immunosensor regarding diagnostic sensitivity, diagnostic specificity, positive predictive value (PPV) and negative predictive value (NPV) was found to be 100%, indicating that the developed immunosensor is fully capable of detecting dengue NS1 and IgM from real serum samples with high sensitivity, specificity. The assay time of electrochemical immunosensor was comparable to ELISA. However, the advantage using immunosensor is that it is more sensitive than ELISA. Apart from these features, the developed immunosensor found to be stable for one year at ambient temperature with the help of preservative trehalose.

In conclusion, the developed immunosensor can be used for the diagnosis of dengue during acute and late phase with high sensitivity and specificity and has the potential to be commercialised. However, further modifications are needed to ensure the assay can be a point of care test.

Supervisor:
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Co-Supervisor:
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THE MECHANISM OF ANTICARCINOGENIC EFFECTS OF TUALANG HONEY (TH) ON INDUCED BREAST CANCER IN RATS

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PhD (Pathology)

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Introduction: The multifloral Tualang honey (TH) and the monofloral Manuka honey (MH) have been reported to have antimicrobial, anti-inflammatory, antioxidant and anticancer effects. Unlike the MH, TH is not extensively studied.

Objectives: This study was conducted to evaluate the mechanisms of the preventive and therapeutic effects of Tualang honey (TH), Manuka honey (MH) and honey sugars analogue (HSA) on experimental breast cancer induced rats using carcinogen 1-methyl-1-nitrosourea (MNU).

Methodology: A total of 130 female Sprague-Dawley rats were used. Sixty female rats were randomly divided into six groups with 10 animals per group in each study. Group 'o' (negative control; normal rats); Group 1 (positive control; tumour induction but no treatment). Groups 2, 3 and 4 were fed orally with 0.2, 1.0 and 2.0 g/kg body weight of TH. Group 5 received 1.0 g/kg of MH, and Group 6 received 1.0 g/kg HSA. For the "cancer-preventive" study, honey was given one week prior to MNU-induction and for the "cancer-therapeutic" study; treatment was given after breast cancer development. The treatment continued until the 120th day when the rats were sacrificed for samples collections.

Results: Results showed that TH and MH treated rats of "cancer-preventive" groups had a lower tumor incidence, and a longer latency period compared to the non-treated control group. The tumors developed in all treated groups of preventive and therapeutic measures were lesser in number, size and weight compared to the non-treated control. The majority of the tumors in the treated groups were of better grade (grade I and II) compared to the non-treated control group (grade III). The haematological parameters showed that varying strengths of TH, MH and HSA had a potentiating effect on haemoglobin, red blood cells, packed cell volume, mean corpuscular volume, lymphocytes and eosinophils, and a lowering effect on total white blood cells, red cell distribution width, polymorphs, monocytes and platelets compared to the non-treated control. These treatments showed no hyperglycemic effects and no body weight loss. The systemic administration of TH, MH and HSA exerts anti-cancer effects through up-regulation of the expression of pro-apoptotic proteins such as caspase 9, Apaf-1 (apoptotic protease activating factor 1), p53, IFN-γ (interferon gamma) and IFNGR1 (interferon gamma receptor 1), and a concomitant down-regulation of the expression of anti-apoptotic proteins such as Bcl-xL (B-cell lymphoma-extra large), TNF-α (tumor necrosis factor alpha), COX-2 (cyclooxygenase-2), E2 (estradiol) and ESR1 (estrogen receptor 1) at serological and or breast cancer tissues levels.

Discussion: Our study shows that the treatment with TH and MH appears to exert cancer-preventive and or cancer-therapeutic effects, is through the modulation tumour

grading, body weight, haematological parameters of immune regulatory response, and modulation of pro and anti-apoptotic proteins of mitochondrial apoptotic pathway at serum and breast cancer tissues level. HSA also acts akin to honey.

Conclusion: Tualang honey, Manuka honey and honey sugars analogue can be used as prophylactic cancer-preventive and cancer-therapeutic agents. The mechanism is through the modulation of tumour grading, haematological parameters, and the modulation of pro and anti-apoptotic proteins at serum and cancer tissues level.

Supervisor:

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COGNITIVE, PSYCHO-PHYSIOLOGICAL AND PHYSICAL BENEFITS OF AEROBIC EXERCISE AND MILK CONSUMPTION AMONG FEMALE SECONDARY SCHOOL STUDENTS

Sedigheh Moghaddam
Doctor of Philosophy

The objectives of the present study were to identify the cognitive, psycho-physiological and physical benefits of aerobic exercise and milk consumption among female secondary school students. The intervention was conducted in two preliminary and main studies, separately. In the preliminary phase, ninety three female students aged 16 years old were randomly assigned in the four study groups: milk, exercise, combined and control groups. The participants in the milk group consumed 250 mL/day low fat milk for five days of school days at specific time and the participants in the exercise group attended an aerobic dance exercise twice a week and the participants in the combined group consumed 250 mL/day low fat milk consumption and attended aerobic exercise. The main phase of the present study was conducted with same participants of the preliminary phase, however, it followed different intervention procedures. Participants in the combined and exercise groups were required to attend aerobic exercise class three times/week, whereas participants in the milk and combined groups were taking 500 mL/day low fat milk (first serving in the morning and second serving in the evening). Selected parameters were assessed after the 6th and 12th weeks of the intervention. The results of the two-way repeated measure ANOVA from the preliminary phase revealed that the participants of the combined intervention group (two times/week aerobic exercise plus 250 mL/day milk consumption) had significantly lower waist circumference, fat percentage and HDL Cholesterol ($P < 0.05$) compared to their counterparts in the control group. Furthermore, combination of aerobic exercise plus intake of milk consumption significantly influenced higher improvement of short term memory and sustained attention ($P < 0.001$, $P < 0.05$) compared to those in the control and milk groups. Outcomes of the main phase over three months intervention however

revealed that the participants in the combined, exercise and milk groups exhibited significantly lower fat % and waist circumference compared with the participants in the control group with higher mean difference for combined group ($P < 0.01$). Moreover, the participants of the combined group had significantly positive change in blood lipids compared to the control group. According to the results of main phase, scores of emotional distress of the all participant in the intervention groups decreased significantly more from baseline to post intervention with greater mean differences in the combined group (mean differences = 5.21, $P < 0.01$). Furthermore, additional benefits of aerobic exercise and milk intake for muscular power surfaced just in the main phase with significant improvement in the combined and exercise groups compared to the control and milk groups. In conclusion, the frequency and duration of aerobic exercise and amount of milk consumption as well as combination of aerobic exercise plus intake of low fat milk improved selected parameters. Although, combining aerobic exercise and milk consumption was observed to be more effective to produce sizable changes on the mentioned parameters.

Supervisor:

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THE ROLE OF MICROVASCULAR ENDOTHELIAL DYSFUNCTION AND GENETICS ON SEVERITY AND PROGRESSION OF PRIMARY OPEN ANGLE GLAUCOMA IN MALAYS

Syed Muddassar Imran Bukhari
Doctor of Philosophy

There is lack of knowledge of clinical presentation and risk factor for primary open angle glaucoma (POAG) in Malays. Identification of the risk factors for severity and progression of POAG in Malays is important to strategies prevention of blindness and effective management. This study was conducted to determine the severity and progression of POAG in Malay patients and to determine the role of microvascular endothelial function and genetics in progression and severity of POAG.

A cross-sectional study was conducted involving 215 Malay (114 POAG patients and 101 controls) subjects. Progression was determined based on Humphrey visual field analysis (HVF) of 114 POAG patients using combination criteria of Advanced Glaucoma Intervention Study (AGIS) scoring and Hodapp, Parish and Anderson classification. Severity of POAG was based on modified AGIS scoring of HVF.

Microvascular endothelial function was assessed using Laser Doppler Fluximetry (LDF) with the process of acetylcholine (ACh) and sodium nitroprusside iontophoresis. Venesection was also conducted. High purity genomic DNA was extracted. Microarray Human Omni Express-12

platform was used to identify genetic markers. rs1392912 and rs1660029 from KALRN gene, and rs1210977 of COL9A1 gene were identified as potential markers for progression and microvascular endothelial function. These single nucleotide polymorphisms (SNPs) were then subjected to DNA sequencing.

After the mean 4.1 (3.0) years of follow up, 35 patients showed evidence of visual field progression. Based on HVF at recruitment, 55 patients were mild, 29 moderate and 30 severe POAG. There was significant reduction of microvascular endothelial function in POAG patients compared to control ($P < 0.001$). ACh and sodium nitroprusside response was significantly reduced in severe POAG ($P < 0.001$). There was significant reduction of microvascular endothelial function in patients who showed visual field progression ($P < 0.001$). The risk of progression is 4.8 folds (95% CI 1.52, 14.86) in patients with rs1392912GA and 5.8 folds (95% CI 1.85, 18.61) in patients with rs1660029AG. However, there was no association between rs1210977 of COL9A1 and microvascular endothelial function of Malay patients with POAG. The progression rate of POAG in Malay patients was 8.5 patients/year.

Microvascular endothelial function play a role in progression and severity of POAG in Malays. rs1392912GA and rs1660029AG of KALRN gene are potential genetic markers for progression of glaucoma. Perhaps, improvement in microvascular endothelial function and early detection of patients with genetic variations of KALRN gene may retard the progression of POAG in Malays.

ROLES OF SELECTED GENETIC VARIATIONS AND MOLECULAR ALTERATIONS IN HUMAN PAPILLOMAVIRUS-MEDIATED CANCER OF UTERINE CERVIX

Tan Shing Cheng
Doctor of Philosophy

Although human papillomavirus (HPV) is essential for cervical carcinogenesis, it alone is insufficient to result in the malignant transformation of the cervix. Information on the roles of selected genetic variations as well as molecular alterations (in the forms of gene expression, DNA copy number alterations and loss of heterozygosity) in cervical cancer is currently lacking among Malaysian women. The present study was therefore undertaken to fill this gap of the literature. For this purpose, the associations of 12 genetic polymorphisms in nine candidate genes involved in various carcinogenic pathways with cervical cancer risk were evaluated on 185 histopathologically confirmed cervical cancer patients and 209 cancer-free female controls. The mRNA expression levels of these nine candidate genes, as well as the genome-wide copy number alterations and allelic imbalances were also analysed in cancerous and non-cancerous tissues of 72 of the subjects. All data obtained were subsequently stratified by ethnicity and HPV subtypes involved. In addition, data on tumor molecular alterations was also stratified by stages and histopathology of the cancer. Besides, the association between the genetic polymorphisms and their respective gene expression levels was investigated. It was demonstrated that 154 (83.2%) of the cervical cancer patients and none (0.0%)

of the cancer-free female controls were positive for HPV infection. Among the HPV-positive subjects, 141 (91.6%) had single-type HPV infections (of which HPV16, HPV18 and HPV58 predominated), while the remaining 13 (8.4%) were simultaneously infected by two HPV types (with HPV16 + HPV18 being the most common multiple-type infection). It was also observed in the present study that after adjustment to known risk factors of cervical cancer, TNF c.-488G>A, CTLA4 c.49A>G, FAS c.-671A>G, MDM2 c.14+309T>G and CCND1 c.723G>A polymorphisms showed statistically significant associations with the risk of the cancer when analysed singly. In addition, statistically significant observations were noted for the several combinations of CTLA4 c.-319C>T polymorphism with TNF c.-418G>A, CDKN1A c.93C>A and CCND1 c.*687C>G polymorphisms. Apart from that, it was shown in the present study that PUM1, YWHAZ and RPLP0 were the most stably expressed reference genes in cervical cancer, and normalisation of expression levels of the nine candidate genes against these reference genes showed no significant relative expression difference between cancerous and non-cancerous tissues of the cervix. However, an association was found between a higher CTLA4 expression and the variant allele of CTLA4 c.49A>G polymorphism, and between a lower FAS gene expression and the variant allele of FAS c.-671A>G polymorphism. The present study also successfully characterised the landscape of genome-wide copy number alterations and loss of heterozygosity in cervical cancer tissues, and observed that the most common loci with recurrent genomic alterations were 3q21.3, 10q26.3 and 5p15.33 (for copy number gains), 11p11.12, Xp11.1 and 12q11 (for copy number losses), and Xq11.1, Xq22.3 and 16p11.2 (for losses of heterozygosity). In conclusion, the present study has successfully determined the prevalence and distribution of HPV types among Malaysian women, identified several host genetic polymorphisms associated with risk of cervical cancer, and identified some major molecular alterations which occurred in the cancerous and non-cancerous tissues of cervical cancer patients. These results have a potential prospect in the promising field of individualised preventive medicine.

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THE MECHANISM OF RAPAMYCIN AND ANDROGRAPHOLIDE ACTION ON THE GROWTH OF BREAST CANCER BY IN VIVO AND IN VITRO STUDY

Wirdatul-Nur binti Mohd Khairi
Doctor of Philosophy

Breast cancer is a major disease that kills women worldwide. Recent advancement in breast cancer treatments such as surgery, chemotherapy, radiation therapy and hormone dependent targeted therapy have improved patient

survival rate. However, the results of chemotherapy to date remain unsatisfactory, prompting a need to identify new potential therapeutic agents that could target cancer cells efficiently. Rapamycin, a macrolide isolated from *S. hygrosopicus* and Andrographolide which isolated from *A. paniculata* (*Hempedu Bumi*) have been reported to exert impressive anti-cancer properties against various human malignant diseases. Therefore, this study aims to investigate the effect of Rapamycin and Andrographolide together with their combination on apoptosis signaling pathway and cell cycle arrest in in vivo NMU-induced rat mammary carcinoma model as well as in vitro breast cancer model. In the in vivo study, the histopathology of breast tumour samples were evaluated by Haematoxylin and Eosin staining, while the gene and protein expression of apoptosis related markers such as p53, Fas-Ligand, Bcl-2, Bax, Caspase 3, Caspase 8 and Caspase 9 were analysed using immunohistochemistry staining and Real-Time PCR assay. For in vitro study, the minimal inhibition concentration (IC₅₀) values of Rapamycin and Andrographolide as mono or dual therapy were determined using MTS assay. Cell morphological changes was examined by microscopy. Meanwhile, apoptosis and cell cycle distribution and apoptosis proteins expressions were determined by flow cytometry and western blot, respectively. The in vivo results showed that Rapamycin (0.2 µg/µL), Andrographolide (100 mg/kg) and combination (0.2 µg/µL + 100 mg/kg) treatments significantly inhibited breast tumour growth in NMU-induced rat model. In addition, Rapamycin, Andrographolide and combination treatments effectively inhibited proliferation of MCF-7 and MDA-MB-231 breast cancer cells in a time and dose dependent manner with IC₅₀ of 0.5 µM, 25 µM and 0.1 µM + 20 µM (MCF-7) and 0.8 µM, 35 µM and 0.1 µM + 30 µM (MDA-MB-231), respectively. The anti-cancer activity of Rapamycin and Andrographolide in both in vivo and in vitro model were associated with up regulation of p53, Fas-Ligand, Bax, Caspase 3, Caspase 8, Caspase 9 and down regulation of Bcl-2 protein expression as well as induction of G₀/G₁, S and G₂/M phase cell cycle arrest. Unfortunately, Rapamycin in combination with Andrographolide do not synergistically inhibited the growth of NMU induced breast tumour, MCF-7 and MDA-MB-231 breast cancer cells. Indeed, combination treatment do not synergistically increased the expression of p53, Fas-Ligand, Bax, Caspase 3, Caspase 8, Caspase 9 as well as down regulation of Bcl-2 protein. In conclusion, Rapamycin and Andrographolide as a single agent represent a potential effective anti-cancer drugs for treatments in both breast cancer models but their combination is likely to be antagonistic to reduce breast cancer cell growth.

Supervisor:

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ACE AND ACTN3 POLYMORPHISMS, AEROBIC AND ANAEROBIC CAPACITIES, BONE AND MUSCULAR PERFORMANCE IN MALAY ATHLETES AND NON-ATHLETES

Xiao Li
Doctor of Philosophy

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Introduction: Efficient human movement is influenced by environmental and behavioral factors including training, diet and genetic endowment, and it is believed that genetic endowment is one of the factors that can increase the possibility of an individual to become an elite athlete.

Objectives: This study investigated the association between ACE gene I/D polymorphism and ACTN3 gene R577X polymorphism, aerobic and anaerobic capacities, bone and muscular performance in Malay athletes and non-athletes.

Methods: A total of 132 participants were recruited in this study. Malay athletes (male athletes, $n = 33$; female athletes, $n = 33$) and non-athletes (male non-athletes, $n = 33$; female non-athletes, $n = 33$) participants were genotyped for ACE gene I/D polymorphism and ACTN3 gene R577X polymorphism by using PCR technique. Forced expiratory ratio (FER), maximal oxygen uptake (VO_{2max}) and Wingate anaerobic power were measured. Meanwhile, the quantitative ultrasound measurements of bone speed of sound (SOS) and T-score of the participants' dominant and non-dominant legs and arms were measured using a bone sonometer. Participants' flexibility, handgrip strength, back and leg strength, leg explosive jump power were also measured. Muscular peak torque (PT, an indicator of muscular strength), peak torque per body weight (PT/BW) and average power (AVG.P) of the participants' dominant and non-dominant knee and shoulder extension and flexion at 60°·s⁻¹, 180°·s⁻¹ and 300°·s⁻¹ were measured using BIODEX isokinetic dynamometer.

Results: The present study found that ACE II genotype was associated with higher VO_{2max} in female and male athletes, and was associated higher muscular PT in female athletes. Meanwhile, ID genotype was associated with higher leg explosive jump power and lower fatigue index in female athletes, and was associated with higher muscular PT i.e. strength and power in male athletes. In female non-athletes, DD genotype was associated with better bone health status. This study also found that ACTN3 RR and RX genotypes were associated with higher flexibility in female athletes. Meanwhile, RR genotype was associated with leg explosive jump power in female athletes. In male athletes, RR genotype was associated with higher mean power. In both female and male athletes, RR genotype was associated with higher muscular PT and AVG.P, i.e. muscular strength and power. In female non-athletes, RR genotype was associated with better bone health status.

Conclusions: The present findings obtained from this study can be used to guide the decisions of sports bodies and coaches in talent identification and selection of elite athletes in Malaysia, especially Malay ethnic group.

Supervisor:

Associate Professor Dr Ooi Foong Kiew

Co-Supervisor:

Professor Dr Zilfalil bin Alwi

KNOWLEDGE, ATTITUDE AND PREVENTIVE PRACTICES ON CENTRAL NERVOUS SYSTEM TUBERCULOSIS AMONG HEALTHCARE WORKERS

Farhanah binti Abd Wahab
MSc (Epidemiology)

A bacterium called *Mycobacterium tuberculosis* which affected the central nervous system (CNS) has caused the emergence of CNS tuberculosis which covered approximately 15% of the total cases of extra-pulmonary TB cases. The first phase of this study was intended to determine the level of KAP on CNS tuberculosis among healthcare workers as well as its associated factors and to determine the association between KAP and self-sufficient perception among the HCWs towards the disease. This study sequentially also explored the themes that influence KAP on CNS tuberculosis prevention among the HCWs in the second phase. A two-phase mixed methods study approach was used in this cross-sectional study underpinned by positivism paradigm. A total of 134 HCWs from medical wards, neurology wards and forensic units of Hospital USM and HKL participated in phase one which were evaluated by using a newly developed self-administered questionnaire of KAP. In phase two, a number of 21 HCWs participated in four focus group discussions by using a semi-structured interview guide. Data collected from first phase was analysed by using logistic regression while in phase two, generation of themes was applied through thematic analysis. In phase one, the profile of HCWs showed that their mean (SD) age was 33.0 (9.2) year-old who have worked about 7.0 (9.0) years in median (IQR). Out of 134 HCWs, 56.7% had good knowledge on CNS tuberculosis while majority of them, 53.7% had negative attitude and there was no difference in their level of practice. The healthcare workers' age and duration of employment were associated by both 5% times the likelihood on getting poor knowledge while respectively by 4% and 5% times the likelihood to have negative attitude towards CNS tuberculosis. In the meantime, age of HCWs and their workplace of neurology ward were associated respectively by 4% more likely and 96% less likely to have poor practice. The associated factors of self-sufficient knowledge perception of HCWs were their negative attitude and duration of employment respectively by 65% less likely and 6% more likely to perceive themselves as having sufficient level of knowledge on CNS tuberculosis. In the second phase, the factors of transmission of CNS tuberculosis and the willingness of HCWs affected their KAP towards the disease prevention. Despite the rare occurrence of admitted patients with CNS tuberculosis, the HCWs unexpectedly gain good knowledge on the disease although majority of them presented with negative attitude which depicted by their way of thinking and reacting while handling the CNS tuberculosis patients.

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Co-Supervisors:
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ASSOCIATION BETWEEN INDOOR ENVIRONMENTAL QUALITY AND SICK BUILDING SYNDROME AMONG NURSES WORKING IN THE WARDS OF HOSPITAL UNIVERSITI SAINS MALAYSIA

Noor Asyikin Aziz
MSc (Epidemiology)

Bad indoor environmental quality can lead to Sick Building Syndrome. Sick Building Syndrome described as a complex of non-specific symptoms caused by working in buildings with bad indoor environment. The aim of this study is to determine status of indoor environmental quality in Hospital Universiti Sains Malaysia wards and factors associated with 'Sick Building Syndrome'. A total of 11 wards and 263 nurses grade U29 from Hospital Universiti Sains Malaysia (HUSM) were recruited on this study. Indoor air assessment was done to determine the selected physical, chemical and biological parameters in the wards. Self-administered questionnaire was distributed to the respondents to identify sociodemographic, work environment and symptoms of sick building syndrome. Physical parameters for temperature (°C) and relative humidity (%) were above the standard level and light below the standard level. Meanwhile concentration of the chemical parameters and biological parameters were within the normal value. Prevalence of Sick Building Syndrome among nurses in Hospital Universiti Sains Malaysia is 39.9 (34.00–45.80). Multiple logistic regression analysis showed that the significant risks were being exposed to varying of room temperature (adjusted OR:2.147; 95% CI: 1.24,3.73; $P = 0.007$) and unpleasant odour (adjusted OR: 3.787; 95% CI: 2.08, 6.90; $P < 0.001$) at working environment were more likely having sick building syndrome compared to those who are not exposed. The prevalence of sick building syndrome was considered high. Individual who exposed to varying of room temperature and unpleasant odour in work environment were risk factors of sick building syndrome. Medical follow up should be carried out for the affected worker with regular indoor air monitoring in the workplace.

Supervisor:
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CHARACTERISATION OF HAIR FOLLICLE DERIVED STEM CELLS AND KERATINOCYTES INDUCTION FOLLOWING SEEDING ON CHITOSAN SCAFFOLD

Norhayati binti Mohd Noor
MSc (Epidemiology)

Hair follicles repeatedly regress and reconstitute themselves, suggesting the presence of intrinsic tissue stem cells. Adult stem cells isolated from hair follicle have a unique

characteristic which is differentiating into keratinocytes. Chitosan skin regenerating template (SRT), produced by AMREC-SIRIM has been successfully used as a scaffold in skin tissue engineering. This study aims to investigate isolation of HFSCs from scalp tissues and the characterisation of the stem cells was performed. The HFSCs attachment, growth and differentiation ability on chitosan SRTs were evaluated. HFSCs were isolated from human scalp tissues using cell dissociation method and then cultured in CnT-07 growth media. The squamous shaped HFSCs formed groups of cells and grown well in the CnT-07 growth media. The characterisation of the cultured HFSCs was performed by using the stem cell marker of K15 and CD200. HFSCs culture were positive for the presence of K15 and CD200. Meanwhile, the attachment and growth of the HFSCs on the chitosan SRTs were evaluated using scanning electron microscope (SEM), Live/Dead assay and Alamar blue assay. The SEM images revealed that HFSCs were shown to attach and grown on chitosan. A live/dead assay shown that living HFSCs population on chitosan at day 1 was 216 ± 6 meanwhile the dead HFSCs was 99 ± 9 ($P = 0.068$). At day 2, the population of viable HFSCs on the chitosan was 367 ± 18 , while the dead population of HFSCs was 213 ± 3 ($P = 0.068$). At day 3, the population of viable HFSCs was 452 ± 18 compared with the dead HFSCs was 221 ± 9 ($P = 0.068$). The population of viable and dead HFSCs grown on chitosan showed no significant differences at day 1, day 2 and day 3. Alamar Blue assay also shown the OD from day 1 to day 7 continues to increase as the days increase, indicating HFSCs able to grow and proliferate on chitosan. The mean of the OD values of HFSCs grown on chitosan on the day 7 was the highest compared to 1, 3, and 5 days of the culture (0.0207 ± 0.001 for day 1; 0.0763 ± 0.003 for day 3; 0.0746 ± 0.003 for day 5; 0.1317 ± 0.020 for day 7). These stem cells were also induced to differentiate into epidermal keratinocytes using CnT-02 differentiation media. The characterisation of the epidermal keratinocytes was confirmed by the presence involucrin and K6 positive cells. In this present study, the HFSCs were successfully isolated, grown in CnT-07 growth media and expressing stem cell markers K15 and CD200. The study also proved that the chitosan SRT is suitable for HFSCs to attach, grow and also support the differentiation of HFSCs into epidermal keratinocytes. This study provides knowledge on HFSCs isolation and their growth and differentiation on chitosan that in future can be used as an alternative method in treating burn patients.

Supervisor:

Professor Dr Ahmad Sukari Halim

Co-Supervisors:

Professor Zamzuri Idris

Dr Saidi Jaafar

DEVELOPMENT AND EVALUATION OF THERMOSTABILISED MULTIPLEX POLYMERASE CHAIN REACTION FOR SIMULTANEOUS DETECTION OF *Klebsiella pneumoniae* AND *Haemophilus influenzae*

Nur Amalina binti Khazani
Master of Science (Epidemiology)

Klebsiella pneumoniae and *Haemophilus influenzae* are important pathogens associated with the various types of infections such as pneumonia, respiratory tract infections, meningitis and also septicemia. The identification of these pathogens using culture methods are time-consuming, and insensitive, while conventional polymerase chain reaction (PCR) still require cold-chain storage and trained personnel to perform the assay. Thus, the aim of this study is to develop and evaluate the thermostabilised multiplex PCR for simultaneous detection of *K. pneumoniae* and *H. influenzae*. Three sets of primer, *php* gene of *K. pneumoniae*, *p6* gene of *H. influenzae* and *glmM* gene of *Helicobacter pylori* (internal control) were designed and optimised in this study. All PCR reagents such as Taq DNA polymerase, $MgCl_2$, dNTPs, 10 X buffer and primers were optimised and lyophilised into a pellet form with an enzyme stabiliser (trehalose). The concentrations of enzyme stabiliser and Taq DNA polymerase were optimised for thermostabilised multiplex PCR. The analytical sensitivity of the assay was evaluated both at the genomic and bacteria levels. While, the analytical specificity of thermostabilised multiplex PCR was evaluated using 30 different bacteria. The stability of thermostabilised multiplex PCR was determine using accelerated stability test at three different temperatures ($4^\circ C$, $25^\circ C$, and $37^\circ C$). The results showed that thermostabilised PCR was stable at the concentrations of 8% stabiliser and 200% Taq DNA polymerase. The limit of xviii detection (LOD) at genomic level for multiplex *K. pneumoniae* and *H. influenzae* was 1 pg of DNA. On the other hand, the LOD at bacterial level multiplex PCR of *K. pneumoniae* and *H. influenzae* was 1×10^3 CFU/mL. The thermostabilised multiplex PCRs demonstrated specificity of 100% with no amplification was observed with other bacteria strains. Based on the stability tests, the thermostabilised multiplex PCR was estimated to be stable for at least 3.02 months at $25^\circ C$. The thermostabilised multiplex PCR for detection of *K. pneumoniae* and *H. influenzae* is simple, specific, easy to perform, cost-effective and minimise the preparation time of PCR mixture. Hence, this assay has potential to be used in routine diagnosis, hospital settings and fields.

EFFECTS OF *Nigella sativa* ON INDICATORS OF RECOVERY FOLLOWING EXERCISE-INDUCED MUSCLE DAMAGE (EIMD) AS A MODEL OF INFLAMMATION

Nur Fatimah binti Raimi
Master of Science (Sport Science)

Unaccustomed, intense exercise is associated with delayed onset muscle soreness (DOMS), a symptom of exercise-induced muscle damage (EIMD). As EIMD induce inflammation to muscles, *Nigella sativa* (NS) was seen as a potential natural remedy to cure inflammatory problems to replace non-steroidal anti-inflammatory drugs (NSAIDs), which are believed to share certain unwanted effects on gastrointestinal and respiratory tract, kidneys, cardiovascular and liver. This study examined the effectiveness of NS in attenuating EIMD

as a model of inflammation, and determined the effective dosage of NS to increase the speed of recovery following EIMD. Subjects ($n = 33$) were assigned to three groups based on the doses of NS, which were either NS 3000 mg, NS 1500 mg or placebo. They had undergone 10 sets of 10 repetitions of counter-movement jump (CMJ) with 30 second intermittent rest between set, adopting a squat stance in starting and landing position to induce muscle damage. A set of tests were conducted to measure muscular power, soreness, tenderness, thigh circumference, range of motion (ROM), serum creatine kinase (CK) and lactate dehydrogenase (LDH) at pre-exercise, 30 minutes, one day, two days, three days and four days post-exercise. Right after the exercise bout, a single one-off dose of NS (either 3000 mg or 1500 mg) or placebo was administered. As expected, exercise conducted decreased muscular power (post 30 min to 1 day) ($P < 0.05$) and ROM (post 30 min to 1 day) ($P < 0.05$), and increased soreness (post 30 min to 1 day) ($P < 0.05$), tenderness (post 30 min to 1 day) ($P < 0.05$), thigh circumference (post 30 min to 1 day) ($P < 0.05$), CK (post 30 min to 1 day) ($P < 0.05$), and LDH (post 30 min to 1 day) ($P < 0.05$). Findings in all parameters related to EIMD suggested that CMJ protocol used in this study was sufficient to induce muscle damage. However, no significant interaction was found on all measured parameters on three different groups across the measurement sessions ($P > 0.05$). The effective dosage of NS to increase the recovery speed was unable to be determined because regardless the dose of NS given, a single one-off intake is of no significant benefit to increase the speed of recovery following EIMD. These results did not support the hypothesis that ingestion of NS would attenuate EIMD, and the intake of NS in a single one-off method might be the possible cause.

Supervisor:

Dr Mohd Nizam bin Mat Jawis

Co-Supervisors:

Associate Professor Dr Hairul Anuar bin Hashim

Associate Professor Zainal Abidin bin Zainuddin

VALIDATION OF THE MALAY VERSION OF PREGNANCY PHYSICAL ACTIVITY QUESTIONNAIRE (PPAQ) AND THE ASSESSMENT OF PHYSICAL ACTIVITY, DIETARY INTAKE AND GESTATIONAL WEIGHT GAIN RATE AMONG PREGNANT WOMEN IN KOTA BHARU, KELANTAN

Puteri Sulwani binti Mamat @ Mohamad
MSc (Sport Science)

Gestational weight gain (GWG) plays a vital role in determining pregnancy outcomes. Excessive GWG is the greatest public health concerns as it is related to postpartum weight retention and higher body mass index later in life. Therefore, the present study aimed at assessing validity of Malay Pregnancy Physical Activity Questionnaire (PPAQ-M), dietary intake and physical activity (PA) and also determined GWG predictor factors among pregnant women. Single 24-hour dietary recall was used to assess dietary intake whereas

pedometer and validated PPAQ-M were used to assess PA among subjects. The study consisted of two phases, phase I was a validation of PPAQ-M which involved 60 pregnant women wherein phase II was the determination of dietary intake, PA and GWG predictor factors which involved 210 pregnant women who visited selected health clinics for an antenatal check-up in Kota Bharu, Kelantan. Intraclass correlation coefficient (ICC) analysis was used to assess PPAQ-M reliability. Pearson correlation coefficient between total activity value derived from PPAQ-M with step counts obtained from pedometer was used to determine the PPAQ-M validity. Multiple logistic regression was used to determine the GWG predictor factors. ICC value was 0.679 (95% CI 0.515, 0.795) for total activity and ranged from 0.542 to 0.679 for activity intensity including sedentary, light, moderate and vigorous activity. As for type of activity, the ICC value ranged from 0.236 to 0.776 which involved household and caregiving, occupational, sports or exercise, transportation activity and inactivity. Pearson correlation coefficient showed there was significantly moderate and positive correlation between the total activity with step counts ($r = 0.394$, $P = 0.002$). There was a high proportion of inadequate (34.8%) and excessive (44.8%) GWG among subjects. Adjusted multiple logistic regression showed only household income level was a significant predictor of excessive GWG. The current study showed the PPAQ-M had a reasonable reliability and validity which could be used to assess physical activity among pregnant women. The findings on GWG predictor factors suggested pregnant women who were at risk of excessive GWG could be identified early in pregnancy and should be targeted for weight-management interventions during pregnancy or postpartum delivery.

Supervisor:

Associate Professor Dr Rohana Abdul Jalil

Co-Supervisor:

Dr Soo Kah Leng

DETECTION OF CYP2C9 AND CYP2C19 SINGLE NUCLEOTIDE POLYMORPHISMS (SNPs) AMONG ABORIGINAL JAHAI AND MALAY POPULATIONS IN MALAYSIA

Rasmaizatul Akma binti Rosdi
MSc (Human Genetics)

CYP2C9 and *CYP2C19* are highly polymorphic genes in cytochrome P450 (CYP). They encode enzymes that catalyse the biotransformation of many drugs such as S-warfarin, nonsteroidal anti-inflammatory drugs (NSAIDs), antitumor and antimalarial. However, polymorphisms in the genes affect the efficacy and toxicity of the drugs inter-individually or inter-ethnically. Hence, the objective of the study is to investigate the single nucleotide polymorphisms (SNPs) of *CYP2C9* and *CYP2C19* genes using nested allele-specific multiplex polymerase chain reaction (PCR) and high resolution melting (HRM) methods among aboriginal people of Jahai and Malays in Malaysia, respectively. Moreover, it is also to develop an HRM genotyping method for *CYP2C19* SNPs detection. This

study was approved by the Research and Ethics Committee of USM. Genomic DNAs were extracted from whole blood of 155 Jahais and 183 Malays using the commercialised extraction kit. The DNA was subjected to PCR method for four *CYP2C9* SNPs. While the HRM technique was used to genotype another four of *CYP2C19* SNPs. Direct DNA sequencing analysis was performed to validate the genotyping results. Four SNPs were found in Jahai; *CYP2C9*3*, *CYP2C19*2*, *CYP2C19*3* and *CYP2C19*17* and appeared to be significantly differences with Malays. *CYP2C9*2* allele frequency was only found in Malay, however, was not different significantly with Jahai. The allelic frequency of *CYP2C9*3* in Jahai was 36.2% making them the highest allele carriers thus far in Southeast Asia. The developed HRM method had showed 100% robust, sensitive and specific as *CYP2C19* SNPs genotyping method. Besides, it also demonstrated to be more rapid, time saving and less laborious than PCR method. According to the genotyping results obtained, Jahai may need the drug dosage adjustment of the particular drugs. Meanwhile, HRM is more suitable to be used in daily clinical setting to detect the gene polymorphisms. By investigating the polymorphisms in the gene, it will help to determine more appropriate drug dosage and reduce adverse drug reactions in individual or ethnic.

Supervisor:

Dr Surini binti Yusoff

Co-Supervisor:

Professor Dr Narazah binti Mohd Yusoff

DRINKING MOTIVES AS MEDIATOR IN THE RELATIONSHIP BETWEEN SOCIAL ANXIETY AND ALCOHOL USE AMONG PRIVATE UNIVERSITY STUDENTS IN THE KLANG VALLEY

Sharivini Lekha a/p Youva Raj
MSc

As social anxiety becomes a threat, drinking alcohol becomes a trend in experiencing relaxation, acceptance and decreases performance fear. Alcohol use continues to be a major concern among people within the age group 15–29, particularly first year university students. This thesis sought to assist in integrating a detailed analysis of potential unique mediator of alcohol use among socially anxious people through a quantitative study among 600 private university students in the Klang Valley using Social Interaction Anxiety Scale, Alcohol Use Disorders Identification Test and Drinking Motive Questionnaires-Revised. Coping and conformity motives were hypothesised to be the most significant mediator in the relationship between social anxiety and alcohol use. By examining the beta weights, coping motives ($\beta = 0.27, P < 0.001$) followed by conformity motives ($\beta = 0.13, P < .05$) were making relatively large contributions to the prediction model, followed by social anxiety ($\beta = 0.15, P < 0.01$) while controlling the mediators. Students with high social anxiety endorsed greater negative reinforcing drinking motives (coping, conformity) which independently mediated the

relation between the two variables studied; in which the coping motives were believed to lead to adverse long-term consequences because the discrepancies that foster negative affects have never been adequately addressed.

Supervisor:

Dr Mohd Azhar Mohd Yasin

Co-Supervisors:

Dr Zahiruddin Othman

Dr Azizah Othman

EXON-WIDE CHARACTERISATION OF GENETIC VARIATION FOR SMAD7 AND ITS PRELIMINARY ANALYSIS OF GENETIC ASSOCIATION IN MALAY PATIENTS WITH VENTRICULAR SEPTAL DEFECT (VSD)

Siti Aisyah Faten Mohamed Sa'dom
Msc (Human Genetics)

Congenital heart defects (CHD) occurs in approximately 8 out of 1000 live births worldwide. Ventricular septal defect (VSD) is the most common type and accounts for about 20% of all CHD. SMAD7 is an inhibitory protein that antagonises the TGF- β signaling and was implicated to be involved in the embryogenesis of the mouse model, particularly in the formation of ventricular septum. It was hypothesised that SMAD7 could influence the risk of VSD. Therefore, this study was conducted to investigate SMAD7 in susceptibility to VSD in Malay patients. This case-control study involves 60 study subjects with 30 non-syndromic VSD patients and 30 healthy controls. Peripheral blood and saliva samples were collected from the study subjects. The genomic DNA was subjected to PCR amplification encompassing six exons of SMAD7 and subsequently, re-sequencing was conducted in the patients. Observed polymorphisms then were genotyped in the controls utilising both re-sequencing and allele-specific PCR (ASPCR) techniques. A total of 10 variants were identified from the sequencing analyses which were located in the 5' upstream promoter region (rs7236774), exonic regions (rs368427729, rs145686330, rs3764482, rs3809922, rs780863704 and rs3809923), intronic regions (rs3736242) and 3'UTR region (rs375444823 and rs16950113). Statistical analysis of all 10 variants did not show any significant differences between the cases and controls groups in terms of genotype and allele frequency as well as risk association. Haplotype analysis of the major allele of rs36842779 (G) and minor allele of rs7236774 (C) significantly increase the association risk of VSD ($P = 0.0475$). This study revealed two variants, rs3809922 and rs3809923 has a complete linkage disequilibrium (LD) with each other implicating that the allele from both SNPs is completely associated with identical allele frequency. Even though all of these variants did not affect amino acid changes and thus did not affect the SMAD7 protein, they might influence the transcriptional efficiency and stability at the mRNA level later on. Hence, this study concludes the identification of genetic polymorphisms in Malay VSD patients

in Kelantan for the first time which provides a new perspective on the causation of VSD.

Supervisor:

Dr Tan Huay Lin

Co-Supervisors:

Dr Wan Pauzi Wan Ibrahim

Dr Mohd Rizal Mohd Zain

THE QUALITY OF LIFE AND FACTORS ASSOCIATED WITH IT AMONG DISABLED CHILDREN AND ADOLESCENTS REGISTERED WITH SELECTED COMMUNITY BASED REHABILITATION (CBR), DEPARTMENT OF SOCIAL WELFARE, KELANTAN

Siti Fairuz binti Ismail
MSc

Determination of quality of life status and its associated factors among disabled children and adolescents is important because it can reflect the true feelings experienced by them. To determine the QoL status and factors associated with it, a cross-sectional study was conducted at the Community-Based Rehabilitation (CBR) centres in five districts in Kelantan. The study involved 419 disabled children and adolescents ages between 2 to 18 years old. The QoL status was measured using Paediatric Quality of Life Inventory (PedsQL) core scales and it showed that the QoL status among the disabled children and adolescents are increasing with their age. Study showed that the presence to CBR is one of the factors associated with the QoL status. Besides, gender and household income also has a relationship with the QoL status. The Multiple Logistic Regression (MLR) analysis was applied and four types of disability were found to be associated with the QoL status includes cerebral palsy (CP), Down syndrome, autism and medical problem. The probability of children and adolescents who have had CP, autism and medical problems to have a lower QoL status is increased by 13.1, 5.7 and 2.8 times. However, children and adolescents diagnosed as Down syndrome have a protective effect, by 0.4 times to have lower QoL status. Indirectly, this research will help professionals involved to improve the intervention programs and give special attention to the disabled who have disabilities such as CP, autism, Down syndrome and medical problem.

Supervisor:

Dr Mohd Ismail bin Ibrahim

Co-Supervisor:

Professor Dr Hans Van Rostenberghe

SURGICAL SITE INFECTIONS AMONG PATIENTS UNDERWENT CLEAN AND CLEAN-CONTAMINATED SURGERY IN HOSPITAL UNIVERSITI SAINS MALAYSIA: RISK FACTORS, MICROBIOLOGICAL AND *Staphylococcus aureus* MOLECULAR PROFILE

Wong Jun Leong
MSc

Surgical site infections (SSI) are among the most commonly encountered healthcare associated infection. The incidence were closely been monitored as it is associated with considerable morbidity and mortality. The common aetiological agents responsible for the infection include *Staphylococcus aureus*, *Streptococcus* spp, *Enterococcus* spp, and *Pseudomonas aeruginosa*. The identification of the causative agents as well as their antimicrobial sensitivity pattern helps in the treatment plan. Therefore the aims of this study were to determine the incidence and risk factors of SSI as well as to identify the causative microorganisms and their sensitivity profile.

This prospective cohort study was conducted from June 2013 until July 2014 at Hospital Universiti Sains Malaysia. Seventy-two patients underwent clean and clean-contaminated surgeries were consented preoperatively and strictly followed up for any signs of SSI for duration of 30 days post-operation. Nasal screening for *Staphylococcus aureus* and Methicillin-resistance *Staphylococcus aureus* was carried out pre-operatively. Tissue samples or wound swab from infected patients were taken for microbial identification and its sensitivity pattern. *Staphylococcus aureus* strain isolated were proceed to polymerase chain reaction analysis to detect the virulence genes (TSST, PVL, cna, hlg, icaA, and SdrE). The overall incidence rate of SSI was 18.1% specifically for clean and clean-contaminated surgeries are 20% and 11.8%, respectively. Significant risk associated with SSI by simple logistic regression analysis included patients admitted two days or more prior to surgery (OR 12.67; 95% CI, 2.02 to 79.53), underwent CABG surgery (OR 10.20; 95% CI, 2.66 to 39.08), underlying diseases (OR 9.46; 95% CI, 1.15 to 77.50), history of diabetes mellitus (DM) prior to the surgery (OR 9.40; 95% CI, 2.36 to 37.39), total hospitalisation period more than seven days (OR 7.84; 95% CI, 2.12 to 29.0), duration of surgery more than four hours (OR 7.08; 95% CI, 1.84 to 27.27), and discharged home three days or longer after surgery (OR 5.13; 95% CI, 1.39 to 18.84).

Multiple logistic regression method demonstrated that the patients who have history of DM (OR 6.97; 95% CI, 1.49 to 32.71) and underwent CABG surgery (OR 5.54; 95% CI, 1.22 to 25.03) had significant risks of SSI. Gram negative microorganism was the leading causative microorganism and in *Staphylococcus aureus* strains, icaA gene was the most common virulence gene detected.

In conclusion, SSI among clean and clean-contaminated surgeries are high in our setting. DM and patients underwent CABG operation are at high risk to get SSI. Gram negative microorganisms are common as compare to Gram positive, however they are all sensitive strains.

Supervisor

Associate Professor Dr Siti Asma' binti Hassan

Co-Supervisors:

Professor Dr Habsah binti Hasan

Professor Dr Mohamad Ziyadi bin Hj Ghazali

Dr Zaidi bin Zakaria

BREAST CANCER DEVELOPMENT IN RATS UNDER THE INFLUENCE OF PLATELET FACTOR-4 (PF4) AND/OR RAPAMYCIN

Zaihassni binti Mat Yaman
MSc

Breast cancer is a leading cause of morbidity and mortality among women worldwide. Steroid hormone receptors such as Estrogen Receptor (ER) and Progesterone Receptor (PR) play a critical role in breast cancer growth. In this study, ER and PR were selected as markers for steroid receptor determination due to the strong association between breast cancer development and the influence of steroid hormones as demonstrated in many studies. On the other hands, the Peroxisome Proliferator Activation Receptor γ (PPAR γ), a family of nuclear hormone receptor was also determined as it was a potential effector for tumour cell differentiation. Rapamycin, a drug from bacteria microlide and Platelet Factor-4 (PF4), a platelet-derived chemokine have anticancer properties. Therefore, it will be interesting to analyse the effect of Rapamycin and PF4 in blocking the growth of breast cancer from responding to hormone stimulation. In this study, invasive mammary carcinoma was induced with 70 mg/kg body weight 1-Methyl-1-Nitrosourea (MNU) in 80 young female Sprague Dawley rats. The gene and protein expressions of ER, PR and PPAR γ markers were evaluated by using semiquantitative immunohistochemistry analysis and quantitative real-time PCR assay. Findings from the untreated-control group demonstrated that all mammary lesions are 100% malignant, histopathologically characterised with invasive ductal carcinoma (IDC) of three major type ie. cribriform, papillary and Not Otherwise Specified (NOS). Rapamycin treatment showed significant inhibition of mammary tumour progression as well as reduction of tumour aggressiveness. Even though treatment with Rapamycin significantly overexpressed ER and PR, activation of PPAR γ promotes differentiation of tumour cells which lead to a more differentiated mammary tumour and consequently reversing the aggressive phenotype of the lesion. Meanwhile, treatment with PF4 did not regress tumour growth and consequently showed no significant expression of ER, PR and PPAR γ . Upregulation of all these three markers in combination treatment lead to significant tumour regression and phenotypically decreased aggressiveness. It was predicted that Rapamycin predominantly showed anticancer effect rather than PF4. Thus, present findings suggested that Rapamycin is neither synergistic nor additive with PF4. It was concluded that Rapamycin is a potent anticancer agent for breast cancer because it halts tumour growth and thus promote tumour cells differentiation through a positive expression of hormone receptors analysis. Further study will be needed to analyse the regulation of ER isoforms (ER α and ER β) and PR

isoforms (PR-A and PR-B) to improve potential therapeutic strategy in breast cancer treatment through anticancer effects of Rapamycin.

Supervisor:

Professor Dr Hasnan Jaafar

Co-Supervisor:

Associate Professor Dr Azman Seeni Muhamad

AWARENESS AND PREPAREDNESS IN SMOKING CESSATION AMONG SMOKER PATIENT SCHEDULED FOR ELECTIVE SURGERY IN HOSPITAL UNIVERSITI SAINS MALAYSIA

Dr Al Jadidi bin Sulaiman
MMed (Anaesthesiology)

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Introduction: Smoking is the single most cause of preventable disease and premature death. Perioperative smoking is linked to various complications and morbidity and to a significant economic burden. Elective surgery offers a powerful opportunity for surgeon and anesthetist to help smokers quit.

Objectives: This study set out to identify factor or predictor toward smoking cessation among smoker patients prior to scheduled surgery; and to determine how sociodemographic background, smoking status and knowledge on the health risks of smoking contribute toward development of such attitude.

Patients and Methods: A total of 106 smoker patients who scheduled for elective surgery in Hospital Universiti Sains Malaysia were enrolled from April till September 2015. This paper reports the results of a cross-sectional study on these patients by filling pre-determined questionnaire before anesthesia and surgery or on the first operative day. The survey included three sections exploring demographical profile of respondent, smoking status and knowledge regarding smoking-related risks.

Results: Mean age of respondent was 37 (SD, 17.3). 60.4% ($n = 64$) patients stopped smoking more than 24 hour prior to surgery while the other 39.6% ($n = 42$) had cessation less than 24 hour preoperatively. Intention to quit turned out to be the most significant predictor for early smoking cessation in this study. Smoker patients who did not have intention to stop smoking had 4.32 higher odds of cessation less than 24 hour compare to those who had intention to stop smoking (95% CI: 1.85, 10.10, P -value < 0.001).

Conclusion: Considering many beneficial effects of preoperative smoking cessation, both surgeon and anesthetist should play their role to achieve this; to the least of brief smoking cessation advice, and to the extent of any form of smoking cessation interventions. Introduction of nicotine replacement therapy will double the chance of abstinence and cure among smokers.

Supervisor:
Dr Laila bt Ab Mukmin

Co-Supervisor:
Prof Dr Mahamarowi Omar

POLYMYXIN B THERAPY FOR MULTIDRUG RESISTANT GRAM NEGATIVE INFECTIONS: OUTCOME AND RISK FACTORS FOR TREATMENT FAILURE IN CRITICAL CARE

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MMed (Anaesthesiology)

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Objectives: Polymyxins have re-administered in clinical practice due to the dry antibiotic development pipeline and worldwide increasing infections caused by multi-drug resistant (MDR) gram negative bacteria. The aim of this study is to investigate the use of polymyxin B antibiotic therapy in Intensive Care Unit, Hospital Universiti Sains Malaysia (HUSM) and to identify the risk factors for polymyxin B treatment failure. Outcomes will be classified into clinical cure and clinical failure.

Methodology: This was a cross-sectional study using secondary data done in Intensive Care Unit (ICU) Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan. This study involved 96 cases of gram negative infections (blood-stream infection and pneumonia), particularly *Acinetobacter* spp, *Acinetobacter baumannii*, *Klebsiella pneumonia* and *Pseudomonas aeruginosa*, isolated from blood, endotracheal aspirate (ETA) as well as bronchoalveolar lavage (BAL) sample, all were treated with polymyxin B. The patient selections were from pharmacy databank on polymyxin B usage from 1 January 2010–31 December 2014. Ninety-six cases treated with polymyxin B from ICU were randomly selected and their medical record were traced from Record Office and reviewed. Their demographic profiles, underlying diseases, potential risk factors, antibiotic usage, possible adverse effects, microbiology results and outcome were reviewed.

Results: Clinical outcome was evaluated for the 96 samples. Clinical cure contributed to 51% of the cases (49 cases) meanwhile another 47 cases (49%) contributed to clinical failure. Percentage of clinical cure was slightly higher compared to clinical failure for this study. 47 clinical failure subject (49.0%) reported death and all were referred to attributable mortality. Associated risk factors for polymyxin B treatment failure by Multiple Logistic Regression model were primary bacteremia ($P = 0.005$) and inappropriate dose of polymyxin B ($P = 0.005$). Polymyxin B was well tolerated by almost all of our sample, whereby only 7 out of 96 cases experienced deteriorating renal function, and it was not lead to discontinuation of the treatment.

Conclusions: In conclusion, mortality associated with multidrug resistant gram negative pathogens continues to be high. The early susceptibility, prompt and optimal antibiotic such as polymyxin B and also combination of antibiotic in

particular with sulperazaone seems to have a survival benefit in this critically ill population.

Supervisor:
Associate Professor Dr Mahamarowi Omar

Co-Supervisors:
Associate Professor Dr Saedah Ali
Associate Professor Dr Zakuan Zainy Deris

THE COMPARATIVE STUDY OF PROPOFOL TARGET CONTROLLED INFUSION VERSUS SEVOFLURANE ON SERUM LACTATE ACCUMULATION

Dr Constance Liew Sat Lin
MMed (Anaesthesiology)

Department of Anaesthesiology and Intensive Care Unit, School of Medical Sciences, Universiti Sains Malaysia, Health Campus, 16150 Kubang Kerian, Kelantan, Malaysia

Introduction: This research was conducted considering the fact that today, there are still very few studies comparing Sevoflurane or Target Controlled Infusion using Propofol in term of serum lactate accumulation during general anaesthesia.

Objectives: The goal of this study is to investigate the effect of Propofol target controlled infusion (TCI) versus Sevoflurane on serum lactate accumulation. We will compare Propofol target controlled infusion (TCI) versus Sevoflurane in serum lactate accumulation at every hour after induction until post operation.

Methodology: There were 92 patients aged 18–65 years old, classified under ASA I, were involved in this prospective study. They were divided into 2 groups and this study was done in a double-blind manner. All patients were pre-medicated with tablet midazolam 7.5 mg at night, and in the morning when called to the operating theater. After pre-oxygenation, IV Fentanyl 2 mcg/kg was given. Patients received either Sevoflurane or Propofol infusion using target plasma concentration of 4 mcg/ml according to Marsh model during operation. All the patients received anaesthesia in a standard practice and blood samples were taken at every hour until completion of operation. The blood samples were tested for acid-base values and lactate level.

Results: There were significant differences in the mean values of serum lactate levels at 1st, 2nd, 3rd and 4th hour of surgery within propofol and sevoflurane group with P -value of < 0.05 . Nevertheless, when comparing differences in the mean values of serum lactate levels between propofol and sevoflurane group showed no significant difference of serum lactate change with $P = 0.186$.

Conclusions: Propofol group and sevoflurane group showed progressive increment of serum lactate level in both groups; however there was a noticeable drop in serum lactate level in propofol group after 3 hours of surgery. The rate of increase of serum lactate level in sevoflurane group was the highest after 2 hours of surgery, followed by a slower rate

of increase in serum lactate level after 3 hours of surgery in sevoflurane group.

ADEQUACY OF EMPIRICAL ANTIBIOTIC THERAPY FOR PATIENT ADMITTED TO ICU WITH SEPSIS

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Introduction: Sepsis is one of the commonest causes of ICU which lead to high mortality and morbidity. Early empirical antibiotic treatment is important to improve the patient's outcome.

Objective: The aim of this study was to assess the adequacy of empirical antibiotic therapy for sepsis patients in Intensive Care Unit (ICU), Hospital Sultanah Nur Zahirah (HSNZ), and Kuala Terengganu.

Patients and Methods: This was a retrospective, observational study to evaluate the adequacy of empirical antibiotic given to patients who were diagnosed with sepsis in ICU. 130 cases who were admitted to ICU for sepsis from January 2013 to December 2013 were selected and their medical record were traced from HIS (Hospital Information System) and reviewed. Their demographic profiles, underlying comorbidities, antibiotic usage, culture and sensitivity results as well as patient's outcome were reviewed. The adequacy of empirical treatment in each case was determined. Adequate empirical antibiotic treatment was considered adequate if spectrum, dose, application modus, and duration of therapy were appropriate according to MSIC (Malaysian Society of Intensive Care) guidelines.

Results: Among 130 intensive care unit patients with sepsis, 119 (91.5%) received adequate antimicrobial treatment. In this group, the mean age of patients was 51.8 year old and 51.3% of them were men. A total of 112 (86.2%) patients presented with septic shock and 104 (87.4%) of them were given adequate empirical antibiotic. The main sources of bacteremia in this group were from lungs (42%), abdomen (21%) or skin and soft tissue (15.1%). The microorganisms most frequently isolated were *Escherichia coli* 13 (37.1%), *Burkholderia pseudomallei* 7 (20.0%), followed with *Klebsiella pneumoniae* 6 (17.1%), *Acinobacter baumannii* 4 (11.4%) and *Leptospira interrogans* 2 (5.7%). For patients with gram positive culture, which affected 25 patients with adequate treatment, coagulase negative staphylococcus, 11 (44.0%), and *Staphylococcus aureus*, 11 (44.0%), were the most common organisms. This was followed with *Streptococcus pneumoniae* in 3 (12.0%) patients. Among the adequate group of patients, cephalosporin was the most frequently used, 63 (52.9%), carbapenem in 21 (17.6%) patients became the second option followed with piperacillin/tazobactam in 17 (14.3%) patients and amoxicillin/clavulanic acid 6 (5.0%). Comparing both group of patients who received adequate and inadequate empirical antibiotics therapy, the outcome were not statistically significant in terms of the duration of ventilation and ICU stay, duration of hospitalisation as well as patient

mortality and survival. However there was 10% reduction of mortality in adequate treatment group.

Conclusion: More than 90 percent of patients with sepsis were given adequate empirical antibiotic treatment. The most common empirical antibiotic used was cephalosporin group (52.9%), whereas, macrolides was the most common second types of empirical antibiotics. However, there were no significant differences in term of outcome between adequate and inadequate group of therapy.

Supervisor:

Professor Dr Shamsul Kamalrujan Hassan

Co-Supervisors:

Dr Rhendra Hardy

Dr Nik Azman Nik Adib

A PROSPECTIVE DOUBLE-BLIND RANDOMISED CONTROLLED TRIAL ON THE EFFECT OF DEXMEDETOMIDINE TOWARDS PREVENTING EMERGENCE AGITATION IN PATIENTS UNDERGOING GENERAL ANAESTHESIA FOR LIMB SURGERIES

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Background: Emergence agitation is a common occurrence after general anaesthesia with reported prevalence ranging from 10% to 80%. It can cause adverse implications on patients' outcome, also can be traumatising for the anaesthetists, staff, patients and the family members. Many theories postulates the causes and risks for emergence agitation but the exact answer is still unknown.

Objectives: To investigate whether dexmedetomidine can reduce the incidence of emergence agitation, to determine whether patients' demographic (age, gender and race), pre-operative anxiety level, duration of anaesthesia and type of procedures are risk factors for emergence agitation and to observe the side effects associated with intra-operative infusion of dexmedetomidine.

Design: Prospective randomised double-blind controlled trial.

Methods: Fifty patients undergoing limb surgeries were recruited. Their pre-operative anxiety levels were assessed using the Hamilton anxiety rating scale prior to the operative procedure. They were randomised into two groups; the dexmedetomidine group received dexmedetomidine infusion at a rate of 0.4 mcg/kg/hr starting 10 minutes after induction of anaesthesia until right after extubation while the control group received volume-matched normal saline as placebo. Sevoflurane was used for maintenance of anaesthesia. Patients were assessed for emergence agitation using the Richmond agitation-sedation scale around the time of extubation. The incidence of agitation, time-to-extubation and risk factors

were evaluated. Side effects of dexmedetomidine (bradycardia, hypotension and delayed awakening) were documented.

Results: The incidence of emergence agitation was lower in the dexmedetomidine group than the control group (8.3% versus 40%), and this was statistically significant ($P = 0.008$). Although there was a considerable number of side effects (10 cases from dexmedetomidine group from total of 11 cases of side effects), the complications were mild and did not result in serious sequelae. There was no statistical significance in the difference of the mean extubation time between dexmedetomidine and control group ($P = 0.098$).

Patient's demographic (age, gender and race), pre-operative anxiety level, duration of anaesthesia and type of surgery was determined not to be the risk factors for emergence agitation from this study.

Conclusion: Dexmedetomidine infusion intra-operatively can effectively reduce the incidence of emergence agitation and its use is relatively safe without serious side effects and without prolonging the extubation time.

Supervisor:

Professor Dr Shamsul Kamalrujan Hassan

Co-supervisor:

Dr Wan Mohd Nazaruddin Wan Hassan

COMPARISON BETWEEN THE EFFICACY OF NEOSTIGMINE VERSUS SUGAMMADEX REVERSAL OF ROCURONIUM INDUCED NEUROMUSCULAR BLOCKADE IN PAEDIATRIC PATIENTS

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Introduction: A reversal agent is commonly given to improve neuromuscular function after intra-operative administration of non-depolarising neuromuscular blocking agents. The administration of conventional reversal agent neostigmine is associated with many undesirable side effects. For almost a decade, a new novel drug sugammadex has been used to specifically antagonise the effect of aminosteroidal neuromuscular blocking agents.

Objective: The aim of this study is to compare the recovery time, haemodynamic stability and complications between these 2 reversal agents in antagonising the effects of rocuronium in the paediatric population.

Methodology: This was a prospective, double-blinded, randomised controlled trial involving 80 paediatric patients aged between 2–12 years old scheduled for surgery under general anaesthesia requiring rocuronium induced neuromuscular blockade. They were randomised equally into two groups, 40 patients each group for reversal with neostigmine or reversal with sugammadex. All patients were induced with sevoflurane, intravenous access obtained, then 2 mcg/kg of fentanyl was administered. Neuromuscular

function monitoring (acceleromyography) of the adductor pollicis muscle was done using train-of-four (TOF) method. TOF-Watch Sx was placed along the ulnar groove of the hand and calibrated. After a baseline TOF reading was taken, and 0.6 mg/kg of rocuronium was given. Patients were intubated once TOF count was less than 1. TOF was monitored and maintained at count of 2–3 throughout the surgery by administering 0.2 mg/kg of rocuronium once TOF count was more than 3. The haemodynamic parameters pre-reversal and post-reversal was documented. The neuromuscular recovery time, from reversal administration at TOF count 2 or 3 to TOF ratio 0.9 was documented. Any complications observed post-extubation were documented.

Results: The neuromuscular recovery time from TOF count 2 or 3 to TOF ratio 0.9 post-reversal was significantly higher in the neostigmine group, with a mean of 501.58 seconds as compared to only 84.45 seconds in the sugammadex group. The mean difference was 417.13 seconds. This difference was statistically significant evidenced by $P < 0.05$. There were also significant changes in the means of systolic blood pressure, diastolic blood pressure and mean arterial pressure pre-reversal and post-reversal in both groups. However the mean differences were much lower in the sugammadex group, ranging from -2.38 to -2.93 as compared to the neostigmine group, which were from -4.85 to -6.80. The mean heart rate pre-reversal and post-reversal showed significant changes in the neostigmine group, but the changes were not significant in the sugammadex group. The incidence of complications post-reversal was higher in the neostigmine group with 17.5% (7 patients) post-operative nausea vomiting and 2.5% (1 patient) sweating. There were no complications noted in the sugammadex group.

Conclusion: Sugammadex has a significantly shorter recovery time (from TOF count of 2 or 3 to TOF ratio of more than 0.9) as compared to neostigmine. Sugammadex has a more stable haemodynamic profile as compared to neostigmine when used to reverse rocuronium induced neuromuscular blockade in paediatric patients. Sugammadex causes less complications or side effects when used in paediatric patients as a reversal for rocuronium induced neuromuscular blockade.

Supervisor:

Dr Rhendra Hardy bin Mohamad Zaini

Co-supervisor:

Associate Professor Dr Shamsul Kamalrujan bin Hassan

SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK IN THE CREATION OF ARTERIOVENOUS FISTULA: A STUDY ON MICROCIRCULATORY CHANGES

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Introduction: Supraclavicular brachial plexus block (BPB) causes vasodilatation and an increase in blood flow, hence increase the skin perfusion and temperature to the ipsilateral upper limb. However, no reports have comprehensively evaluated these microcirculatory changes after a BPB.

Objectives: To compare the skin perfusion changes before and after supraclavicular BPB and to compare the temperature changes before and after supraclavicular BPB.

Patients and Methods: Thirty two adult patients with chronic renal failure scheduled for AVF surgery were studied in a prospective cross sectional study design. The supraclavicular BPB was performed under ultrasound guidance using 20 mls of levobupivacaine 0.5%. The skin perfusion (AU–Arbitrary Unit) and temperature (°C) of both arms were recorded every 5 minutes for 15 minutes pre-block and compared post-block for another 15 minutes, recorded every 5 minutes. To avoid bias, ten healthy adults were recruited for control group and both perfusion and skin temperature of both arms were recorded for 15 minutes. Both skin perfusion and temperature were recorded using Laser Doppler Fluximetry (LDF) machine in both groups.

Results: There is a significant difference found between skin perfusion value in anaesthetised arm of studied group (12.80 ± 4.89 ; $P < 0.05$), but not the contralateral arm (6.25 ± 2.35 ; $P = 0.306$), before and after a supraclavicular brachial plexus block. There is an increment of 5.46 ± 4.10 AU in the anaesthetised arm, post block. Whereas for the contralateral arm, the increment post block was not significant (0.19 ± 1.04 AU). There is a significant difference found between skin temperature changes in both anaesthetised and contralateral arms of studied group before and after a supraclavicular brachial plexus block. There is an increase in skin temperature in anaesthetised arm (33.36 ± 3.01 ; $P = 0.004$), as well as contralateral arm (32.16 ± 1.49 ; $P = 0.014$) of studied group after a supraclavicular brachial plexus block. There were no significant haemodynamic changes post block in all patients (Systolic blood pressure, 153.49 ± 8.34 , $P = 0.061$; diastolic blood pressure, 74.89 ± 8.34 , $P = 0.953$; heart rate, 74 ± 12 , $P = 0.327$). In the control group, there is no significant difference between right arm and left arm in term of skin perfusion and temperature (10.42 ± 2.45 , $P = 0.597$ and 27.79 ± 1.01 , $P = 0.896$ for skin perfusion and temperature, respectively).

Conclusion: Microcirculatory changes that occur after supraclavicular BPB include an increase in skin perfusion and an increase in temperature with stable hemodynamic parameters.

Supervisor:
Dr Saedah Ali

Co-Supervisors:
Dr Arman Zaharil Mat Saad
Dr Aida Hanum Ghulam Rasool
Dr Laila Abdul Mukmin

THE EFFECT OF PRE-OPERATIVE PREGABALIN ON POST-OPERATIVE PAIN AND MORPHINE CONSUMPTION AFTER OPEN GYNAECOLOGICAL SURGERY

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Introduction: Pre-operative pregabalin has been shown to reduce post-operative pain scores and morphine consumption in certain surgical groups. We studied the effect of pre-operative pregabalin on post-operative pain relief among patients undergoing open gynaecological operation.

Objective: This was a prospective, randomised, double blinded study on the efficacy of pre-operative oral pregabalin 150 mg in reducing post-operative morphine consumption and pain scores after undergoing open gynaecological operation.

Methodology: Sixty patients undergoing open gynaecological operation that fulfilled inclusion and exclusion criteria were recruited in Hospital Universiti Sains Malaysia and randomised into two groups. Oral pregabalin 150mg was given to the pregabalin group ($n = 30$) one hour prior to operation while placebo was given to the control group ($n = 30$). A standardised regime of general anaesthesia was given to both groups and intravenous morphine was delivered via a patient controlled analgesia machine. Post-operative pain scores at rest and movement were recorded using numeric rating scale at 0, 1, 4 and 24 hours post-operatively. Total morphine usage was also recorded at those intervals.

Results: There were no significant differences in resting pain scores ($P = 0.083$), moving pain score ($P = 0.680$) or morphine consumption ($P = 0.740$) at 24 hours post-operatively between pregabalin and control group.

Conclusion: The use of 150mg oral pregabalin pre-operatively given one hour prior to operation did not decrease post-operative pain score and morphine consumption for patients who underwent open gynaecological operation under general anaesthesia.

Supervisor:
Professor Dr Shamsul Kamalrujan Hassan

Co-Supervisor:
Professor Dr Nik Abdullah Nik Mohamad

THE PREVALANCE AND RISK FACTORS OF VENTILATOR ASSOCIATED PNEUMONIA IN INTENSIVE CARE UNIT IN HOSPITAL SULTANAH BAHYAH, KEDAH MALAYSIA

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Introduction: Ventilator associated pneumonia (VAP) is the commonest nosocomial infection in intensive care unit (ICU). We conducted a first study to collect local data

on prevalence and risk factors of VAP in Hospital Sultanah Bahiyah (HSB), Kedah.

Methodology: This prospective cohort surveillance was conducted on patients admitted to an adult medical-surgical ICU of a tertiary hospital from 1 August 2104 to 31 July 2105. VAP was diagnosed using Malaysia Registry of ICU (MRIC) criteria which included clinical manifestation, imaging and investigations.

Results: In total, 297 patients were enrolled in this study. The prevalence of VAP was 22.0%. The most common causative pathogen was *Acinetobacter* sp. (31.8%). Multivariate analysis using simple logistic regression showed that risk factors for VAP were elderly patients ($P = 0.02$; OR 1.02; 95% CI 1.00, 1.04), increase duration of ventilation ($P < 0.001$; OR 1.49; 95% CI 1.35, 1.63), length of stay in ICU ($P < 0.001$; OR 1.45; 95% CI 1.33, 1.59), length of stay in hospital ($P < 0.001$; OR 1.07; 95% CI 1.04, 1.09), respiratory diseases ($P = 0.02$; OR 2.25; 95% CI 1.17, 4.33), lung malignancy ($P < 0.001$; OR 22.35; 95% CI 6.24, 80.09), previous antibiotic within three months ($P = 0.02$; OR 2.25; 95% CI 1.17, 4.33), tracheostomy ($P < 0.001$; OR 18.42; 95% CI 9.36, 36.23), reintubation ($P < 0.001$; OR 25.69; 95% CI 12.73, 51.82), transportation for remote procedure ($P < 0.001$; OR 20.76; 95% CI 9.65, 44.76), central venous line (CVL) insertion ($P = 0.04$; OR 2.22; 95% CI 1.04, 4.76), continuous sedation ($P = 0.03$; OR 1.85; 95% CI 1.04, 3.26) and without venous thromboprophylaxis ($P = 0.03$; OR 2.05; 95% CI 1.09, 3.87).

Conclusion: The prevalence and risk factors in our study were comparable to national and international data. We identify one new risk factor which is CVL insertion.

Supervisor:

Dr Laila Abdul Mukmin

Co-Supervisors:

Professor Mahamarowi Omar

Dr Ahmad Shaltut bin Othman

A COMPARISON OF PERINEURAL DEXMEDETOMIDINE IN 0.75% ROPIVACAINE BETWEEN ULTRASOUND-GUIDED SUPRACLAVICULAR AND INFRACLAVICULAR BRACHIAL PLEXUS BLOCK FOR UPPER LIMB SURGERY

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Introduction: Dexmedetomidine is α_2 agonists which is potential as an adjuvant drugs to improve quality of peripheral nerve block using local anaesthetic as well as able to provide haemodynamic stability. We compared the effect perineural dexmedetomidine 1 mcg/kg in 0.75% Ropivacaine for ultrasound-guided supraclavicular block (SCB) and infraclavicular block (ICB).

Objectives: The aims of this study are to determine which approach of brachial plexus block (BPB) has the better benefit of perineural Dexmedetomidine and to determine which approach of BPB has safer effect of perineural Dexmedetomidine in terms of haemodynamic and sedative effects because both block are close to major vessels (SCB is close to subclavian artery and ICB is close to axillary artery).

Method: This was a randomised, assessor blinded, controlled trial. They were randomized into two groups: group SCB (supraclavicular block) ($n = 39$) and group ICB (infraclavicular block) ($n = 39$). The block was performed by single operator and the assessment was done by second medical officer who was blinded with the technique. Both groups received total of 20 mL 0.75% Ropivacaine and 1 mcg/kg of dexmedetomidine. The assessment parameters were onset of sensory and motor block, duration of sensory and motor block, bispectral Index (BIS) score as well as haemodynamic changes.

Result: There were significant difference between Group SCB and Group ICB block in the onset of sensory (9.21 (2.18) versus 10.62 (2.23) minutes, $P = 0.006$), the onset of motor (14.15 (2.24) versus 15.15 (1.66) minutes, $P = 0.028$). There were significant differences between the two groups based on time (within-between group comparison) in SBP ($F = 6.99$, $P < 0.001$), DBP ($F = 3.63$, $P = 0.016$) MAP ($F = 5.32$, $P < 0.001$) and HR ($F = 3.59$, $P = 0.010$). In general, there were no significant differences in duration of sensory and motor block. Both group also showed a good sedative effect changes based on time but there was no significant difference between the groups.

Conclusion: Perineural dexmedetomidine in 0.75% ropivacaine produced faster onset of sensory and motor blockade in ultrasound guided SCB than ICB. However, it produced comparable sedative effect and haemodynamic stability in both groups.

Supervisor:

Dr Wan Nazaruddin Wan Hassan

Co-Supervisor:

Dr Rhendra Hardy Md. Zaini

COMPARISON OF THE EFFECTS OF PROPOFOL-KETAMINE (KETO FOL) MIXTURE IN COMBINATION OF IV FENTANYL PRE-TREATMENT DURING INDUCTION AND PROSEAL LARYNGEAL MASK AIRWAY (LMA) INSERTION

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Introduction: The renewed interest in combination of propofol-ketamine as a mixture for sedation and anaesthesia had led us to search for a suitable mixture to be used for induction of anaesthesia.

Objectives: This study was conducted to compare the effects of two different mixture of propofol–ketamine on haemodynamic stability, adequate condition for Proseal LMA insertion and occurrence of apnoea after induction.

Settings and Design: A randomised double-blinded, controlled trial was conducted in Hospital Universiti Sains Malaysia between June 2014 and October 2014.

Patients and Methods: A total of 88 patients were recruited and randomised into two groups using block randomisation. One group of patients was given propofol-ketamine with 1:1 ratio; whereas another group was given propofol-ketamine 1:0.5 ratio. Haemodynamic monitoring was measured at baseline, 1 minute, 5 minute and 10 minutes after induction. Proseal was inserted in each patient after successful induction. LMA scoring and apnoea scoring were recorded.

Results: In regard to within-intervention-group-effect comparisons, both 1:0.5 and 1:1 propofol/ketamine ratio groups showed statistically significant changes in SBP, DBP, MAP and HR nearly across all time points. However, regarding between-and-within-intervention-group comparisons (i.e. comparison of SBP, DBP, MAP and HR between intervention groups across time points), there were no significant marginal mean differences noted between both propofol/ketamine ratio groups across time. The medians percentage of oxygen saturation was exactly the same for both groups of intervention. There was no significant difference in mean Proseal LMA score between the two groups. There were also no significant predictors between associated with Proseal LMA score. The 1:1 propofol/ketamine ratio group has higher percentage of prolonged apnoea than 1:0.5 propofol/ketamine group (90.9% versus 13.6; $P < 0.001$). There were two significant predictors for apnoea score which were BMI (adjusted OR 1.148, 95% CI 0.964, 1.583) and intervention group (adjusted OR 49.765, 95% CI 12.789, 193.649)

Conclusions: Propofol/ketamine mixture with 1:0.5 ratio was better than propofol/ketamine 1:1 because it caused lesser association to apnoea occurrence. However the haemodynamic response were stable and comparable in both groups.

Supervisor:

Dr Wan Mohd Nazaruddin bin Wan Hassan

RETROSPECTIVE STUDY OF THE OUTCOME OF NECROTISING FASCIITIS IN INTENSIVE CARE UNIT, HOSPITAL RAJA PEREMPUAN ZAINAB 11, KOTA BHARU, KELANTAN

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Introduction: Necrotising fasciitis is rapidly progressive soft tissue infection involving deep fascia which carries relatively high mortality rate worldwide. It is associated with

extensive soft tissue necrosis, profound septic shock and high morbidity.

Objectives: The aim of this study is to determine the mortality rate in our local general hospital and to investigate the factors that determine the outcome of the necrotising fasciitis patient treated in Intensive Care Unit.

Patients and Methods: This is retrospective cross sectional study in which we evaluates few variables including comorbidities, Acute Physiology And Chronic Health Evaluation (APACHE) 11 score, criteria of sepsis and severe sepsis, time to surgical debridement, organism isolated and morbidity include requirement of vasopressor, renal replacement therapy and ventilation in 71 patients admitted to HRPZ 11 from 2012 to 2015.

Results: The median age was 57.7 years. Common comorbidities were diabetes (83.1%) and hypertension (62%). Common organism isolated was *Klebsiella sp* (24%), Group A *Streptococcus* (18.3%) and *Proteus mirabilis* (14.1%). The overall mortality was 22/71(31%). The mean APACHE II score was 19.2 (SD = 6.57) and the median time to operation was 50 hours (IQR = 70.0). Factors directly contributing towards mortality were higher APACHE II score (adjusted OR 1.41, 95%CI: 1.20, 1.66, $P < 0.001$) and an increase in time to surgical debridement (adjusted OR 1.03, 95%CI: 1.01, 1.05, $P = 0.003$).

Conclusion: Early surgical debridement was crucial in the treating the necrotising fasciitis patients and high APACHE 11 score during admission was associated with increase mortality.

Supervisor:

Associate Professor Saedah Ali

Co-Supervisors:

Professor Shamsulkamalrujan Hassan

Dr Mohd Nazri Ali

RISK FACTORS AND OUTCOMES OF CARBAPENEM-RESISTANT GRAM-NEGATIVE BLOOD STREAM INFECTION IN INTENSIVE CARE UNIT, HUSM

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Objectives: Carbapenem-resistant (CR) gram-negative pathogens have increased substantially and is worrisome. This study was performed to identify the risk factors for development as well as outcomes of CR Gram-negative bacteremia (GNB) among patients in Intensive Care Unit (ICU), Hospital Universiti Sains Malaysia (HUSM).

Methods: Retrospective, case-control study; risk factors for development of CR-GNB were investigated using two groups of patients: the first group (control) consisted of patients who acquired carbapenem susceptible (CS) GNB and the second group (case) included patients with CRGNB. The

case groups were compared to the control group defined as patients hospitalised in the ICU during the same period, with similar inclusion and exclusion criterias. A total of 96 cases of Gram-negative bacilli BSI from ICU were randomly selected and their medical record were traced from Record Office and reviewed. Their demographic profiles, underlying diseases, potential risk factors, antibiotic usage, microbiology results and outcome were reviewed.

Results: Total 96 patients were included for the study, 48 patients with CR were compared to 48 patients with CS-GNB. Increased length of ICU stay (OR 2.09, 95 % CI 1.01–33.18, $P = 0.019$), DM (OR 3.5, 95 % CI 1.61–13.24, $P = 0.016$), presence of tracheostomy and chest drain (OR 5.17, 95% CI 1.94–18.92, $P = 0.010$) and (OR 5.79, 95% CI, 4.27–24.40, $P = 0.016$) respectively, prior exposure to carbapenems (OR 5.90, 95% CI, 4.63–7.40, $P = 0.002$) and those who have infected by *Acinetobacter baumannii* (OR 6.18, 95% CI, 2.56–8.68, $P = 0.010$) and *Pseudomonas aeruginosa* (OR 4.29, 95% CI, 0.22–8.48, $P = 0.034$) were independent risk factors associated with CR-GNB. Crude mortality in CS-GNB was greater compared to CR group, however, statistically not significant ($P = 0.679$). Meanwhile, the attributable mortality in CR-GNB was noted higher than CS-GNB (24 patients in CR compared to 17 patients in CS-GNB), with $P = 0.011$.

Conclusions: This study indicates the importance of preventing CR-GNB blood stream infections and the appropriate use of antimicrobial agents to reduce attributable mortality.

Supervisor:

Professor Dr Shamsul Kamalrujan Hassan

Co-Supervisors:

Dr Rhendra Hardy Mohamad Zaini

Associate Professor Madya Dr Zakuan Zaini Deris

NEOSTIGMINE INFUSION VERSUS SYRUP LACTULOSE FOR THE TREATMENT OF CONSTIPATION IN INTENSIVE CARE UNIT (ICU): A RANDOMISED, CONTROLLED STUDY

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Introduction: Constipation and its implications have received very little attention even though this gastrointestinal motility disorders are common in critically ill patients. Constipation is defined as failure of the bowel to open for three consecutive days. This condition can give rise few adverse implications in critically ill patients such as more constipated patient failed to wean from mechanical ventilation, the median length of stay in intensive care increase and the proportion of enteral feeding intolerance were greater than non-constipated patients.

Objective: To compare bowel opening between groups of patients who receive neostigmine infusion versus syrup lactulose for treatment of constipation in ICU.

Methodology: This is a prospective study. The ventilated patients who fulfilled the inclusion criteria and were admitted to HUSM ICU between February till October 2015 were randomly received either neostigmine infusions 0.4–0.8 mg/hour or syrup lactulose 15 mL TDS. Incidence of bowel opening, time to first bowel opening and any adverse reactions were recorded.

Results: Forty patients were randomised where 20 patients in each group either neostigmine infusion or syrup lactulose. Neostigmine infusion group significantly had bowel opening (P -value = 0.027) and markedly had faster onset of bowel opening (P -value < 0.001) compared to syrup lactulose group. There was no significant mean difference in term of length of mechanical ventilation between two group of therapy (P -value = 0.542). No complications occurred from the neostigmine infusion.

Conclusion: Neostigmine infusion was effective for treatment of constipation in ICU compared than standard therapy syrup lactulose. Continuous intravenous neostigmine infusion of up to 0.8 mg/hour to critically ill patients appears to be safe.

Supervisor:

Professor Dr Nik Abdullah Nik Mohamad

THE EFFECTS OF INTRAVENOUS DEXMEDETOMIDINE PREMEDICATION ON INDUCTION OF ANAESTHESIA USING TARGET-CONTROLLED INFUSION OF PROPOFOL AND REMIFENTANIL

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Introduction and Objectives: Dexmedetomidine (Dex) is a selective α -2 agonist, which is beneficial as an adjunct drug for anaesthesia. The aims of this study were to determine the effects of loading dose of Dex on induction using target-controlled infusion (TCI) propofol and remifentanil in terms of induction time, target plasma concentration (Cpt) requirement for induction, effect-site concentration (Ce) at induction and haemodynamics changes.

Patients and Methods: 54 respondents, aged between 18–60 year-old and ASA I-II, scheduled for elective surgeries under general anaesthesia with endotracheal intubation were randomised into two groups; Group I: Dex ($n = 27$) received infusion loading dexmedetomidine 1 mcg/kg over ten minute. Group II: Control ($n = 27$) received 0.9% normal saline solution of the same calculated dose over ten minute. After loading dose, both groups will receive TCI remifentanil at target effect concentration of 2 ng/mL and Cpt propofol using Marsh model of 2 mcg/mL. If patients were still conscious after 1 min, Cpt propofol was titrated every 0.5 mcg/mL in

every 30 seconds until successful of induction. After successful induction, intravenous rocuronium 0.9 mg/kg was given and endotracheal intubation performed after one minute. After intubation, TCI remifentanyl must be tapper up by 1 ng/mL if there were any tachycardia and hypertension until stable. The following data were recorded; target plasma concentration and effect-site concentration of propofol at successful of induction, the induction time from starting of TCI propofol to loss of consciousness and any supplementation of TCI remifentanyl after intubation. The following parameters were recorded; blood pressure (BP), mean arterial pressure (MAP), heart rate (HR) and bispectral index score (BIS) at T baseline, T after completed loading drug study, T after TCI remifentanyl, T after successful TCI propofol, T before intubate, T 1 minute after intubate and T 5 minute after intubate.

Results: Dex group showed significantly lower Cpt of propofol [2.44 (0.54) versus 4.20 (1.11) mcg/mL; $P < 0.001$], lower Ce of propofol [1.60 (0.67) versus 3.43 (1.09) mcg/mL; $P < 0.001$] and shorter induction time [71.59 (38.13) versus 182.48 (62.64) seconds; $P < 0.001$]. Mean of HR in Dex group was significantly lower than control group at T after loading dose; [64.48 (CI 95% 59.94, 69.03) versus 81.22 (CI 95% 76.68, 85.79) bpm] and at T after TCI remifentanyl; [64.00 (CI 95% 59.16, 68.83) versus 79.37 (CI 95% 74.53, 84.21) bpm] ($F = 35.64$, $P < 0.001$). Mean of MAP in Dex group was significantly lower than control group at T after TCI remifentanyl; [85.93 (CI 95% 80.85, 91.01) versus 94.89 (CI 95% 89.81, 99.97) mmHg]. After endotracheal intubation, there were significant differences of mean MAP between the two groups ($P < 0.001$) regardless of time and significant differences of mean HR between the two groups ($P = 0.004$) regardless of time.

Conclusion: Pre-medication of dexmedetomidine reduced the requirement of target plasma concentration and effect-site concentration of TCI propofol for induction. It also produced reduction of induction time and more stable haemodynamic changes during induction of anaesthesia as well as during intubation using TCI.

Supervisor:

Dr W Mohd Nazaruddin W Hassan

Co-Supervisor:

Professor Dr Shamsul Kamalrujan Hassan

COMPARISON ON THE EFFICACY OF IMMEDIATE RELEASE OXYCODONE AND TRAMADOL IN REDUCING POSTOPERATIVE PAIN, NAUSEA AND VOMITING IN POST LAPAROTOMY PATIENTS WEANED FROM PCA MORPHINE

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Introduction: The introduction of oxycodone into the Malaysian health care system in recent years has opened up

another option for post-operative pain relief. We assess the clinical efficacy of oral oxycodone IR in reducing pain as well as nausea and vomiting and compare it to oral tramadol in this post-operative study.

Objective: This was a prospective, randomised, double blinded study on the efficacy of oxycodone IR as oral maintenance analgesia in reducing post-operative pain, analgesic requirement and incidence of nausea and vomiting in patients post laparotomy after PCA morphine is weaned off. This study was conducted in Hospital Universiti Sains Malaysia.

Methodology: We recruited 40 patients undergoing an elective laparotomy for gynaecological surgery. These patients were randomly selected to receive oral oxycodone IR once PCA morphine was weaned off 48 hours post-surgery. The other group of patients received the standard oral tramadol. Post-operative pain scores were assessed using the Combination Rating Scale and requirement of rescue analgesia at 2 hours, 6 hours, 24 hours and on day 3 of oral analgesia. Incidence of nausea was documented along with the requirement of rescue antiemetics at the same intervals. Assessment was made by pain services nurses and data was entered using Statistical Package for Social Science SPSS Version 22.

Results: This study revealed that patients receiving oral oxycodone IR had significantly lower pain scores of less than 4 which was achieved within 6 hours of treatment. This level was only achieved by the tramadol group at 24 hours of treatment. This is significant with a P -value < 0.001 based on time and treatment effects. Requirement of 1st and 2nd line rescue analgesia was significant between groups. Ten percent of the oxycodone group and 60% of the tramadol group needed 1st line rescue and 5% of the oxycodone group against 40% of the tramadol required rescue analgesia. Incidence of nausea was significantly lower in the oxycodone group only at 2 hours with a P -value of 0.022. The requirement of 1st and 2nd line rescue anti-emetics was lower in the oxycodone group however remained insignificant with a P -value of > 0.05 . Finally the mean satisfaction score for patients on oxycodone was 6.85 compared to 5.75 over a score of 10 with a significant mean difference of P -value < 0.001 .

Conclusion: The introduction of oral oxycodone IR in the post-operative period for post laparotomy patients who were weaned from PCA morphine showed better pain scores and less analgesic requirement. These patients also had reduced incidence of nausea at 2 hours and better overall patient satisfaction scores compared to the tramadol group. However, there was no significant difference in the antiemetic requirement between the two groups.

Supervisor:

Dr Laila Ab Mukmin

Co-Supervisor:

Associate Professor Dr Saedah Ali

LIMITATION OF MOBILE HEAD CT SCANNER (CERETOM) IMAGE QUALITY IN A NEUROSURGERY CENTER

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Introduction: Computed tomography (CT) has become the preferred technique in the diagnostic toolkit for head and brain imaging and superior to Magnetic Resonance Imaging (MRI) for the assessment of head injury. Indications for head imaging includes head injury, acute stroke, subarachnoid haemorrhage etc. A more recent development in CT imaging has been the development of a mobile CT scanner which can be beneficial from clinical and economical point of views.

Objective: To compare the image quality of CT brain images produced by mobile head CT scanner, CereTom, to standard fixed CT scanner.

Methods: This was a single center retrospective study involving CT brain images of 112 neurosurgical patients admitted to Hospital Sultanah Aminah Johor Bahru from December 2014 until March 2015. Hounsfield unit (HU) of all the selected images from CereTom were measured for: air, water and bone. Three observers (two neurosurgeons and a radiologist) evaluated independently the CT brain images acquired on standard fixed CT scanner within 48 hours apart with the CereTom. Each images were evaluated for visualisation of lesions, grey-white matter differentiation and streak artifacts at three different levels which were centrum semiovale, basal ganglia and middle cerebellar peduncles. Each evaluation was scored either 1 (poor), 2 (average) or 3 (good). The scores were sum up forming an ordinal reading of 3 to 9.

Results: Hounsfield unit (HU) for measured air, water and bone from CereTom were within the range of recommended by ACR. Evaluation of streak artifacts demonstrated scores of 8.54 (IQR 0.24) with fixed CT scanner versus 7.46 (IQR 1.16) for CereTom at centrum semiovale (z -5.67), 8.38 ± 1.12 versus 7.32 ± 1.63 at the basal ganglia and 8.21 ± 1.30 versus 6.97 ± 2.77 at the middle cerebellar peduncles. Comparison of grey-white matter differentiation showed scores of 8.27 ± 1.04 with fixed CT scanner versus 7.21 ± 1.41 for CereTom at centrum semiovale, 8.26 ± 1.07 versus 7.00 ± 1.47 at the basal ganglia and 8.38 ± 1.11 versus 6.74 ± 1.55 at the middle cerebellar peduncles. Evaluation for visualisation of lesions showed scores of 8.86 (IQR 0.09) with fixed CT scanner compared to 8.21 (IQR 0.34) for CereTom at centrum semiovale (z -4.24), 8.93 (IQR 0) versus 8.18 (IQR 0.57) at the basal ganglia (z -5.32) and 8.79 (IQR 0.11) versus 8.06 (IQR 0.41) at the middle cerebellar peduncles (z -4.93). All the results were significant with P -value < 0.01 .

Conclusion: The results of this study showed there were significant differences in terms of image quality between the images produced by fixed standard CT scanner and CereTom with the latter being more inferior. However, Hounsfield unit (HU) of images produced by CereTom do fulfil the recommendation by ACR.

Supervisors:

Dr Johari Siregar Adnan

Dr Noor Azman A Rahman

PRE-OPERATIVE AND POST-OPERATIVE DIFFUSION TENSOR IMAGING IN PATIENTS WITH EXTRA-AXIAL LESIONS AT THE FRONTAL OR TEMPORAL REGIONS OF THE BRAIN AND THEIR CORRELATIONS WITH NEUROPSYCHOLOGICAL OUTCOMES

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Background: The underlying changes in the neuronal connectivity adjacent to brain tumours cannot always be depicted by conventional MR imaging. The hypothesis of this study was that pre-operative neuropsychological deficits are associated with impairment of diffusivity in association fibre bundles. Hence, we investigated the potential of combined diffusion tensor imaging (DTI) fibre tracking and fractional anisotropy (FA) values of the fibres to determine changes in association fibres and their correlation to neuropsychological scores.

Methods: Our study consisted of eighteen patients with extra-axial brain tumours in areas adjacent to the frontal and temporal lobes. They were assessed pre-and post-operatively with DTI and neuropsychological assessments. MR examinations were performed on a 3T-scanner. FA values were calculated for the uncinate fasciculus, arcuate fasciculus, superior fronto-occipital fasciculus, inferior fronto-occipital fasciculus and corticospinal tracts ipsilateral and contralateral to the tumor. These values were compared with neuropsychological scores for language, memory and attention.

Results: The analysis revealed marked differences in pre- and post-excision of the tumor in both FA values and neuropsychological scores. Quantitative DTI was able to show significant differences in diffusivity of the association fibres before and after the surgery.

Conclusion: The additional use of DTI-fibre integrity and neuropsychological tests may aid in prognostication and decision making prior to surgery.

Supervisor:

Professor Dr Zamzuri Idris

Co-Supervisors:

Dr Salma @ Win Mar

Wan Nor Azlen Wan Mohamad

COMPARISON BETWEEN VENTRICULOSUBGALEAL SHUNT AND EXTRAVENTRICULAR DRAINAGE TO TREAT ACUTE HYDROCEPHALUS IN ADULTS AT HOSPITAL QUEEN ELIZABETH BETWEEN 2013 AND 2015: A RETROSPECTIVE STUDY

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Introduction: Hydrocephalus is defined as an inappropriate amount of cerebrospinal fluid (CSF) within the intracranial space at an inappropriate pressure. The decision to treat hydrocephalus is based on its various aetiologies. Transient alterations of CSF hemodynamics due to conditions such as subarachnoid and intraventricular haemorrhages, meningitis, and external compression from tumours may resolve after treatment; thus, temporary CSF diversion can be considered. A ventriculosubgaleal shunt (VSGS) can be used for temporary CSF diversion because it is a simple and rapid method, and establishes CSF decompression without causing electrolyte and nutritional losses.

Objectives: To study the efficacy of VSGS as a means of temporary CSF diversion, compared to EVD in adult hydrocephalus patients; to evaluate the outcome in terms of avoiding a permanent shunt, and to look for incidences of intracranial complications such as ventriculitis and modified Rankin scale, between the year 2013 and 2015.

Patients and Methods: This is a retrospective review of records. The data has been acquired from case notes of 50 patients with acute hydrocephalus: 26 secondary to intraventricular haemorrhage, ten from aneurysm rupture, eight post-trauma and six from infection. All these patients had undergone cerebrospinal fluid diversion in Hospital Queen Elizabeth II between 2013 and 2015. The patients were followed-up from the date of treatment until the resolution of hydrocephalus, where parameters such as shunt dependency and complications were documented in a pro forma.

Results: A total of 21 (42%) patients underwent EVD insertion and 29 (58%) underwent VSGS. Thirty-seven (74%) patients did not require a permanent shunt; 24 (64.8%) of them were from the VSGS group ($P = 0.097$). EVD had more intracranial complications (44.1%) compared with VSGS (23.5%), with a statistically significant P -value of 0.026.

Conclusion: While each treatment modality has its own complications, this study shows that VSGS is comparable with EVD as a temporary CSF diversion measure. As there are no statistical differences between these two modalities, VSGS is a viable option that has clinical value, with the possibility of continuation of treatment for such patients in non-neurosurgical centres, as opposed to patients with EVDs. Also, VSGS has statistically significant less intracranial complications compared with EVD.

Supervisors:

Dr Pulivendhan Sellamuthu
Dr Rahmat Harun @Haron

Co-Supervisor:
Professor Zamzuri Idris

FLUORESCENCE GUIDED VERSUS CONVENTIONAL SURGICAL RESECTION OF HIGH GRADE GLIOMA: A SINGLE CENTRE SEVEN YEARS COMPARATIVE EFFECTIVENESS STUDY

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Introduction: High grade gliomas (HGGs) are locally invasive brain tumors that carry dismal prognosis. According to National Comprehensive Cancer Network (NCCN) Guideline, the current standard management of HGGs includes maximum safe microsurgery resection followed by chemotherapy and radiotherapy. Although complete resection increases median survival, difficulty to demonstrate the tumor border reliably intraoperatively is a norm. Department of Neurosurgery Hospital Sungai Buloh has adopted fluorescence guided (FG) surgery using 5-aminolevulinic acid (5-ALA) as the first public hospital in Malaysia to overcome this shortcoming.

Objectives: The aims of this study were to evaluate the effect of FG surgery on overall survival and functional outcome as compared to conventional surgery. It also aimed to identify the significant independent predictors of survival in HGGs patients. Lastly, the effect of the extent of surgical resection on overall survival and functional outcome in FG patients was also evaluated.

Patients and Methods: This study was a retrospective observational study. A total of 74 patients with histologically proven high grade gliomas (HGGs) were recruited between January 2008 and December 2014. A total of 37 HGG patients who underwent FG surgery from January 2010 until 31 December 2014 and fulfilled the inclusion criteria were recruited. Another 37 patients from the conventional group were recruited consecutively from January 2008 until 31 December 2014 as the comparison group. The follow-up periods were done according to the scheduled appointment date (mostly at 6 weeks and 6 months) from the date of operation, which ended on 30 June 2015. Statistical Package for Social Sciences (SPSS) software version 22.0 was used in the statistical analysis.

Results: Significant longer survivals were observed in FG group compared with conventional group (12 months versus 8 months), $P < 0.02$. Even without adjuvant therapies, HGG patients from FG group survived longer than those from conventional group (8.0 months versus 3 months), $P = 0.006$. No significant differences of post-operative Karnofsky performance scale (KPS) between groups at 6 weeks and 6 months after surgery. Multivariate analysis identified four independent predictors of survival: $KPS > 80$ ($P = 0.01$),

histology ($P < 0.001$), surgical method ($P < 0.001$) and adjuvant therapy ($P < 0.001$). Multiple logistic regression analysis showed only three predictors of survival: tumor located in non-eloquent or near eloquent area ($P = 0.092$), surgical method (0.087) and adjuvant therapy (0.094). Although FG patients did not demonstrate significant influence of extent of surgical resection on patients' survival and functional outcome, patients with GTR/ NTR appeared to survive longer than STR (10.0 months vs 8.0 months).

Conclusion: This study showed a significant clinical benefit for HGG patients in terms of overall survival using FG surgery without resulting in worsening of postoperative function outcome when compared with conventional surgical method. However, the results might not be conclusive as this is a single centre study with small sample size. We advocate a further multi-centered, randomised control trial to support these findings before FG surgery being implemented as a standard surgical treatment for all HGG patients in local practice.

Supervisor:

Dr Azmin Kass Rosman

Co-supervisor:

Dr Marymol Koshy

A REVIEW OF OVARIAN TERATOMA IN HOSPITAL UNIVERSITI SAINS MALAYSIA TEN YEARS EXPERIENCE: 2003 TO 2012

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Introduction: Ovarian cancer is the fourth most common cancer among women in United Kingdom (UK) and in Malaysia. It constituted 6.5% of total female cancer with age standardised incidence rate (ASR) of 8.6 per 100,000, and is a major source of morbidity and mortality among women coming only after cancers of lungs, breast and colon in Malaysia. Mature ovarian teratoma is commonly benign; however it is associated with malignant transformation in up to 15% and no reliable pre-operative diagnostic procedures to detect this transformation. Immature teratoma represents 3% of total ovarian teratoma but constitutes 20% of germ cell malignancies, it occurs commonly among women below 20 years old and has tendency of recurrence. Fertility preservation approach of management is highly crucial but in advance stage may be difficult and occasionally the fatal complication associated with chemotherapy is a concern.

Objective: We aim to review the clinico-pathological pattern and outcome of management of ovarian teratoma patients in Hospital Universiti Malaysia (HUSM).

Patients and Methods: A total of 160 women diagnosed with ovarian teratoma and managed in HUSM from 2003 to 2012 were reviewed retrospectively. List of patients with confirmed histological diagnosis was obtained from

pathology department record and their folders were traced, data collected and analysed using SPSS 21 software (Inc., Chicago, USA).

Results: Ovarian teratoma is seen from 4 years to 75 years old women and commonest among 21–40 years age group (59.4%). Majority were married (74.4%) and most of them never use oral contraceptive pills (OCP), 64% have 1–4 children and breast fed for at least one year and 53 (33.1%) of them were pregnant during diagnosis. Abdominal mass or distension and abdominal pain were the commonest presenting symptoms in 32 cases, 45 cases were incidental diagnosis while 18 presented with acute abdomen. 43.1% of the cases were obese. Mature cystic teratoma is the commonest histological type (91.9%), monodermal 3.1%, immature 2.5% while, malignant transformation and mixed germ teratoma have 1.25% each. Ultrasound features were unilateral 108 (67.5%), bilateral 14 (8.8%). There were mixed solid cystic tumors in majority of cases 89 (55.6%), 29 (18.1%) were pure cystic while 4 (2.5%) were pure solid tumors. Only in 38 (31.1%) cases had discrete echogenic mass reported. Laparotomy was the commonest surgical approach 114 cases (71.3%), removal of tumor in the same setting during lower segment Caesarean section (LSCS) were 34 cases (21.3%) and laparoscopic approach was 12 cases (7.5%). The rate of spillage was found to be 21.1%, 20.6% and 58.3% for laparotomy, LSCS and laparoscopic approach respectively. Two cases had adjuvant chemotherapy with Bleomycine, Etoposide and Platinum regimen (BEP) involving one case of immature teratoma and the other of mature teratoma with malignant transformation. Follow up period was 3–60 months and two cases of recurrent mature ovarian teratoma occurred but no chemical peritonitis reported.

Conclusion: Teratoma is the commonest ovarian tumor in the reproductive age women, however, we found no significant association with factors such as marital status, parity, breast feeding, use of combine oral contraceptive and body mass index despite the presence of these factors in majority of our cases, this might be as a result of low power of the study to detect such an association. Fertility conservation is a great concern; ultrasonography is a reliable means for diagnosing and careful selection of patients for expectant management or surgical intervention. This study reveals that majority (122/160) of ovarian teratoma cases had ultrasound done pre-operatively and diagnosis of teratoma was suspected or made but only one out of many presumed pathognomic features of teratoma was reported in 38/112 cases. As such there is a need to improve in sonographic reporting of suspected cases of ovarian teratoma. Twelve cases of ovarian teratoma had laparoscopic removal of the tumor with 58.3% spillage rate, however none of the cases had a recurrence or chemical peritonitis therefore laparoscopic approach can be consider as an alternative to traditional laparotomy approach.

Supervisor:

Dr Ramli Ibrahim

Co-Supervisors:

Dr Nik Rafiza Affendi

Dr Akram Omar

USE OF GLARGINE + LISPRO VERSUS INSULATARD + ACTRAPID IN PREGNANT WOMEN WITH DIABETES DURING RELIGIOUS FASTING PERIOD – A PILOT STUDY

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Introduction: Large proportions of diabetic patients including pregnant women who fast during Ramadan represent a challenge to their physicians. Due to the lack of studies on safety and the absence established guidelines on management of diabetic pregnant women who wish to fast during Ramadan, women with pre-gestational or gestational diabetes are at a very high risk and may be strongly advised not to fast. In reality, many of them insist on carrying out this religious duty and some may not consult their physician at all, causing difficult management to the physician. The aim of this study was to find a better insulin regime for glycaemic control among diabetic mothers.

Objectives: To compare the glycaemic control and the incidence of hypoglycaemic event for pregnant women with diabetes among those using Glargine + Lispro with those using Insulatard + Actrapid during period of religious fasting.

Methodology: A prospective randomised controlled open-labelled study conducted in Hospital USM during fasting month involving 16 pregnant women with diabetes using insulin who wished to fast during Ramadan. They were divided into two groups; Group 1 given glargine + lispro and Group 2 given insulatard + actrapid. For Group 1, the total daily insulin dose calculated reduced by 70% for fasting and divided in ratio of 6:4 (glargine: lispro), glargine given at 10 p.m. while lispro given at sahur and iftar meal. For Group 2, 2/3 of calculated insulin requirement given at iftar and 1/3 given at sahur; for each dose, 2/3 given in the form of actrapid and 1/3 in the form of insulatard. The participants were required to break their fast should they experience hypoglycaemic symptoms.

Initially, they were admitted in the ward for glucose monitoring for 2 days. Capillary blood glucose measured 8 times throughout the day. During Ramadan, they were monitored in antenatal clinic with weekly blood sugar profile taken 4 times at 4:00 a.m., 8:00 p.m., 5:00 p.m. and 10:00 p.m. The glycaemic control was measured by median of the glucose level per day, and compared between the two groups. The glucose control throughout month of Ramadan also compared with the level prior to Ramadan. Mann Whitney test was used to compare independent samples and Wilcoxon signed rank test for dependent samples. Statistical analysis done using Stastical Package for Social Sciences (SPSS) version 22.

Results: All participants were able to fast without major problems and no hypoglycaemic event noted. The glucose level per day for whole Ramadan was lower in Group 1 (6.39 mmol/L, IqR 2.14) compared to Group 2 (6.70 mmol/L, IqR 1.13) with *P*-value of 0.749. Post-prandial glucose control (after sahur and after iftar) was better in Group 2 (7.05 mmol/L, IqR 4.04 for sahur and 7.02 mmol/L, IqR 2.32 for

iftar) compared to Group 1 (7.47 mmol/L, IqR 2.87 for sahur and 7.03 mmol/L, IqR 3.81 for iftar).

For both groups, the glucose level during fasting was significantly higher compared to prior to Ramadan (6.58 mmol/L compared to 5.59 mmol/L with *P*-value 0.023).

Conclusion: This study suggests that pregnant women with diabetes requiring insulin can fast safely in Ramadan month. The use of glargine + lispro was as effective as the use of insulatard + actrapid for pregnant women with diabetes during Ramadan fasting. In our group of patients, glycaemic control was relatively poorer during Ramadan fasting compared to prior to Ramadan.

GESTATIONAL TROPHOBLASTIC DISEASE IN HOSPITAL USM: A RETROSPECTIVE REVIEW

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Introduction: Gestational trophoblastic disease (GTD) forms a group of disorders spanning the conditions of complete and partial molar pregnancies through to the malignant conditions of invasive mole, choriocarcinoma and the very rare placental site trophoblastic tumour (PSTT). The World Health Organisation classification divides Trophoblastic Disease into the Pre malignant condition which is Partial Hydratirform moles, Complete hydatidiform moles and malignant condition such as Persistent Trophoblastic Disease, Invasive Mole, Choriocarcinoma, Placental Site Tumours. Molar pregnancies can be sub-divided into complete (CM) and partial moles (PM) based on genetic and histopathological features. GTD is a rare event in the Europe, with a calculated incidence of 1/714 live births.

Objectives: To determine prevalence of different types of Gestational Trophoblastic diseases, assess the associated factors of malignant condition compared to pre malignant condition and to determine the outcome of the chemotherapy treatment for patient with GTD.

Methodology: A retrospective review was conducted on all GTD cases over the 10 year period between January 2002 and December 2011. The diagnosis and staging was classified using FIGO anatomical staging (Appendix A) and had histopathological confirmation of the disease, data was compiled through a clinical research form for analysis and data analysis was carried out with SPSS version 22.

Results: A total of 123 cases were diagnosed with GTD within ten years span, there were 98 cases of Benign form of GTD and 25 cases of malignant form of GTD. Among the benign form of GTD there were 53 (43.1%) patients with partial hydatidiform mole and 45 (36.6%) with complete hydatidiform mole diagnosed clinically and conformed by histopathological evaluation. Malignant form of GTD accounted for total of 25 (20.3%) patients, among which persistent trophoblastic disease (PTD) consist of 22 patients (17.9%) and 3 (2.4%) patients with choriocarcinoma. Among the associated factors of malignant disease studied was age, ethnicity, pre-treatment hCG level, parity, child birth spacing, size of the uterus, size

of molar tissue, history of molar pregnancy, previous usage of oral contraceptive pills and presence of thecal luteal cyst. Among the risk factors, age was strongly associated with malignant GTD, it was noted that with increase in every year of age the odds of developing malignant GTD was increased by 5%. The outcome of two major treatment groups namely MTX regimen and EMA-CO regimen was studied, total of 22 patients received MTX as a single agent therapy, all of them were diagnosed with PTD and 19 patients had FIGO stage I disease and one patient with FIGO stage II disease and each one patient in stage III and stage IV disease, the patients in stage II and III needed second line chemotherapy with Actinomycin D and achieved full recovery, 19 patients in stage I received single agent MTX and complete recovery was achieved in 12 patients resulting in a success rate of 63% when used a single agent in stage I disease. There were 7 patients with stage I disease who failed to achieve satisfactory response with MTX alone and eventually requiring Actinomycin D (37%) achieved complete recovery from the disease. In this study 3 patients received EMA-CO regime as treatment, all of them were diagnosed with choriocarcinoma, two patients had stage I disease. One of them had hysterectomy done prior to treatment with EMA-CO and another received only EMA-CO after evacuation. Another one patient had stage IV disease with brain and liver metastasis, she was primarily started on EMA-CO and eventually succumbed to death. The remaining 2 patient had complete remission after treatment with EMA-CO. The success rate of EMA-CO in high risk patients at our center remains good as seen in previous studies.

Conclusion: In this study there was no major changes in term of the epidemiology of the disease, it was well within the generally accepted prevalence for GTD. Perhaps the one of the most interesting finding in this study was the associated risk factors to develop malignant disease, in this study factors which had high association were age, high parity, and long interval of last child birth. Most patients had FIGO stage I disease, the response to single agent MTX treatment achieved an acceptable outcome, while the rest of the patients who received second line therapy also had a complete recovery. Patients who were in stage II and III had complete recovery with EMA-CO regime. MTX remains as our first line treatment in low risk patients while the usage of Actinomycin also proved beneficial in cases of resistant. For the patients in high risk category this study supports the use of EMA-CO.

Supervisor:

Associate Professor Dr Mohd Pazudin bin Ismail

THE ACCURACY OF ULTRASONOGRAPHY IN THE ANTENATAL DIAGNOSIS OF PLACENTA ACCRETA IN HOSPITAL UNIVERSITI SAINS MALAYSIA

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Introduction: The incidence of placenta accreta is on the rise, owing to the increasing number of Caesarean sections. The incidence of placenta accreta has steadily increased in recent decades. It is a potential life threatening condition, and associated with significant morbidity and mortality to the patients. Multidisciplinary approach is fundamental when it comes to strategies to minimise the complications.

Objectives: The aims of this study are to determine the sensitivity and specificity of ultrasonography in the antenatal diagnosis of placenta accreta in patients with placenta praevia and previous uterine surgery and to compare the morbidity associated with placenta accreta to that of placenta praevia alone.

Methodology: This was a retrospective cohort study with the study population consisted of women with diagnosis of placenta praevia with previous uterine surgery, such as Caesarean section(s), dilatation and curettage (D&C), myomectomy or retained placenta who delivered at Hospital Universiti Sains Malaysia between January 2005 and December 2015. The hospital records system was used to identify all patients with the diagnosis of placenta praevia with previous uterine surgery, diagnosed after 28 weeks of gestation. Hospital charts were then traced and reviewed for data collection. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of ultrasound in the diagnosis of placenta accreta were calculated.

Results: Out of 80 patients included in the study, 15 (18.75%) of them were confirmed to have placenta accreta. The sensitivity and specificity of ultrasound in the diagnosis of placenta accreta were 84.62% and 94.03%, respectively. The positive predictive value (PPV) for ultrasound was 73.33% and the negative predictive value (NPV) was 96.92%. In terms of morbidity, patients with placenta accreta had significant intraoperative blood loss, hysterectomy rate, ICU admission rate, number of packed cells and DIC regime transfusions and longer hospital stay. More neonates in the accreta group required NICU admission.

Conclusions: Placenta accreta is associated with significant morbidity compared to placenta praevia alone. Ultrasound is a good diagnostic tool in the diagnosis of placenta accreta. This finding is consistent with other studies.

Supervisor:

Associate Professor Dr Adibah binti Ibrahim

Co-Supervisor:

Dr Nik Rafiza binti Nik Affendi

Co-Researcher:

Dr Nik Ahmad Zuky bin Nik Lah

ENDOMETRIAL CARCINOMA REVIEW: A 10-YEAR HOSPITAL UNIVERSITI SAINS MALAYSIA (HUSM) EXPERIENCE (JANUARY 2002–DECEMBER 2011)

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Introduction: Endometrial carcinoma is the most common gynaecological malignancy in the developed nations. It is the sixth of most frequent cancer that affect the women worldwide. In Malaysia, endometrial cancer is the sixth most frequent cancer that affects the Malaysia women. The life time risk of developing endometrial cancer is estimated to be as high as 2.6%. The peak incidence of endometrial cancer is in the early sixth decade. However, endometrial cancer is being diagnosed increasingly in younger women. It was found that 1.6% of all endometrial cancers were diagnosed between the ages of 20 and 34 years and 6.1% between the ages of 35 and 44 years. Most of these are Type 1 or hormone-dependent cancers associated with endometrial hyperplasia. In most women, endometrial cancers are diagnosed at early stage and are usually associated with a good prognosis. With appropriate treatment, the 5-year survival for disease confined to the uterus is as high as 96%. As the current trend of this disease continues to persist, this study tries to look into the trend of endometrial carcinoma cases that had been managed in HUSM from January 2002 until December 2011.

Objectives: This study was conducted to determine the prevalence, and to evaluate the response of all treatment modalities, and to determine the incidence of recurrence, and to determine the survival rate of endometrial carcinoma cases that was managed in Hospital University Sains Malaysia from January 2002 until December 2011.

Methodology: This is a retrospective study, which conducted by reviewing the patients' medical records with diagnosis of "endometrial cancer, endometrial carcinoma, or uterine cancer". Relevant information was obtained, recorded then analysed using descriptive statistics. The one sample *t*-test was used to determine the significant mean for some of the associated factors. For survival analysis, simple univariate and multivariate Cox regression model was used.

Results: A total of 56 cases were included in this study. Majority of the patients were Malays (89.3%), and Chinese (8.9%). The factors that associated incidence of endometrial carcinoma were post-menopausal age with peak incidence was in age group of 50–55 years, mean age 54.3 years (SD 11.77, $P = 0.036$), nulliparity and low parity (mean 2.75, SD 2.63, $P = < 0.001$), increase body mass index (BMI) with mean BMI 27.2 kg/m² (SD 5.43, $P = 0.003$) and those with underlying hypertension (53.6%) and diabetes mellitus (21.4%). Almost all patients were symptomatic at time of presentation (96.4%) with the main presenting symptoms of per vaginal bleeding in 91.1% and abdominal pain in 19.6% of patients. However, majority of the patients (55.4%) did not have any remarkable physical finding when they presented. For the rest of them, the commonest physical finding was the presence of abdominal mass (39.3%). Ultrasound was the main imaging modality. The main sonographic features of patients with endometrial carcinoma were abnormal thickened endometrium equal or greater than 5 mm (85.7%) which were common in the post-menopausal patients (46.4%) and enlarged uterus (48.2%). The preferred first line of diagnostic test was pipelle sampling (42.9%), followed by hysteroscopic tissue biopsy (28.6%). When the disease was staged, majority of patient were in stage I (67.9%). For other stages, 8.9% of patients were in stage II,

19.7% were in stage III and 3.6% in stage IV. The commonest histological type was the endometrioid adenocarcinoma with its sub-types (87.5%). The other types of histology were less common, with serous cell type in 3.6% of cases, clear cell type in 3.6%, mixed adenocarcinoma in 3.6% of cases and undifferentiated type in 1.8%. With regards to histological grades, many tumours were grade 1 (41.1%) and grade 2 (39.3%) and only 19.6% were grade 3 tumours. The predominant histological type of tumours with grade 1 and grade 2 were endometrioid adenocarcinoma, whereas for the grade 3 tumours were usually the other carcinoma sub-type (serous cell, clear cell, mixed adenocarcinoma, and undifferentiated). The endometrioid adenocarcinoma types of tumours were commonly occurred in early stages and in patient at age below 60. From the aspect of treatment, all patients had undergone surgery through the course of treatment. For modalities of treatments, majority had surgery followed with adjuvant radiotherapy (46.4%), while other 39.3% of patients had undergone surgery only. For the types of surgery, the type of surgery performed on most number of patients was extrafacial hysterectomy and bilateral salphingo-oophorectomy (BSO) (46.4%), followed by simple hysterectomy and BSO (41.1%). Despite appropriate treatment, a small number of the patients still developed recurrence, and later death. 75.0% of patients were disease free after 24 months, while the rest of 25.0% developed recurrence within less than 24 months, with the most of the patients (12.5%) developed persistence disease within less than 6 months following treatment. 80.4% of patients were still alive after 24 months following treatment, while other 19.6% of patients died in less than 24 months, with the most death (12.5%) occurred in less than 6 months. The significant prognostic factor were stage (stage III, $P = 0.003$, adjusted HR 26.243) and histological tumour grade ($P = 0.015$, adjusted HR 10.887). The 2-years survival rate was 97.4% for stage I, 60.0% for stage II, 36.4% for stage III, and 50.0% for stage IV.

Conclusions: Despite the inability to come up with survival rate of 5 years due to limitation of the study, the survival rates at 2 years had managed to show the strong prognostic influence of stage and grade.

Supervisor:

Dr Mohd Pazudin bin Ismail

THE EFFECT OF ANTENATAL PERINEAL MASSAGE ON THE OUTCOME OF PERINEAL TEAR AMONG PRIMIPAROUS WOMEN: A PROSPECTIVE RANDOMISED CONTROLLED TRIAL

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Introduction: Perineal trauma is a highly prevalent condition particularly those giving birth for the first time. The short and long term morbidity associated with perineal tear

can lead to major physical, psychological and social problems affecting the woman's ability to care for her newborn baby and other members of the family. Perineal massage performed during the last weeks of pregnancy has been shown probability of delivering with an intact perineum.

Objectives: To evaluate the effect of antenatal perineal massage on perineal tear outcome in primiparous women, specific location of tear, suturing time and to assess perineal pain score 12 hour post-delivery.

Patients and Methods: A 12-months randomised controlled trial in Hospital Raja Perempuan Zainab II, Kota Bharu was conducted from 1 February 2015 until 31 January 2016. The trial included 266 primigravida with singleton fetus beyond 34 weeks gestation who expected vaginal delivery, and randomly assigned to massage and non-massage groups. Women allocated to the study group were instructed to practice a 10 minute perineal massage daily from the 34th week of gestation until delivery. The types of perineal trauma following childbirth, specific tear location, suturing time and perineal pain score 12 hour post-delivery were evaluated.

Results: Women in the massage group had higher rate of an intact perineum (86.2% versus 13.8%, $P < 0.001$). Primiparous women in non-massage group were 2.17 more likely to have tear compared to massage group. Overall, there is no difference in the proportion of women who sustained first- or second-degree perineal tears or third/fourth degree perineal trauma comparing those who massage with controls. The rates of non-posterior perineal tears were significantly higher in the massage group (75.8% versus 24.2%, $P < 0.001$), whereas suturing time and perineal pain score were similar in both groups.

Conclusion: Antenatal perineal massage is an effective approach to increasing the chance of delivery with an intact perineum for primiparous women.

Supervisor:

Associate Professor Dr Mohd Pazudin bin Ismail

Co-Supervisor:

Dr Zainal Abidin bin Hanafiah

EFFECTS OF DIETARY COUNSELING ON GESTATIONAL WEIGHT GAIN AND PREGNANCY OUTCOMES IN OBESE PREGNANT WOMEN PROSPECTIVE RANDOMISED CONTROLLED TRIAL IN HOSPITAL SULTANAH BAHYAH, ALOR SETAR, KEDAH

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Introduction: Obesity is a serious and increasing health problem in the Western World and also in Malaysia. Prevalence of obesity in Malaysia is 7.5% and estimated prevalence of obesity in women in Malaysia was 16.6%. The

numbers keep increasing each year and it gives a significant impact to the reproductive age women. Obese women who get pregnant carried higher maternal morbidity and perinatal morbidity and mortality. Pregnancy complications such as Gestational Diabetes Mellitus (GDM), Pre-Eclampsia (PE), Caesarean Section, infections and thromboembolic disease significantly associated with obese mother.

Observational studies indicate that the rate of pregnancy complications among obese pregnant women can be limited if weight gain during pregnancy is restricted. Heavier women may benefit from avoiding high and very high gestational weight gain (GWG), which brings only a slight increase in the risk of growth restriction for the infant. On recent data, especially in Asian population, there is no evidence-based prenatal counseling protocol available to prevent excessive gestational weight gain.

Objective: To evaluate the effects of dietary counseling in obese pregnant women on gestational weight gain and pregnancy outcomes in Hospital Sultanah Bahiyah, Alor Setar, Kedah.

Patients and Methods: This was a prospective randomized controlled trial, commenced on the 1 December 2013 and ended on the 30 December 2014. It was carried out in Hospital Sultanah Bahiyah, Alor Setar, Kedah. There were 120 patients with obesity Class I, II and III recruited in this study, equally randomised into two groups; obese patients in intervention group with dietary counseling and control group with routine prenatal care group. The intervention group received dietary counseling from the only one dedicated nutritionist for at least once in each trimester of pregnancy. The main dietary counseling remains on diet and caloric restriction. The main outcome measured was the mean difference of gestational weight gain between two groups. Secondary outcomes included maternal outcome such as incidence of Gestational Diabetes Mellitus, Pregnancy Induced Hypertension, Pre Eclampsia, mode of delivery, Post Partum Haemorrhage; and fetal outcomes included mean gestational age, mean birth weight, shoulder dystocia and Apgar Score.

Results: A total of 120 women were randomised into two groups of 60, the dietary counseling and routine prenatal care groups. Baseline demographic characteristics were similar between the study groups. The dietary counseling group gained significantly less gestational weight gain than did the routine prenatal care group 7.6 kg (SD 1.54) compared with 9.1kg (SD 1.86), $P < 0.001$ with 95% CI: 0.83–2.07. In a multiple logistic regression, statistically significant variables in the maternal outcome include gestational age, GDM and spontaneous labour. Fetal outcome with significant variables include Apgar score in 1 minute, 5 minutes, 10 minutes and diagnosis of pneumonia.

Conclusions: The study shows dietary counseling in obese pregnant women has significant benefit in reducing gestational weight gain and improving pregnancy outcomes in maternal side such as prolonged gestational age of delivery, reducing occurrence of GDM and higher proportion goes into spontaneous labour. Fetal outcomes also significantly improved in term of Apgar Score and reducing number of fetus develop pneumonia.

Supervisor:

Professor Dr Mohd Shukri Othman

Co-Supervisor:

Dr Ahmad Amir Ismail

COMPARISON BETWEEN TWO DIFFERENT ANTIBIOTIC REGIMES (2 GRAMS STAT THEN 1 GRAM 4 HOURLY AMPICILLIN VERSUS 1 GRAM STAT THEN 500 MG 6 HOURLY OF AMPICILLIN) AS ANTIBIOTIC PROPHYLAXIS OF MATERNAL AND NEONATAL SEPSIS IN PROM \geq 18 HOURS, PROSPECTIVE RANDOMISED CONTROLLED TRIAL IN HOSPITAL SULTAN ISMAIL, JOHOR BAHRU, JOHOR

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Introduction: Pre-labour rupture of membranes is a common clinical problem with the predominant risk to the fetus is ascending infection. The risks to the mother are of uterine infection, via either chorioamnionitis or postpartum endometritis. Ampicillin group antibiotic is currently used as prophylaxis. Across the region, many antibiotic regime and dosage is recommended. Several studies showed conflicting outcome in search for optimal dosage.

Objective: The aim of this study is to evaluate maternal and fetal outcome of two different regimes of Ampicillin dosage for antibiotic prophylaxis.

Patient and Methods: A total of 292 patients were recruited in this study. Patients with term uneventful antenatal whom demonstrated PROM more than 18 hours were randomised into two different Ampicillin dosage regimes; a) 2 grams stat and 1 gram 4 hourly, b) 1 gram stat and 500 mg 6 hourly. Maternal outcome in term of duration of PROM, prostin insertion, level of WCC, temperature of 38 °C, dosage of antibiotic given prior to delivery, numbers of vaginal examinations, maternal chorioamnionitis and incident of postpartum endometritis were recorded. Fetal outcome measured include Apgar score at 1 minute, Apgar score at 5 minutes, NICU admission, early onset of neonatal sepsis and perinatal mortality. Both group were compared and *t*-test performed with significant level of $P < 0.05$ is used.

Results: A number of 146 patients in each armed fulfilled the inclusion criteria. There were no cases of postpartum endometritis and perinatal mortality recorded.

Majority of patients delivered vaginally (88% in 2 gram groups, 99% in 1 gram group) followed by LSCS (23.35 in 2 grams group, 19.2% in 1 gram group). There were three cases of chorioamnionitis in 2 grams group (2.1%) and two cases (1.4%) in 1 gram group. Apgar score at 1 minute showed significant difference between two group with a number of nine cases (6.2%) less than 7 in 2 grams group and six cases (4.2%) in 1 gram group ($P = 0.049$). There were 5 babies diagnosed as early onset of neonatal sepsis in 2 grams group (3.4%) and 3 babies in 1 gram group (2.1%). However, there were no significant different between two group Ampicillin regimes

in relation to duration of PROM, prostin insertion, level of WCC, temperature of 38 °C, dosage of antibiotic given prior to delivery, numbers of vaginal examinations, Apgar score at 5 minutes, NICU admission and early onset of neonatal sepsis.

Conclusion: Data from this study showed that there is no significant difference between the different dosage used as antibiotic prophylaxis for PROM patients with respect to maternal and fetal outcome (short and medium term outcome).

Supervisor:

Dato Dr Ghazali bin Ismail

Co-Supervisor:

Associate Profesor Dr Pazudin bin Ismail

A COMPARISON FOR THE MATERNAL AND PERINATAL OUTCOME BETWEEN METFORMIN AND INSULIN IN THE TREATMENT OF GESTATIONAL DIABETES MELLITUS

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Background: Diabetes mellitus (DM) is an important complication of pregnancy which may carry adverse effects on both mother and fetus. While insulin is effective in controlling high blood glucose levels, otherwise resistant to diet and exercise management, several factors hinder its usage. Metformin has been found to be a convenient, cheap, effective and safe hypoglycaemic agent in some countries. It is possible that metformin will have similar beneficial effects among Malaysian pregnant women.

Aim: The main aim of this study was to determine that metformin is an effective treatment for glycaemic control in the gestational diabetes mellitus (GDM) population in Malaysia as compared to insulin. It is also to assess the safety of these treatments by evaluating the maternal and fetal outcomes in GDM patients treated either with metformin or insulin.

Methodology: A prospective, open label, randomised controlled study involving 99 pregnant women recruited between 12–32 weeks gestation, diagnosed with GDM. Patients were randomised to be either in the insulin group ($n = 48$) or metformin group ($n = 51$). Participants were followed-up throughout their pregnancy with a 2-weekly BSP monitoring till date of delivery. Mother and perinatal outcomes were followed-up until mother and baby were discharged from the ward post-natally. Both laboratory and clinical data were recorded and analysed.

Results: Ninety eight percent and 95% of participants in the metformin and insulin groups, respectively, completed the study. The primary outcomes in comparing the differences of capillary blood glucose (BSP) levels between metformin group and insulin group shown that there is no significance

difference between metformin group and insulin group at all different treatment periods.

Maternal weight gains between both groups were no significantly different at 8.8 kg (\pm 4.27) in metformin group to the 8.8 kg (\pm 3.43) insulin group ($P > 0.950$). The rates of maternal hypertension complications did not differ significantly between the two groups. Higher reported cases of urinary tract infection (UTI) in metformin group as in 30% while only 6.5% in the insulin group ($P = 0.003$).

Average birth weight in the metformin group [3.1 kg (\pm 0.26)] is similar to the insulin group [3.0 kg (\pm 0.48)]. No significance difference in neonatal morbidity; hypoglycemia, hyperbilirubinaemia or respiratory disorder, was observed between metformin and insulin group.

Conclusion: Efficacy of metformin therapy was similar to insulin in giving good optimum glycaemic control in GDM women in Malaysia and carries similar low risk in term of maternal and perinatal outcomes. However, more studies with larger sample numbers, wider sample population are needed to collaborate these findings.

Supervisors:

Dr Krishna Kumar

Professor Nik Ahmad Zuky bin Nik Lah

OPTIC NERVE HEAD AND RETINAL NERVE FIBER LAYER ANALYSIS IN EMMETROPIC MALAY CHILDREN

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Introduction: Optic nerve head (ONH) parameters and retinal nerve fiber layer thickness (RNFLT) of normal children have been described in previous published reports. None of these measurements was described among Malay children population using Cirrus spectral domain optical coherence tomography (SD-OCT). The aim was to report normative values for ONH parameters and RNFLT in emmetropic Malay children. The possible correlations between these parameters were also evaluated.

Objectives: To determine the mean of ONH parameters and mean RNFL in emmetropic Malay children by using Cirrus SD-OCT; and to determine correlation between the ONH parameters and RNFL thickness.

Patients and Methods: Ninety-five Malay children with no ocular abnormality aged between 7 to 17 years were recruited into this cross sectional study. It was conducted in Hospital Universiti Sains Malaysia, Malaysia from January 2014 to December 2015. All children underwent a complete ocular examination including refraction and axial length measurement. ONH parameters and RNFLT measurement were performed using Cirrus SD-OCT machine. One eye of each subject was randomly selected for analysis. The correlations in between the parameters and influence of age, gender, axial

length and spherical equivalent (SE) on measurements were statistically evaluated.

Results: Ninety-five children were included in the study with 65 females (68.4%) and 30 males (31.6%). Mean age was 10.6 (2.82) years, mean IOP was 14.8 (2.81) mmHg, mean SE refraction was -0.12 (0.28) diopters and mean axial length was 23.03 (0.76) mm. Mean (SD) disc area, rim area and cup volume were 2.32 (0.40) mm², 1.53 (0.33) mm² and 0.204 (0.16) mm³, respectively. The average cup to disc ratio (SD) and vertical CDR were 0.55 (0.13) and 0.50 (0.14). Mean (SD) RNFLT for all patients was 102.08 (11.08) μ m. The average, superior and inferior RNFLT showed a significant positive correlation with the optic disc area. A significant correlation was also observed between the rim area and average, superior, inferior and nasal RNFLT. The inferior RNFLT was negatively correlated with average CDR. There was also significant effect of gender on disc area. There were no significant effects of age, axial length and SE on the measurements.

Conclusion: This study provides normative data of ONH parameters and RNFLT in emmetropic Malay children. Emmetropic Malay male had a significantly larger optic disc area. Increase in RNFLT is associated with significant increase in disc and rim areas.

Supervisor:

Professor Dr Shatriah Ismail

EVALUATION OF RETINAL VASCULAR CALIBER IN MALAY CHILDREN

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Introduction: Digital retinal vessel imaging is evolving as a non-invasive method of evaluating the microvasculature. In children, the general absence of disease-related confounding factors makes them an ideal study population. However, childhood studies in this field are limited, especially among Malays, the main ethnicity in South East Asia.

Objectives: The present study aims to evaluate the influence of ocular and systemic factors on retinal vessel caliber in a childhood Malay population.

Methods: This was a cross-sectional study involving 86 Malay children aged 6 to 12 years old in Hospital Universiti Sains Malaysia, Malaysia. Ocular examination, refraction, retinal photography and axial length were performed by standardised protocols. Anthropometric measurements including blood pressure were likewise obtained. Retinal vessel diameters were summarised as the central retinal arteriolar equivalent (CRAE) and central retinal venular equivalent (CRVE) using validated computer-based methods. Multiple linear regression was used to determine the effect of systemic and ocular biometry on CRAE and CRVE.

Results: After correcting for ocular magnification, the mean CRAE and CRVE were 171.40 μ m and 248.02 μ m, respectively. Blood pressure (SBP, DBP, MAP) and axial length

were the main factors affecting the CRAE. After multivariable adjustment, each unit (1 mm Hg) increase in mean arterial pressure was associated with a 0.451 mm reduction in CRAE ($P = 0.013$). Each 1 mm increase in axial length was associated with a 4.582 mm narrowing of CRAE ($P = 0.024$). All variables analysed in our study had no statistically significant effect on the CRVE.

Conclusion: The mean retinal CRAE and CRVE in Malay children were 171.40 mm and 248.02 mm. Retinal arteriolar calibers are narrower in healthy children with higher blood pressure and longer axial lengths. These associations suggest that the pathological changes in the microvasculature seen in hypertension and pathological myopia may be an amplification of the normal physiological response of blood vessels to various systemic and ocular dynamics.

Supervisor:

Professor Dr Wan Hazabbah Wan Hitam

Co-Supervisor:

Professor Dr Shatriah Ismail

COMPARISON OF OXIDATIVE STRESS LEVELS AMONG PATIENTS WITH PRIMARY OPEN ANGLE GLAUCOMA (POAG) AND PRIMARY ANGLE CLOSURE GLAUCOMA

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Introduction: Oxidative stress has been postulated to cause retinal ganglion cells death, trabecular meshwork degeneration leading resistance of aqueous outflow. Subsequently, it may lead to IOP elevation and glaucomatous optic neuropathy. Thus, it is worthwhile to look for the oxidative stress level in glaucoma patients. Detection of oxidative stress level in ocular tissue may perhaps provide insight into a role of oxidative stress in pathogenesis of glaucoma.

Objective: Our objective was to compare the oxidative stress level in tears between glaucoma and age-matched controls. The comparison of SOD, catalase and MDA level between POAG and PACG patients were also conducted.

Methods: A cross sectional study was conducted between May 2014 and November 2015 involving patients with confirmed diagnosis of POAG and PACG attending eye clinic of two tertiary hospitals in Malaysia; Hospital Universiti Sains Malaysia and Hospital Raja Permaisuri Bainun. Age-match non-glaucoma patients were recruited as controls. The detail medical history, ocular history and drug history such as antioxidant supplement were obtained through direct questioning from patients and medical record. Complete ophthalmic evaluations were conducted including Humphrey visual field analysis. Tear samples collected by using schirmer paper. Laboratory analysis was performed to test on SOD, catalase and MDA level of tears using commercially available immunological kits. Statistical analysis was done using

Statistical Package for the Social Science (SPSS Inc Version 20). Independent *t*-test was used to compare the SOD, catalase and MDA level in tears between glaucoma and controls.

Results: A total of 62 POAG patients, 57 PACG patients and 72 controls were recruited. Patients with glaucoma were older. Mean SOD and catalase level were slightly higher in glaucoma patients as compared to controls. Meanwhile mean MDA level was slightly lower in glaucoma patients compared with controls. However, there was no significant difference of SOD level ($P = 0.191$), catalase level ($P = 0.259$) and MDA level ($P = 0.309$) between glaucoma and controls using multivariate analysis. There was no significant difference of SOD, catalase and MDA level between POAG and PACG patients. However, mean SOD activity was statistically significant higher in patients with POAG compared to controls after adjusting confounding factors (351.67 U/mL versus 315.12 U/mL), $P = 0.006$.

Conclusions: Quantification of oxidative stress level in tears is non-invasive and easy. Catalase and MDA may not a play role in oxidative stress in glaucoma. SOD is a potential oxidative stress marker for POAG.

Supervisor:

Professor Dr Liza Sharmini Ahmad Tajudin

Co-Supervisor:

Associate Professor Dr Che Badariah Abd Aziz

ASSOCIATION OF CIGARETTE SMOKING AND PHYSICAL ACTIVITY WITH PRIMARY OPEN ANGLE GLAUCOMA IN MALAY PATIENTS

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Introduction: Glaucoma is the second leading cause of blindness worldwide, with Asians accounting for approximately half of the world's glaucoma cases. Primary Open Angle Glaucoma (POAG) is the most common form of glaucoma. Malays are among the affected races in Asia with a prevalence of about 2.5%. Modifiable risk factors have not been identified, apart from intraocular pressure (IOP). The effects of cigarette smoking and physical activity has not yielded any concrete evidence in its effects towards IOP and POAG.

Objectives: To determine association between cigarette smoking and physical activity with the risk for POAG in Malays.

Methodology: A case-control study was conducted involving 250 Malay POAG patients and 250 Malay control subjects. Demographic data consisting of age, gender and level of education were obtained. A pedigree chart consisting of the last 3 generations was documented to ascertain the Malay status of participants. Body Mass Index (BMI) was measured and control subjects underwent ocular examination which included IOP, gonioscopy and optic disc

assessment. Humphrey Visual Field (HVF) testing was also done. An adapted and validated interviewer-based lifestyle questionnaire was administered to assess smoking status and physical activity of participants. Statistical analysis using multiple logistic regression was done.

Results: Mean age was 62.4 ± 7.7 years and 61.0 ± 10.0 years among POAG patients and control subjects respectively. There was a male preponderance in both groups. In simple logistic regression, there was statistically significant association of status of smoking (OR 1.54 [95% CI; 1.07, 2.21]) ($P = 0.021$), duration of smoking (OR 1.01 [95% CI; 1.00, 1.02]) ($P = 0.030$) and smoking 1 to 10 sticks of cigarettes per day (OR 1.82 [95% CI; 1.15, 2.90]) ($P = 0.011$) towards increasing risk of developing POAG. Presence of physical activity (OR 0.50 [95% CI; 0.29, 0.85]) ($P = 0.010$), moderate levels of physical activity (OR 0.43 [95% CI; 0.25, 0.76]) ($P = 0.003$), number of days per week of physical activity (OR 0.90 [95% CI; 0.83, 0.97]) ($P = 0.004$) and minutes per day of physical activity (OR 0.98 [95% CI; 0.98, 0.99]) ($P < 0.001$) were found to be protective against POAG. In multiple logistic regression analysis, after adjusting for age, gender and BMI, there was statistically significant association of status of smoking (OR 2.05 [95% CI; 1.25, 3.36]) ($P = 0.005$), duration of smoking (OR 1.02 [95% CI; 1.00, 1.03]) ($P = 0.010$), smoking 1 to 10 sticks of cigarettes per day (OR 2.44 [95% CI; 1.39, 4.28]) ($P = 0.002$) and smoking more than 20 sticks of cigarettes per day (OR 4.41 [95% CI; 1.11, 17.52]) ($P = 0.035$) towards developing POAG. Presence of physical activity (OR 0.49 [95% CI; 0.28, 0.84]) ($P = 0.010$), moderate levels of physical activity (OR 0.46 [95% CI; 0.23, 0.90]) ($P = 0.023$), number of days per week of physical activity (OR 0.90 [95% CI; 0.82, 0.98]) ($P = 0.011$) and minutes per day of physical activity (OR 0.98 [95% CI; 0.97, 0.99]) ($P < 0.001$) decreased the risk of POAG.

Conclusion: There was statistically significant association of cigarette smoking and risk of POAG in Malays. There was statistically significant association of physical activity towards decreasing the risk of POAG in Malays.

Supervisor:

Associate Professor Dr Mohtar Ibrahim

Co-Supervisor:

Professor Dr Liza Sharmini Ahmad Tajudin

EVALUATION OF VISUAL ACUITY AND MACULAR THICKNESS POST FOCAL LASER WITH AND WITHOUT SUPPLEMENTARY HONEY IN DIABETIC MACULAR OEDEMA

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Introduction: Diabetic macular oedema (DMO) is a significant cause of vision loss in the diabetic patients. Laser is the standard treatment for DMO. Chronic inflammatory also has an important role in the pathogenesis of DMO. Tualang

honey with anti-inflammatory and anti-oxidant properties has a potential as an adjunct treatment for DMO.

Objective: To compare LogMAR best corrected visual acuity (BCVA) and central macular thickness (CMT) at 3 months post laser treatment between those with and without honey supplement in DMO.

Methods: A prospective randomised controlled study was conducted in Hospital Universiti Sains Malaysia between April 2013 and August 2015. Patient with clinically significant macular oedema (CSMO) was selected and was randomised by using randomised envelope technique into 2 groups; laser without honey group and laser with honey group. Patients were evaluated for LogMAR BCVA and CMT pre-treatment and at 3 months post-treatment. LogMAR BCVA was assessed using LogMAR chart and CMT was measured using Heidelberg Spectralis OCT.

Results: A total of 52 patients were recruited (laser group without honey: 26 patients and laser with honey group: 26 patients) into this study. There was a significant improvement of mean LogMAR BCVA at 3 months post treatment in DMO patients treated with laser alone ($P = 0.002$). However, there was no significant difference of the mean LogMAR BCVA in DMO patients treated with laser between those with and without honey supplement at 3 months post treatment ($P = 0.448$). There was also no significant difference of mean CMT ($P = 0.881$) at 3 months post laser treatment between those with and without honey supplement. There was no side effect of honey noted in patients consumed tualang honey.

Conclusion: Tualang honey used as adjunct with standard focal/grid laser has no additional improvement in both visual acuity and CMT compared to laser alone.

Supervisor:

Associate Professor Datin Dr Zunaina Embong

Co-Supervisor:

Professor Dr Siti Amrah Sulaiman

COMPARISON OF MACULAR THICKNESS, RETINAL NERVE FIBER LAYER THICKNESS AND OPTIC NERVE HEAD PARAMETERS IN HBE/ BETA THALASSEMIA AND CONTROL

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Introduction: HbE/ β -thalassemia is one of the hemoglobinopathy that commonly found in South East Asia (SEA) and it has become a severe public health problem today. Apart from the pathological anemia, they also share other common features like hepatosplenomegaly and craniofacial bony deformities. Ocular biometry can be affected as well due to abnormal growth of the orbital bone. Other than these, structure of the retina and the optic nerve may be altered in these patients.

Objectives: To compare mean macular thickness, retinal nerve fiber layer (RNFL) thickness and optic nerve head (ONH) parameters between HbE/ β -thalassemia group and control.

Patients and Methods: This is a cross-sectional study conducted in Hospital Universiti Sains Malaysia from June 2014 till March 2016. Patients with confirmed HbE/ β -thalassemia and healthy population were selected based on the inclusion and exclusion criteria. Baseline macular thickness, RNFL thickness and ONH parameters were measured by using Cirrus HD-OCT. Statistical analysis was performed using SPSS version 22.0.

Results: A total of 132 participants were recruited (66 participants in HbE/ β -thalassemia group and 66 participants in control). There was no significant difference in mean macular thickness in between the two groups. No significant difference found in the mean RNFL thickness in between HbE/ β -thalassemia and control. There was also no significant difference in ONH parameters between two groups.

Conclusion: The study revealed that there was no significant differences in both mean macular thickness, RNFL thickness and ONH parameters in between HbE/ β -thalassemia and normal population.

Supervisors:

Associate Professor Dr. Adil Hussein
Dr Suresh Kumar a/l Vasudevan

Co-supervisor:

Dr Khairy Shamel bin Sonny Teo

QUALITY OF LIFE AND DEPRESSION IN PATIENTS WITH PRIMARY OPEN ANGLE GLAUCOMA USING MALAY VERSION GLAUCOMA QUALITY OF LIFE 36 (GLAUQoL 36) AND MALAY VERSION GERIATRIC DEPRESSION SCALE 14 (mGDS 14)

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Introduction: Glaucoma is a chronic disease requiring life long treatment. Quality of life (QoL) is often under emphasised during the course of glaucoma management. Understanding the quality of life and detection of early depression at different severity stage of POAG not only helps in coping with the disease but also in customisation of the management. There is still a wide gap in understanding the QoL and depression in elderly with POAG in Malaysia.

Objectives: To evaluate quality of life and depression in patients with primary open angle glaucoma using the Malay version of the Glaucoma Quality of Life- 36 (Glau-QoL 36) and Malay version Geriatric Depression Scale 14 (mGDS 14) questionnaires. This study also aims to compare the QoL and depression with severity of POAG. The potential correlation between QoL and depression was also studied.

Patients and Methods: A cross sectional study was conducted in Hospital Universiti Sains Malaysia, Kelantan and Hospital Selayang, Selangor between July 2014 and February 2016. POAG patients who were ≥ 60 years old at the time of recruitment had mLOCS II grade 1 or less, underwent cataract or trabeculectomy surgery at least 3 months prior and were on medical or combined medical and surgical treatment. Severity of POAG was based on modified Advanced Glaucoma Intervention Study (AGIS) based on two reliable reproducible Humphrey visual field SITA program 24-2 analysis. Face to face interview was conducted using validated *Bahasa Malaysia* version of GlauQoL 36 and mGDS 14 questionnaires.

Results: A total of 360 patients were recruited. Majority of recruited patients were between ages 60–67 (38.3%). Overall 64 (17.8%) have mild POAG, 93 (25.8%) have moderate POAG, 115 (31.9%) have severe POAG and 88 (24.4%) have end stage POAG. Majority of the recruited patients were not working (88.9%) and live with their families (68.1%). There was significant association between GlauQoL 36 score among POAG patients according to severity and domains: daily living, driving, physiological well being, self image, anxiety, burden of treatment and confidence in healthcare. Increased severity of POAG was associated with decreased quality of life in all GlauQoL 36 domains except confidence in healthcare. There were more depressive patients as severity of POAG increased. There was poor correlation between quality of life and depression among POAG patients ($r < 0.25$).

Conclusion: Bahasa Malaysia version of GlauQoL 36 and mGDS 14 is a useful tool to assess QoL and depression of POAG patients in Malaysia. GlauQoL 36 scores increased as the severity of glaucoma increases suggestive of poorer quality of life. The mGDS 14 score also increases as the severity of glaucoma increases. However, there was poor correlation between QoL and depression based on the mGDS 14 and GlauQoL 36 questionnaire.

Supervisor:

Professor Dr Liza Sharmini Ahmad Tajudin

Co-Supervisor:

Associate Professor Dr Azhany Yaakub

CORRELATION OF THE ANTERIOR OCULAR SEGMENT BIOMETRY AND HbA1c LEVEL IN TYPE 2 DIABETES MELLITUS PATIENTS

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Introduction: Anterior ocular segment is an important structure in the eye that showed to be damaged in diabetic retinopathy. Hyperglycaemia is one of the factors that associated with the progression of diabetic complications.

Objectives: To compare the mean anterior ocular segment biometry and mean HbA1c among Type 2 diabetes mellitus [no diabetic retinopathy and non-proliferative

diabetic retinopathy (NPDR)] and to evaluate the correlation of anterior ocular segment biometry and HbA_{1c} level.

Methodology: A cross-sectional study was conducted in Hospital Universiti Sains Malaysia, Kelantan from November 2013 till May 2016 among non-diabetes mellitus and Type 2 diabetes mellitus (diabetic with no diabetic retinopathy and diabetic with NPDR) patients. The patients were evaluated for anterior ocular segment biometry [central corneal thickness (CCT), anterior chamber width (ACW), angle opening distance (AOD) and anterior chamber angle (ACA)] by using Anterior Segment Optical Coherence Tomography (AS-OCT). Three mL venous blood was taken for the measurement of HbA_{1c}.

Results: A total of 150 patients were included in this study (non-diabetes mellitus: 50 patients, diabetic with no diabetic retinopathy: 50 patients, diabetic with NPDR: 50 patients). There was significant difference in mean CCT between non diabetes mellitus, diabetic with no diabetic retinopathy and diabetic with NPDR [493.12 (67.08), 524.60 (28.74) and 529.26 (33.88), respectively] ($P < 0.001$) and ACW [11.58 (0.74), 11.76 (0.53) and 11.39 (0.62)] ($P = 0.015$) which was significant between diabetic with NPDR and diabetic with no diabetic retinopathy. There was significant difference of HbA_{1c} level between diabetic with no diabetic retinopathy (8.26, SD 1.77) and diabetic with NPDR (9.65, SD 2.57) ($P = 0.002$). There were poor negative correlation between all the anterior ocular segment biometry with HbA_{1c} in diabetic with no diabetic retinopathy group except the CCT and ACW (poor positive correlation). However, all the correlation was not significant. There was poor negative correlation between all the anterior ocular segment biometry and HbA_{1c} in diabetic with NPDR except ACW (poor positive correlation). However, all the correlation was also not significant.

Conclusion: The CCT was significantly thicker in diabetic patients compared to non-diabetes mellitus. The ACW was significantly widest in diabetic with no diabetic retinopathy compared to diabetic with NPDR. The HbA_{1c} was significantly higher in diabetic with NPDR compared to diabetic with no diabetic retinopathy. There was poor correlation between all of anterior ocular segment biometry with HbA_{1c} in diabetic with NPDR and diabetic with no diabetic retinopathy groups.

Supervisor:

Associate Professor Dr Mohtar Ibrahim

Co-Supervisor:

Associate Professor Datin Dr Zunaina Embong

CORRELATION OF RETINAL NERVE FIBER LAYER AND MACULAR THICKNESS WITH SERUM URIC ACID AMONG TYPE 2 DIABETES MELLITUS

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Introduction: Serum uric acid is a final breakdown product of purine catabolism in humans. It's a potent antioxidant that induces oxidative stress on the vascular endothelial cells, thus mediating progression of diabetic related diseases. Various epidemiological and experimental

evidence suggest that uric acid has a role in the etiology of type 2 diabetes mellitus. We conducted a cross-sectional study to evaluate the correlation of Retinal Nerve Fiber Layer (RNFL) and macular thickness with serum uric acid in type 2 diabetic patients.

Objectives: The aim of this study was to correlate the RNFL and macular thickness with serum uric acid among type 2 diabetes mellitus patients with Non-Proliferative Diabetic Retinopathy (NPDR) and without diabetic retinopathy.

Patients and Methods: A cross-sectional study was conducted in the Eye Clinic, Hospital Universiti Sains Malaysia, Kelantan between the period of August 2013 till July 2015 involving type 2 diabetes mellitus patients with no diabetic retinopathy and with NPDR. An evaluation for RNFL and macular thickness using Spectralis Heidelberg optical coherence tomography was done and 6 mL of venous blood was taken for the measurement of serum uric acid and HbA_{1c}.

Results: A total of 180 diabetic patients were recruited (no diabetic retinopathy: 90 patients and NPDR: 90 patients) into the study. The mean level of serum uric acid for both the groups were within normal range and there was no significance difference between the two groups. The mean level of serum uric acid for both gender was significantly higher in no diabetic retinopathy group ($P = 0.004$ respectively). The mean serum uric acid was significantly higher in patient with HbA_{1c} < 6.5% ($P < 0.031$). Patients with NPDR have thicker RNFL and macular thickness compared to patient with no diabetic retinopathy. However, only the RNFL thickness of the temporal quadrant and the macular thickness of the superior outer, inferior outer and temporal outer subfields were statistically significant ($P = 0.038$, $P = 0.004$, 0.033 and < 0.001 , respectively). There was poor correlation between RNFL and macular thickness with serum uric acid in both the groups.

Conclusion: Serum uric acid showed a poor correlation with RNFL and macular thickness among type 2 diabetic patients.

Supervisor:

Associate Professor Madya Datin Dr Zunaina Embong

COMPARISON OF RETINAL NERVE FIBER LAYER THICKNESS, MACULA THICKNESS AND OPTIC NERVE HEAD PARAMETERS IN OPIOID DEPENDENT AND NORMAL ADULT

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Introduction: Drug abuse is a socioeconomic problem that affects the public of the country. Heroin and morphine, which falls under the opioid group continues to be the commonest drug of abuse in Malaysia. Opioid usage is associated with addiction and dependence, and reported ocular side effects are pupillary miosis, conjunctiva hyperemia, ocular motility disorder and risk of complication such as

endophthalmitis. It was also reported that chronic opioid usage leads to neurological degeneration.

Objectives: To compare the retinal nerve fiber layer thickness, macula thickness and optic nerve head parameters in opioid dependent and normal adult.

Methods: The study design was a case control with opioid dependent individuals and healthy individuals recruited from the Methadone Clinic, Department of Psychiatry and Ophthalmology Clinic, Department of Ophthalmology, Hospital Universiti Sains Malaysia. Thirty five opioid dependent subjects and thirty five healthy subjects with no history of opioid use were recruited. Ophthalmological examination and optical coherence tomography (Heidelberg Spectralis® OCT) were performed.

Results: Compared to normal healthy subjects, opioid dependent group has thinner average retinal nerve fiber layer in the right eye ($P < 0.05$) and in both superior quadrant of the optic nerve ($P < 0.05$). Analysis of other segments did not show any statistical significance.

Conclusion: Early thinning of the retinal nerve fiber layer could be one of the early signs of complication from long term opioid usage. Further studies may be needed to determine if further thinning occurs with time and the implication to the patients' vision.

Supervisor:

Associate Professor Dr Adil Hussein

Co-Supervisor:

Dr Mohd Azhar Mohd Yasin

ENDOSCOPIC DECOMPRESSIVE SURGERY FOR LUMBAR SPINAL STENOSIS: ANALYSIS OF CLINICAL OUTCOME AND PREDICTIVE FACTORS

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Background: Endoscopic approach is one of the approaches that maintained the aim of surgery while minimise the collateral tissue destruction. Its efficacy and safety have been advocated by numerous studies. To our knowledge, there are number of studies done for lumbar stenosis with regards to the outcome and related issues in endoscopic spine surgery, however there are lacked of literature that evaluate the outcome of the decompressive lumbar spine surgery.

Purpose: To assess the outcome result of endoscopic surgery for lumbar stenosis and to determine its predictive factors.

Study Design: A retrospective cohort study of patients with degenerative lumbar spinal stenosis who underwent endoscopic percutaneous surgery using unilateral approach for bilateral decompression.

Patient Sample: Sixty patients with lumbar spinal stenosis underwent endoscopic decompressive surgery between 2009 and 2013.

Methods: Between 2009 and 2013, 60 eligible patients who undergone endoscopic interlaminar decompressive spine surgery (Destandau's method) for lumbar degenerative spinal stenosis in Hospital Universiti Sains Malaysia were selected for the study. The clinical outcome was measured pre and post-operative for Visual Analogue Scale (VAS) for back and leg pain, motor grading, sensory, Oswestry Disability Index (ODI), and MacNab's criteria. The cohort was group into two categories: excellent to good result was grouped into favourable category and fair to poor result was grouped into unfavourable category. Paired t-test and Fisher exact test was used for statistical analysis.

Results: Mean age of patients were 60.82 years old. The mean follow-up period was 30.1 months (range 17.2 to 43 months). There were 23 (38.3%) male and 37 (61.7%) female. The mean operation time was 183.6 minutes (ranging from 124.8 minutes to 242.4 minutes). Mean blood loss was 150.18ml (ranging from 30.82 ml to 269.54 ml). Post-operative hospital stay mean was 2.45 days (ranging from 1.34 days to 3.56 days). Most frequently involved level were L4/L5 in 51 patients (52.6%), followed by L3/L4 in 19 patients (19.6%), L5/S1 in 24 patients (24.7%), and L2/L3 in 3 patients (3.1%). VAS for back pain and leg pain and ODI for pre and post operation was statistically significant ($P < 0.001$). Reduction in neurology is statistically insignificant. Based on Macnab's criteria, 88.4% showed excellent to good outcome and 11.7% showed fair outcome. There was no significant predictive factor for the outcome. As for complication, 13.3% of patients had dural tear; 1.6% had nerve root injury, wrong level and delay wound healing; 11.6 % had leg dysesthesia; 11.6% had recurrent stenosis; and 1.6% and 6.6% had reduced motor and sensory respectively.

Conclusions: Endoscopic decompressive lumbar stenosis surgery is a safe surgery. It has an excellent outcome in term of reducing the back and leg pain, and improve quality of life beside a shorter hospital stay and early mobilisation.

Supervisor:

Associate Professor Dato' Dr Abdul Halim bin Yusof

FUNCTIONAL OUTCOME OF PROXIMAL FIBULAR GRAFTING AFTER WIDE RESECTION OF DISTAL RADIUS TUMOUR IN HUSM FROM YEAR 2000 TO 2013

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Introduction: Distal radius bone tumour surgery is a complicated and challenging procedure which includes resection of the affected bone and reconstruction of the bony defect. Several reconstructive procedures have been described including vascularised and non-vascularised fibular graft,

osteoarticular allograft, prosthetic replacement and ulnar translocation. The proximal fibular graft was used in order to preserve better wrist function due to its similarity in shape and size to the distal radius. The aim of this study is to evaluate and compare the functional outcome between total wrist fusion and wrist reconstruction with proximal fibular grafting after wide excision of distal radius tumour by using Musculoskeletal Tumor Society scoring system (MSTS).

Methods: This study was a cross-sectional, single intervention and retrospectively assessed the selected eleven patients with distal radius bone tumour who had wide excision and reconstructive surgery done with proximal fibular autograft that fulfilled the inclusion and exclusion criteria. All the patients recruited in this study were from year 2000 to 2013 and sampled into two groups; the wrist reconstruction and total wrist fusion groups. Functional outcome was evaluated and compared by using Musculoskeletal Tumor Society scoring system (MSTS). Hand grip strength and union rate were assessed by Jamar hand dynamometer and plain radiographs respectively.

Results: There were 6 patients underwent wrist reconstruction procedure and 5 patients underwent total wrist fusion. The mean age of patients was 36.55 years old. Mean follow up period was 6.3 years. There were 9 patients with Campanacci grade II to grade III giant cell tumours, 1 patient with osteosarcoma and 1 patient with aneurysmal bone cyst in this study. Overall musculoskeletal tumor society (MSTS) score range from 70% to 93.3%, with 4 good and 7 excellent results. The mean MSTS score for wrist reconstruction group was 24.83 (82.78%) and total wrist fusion group was 23.4 (78.0%). Average grip strength compared to the contralateral hand was 60.0% for total wrist fusion which was better than wrist reconstruction, 58.07%. Radiofibular union occurred in 8 out of 11 cases. The union rate for wrist reconstruction was 83.3% whereas for total wrist fusion was 60%. Excluding the 3 non-union cases, average time for union was 18.4 weeks for the wrist reconstruction and 18.7 weeks for the total wrist fusion. There was no tumour recurrence and all the patients were disease free.

Conclusion: Proximal fibular grafting after wide excision of distal radius bone tumour had good to excellent MSTS score for both wrist reconstruction and total wrist fusion. The only significant finding was the scoring for pain component in MSTS was more superior in total wrist fusion. However, there was no significant difference for the overall MSTS score between these procedures. The most commonly encountered complication was fibulocarpal subluxation which found in wrist reconstruction group.

Supervisor:
Dr Norazman Md Zain

Co-Supervisor:
Professor Dr Wan Faisham Wan Ismail

ASSOCIATION OF POSTERIOR CRUCIATE LIGAMENT INJURY IN DIFFERENT TYPES OF FEMUR FRACTURE IN HOSPITAL ALOR SETAR KEDAH, A CROSS SECTIONAL STUDY

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Introduction: Posterior Cruciate injury in association with ipsilateral femur fracture has been historically underdiagnosed as many cases are missed during the initial trauma. The incidence or proportion of this injury has wide variation and the incidence in our setting is not known. Understanding the proportion and association of posterior cruciate injury with femur fracture enables us to detect the injury early and treat the injury accordingly. The aim of treatment to provide a stable and pain free knee while minimalising the risk of OA. This aim can be achieved if the injury is picked up early so than an early physiotherapy regime can be started.

Objectives: To detect the proportion of PCL injury in combination of femur fracture and to determine the relationship between the demographic factors, the cause of injury and different types of fracture femur. Thus by understanding the association of the injury with different types of fracture femur, it will enable us to diagnose the injury more reliably so that it can be detected in acute setting or as early as possible so that early treatment either operative or non-operative by means of physiotherapy can be initiated.

Patients and Methods: This was a single centre cross sectional study in which from Jan 2012 till June 2014, all patient that were diagnosed with femur fracture who meet the inclusion criteria was reviewed to determine the association of PCL injury.

Results: There were a total of 144 patients included in this study. From these 144 patient, 13 patients had PCL injury (9%). Based on the study, 6 out of 13 cases of PCL injury with femur fracture were detected late with one case was detected 6 weeks after injury, three cases were detected 8 weeks after injury, one case was detected 9 weeks after injury and 1 case was detected 10 weeks after injury. The remaining 7 cases of PCL injury was detected early. Out of the 7, 5 were avulsion injury which was picked up by x-ray during the initial assessment and the other 2 were picked up following the fixation of femur.

Conclusions: The proportion of PCL injury with femur fracture is 9% in our setting and distal 3rd femur fracture have higher incidence. Majority of the cases that were missed was due to failure to perform complete knee examination following fixation. We strongly recommend all patient undergoing femur fracture fixation should undergo complete knee examination while still under anaesthesia. These patient, especially with distal 3rd femur fracture should also be repeatedly screen during clinic their follow up.

Supervisor:
Dr Emil Fazliq Mohd

CAST VERSUS PLATE IN THE TREATMENT OF BOTH BONE FOREARM FRACTURE IN OLDER CHILDREN: FUNCTIONAL OUTCOME AT MATURITY

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Background: Both bone fracture at forearm is usually treated with cast using Plaster of Paris for children less than 10 years old but for those 10 and above the treatment is debatable whether surgery is needed or not. The aim of this study was to make a comparison between the treatment of cast and plate fixation for both radius ulna fracture in older children approaching skeletal maturity. The age of patient at time of fracture, post reduction angular correction of radius and ulna and forearm rotational limitation were compared with the functional outcome during the assessment at skeletal maturity.

Methodology: Fifty patients were involved in this study, 25 patients treated with cast and another 25 treated with plate. Individual consent was obtained from all patients and parents. All those chosen are 10 years and above. They were assessed at least 2 years after treatment and at skeletal maturity to allow remodeling. The boys' skeletal maturity age was taken as 16 and girls' as 14.

Those selected were contacted after reviewing their radiological and treatment records and have been asked to come to Hospital Universiti Sains Malaysia for further evaluation. During evaluation, the functional ability of the involved hand and forearm has been assessed. A radiological assessment of affected limb was also done through a proper antero-posterior and lateral radiograph. The functional outcome was assessed based on activity of daily living, the differences of the pronation and supination of the affected forearm with the normal arm and graded using Price method into excellent, good, poor and fair outcome. The angulations of the radius and ulna post reduction and at skeletal maturity were documented. Data was statistically analysed using SPSS version 22.

Results: In this study both the groups treated with cast and plate had either excellent or good functional outcome assessment by Price score. In the cast group, there was a statistically significant correction of both radius and ulna angulation in post reduction and after skeletal maturity ($P < 0.05$). Majority of the patients have excellent price grading with 44 patients (88.0%) and only six patients under good price grading (12.0%) in both the groups.

This shows that even the cast group treated without surgery can achieve excellent (88.0%) and good (12.0%) functional outcome at maturity. However, this is only true if the maximum post reduction angulation of radius and ulna is 15 degrees in the cast group, as angulation more than that may need surgical reduction (Bowman et al. 2011).

Mean age at time of fracture in both the groups were 12.12 with the youngest age at the time of fracture was 10 years old and 15 years old was the eldest patient.

The radius post reduction angulation was within 3 to 15 degrees with the median of 8.00 degrees under cast group and for the plate group, the radius post reduction angulation was within 3 to 7 degrees with the median of 5.00 degrees. At the skeletal maturity the angulation was corrected to within the range of 0 to 15 degrees with the median of 3.00 degrees in the cast group and the angulation was corrected to within the range of 0 to 7 degrees with the median of 2.00 degrees for plating group. For the ulna in cast group, post reduction angulation was within 1 to 15 degrees (median of 7.00 degrees) with improvement to within 0 to 15 degrees (median of 2.00 degrees) at skeletal maturity. For the ulna in plate group, post reduction angulation was within 1 to 4 degrees (median of 2.00 degrees) with improvement to within 0 to 5 degrees (median of 2.00 degrees) at skeletal maturity.

For the limitation of supination in the cast group, there was 5.00 degree of median compared to 0 degree of median in plating group and for the limitation of pronation in the cast group there was 4.00 degrees of median compared to 0 degree of median in plate group.

Conclusion: This study showed that the result of casting is comparable to plate fixation in both bone forearm fracture to achieve excellent functional outcome in older children approaching skeletal maturity provided the maximum radius and ulna angulation post reduction in the cast group is 15 degrees.

Supervisor:
Dr Ismail Munajat

CONVENTIONAL VERSUS DIGITAL PREOPERATIVE TEMPLATING IN PRIMARY TOTAL HIP ARTHROPLASTY AT HOSPITAL SULTANAH BAHYIAH

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Introduction: Templating is part of pre-operative planning for total hip arthroplasty surgery. Conventionally this was done using on acetate transparent films overlaid on hard copy radiographs. With the emergence and implementation of digital radiograph, digital templating software was introduced in total hip arthroplasty.

Objectives: The aim of this study was to compare the accuracy of conventional templating techniques and digital templating system in primary total hip arthroplasty at Hospital Sultanah Bahiyah Alor Setar, Kedah, Malaysia.

Patients and Methods: This was a retrospective study done on 73 cases where primary total hip arthroplasty was performed for osteoarthritis, avascular necrosis of femoral head and femoral neck fracture in Hospital Sultanah Bahiyah Alor Setar, Kedah, Malaysia from June 2011–June 2014. In a separate sitting, conventional templating was performed using hard copy radiographic films with implant specific templates whereas digital templating was performed using

a magnification-calibrated digital radiographic images and TraumaCad™ templating software on a computer workstation. Paired *t*-tests were used to determine the accuracy of conventional templating versus digital templating. We also used Bland-Altman Method and to determine the agreement between conventional method and actual implant as well as digital method and actual implant.

Results: Both the conventional and digital template had quite a good agreement with the actual implant in predicting the acetabular cup and femoral stem size. However, digital templating had higher agreement to the actual implant size as compared to conventional templating in predicting the acetabular cup and femoral stem size.

Conventional templating significantly under predicted cup size (P -value = 0.003) and the digital templating slightly over predicted the cup size but was not statistically significant (P -value = 0.501). Conventional templating significantly over predicted femoral stem size (P -value = 0.004) while digital templating slightly over predicted the femoral stem size but was not statistically significant (P -value = 0.103). Therefore digital templating is more accurate than conventional templating in the preoperative assessment.

Conclusion: Digital templating is more accurate in predicting the acetabular cup and femoral stem size than conventional templating using the available software.

Supervisor:

Associate Professor Abdul Nawfar Sadagatullah

Co-Supervisor:

Dato Dr Suresh Chopra

EVALUATION OF PROGNOSTIC FACTORS AND SURVIVAL OF PATIENTS WITH METASTATIC BONE DISEASE

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Introduction: Management of metastatic bone disease is still challenging, along with the improvement in managing primary solid tumors, patients survive longer and they become potential to have metastatic lesions of bone more than they had before. A variety of treatment options could possibly be given to those patients includes medical treatment, radiation, chemotherapy and surgical intervention. The surgical intervention for metastatic bone lesions gives satisfactory outcome. However, there are few factors affecting the survival of patients with metastatic bone disease such as performance status, type of primary tumor, neurology deficit, pathologic fracture, visceral organ metastasis and chemotherapy administration. This study was conducted to evaluate the prognostic factors affecting the median survival and patient's quality of life.

Objectives: The aims of this study are to determine prognostic factors that are affecting post-operative survival

rate of the patients with metastatic bone diseases, to assess the post-operative survival rate of patients with metastatic bone diseases, and to evaluate the performance status questionnaires of the survived patients within first year after metastatic bone lesion operation

Methods: A total of 40 patients with metastatic bone disease treated surgically between 2008 to 2015 at Orthopaedics Oncology Unit, Hospital Universiti Sains Malaysia were evaluated retrospectively, for survival prognostic factors, while the performance status questionnaire of ECOG (Eastern Cooperative Oncology Group) was used to assess the patient's quality of life at three, six and twelve month after the surgery. Subsequently, survival rate was analysed by the Kaplan-Meier method.

Results: There were 29 female and 11 male, the most common primary tumor was breast cancer with 42.5%, followed by thyroid cancer 17.5%. Over all 14 (37.8%) patients survived, while 23 (62.16%) patients died, and the median survival was 36 months. Mean age at presentation was 54.43 years, and there were 30% (12/40) above 60 years and 70% (28/40) below 60 years. Based on the age groups, the survival rate was statistically significant P -value (0.028). Other prognostic factors include chemotherapy administration and site of bone metastasis (appendicular, axial bone or both together) were also significantly correlated with the survival P -value of (0.003, 0.021), respectively. Types of the surgery was a significant factor associated with the survival (P -value 0.038), resection and endoprosthesis surgery was the most procedure performed in our center for (hip, proximal femur, shoulder and around knee joint lesions) 58.97% ($n = 24$), followed by Harrington procedure for pelvic involvement which was 17.95%. Performance status ECG (0–2) and ECOG (3–5) of patients was evaluated and found to be statistically significant as a prognostic factor for survival.

Conclusion: The prognostic factors that significantly affect the survival of patient with bone metastasis were age which was less than 60, location of bone lesions, previous chemotherapy, and the type of performed surgical procedure. Additionally, the study revealed that the quality of life significantly correlated with the types of surgery and overall survival. Furthermore, the performance status (ECOG) significantly correlated with the types of surgery and age.

Supervisor:

Professor Dr Wan Faisham Nu'man Wan Ismail

THE OUTCOMES OF DELAYED TREATMENT FOR OPEN FRACTURE DIAPHYSEAL FOREARM

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Introduction: Open fractures considered as orthopaedic emergency and need prompt wound debridement to prevent infection. However due to unavoidable circumstances

debridement cannot be performed within 12 hours. Furthermore, sometimes wound debridement was delayed up to more than 48 hours. The purpose of this study to review on the outcome of diaphyseal forearm open fracture when wound debridement was performed according different time classification.

Objectives: The purpose of this study is to review on the outcome of diaphyseal forearm open fracture regarding soft tissue infection, osteomyelitis and non-union when wound debridement was performed according different time classification.

Methods: A five-year secondary data review on the outcome of diaphyseal forearm open fractures patients admitted to our centre between 2008 and 2013. Patients with grade IIIc open fractures were excluded. Demographic data, time of debridement, present of infection and type of union were recorded.

Results: We had 26 cases of open fracture diaphyseal forearm with 10 cases Grade I, seven cases Grade II, 8 cases Grade IIIa and 1 case Grade IIIb. There was one non-union with no soft tissue infection or osteomyelitis among patients with wound debridement done before 12 hours of injury. One soft tissue infection without osteomyelitis cases and one non-union case among patients with wound debridement done with 13–24 hours of injury. There was one soft tissue infection with osteomyelitis case and one non-union case among patients who had debridement after 24 hours of injury.

Conclusion: There was a proportionate higher risk of infection if wound debridement was delayed more than 12 hours. Osteomyelitis was proportionately higher if wound debridement was done after 24 hours of injury. Non-union was proportionately similar if wound debridement was done before 12 hours, within 13–24 or after 24 hours of injury.

BONE MINERAL DENSITY IN PATIENT ADMITTED TO HOSPITAL RAJA PEREMPUAN ZAINAB II WITH PROXIMAL FEMUR FRACTURE

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Introduction: Osteoporosis has been recognised as an established and well-defined disease that affects more than 8.9 million fractures annually worldwide. Most studies of fracture involving the proximal femur claim that generalised osteoporosis is the major etiological factor, although none has established a densitometric fracture threshold above which such fractures would not occur.

Objectives: This is a cross sectional analytical study with aims to identify the bone mineral density of elderly patients admitted for fracture proximal femur in an institution as assessed by Dual Energy X-Ray Absorptiometry (DXA) scan as well as to determine the biodemographics of the said profiles.

Methodology: Bone mineral density of 15 patients admitted for proximal femur fractures were evaluated using

DXA scan. The T-score was further evaluated to see the significance of osteoporosis in these subjects.

Results: The mean age of the subject was 70 years old, and 80% were Malays. 60% of them were non-milk consumer, and 80% were categorised under low socioeconomic group. Only 33% were a smoker. Bone density of neck of hip among the patients had the lowest median with -1.70 and interquartile range of 1.10 . Then, it was followed by bone density for total hip and spine with median value of -1.60 and -1.40 , respectively. Majority of the patients who involved in this study had their bone mineral density value as osteopenia. The highest osteopenia percentage was for the neck of hip, 66.7%. Then it was followed by total hip and spine, 60% and 33.3% respectively. The percentage of patients with osteoporotic group of BMD for total hip, spine and neck of hip were 6.7%, 33.3% and 20%, respectively. Five (33.3%) patients had their BMD total hip as normal, 5 (33.3%) patients for spine and 2 (20%) patient for neck of hip. Out of 15 subjects, only 1 who had all three BMD value of total hip, spine and neck of hip as osteoporosis. Fisher's Exact test analysis found that there were no significant association between studied bio-demographic and bone mineral density at all measured sites.

Conclusion: This study found that there were no significant association between studied bio-demographic and bone mineral density at all measured sites. Majority of the patients who involved in this study had their bone mineral density value as osteopenia. The highest osteopenia percentage was for the neck of hip, 66.7%, followed by total hip and spine, 60 and 33.3%, respectively.

Supervisor:

Associate Professor Dr Abdul Nawfar Sadagatullah

Co-Supervisor:

Dr Muhammad Anwar Hau Abdullah

GROUND REACTION FORCE OF THE HIP, KNEE AND ANKLE JOINTS IN ADOLESCENT IDIOPATHIC SCOLIOSIS: COMPARISON BETWEEN NORMAL POPULATIONS

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Introduction: Scoliosis particularly Adolescent idiopathic scoliosis (AIS) is a relatively common condition seen in orthopaedic practice which can modify human locomotion. Thus far, no report yet on GRF comparison between pre- and post-operative treatment. This data is expected to give clinicians evidence based information on how scoliosis can affect all major weight bearing joints in term of its ground reaction force.

Objectives: This study aimed to establish and compare the GRF on the three main weight-bearing lower limbs joints during a normal walking gait, among normal person, person

with idiopathic scoliosis without spinal fusion, and person with idiopathic scoliosis with spinal fusion.

Patients and Methods: Targeted subjects were recruited from Hospital Raja Perempuan Zainab II and Hospital Universiti Sains Malaysia, the two only referral hospitals for spinal cases in Kelantan, Malaysia. A total of 41 subjects fulfilling the recruiting criteria were recruited, namely control group without scoliosis ($n = 14$), study group with scoliosis without spinal fusion ($n = 14$), and study group with scoliosis with spinal fusion ($n = 13$). The gait analysis was done at Sport Science Unit, School of Health Sciences, USM, equipped with an optical motion capture system consisting of six high-resolution digital cameras. These values were computed during walking on the gait platform over the force plate.

Results: GRF profiles for the three study groups on the three axes of the three weight bearing lower limbs joints versus walking phase was established. There was a noticeable trend observed in changing of X-axis and Z-axis GRFs versus walking phase on the three joints among the three study groups. The GRF was at baseline during the heel strike phase, and then it increased during the early stance and mid stance walking phases, the GRF decreased during the toe off phase and further decreased back to the baseline. Similar trend was also found in Y-axis GRF versus walking phase on the knee and ankle joints, but not the hip joint. In group comparison, there were no significant difference in the GRF of the three axes of the three joints between AIS without spinal fusion and normal groups. There were also no significant difference in the GRF of the three axes of the three joints between AIS with spinal fusion and normal groups. There were no significant difference in the GRF of the X and Z axes of the three joints between AIS without spinal fusion and AIS with spinal fusion groups. There was a significant difference was found between the AIS without spinal fusion group (44.00 ± 26.78) and group of AIS with spinal fusion (17.85 ± 17.21) at left knee Y-axis GRF, in which the GRF is significantly higher by mean difference of 26.15 in AIS without spinal fusion group.

Conclusion: Scoliosis had significant effect on the knee joints Y-axis GRF. Spinal fusion results in rebalancing of the knee joint Y-axis GRF, in which Y-axis force reflects the propulsive or braking force in a joint.

Supervisor:
Professor Dr Mohd Imran Yusof

OUTCOME OF NECK OF FEMUR FRACTURE IN ELDERLY TREATED NON OPERATIVELY IN HOSPITAL SELAYANG

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Introduction: Femoral neck fracture is a common occurrence among the elderly age group especially when the aging population around the world is on the rise. This type

of fracture poses a high mortality and morbidity, hence, they are commonly treated operatively to prevent complications. However, this fractures has been treated non-operatively in certain circumstances. In this study, we assess the functional outcome of elderly patients with femoral neck fracture that was treated non-operatively.

Methods: We recruited 55 patients in this study from January 2010 to January 2014. Out of the total 55 patients, the patients who are still alive are called and interviewed in the clinic. The functional outcome after neck of femur fracture being treated non-operatively were assessed using the SF-36 health survey questionnaire. The reason for opting non-operative treatment were explored and also the major cause of mortality among these patient was also identified.

Results: From our small series conducted, the survival rate for elderly patients with neck of femur fracture treated non-operatively was 58.2%. The mortality rate for elderly patients with neck of femur fractures treated non-operatively was around 41.8% per year. With regards to the quality of life, the functional assessment for our patients revealed that they fare fairly when the mental component is taken into account. With the mean Mental Component Summary (MCS) of 57.5 and mean Physical Component Summary (PCS) of 46.3. This means the functional outcome for elderly patients with neck of femur fracture treated non-operatively was average based on the Mental Component Summary (MCS) score and was below average for the Physical Component Summary (PCS) score. There were two reasons identified for these patients opting for non-operative intervention; that is patients are medically unfit accounting for 54.5% of the total 55 patients and another reason is patient and family refusal which leaves us with 45.5%. The major cause of mortality from the 23 patients who passed away was identified as pneumonia which showed significant association with the mortality status.

Conclusion: Although the standard treatment for neck of femur fractures are operative intervention, under certain circumstances, it can be treated non-operatively. With proper nursing care and rehabilitation, the general health among these patients can be improved.

Supervisor:
Dr Muhammad Paiman

REVISION ENDOSCOPIC INTERLAMINAR LUMBAR SPINE DECOMPRESSION SURGERY USING DESTANDAU ENDOSPINE SYSTEM: A RETROSPECTIVE STUDY OF CLINICAL OUTCOME IN A SINGLE INSTITUTION

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Introduction: Revision surgery is known to be difficult and high risk. It faces serious technical challenges and the outcome is less than the index surgery. Endoscopic spine

surgery is a minimally invasive surgery and is a very promising method with potential of providing better results. So far there is no study on the outcome of the revision endoscopic lumbar surgery.

Objectives: The aim of the study is to determine the feasibility of revision endoscopic interlaminar lumbar spine decompression surgery using Destandau Endospine system and to correlate the clinical outcome with the biodemographic factors.

Methodology: A total of 17 patients who underwent revision endoscopic lumbar spine surgery between December 2009 and September 2014 were followed up at a mean of 2.95 years (0.42–6 years). Three cases had open surgery and others (14) were endoscopic surgery as index operations. Two cases were wrong level of operations and the rest (15) were inadequate surgery as the reason for revision. Two patients were excluded earlier due to loss of follow up. All except one (discectomy) undergone decompressive surgery. In addition to the biodemographic parameters, they were assessed in term of pain using Visual Analogue Scale (VAS), sensory score based on American Spinal Injury Association (ASIA) chart for numbness and muscle power based on Medical Research Council (MRC) grading for strength. While body capacity rating according to MacNab's classification and Oswestry Disability Index (ODI) questionnaires were used for measuring the clinical outcomes. The complications were documented pre-operative and post-operatively.

Results: The results showed significant improvement in mean VAS for back pain (3.1 ± 1.83 to 2.1 ± 1.56 , $P = 0.015$), leg pain (7.0 ± 1.28 to 4.2 ± 2.22 , $P < 0.001$), leg numbness ($P = 0.041$) and muscle weakness ($P = 0.014$). Based on the MacNab's criteria, 9 (53.0%) patients showed excellent or good outcomes while the other 8 (47.0%) patients showed fair or poor outcomes. There were significant improvement in term of ODI with pre-operative and post-operative mean of 57.2 ± 12.78 and 41.5 ± 19.10 , respectively ($P = 0.002$). No significant relationship were found between MacNab's criteria with gender, age group, medical problems, duration of symptoms, pain free interval, side of recurrence, duration of revision surgery and blood loss ($P > 0.05$). The complication rates were low with one patient had delayed wound healing, infection and hamstring tightness, while 5 (29.4%) patients had incidental durotomy. The mean operation time was 3.79 ± 1.11 hours with median blood loss of 190.0 mL (IQR 170.0 mL) and mean post-operative hospital stay of 1.5 ± 0.51 days.

Conclusion: Revision endoscopic lumbar spine surgery using Endospine system provides an adequate and safe decompression with resulted in a significant improvement in the outcome.

Supervisor:

Associate Professor Dato' Dr Abdul Halim Yusof

EARLY REVIEW OF SHOULDER ARTHRODESIS IN BRACHIAL PLEXUS INJURY

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Introduction: Traumatic brachial plexus injury commonly occurs due to road traffic accident, it often leads to long term devastating disability and psychological stress to the affected individual. The injury leads to flail upper limb, impaired sensation and disabling pain. Shoulder arthrodesis is one of the treatment options that improved upper extremities functional outcome. This study intended to evaluate functional outcome of brachial plexus injury after shoulder fusion.

Objectives: The aim of this study were to evaluate functional outcome post shoulder arthrodesis in brachial plexus injury among traumatic brachial plexus injury patients in Universiti Sains Malaysia (USM) Health Campus, Kelantan, using validated QuickDASH and SF36v2 questionnaires

Patients and Methods: A group of 22 patients with traumatic brachial plexus injury who undergone shoulder fusion from January 2010 until December 2013 were selected. In the end 18 patients were included as study subjects. All selected patients were evaluated for pain score, functional assessment using QuickDASH questionnaire, and General well-being using SF36v2 questionnaire during recent clinic follow up.

Results: Shoulder fusion achieved significant reduction in pain among BPI patients. Most of the patient (63.2%) experience moderate difficulty of upper limb function after evaluated with QuickDASH questionnaire. All the patient achieved below average score in Physical Component Summary (PCS) and only 3 (16.7%) patients achieved score average (> 50) in Mental Component Summary (MCS). 16 (88.9%) patients achieved radiological union and only 2 (11.1%) patients had non-union. There were no significant correlation between radiological union and (QuickDASH) functional outcome or (SF36v2) general well-being in this study. Although majority of patient's general health (SF36v2) score below average, they were satisfied and had no regret to undergone shoulder fusion surgery.

Conclusion: Shoulder arthrodesis was able to reduce pain in BPI patients. Although majority of patient experience moderate difficulty in upper limb functional score and below average general health score. Most patients were satisfied with the surgery done. Shoulder arthrodesis helps stabilised the shoulder joint which improved control of upper limb function and lead to better quality of life.

Supervisor:

Associate Professor Dr Abdul Nawfar Sadagatullah

RELEVANCE OF INTRA OPERATIVE BACTERIOLOGY CULTURE IN PRIMARY TOTAL KNEE REPLACEMENT

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Introduction: Prosthetic joint infection following joint replacement is uncommon but can be a devastating complication. The rate of deep infection following primary total knee replacement is less than 2%. However, it remains a challenge to be encountered despite the advances in surgery nowadays.

Objectives: The aim of this study was to determine whether obtaining bacteriology swabs for culture and sensitivity at the time of surgery could help in further reducing the rate of infection following primary total knee replacement.

Patients and Methods: This study was a retrospective cross sectional study. A bacteriology swab of the synovial fluid was taken immediately after opening the capsule of the knee joint and was sent for culture and sensitivity.

Results: Out of 140 swabs sent, none was found to be positive. Post-operatively, 2 (1.4%) of the patients developed deep infection whereas 36 (25.7%) developed superficial infection.

Conclusion: Intra-operative bacteriology swab in primary total knee replacement has limited role in future prediction of incidence and management of post-operative prosthetic joint infection in total knee joint replacement surgery. This study also showed that there was no association found between risk factors such as age, gender, obesity, diabetes mellitus, rheumatoid arthritis, smoking and prolong duration of surgery, with post-operative superficial and deep infection.

Supervisor:

Dr Shaifuzain Abd Rahman

COMPARING THE HEARING THRESHOLD BETWEEN POSTERIOR AURICULAR MUSCLE RESPONSE (PAMR) AND PURE TONE AUDIOMETRY (PTA) IN IMPAIRED HEARING INDIVIDUALS

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Introduction: Posterior Auricular Muscle Response (PAMR) is an objective electrophysiological test to determine hearing thresholds. It is a cochlear myogenic response evoked by a click or tone burst stimuli and the response is measured as potential difference between posterior auricular muscle and rear of ear pinna.

Objectives: The aim of this study is to estimate and to compare the mean hearing thresholds in cochlear hearing loss and CHL using PAMR and PTA. Then, the hearing thresholds of PAMR and PTA in cochlear hearing loss and CHL patient are compared in order to determine the correction factors.

Patients and Methods: This is a cross sectional study conducted at Audiology Clinic, Hospital USM starting from 1 June 2013 until 31 May 2014. It comprised of 76 volunteered subjects and aged ranging between 18 to 60 years.

All patients were examined using otoscope, tympanometry and then PTA. Tone decay test was done for patient with sensorineural hearing loss to exclude retrocochlear hearing loss. Subject with normal tone decay test will proceed with PAMR. Finally, the PAMR were performed by placing the positive electrode at the ear lobule, negative electrode at the posterior auricular muscle while the reference electrode was placed at the forehead. This PAMR were measured at frequencies 500, 1000, 2000 and 4000 Hz using tone burst stimuli and the subject was asked to make 70° lateral eye turned to side of stimulus when the stimulus was being presented and the waves recorded.

Results: The PAMR thresholds noted were higher compared to the PTA thresholds. As there were differences in hearing thresholds between PAMR and PTA, the correction factors were determined. The correction factors decreased with increased in frequencies. In cochlear hearing loss patients, the correction factors were 26.29, 19.00, 16.00, 13.00 for 500, 1000, 2000 and 4000 Hz, respectively. In CHL patients, the correction factors were 20.29, 18.68, 14.12, 12.06 for 500, 1000, 2000 and 4000 Hz, respectively.

Conclusion: PAMR can be used as one of objective tests to determine hearing thresholds since all the subjects had recordable PAMR waves with eye turned position. However, because of difference in PAMR thresholds compared to PTA, the correction factors should be applied to PAMR threshold in order to estimate PTA thresholds.

Supervisor:

Dr Nik Adilah binti Nik Othman

Co-Supervisors:

Dr Mohd Normani bin Zakaria

Associate Professor Dr Rosdan Salim

DEVELOPMENT AND EVALUATION OF THE STANDARD ADENOTONSILLECTOMY CLINICAL PATHWAY IN HOSPITAL UNIVERSITI SAINS MALAYSIA

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Introduction: Patient care variation is an important source of concern in health care delivery. Its main sources are in the area of availability of health care services, lower use of medical evidence, and the professional uncertainties. To reduce this variation many guidelines and evaluating tools were created from evidence based medicine practice; one of these tools is clinical pathway (CP), a multidisciplinary structure care plan that detailed essential steps in the care of a patient with specific clinical problems, it supports and translates clinical guides to the local protocol.

Hospital Universiti Sains (Hospital USM) had implemented clinical pathway in 2012 and currently

conducting a survey on the CP implementation involving eleven specialities, adenotonsillectomy was selected under ORL-HNS.

Objectives: The aims of this study is to evaluate the standard Clinical Pathway of adenotonsillectomy patients in Hospital USM.

Patients and Methods: This was a cross-sectional comparative study conducted over a period of eighteen months in Hospital USM from March 2014 to September 2015.

The Universiti Research Ethics Committee (Human) approval has been obtained. Information used in this study was retrieved from implemented CP patient information form and from (Hospital USM) Medical Record Unit. Case note of patients who fulfill inclusion criteria were selected in non-randomised pattern and reviewed individually for both clinical pathway (CP) and non-clinical pathway (non-CP) groups over a period of six months. The data obtained was stored in software, compared and analyses.

Results: Total of 60 patients were involved in this study, 30 in each CP and non-CP groups. 18 females, 12 males were involved in CP group and 16 females and 14 males were involved in non-CP group. The average age of participant was 13.9 years and 17.1 years in CP and non-CP groups respectively. The estimated length of stay observed in this study were 0.9833 and 1.05 for non-CP and CP group, respectively. The result did not show any statistically observed difference between the groups ($Z = -0.853$; $P = 0.393 > 0.05$).

Two and six post-operative complications were observed in both non-CP and CP groups respectively, $Z = -1.506$, (P -value = 0.132 > 0.05). There was no significant difference in terms of complications rate between non-CP and CP groups.

An average estimated adenotonsillectomy cost for CP and non-CP group were RM3,000 and RM3,010, respectively this value was lower than RM4,725 quoted in MY-DRG casemix system.

An overall 88.4% compliance rate to CP guideline was observed in CP group. Patient complied more with 90%, followed by nurses with 89.9% then doctors with 87.5%.

There were eight observed CP variances in this study, six out of this have their sources from a health care provider's and accounts for 75%, two variances were from patients and accounts for 25%.

Conclusion: This study has evaluated the standard clinical pathway of adenotonsillectomy by looking into specific outcomes of certain parameters such as length of hospital stay, variances, post-operation complications, costing process and overall study effectiveness.

The baseline participant demographic data were almost equal between two study groups, there was no significant difference in terms of duration of hospital stay, costing and complications between the two groups.

Eight variances were observed in this study, two have their sources from the patients and six from health care providers. The overall compliance of pathway has been very good.

We were unable to obtain a cost saving because there was no significant cost difference between the two study groups.

Supervisor:

Dr Hazama Mohamad

Co-Supervisors:

Dr Rosaminah Mohamed

Associate Professor Dr Irfan Mohamad

GENETIC ASSOCIATION STUDY OF TUMOUR NECROSIS FACTOR POLYMORPHISMS IN CHRONIC RHINOSINUSITIS WITH AND WITHOUT NASAL POLYPS

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Introduction: Chronic rhinosinusitis (CRS) is a chronic inflammatory condition which initiates the cascade of inflammatory responses resulting in production of various proinflammatory cytokines. Tumour Necrosis Factor (TNF) is one of the proinflammatory cytokines that has crucial role in the pathogenesis of CRS.

Objectives: This case-controlled study aimed to identify the presence and associations of TNF α -1031 and TNF β +252 gene polymorphisms between CRS and healthy controls as well as between CRSwNP and CRSsNP. Another purpose of this study was to investigate the associations of these genes polymorphisms with factors related to CRS.

Methodology: Forty eight CRS participants which comprised of 24 CRSsNP and 24 CRSwNP participants together with 48 healthy controls were enrolled in this study. All DNA samples were collected from buccal mucosa and subsequently, genotyped for TNF α -1031 and TNF β + 252 genes by mean of polymerase chain reaction (PCR) and restriction fragment length polymorphisms (RFLP). The statistical analysis were carried out using Chi-square Test or Fisher's exact test and multiple logistic regression to determine the associations of TNF α -1031 and TNF β + 252 gene polymorphisms in CRS with and without nasal polyps and risks of CRS.

Results: Our findings confirmed the presence of TNF α -1031 gene polymorphisms in which the homozygous wild-type (TT) and heterozygous mutant-type (TC) were evenly distributed between CRS and healthy controls as well as in CRSsNP and CRSwNP. Homozygous mutant-type (CC) was absent in our population. Similarly, the wild-type allele (T) and mutant allele (C) revealed balance distributions. As for TNF β +252 gene polymorphisms, the heterozygous mutant-type (AG) was identified to be more prevalent in comparison to homozygous wild-type (AA) and homozygous mutant-type (GG). The wild-type allele (A) and mutant-type allele (G) distributed uniformly. Statistical analysis of genotype and allele frequencies of TNF α -1031 and TNF β +252 gene did not show any significant associations between CRS and healthy controls as well as between CRSwNP and CRSsNP. However, a significantly statistical difference of TNF α -1031 was observed in CRS participants with atopy (P -value = 0.037) but not asthma and ASA intolerance. There were no significant

associations of TNF β +252 gene polymorphisms with factors related to CRS.

Conclusion: The presence of TNF α -1031 and TNF β +252 gene polymorphisms in current study did not render any significant associations between CRS and control as well as CRSsNP and CRSwNP. However, this study suggests that the presence of TNF α -1031 gene polymorphisms in CRS patients with atopy may be associated with increase susceptibility towards CRS.

Supervisor:

Professor Dr Suzina binti Sheikh Ab Hamid

Co-Supervisors:

Dr Azlina binti Ahmad

Dr Ramiza Ramza bin Ramli

COMPARATIVE STUDY OF MULLER'S MANEUVER AND DEXMETOMIDINE INDUCED SLEEP ENDOSCOPY IN SNORING ADULTS

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Introduction: Sleep-disordered breathing (SDB) comprises a wide spectrum of sleep-related breathing abnormalities from simple snorer at the one end and obstructive sleep apnoea/hypopnea syndrome (OSAHS) at the other end. It is characterised by repetitive partial or complete collapse of the upper airway during sleep, resulting in intermittent cessations of breathing (apnoeas) and reduction in airflow (hypopneas) despite on-going respiratory effort. Flexible nasopharyngolaryngoscope (FNPLS) can identify and quantify the site and degree of obstruction that caused the snoring. However, we normally evaluate the patient when he or she is awake and in erect position, whereas snoring occurs when patient is in supine and sleeping. The endoscopic findings during awake endoscopy may not accurate to conclude the site responsible for the production of snoring. Sleep endoscopy in the naturally asleep patient is a diagnostic method permits the examiner to better determine the site that is responsible for the production of snoring. The drug used is Dexmedetomidine with or without Midazolam. This can be beneficial for the choice of the different and most appropriate treatment options for optimal benefits to the patients.

Objective: To compare awake endoscopy (Muller's maneuver) and drug-induced sleep endoscopy (DISE) findings in snoring individuals.

Study design: A cross sectional study was performed on patients aged more than 18 years old, with symptom of snoring planned for elective adenotonsillectomy and able to co-operate for FNPLS examination in Hospital Universiti Sains Malaysia.

Methodology: The consented patients who fulfilled the criterias were subjected to FNPLS with Muller's maneuver at

ORL-HNS Clinic, HUSM. After that, patients were admitted to ward one day prior to elective adenotonsillectomy surgery. Pre-operative assessment was done to assess whether patients were suitable and safe for Dexmedetomidine-induced sleep endoscopy. Patients were induced with the drug prior to intubation. FNPLS was repeated once patients reached sleep state based on bispectral index scoring system (BISS) score.

Result: A total of 15 patients with symptom of snoring participated in this study. Sixty-seven percent of them are male. All patients showed only one level airway obstruction which is at retropalatal level. Sixty percent have concentric type and 40% have lateral type of airway obstruction during Muller's maneuver and during DISE, the configuration of airway obstruction was 80% and 20%, respectively. During Muller's maneuver, only 33% of patients showed grade 1 (50-75%) of airway obstruction and 67% showed grade 0 (< 50%) at retropalatal level. However, during DISE, 67% and 33% of patients showed grade 1 and grade 2 (> 75%) of airway obstruction, respectively. All patients showed grade 0 at retrolingual level during both procedures. Our study showed that there was poor agreement between Muller's maneuver and DISE according to its degree and configuration of airway obstruction with ICC value was 0.14. Twenty percent of patients showed changes in the configuration of airway obstruction.

Conclusion: The degree of airway obstruction during DISE was more severe compared with the Muller's maneuver. There was a difference in the configuration of airway obstruction observed between these 2 procedures. DISE permits better evaluation of the degree and level of airway obstruction.

CHARACTERISTICS OF HEARING LOSS IN CHRONIC SUPPURATIVE OTITIS MEDIA PATIENTS

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Introduction: Chronic suppurative otitis media (CSOM) is defined as a chronic inflammation of the middle ear with discharge through a chronic perforation of the tympanic membrane and is a major cause of mild to moderate acquired hearing loss worldwide especially in children, particularly in developing countries. Hearing loss is the commonest preventable sequel of CSOM which typically produces a mild to moderate conductive hearing loss (CHL). However in recent years, an issue that has gained interest is sensorineural hearing loss (SNHL) due to CSOM. Although rare possibilities, there are evidences suggesting that SNHL do occurs in CSOM. Compared to CHL, SNHL consist of a more permanent effect and attenuated only through the use of hearing aid. Knowledge regarding influencing factors and correlations of different parameters of CSOM with SNHL is beneficial for development

of new treatment modalities to improve hearing in patients with chronic ear disease in the near future.

Objective: To study the characteristics of hearing loss in CSOM patients.

Patients and Methods: This was a cross sectional study conducted at Otorhinolaryngology Clinic conducted in Hospital Universiti Sains Malaysia, Kubang Kerian. The consented patients who fulfilled the inclusion criterias were recruited for this study. They were randomised and a total of 100 patients were selected. Patients with cholesteatoma, inner ear diseases, familial hearing loss, history of otologic surgery in the same ear, exposure to noise induced hearing loss and previous exposure to ototoxic drugs (within 6 months) were excluded from the study. Detailed information regarding patient's age, sex, and duration of disease, site and size of the TM perforation was obtained from patient's medical record. Pure tone audiometry was done to determine type, severity, degree and frequency of hearing loss. All these data were then documented in a data collection sheet.

Results: A total of 100 patients with CSOM aged 7–55 years were examined. Data analysis showed majority of the patients has mild CHL (75%) with normal BC (100%). The average frequency affected in both air and bone conduction for all types of hearing loss was the high frequency. Mild SNHL were seen in 2% of the patients and in these patients the degree of BC threshold documented was mild. Size of tympanic membrane perforation documented were majority medium size for CHL and SNHL at 46.4% and 100%. We also found that from this study there was a significant association between size and site of tympanic membrane perforation with the type of hearing loss. However, our study revealed that there was no significant association between duration of disease and type of hearing loss.

Conclusion: The type of hearing loss seen in majority of CSOM patients involved in this study were CHL with most of them having mild degree of AC HL with normal BC. Significant association between severity of AC and BC HL with type of hearing loss were seen. There was also a significant association between site and size of tympanic membrane perforation and type of hearing loss. However, there was no significant association seen between duration of disease and types of hearing loss.

Supervisor:

Professor Dr Mohd Khairi Md Daud

Co-Supervisor:

Associate Professor Dr Rosdan Salim

CLASSIFICATION OF INVASIVE BREAST CARCINOMA ACCORDING TO ST GALLEN CLASSIFICATION 2011 WITH EMPHASIS ON Ki67 INDEX AMONG SABAHAN POPULATION

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Background: Invasive Breast Carcinoma of No Specific Type (IBC NST) is divided into four sub-types using Estrogen Receptor (ER), Progesterone Receptor (PR) and Human Epidermal Receptor 2 (HER2) immunohistochemistry markers. They are classified into Luminal A (LA), Luminal B (LB), HER2 Overexpressed (HO) and Triple Negative (TN) sub-type. The St. Gallen 2011 Classification recognises the use of Ki67 proliferative index to identify LB sub-type from LA group. LB has a worse prognosis and different approach of treatment.

Objectives: This study aimed to identify HER2 negative LB sub-type according to St Gallen Classification 2011 using Ki67 and to compare the clinicopathological features of different sub-types.

Methods: Tissue biopsies of LA sub-type were stained with antibody towards Ki67. LA cases with Ki67 \geq 14% were re-classified as LB sub-type. Luminal sub-types with corresponding stage (tumour size), histological grade and lymph node metastases were compared. Univariate analysis using simple logistic regression was performed to determine the percentage of Ki67 expression among all IBC NST cases. McNemar's test was used for paired categorical analysis. All calculations performed using SPSS version 22 and a *P*-value of < 0.05 was set to denote statistical significance.

Results: LA is the most common sub-type (43%; 68/158), followed by LB (33%; 52/158). Only 37 out of 68 cases were stained with Ki67 due to sample limitations. From these LA cases, 43% (16/37) showed Ki67 \geq 14% (re-classified as LB sub-type). There was significant result when using Ki67 ($P < 0.001$; $P < 0.05$). However, LB sub-type showed statistically insignificant result when compared between stage, grade and lymph node status.

Conclusion: The classification according to the St Gallen Classification 2011 utilised Ki67 marker in addition to ER, PR and HER2 in identifying luminal B sub-type cases, which have a worse prognosis.

Supervisor:

Dr Anani Aila Mat Zin

Co-Supervisors:

Dr Ch'ng Ewe Seng

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A STUDY ON SURVIVIN EXPRESSION IN PROSTATE CANCER AND BENIGN PROSTATIC HYPERPLASIA; AND ITS ASSOCIATION WITH PRE-OPERATIVE SERUM PROSTATE SPECIFIC ANTIGEN LEVELS AND GLEASON SCORE IN PROSTATE CANCER

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Introduction: Prostate cancer (PCa) and benign prostatic hyperplasia (BPH) are common urologic conditions in older men and both conditions are frequently coexisting. Inhibition of apoptosis has been suggested to occur in the development both conditions. The clinical significance of the survivin expression in PCa remains unclear.

Objectives: The aim of this study was to determine the expression of survivin in PCa and BPH tissues; its association with Gleason score and pre-operative serum prostate specific antigen (PSA) level in PCa patients.

Methods: A comparative cross-sectional study was conducted, whereby our study comprised of 159 samples obtained from archived blocks from 2009 to 2014 in Pathology Department, Hospital Universiti Sains Malaysia (HUSM). Each block was sectioned onto a single slide and stained for survivin. The expression of survivin was examined by immunohistochemistry staining. The staining was semiquantitatively scored based on both staining intensity and percentage of positive survivin cells. The percentage of positive cells and the staining intensity were multiplied to produce a weighted score for each case. The results were analysed using the Fisher exact test and Pearson χ^2 test. The value of $P < 0.05$ was considered as statistically significant.

Results: A total of 91 specimens were from transrectal ultrasound (TRUS)-guided biopsy and 68 specimens were from transurethral resection of prostate (TURP). Of that, 79 specimens contained PCa tissue and 80 specimens contained BPH tissue. Survivin was expressed in all prostate specimens. However, the intensity of survivin expression in PCa are significantly greater than that in BPH ($P < 0.001$). The distribution of nuclear and cytoplasmic positivity of survivin in PCa are significantly higher than those in BPH ($P < 0.001$ and $P = 0.014$, respectively). In 96.2% of PCa and 97.5% of BPH cases, the survivin was expressed in both cytoplasmic and nuclear location simultaneously. There were no significant association between intensity of survivin expression in PCa tissue with Gleason score and pre-operative serum PSA in PCa patients ($P = 0.474$ and $P > 0.999$, respectively).

Conclusions: In this study, we report that survivin was expressed in all PCa and BPH tissues; and the expression intensity and percentage distribution of survivin positive cells were significantly greater in PCa as compared to BPH. However this study was unable to demonstrate its association with Gleason score and pre-operative serum PSA in prostate cancer patients.

Supervisor:

Dr Iskandar Zulkarnain Alias

Co-Supervisors:

Dr Julia Omar

Professor Hasnan Jaafar

Dr Azhar Amir Hamzah

FACTORS INFLUENCING PLATELET APHERESIS YIELD AND EFFECT OF DONATION AMONG DONORS

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Introduction: The development in transfusion practice with discovery of advanced cell separators have defined platelet therapy in terms of quality and productivity. Previous studies have shown that transfusion of high yield platelet products could reduce the requirement of transfusion among thrombocytopenic patients

Objective: The aim of this study was to investigate the factors that influence the platelet apheresis yield among apheresis donors by studying the donor variables and machine variables. Differences in donors peripheral count pre- and post-apheresis procedure were also studied. Correlation of serum ferritin level with platelet apheresis yield was also determined in this study.

Methods: A prospective study was conducted from September 2015 to August 2016 at Hospital Universiti Sains Malaysia (HUSM), Kubang Kerian, Kelantan. Thirty five male subjects were recruited for this study.

Full blood count (FBC) and serum ferritin were taken prior to the donation. Post donation, another sample of FBC was taken. FBC and serum ferritin was run by Diagnostic Stago haematology analyser Sysmex XE 5000 and Bio-Architect, respectively. FBC was analysed pre and post donation for haemoglobin level, haematocrit and platelet count. Other donors demographic data which included age, height, weight, frequency of donation and ABO blood group were taken from the donor apheresis registry book. Data regarding machine variables (anticoagulation infusion rate, processing time and plasma volume collected) were retrieved from the apheresis machine. The apheresis machine used in this study was Trima Accel cell separator.

Results: Height, pre-donation platelet count and machine variables revealed significant positive correlations with platelet apheresis yield. There were also significant differences in donor peripheral counts pre- and post-apheresis procedure. Positive correlation of serum ferritin level with platelet yield was seen. No significant IDA was detected among the apheresis donors.

Conclusion: Some of the donors' and all machine related variables showed significant relationship with platelet apheresis yield. There were also significant changes pre- and post-donation peripheral counts. Donors with high pre platelet count with adequate optimisation of machine variables can potentially produce a higher platelet apheresis yield collection.

CLINICAL AND LABORATORY PROFILES OF BLOOD DONORS WITH ERYTHROCYTOSIS

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Introduction: In blood banking setting, every blood donors are mandatory to have their haemoglobin (Hb) values tested before blood donation procedure. In current practice,

donors with high Hb will be deferred from blood donation. Little attention is given to blood donors with high Hb although it is known that high Hb may indicate an underlying hidden pathological condition.

Objective: The aim of this study is to evaluate the possible underlying aetiologies associated with erythrocytosis in blood donors.

Patients and Methods: A pilot cross sectional study was conducted in Hospital Sultanah Aminah Johor Bahru (HSAJB) and Hospital Universiti Sains Malaysia Kubang Kerian (HUSM) over nine-month period involving blood donors with high pre-donation Hb. A total of 175 samples were collected and analysed for haematological tests, Hb analysis, serum ferritin, biochemical tests and molecular study for the detection of JAK2 V617F mutation. All of the data were analysed using SPSS software version 23.0.

Results: The prevalence of blood donors with erythrocytosis was 7.8% ($n = 175$). Among 175 donors, 103 donors were found to have relative erythrocytosis, which mostly contributed by contraction of plasma volume possibly due to dehydration. Another seventy-two (72) donors had absolute erythrocytosis. A total of forty-nine (49) donors had background history of chronic cigarette smoking. We found that there were associations between smoking and thalassaemia/haemoglobinopathy with erythrocytosis in blood donors. We also found positive correlation between the numbers of blood donation with the degree of erythrocytosis ($r = 0.201$). The higher the number of blood donations, the higher Hb level will be observed.

Conclusion: High Hb in blood donors does indicate hidden pathological aetiology. Quite a number of donors were found to have other significant medical conditions such as thalassaemia/haemoglobinopathy and iron deficiency state. We also strongly suggest that blood donors with high Hb level should be investigated thoroughly in order to exclude any significant pathological conditions that are associated with erythrocytosis.

Supervisor:

Dr Noor Haslina Mohd Noor

Co-Supervisors:

Dr Mohd Nazri Hassan

Associate Professor Dr Wan Zaidah Abdullah

Dr Ebrahim Jamian

ASSOCIATION BETWEEN POLYMICROBIAL INFECTIONS AND SEVERITY OF DIABETIC FOOT INFECTION AMONG PATIENTS IN HOSPITAL UNIVERSITI SAINS MALAYSIA

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Background: Foot infections are a major complication of patients with diabetes mellitus (DM). The causative

microorganisms are usually polymicrobial. The aim of the study is to determine the percentage of microorganism in diabetic foot infection, its susceptibility to antibiotic, association between polymicrobial infection and severity of diabetic foot infection and to determine the outcome of diabetic foot infection among patients infected with polymicrobial organisms in Hospital USM.

Materials and Methods: This is a retrospective analysis conducted for one year duration starting from June 2014. A total of 104 patients selected from this study. Their folders were reviewed and assessed for severity and outcome of foot infection in association with polymicrobial infections. Parameters such as glycated haemoglobin (HbA1c), random blood sugar (RBS), total white cell (TWC) and haemoglobin (Hb) were analysed. The result were presented as descriptive and statistically analysed by Fisher exact test.

Results: There were 104 patients involved in this study, with a total 133 microorganisms were isolated with an average of 1.28 organisms per lesion. Gram negative (GN) and Gram positive (GP) microorganisms were 62% and 38% respectively. The most frequently isolated GN microorganism includes *Pseudomonas* spp (28%), *Proteus* spp (11%), *Klebsiella* spp (8%) and *E. coli* (4%). *Staphylococcus aureus* was the predominant (54%) among GP microorganisms followed by Group B *Streptococci* (26%) and *Enterococcus* spp (6%). GN isolates were sensitive to carbapenem and aminoglycoside groups while vancomycin showed good activity to GP microorganism. There was significant association between quantity of microorganisms and severity of diabetic foot infection using Fisher's Exact test ($P = 0.003$). Thirty patients had polymicrobial infections. In severe diabetic foot infection, 77.8% with polymicrobial organisms undergone amputation, meanwhile monomicrobial infection was 33.3%. Majority of polymicrobial or monomicrobial infection was discharged well, 84.0% and 91.1% respectively. There was no significant association between polymicrobial or monomicrobial infection with patient's outcome of severe diabetic foot infection including amputation and discharge of patient ($P = 0.136$ and $P = 0.465$). The mean (SD) for HbA1c, RBS, TWC and Hb in severe polymicrobial infections were 11.8(2.1) %, 16.3 (5.2) mmol/L, 16.6 (2.4) $\times 10^9$ and 9.0 (1.3) g/dL, respectively.

Conclusion: GN microorganisms were predominantly isolated from diabetic foot infections and antibiogram showed that the common organisms remain sensitive to a number of widely used agents. Polymicrobial infections were associated with the severity of its infection meanwhile quantities of organisms was not associated with patient's outcome of diabetic foot infection. There were higher glucose level and TWC count with lower Hb in severe polymicrobial diabetic foot infection.

Supervisor:

Professor Madya Dr Siti Asma' binti Hassan

Co-Supervisor:

Dr Nurahan binti Maning

PREVENTIVE MEASURES AND ASSOCIATED FACTORS OF RESPIRATORY ILLNESS AMONG MALAYSIAN PILGRIMS 2013

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Introduction: Respiratory illness continues to exert a burden on hajj pilgrims in Makkah. An expanded definition of respiratory illness was used for this study. Respiratory illness was defined as when the person is having at least one of the respiratory symptoms (non ILI) or influenza-like illness (ILI). The transmission of all respiratory infections, including influenza can be prevented by implementing infection control measures at the first point of contact with a potentially infected person

Objectives: The purpose of this study is to determine the prevalence of the respiratory illness among Malaysian hajj pilgrims in 2013, to describe its preventative measures including hand hygiene and face mask practices, vaccination coverage and supplement intake, and also to determine the association between socio-demographic, previous experience of hajj/umrah, co-morbidity, smoking habits, vaccination and the practice of preventative measures including religious practices with respiratory illness or ILI. In this study, apart from those preventive measures, we also explored the association between good hand hygiene practice and good standard face mask practice with the occurrence of respiratory illness/ILI.

Patients and Methods: A cross-sectional study was conducted in Makkah and Malaysia involving all consented Malaysian pilgrims in 2013 hajj season. A self-administered form on social demographics, previous experience of hajj or umrah, smoking habits, co-morbid illness and practices of preventive measures against respiratory illness and ILI were obtained. Altogether 468 forms were analysed.

Results: The prevalence of the respiratory illness was 93.4% with a subset of 78.2% fulfilled the criteria for influenza-like illness (ILI). Most of them (77.8%) had a respiratory illness of less than 2 weeks duration. About 61.8% were administered antibiotics, but only 2.1% of them had been hospitalised. Most of them acquired the infection after a brief stay at Arafat (81.2%). Vaccination coverages for influenza virus and pneumococcal disease were quite high, 65.2% and 59.4%, respectively. For other preventive measures practices, only 31.8% of them practiced good hand hygiene. Three hundred and twenty two of our pilgrims had worn standard face masks (83.0%) and out of these numbers, 45.3% of them used in proper way. Malaysian hajj pilgrims with previous experience of hajj (OR 0.24; 95% CI 0.10–0.56) or umrah (OR 0.19; 95% CI 0.07–0.52) were significantly associated with lower risk of respiratory illness. Otherwise, pilgrims having contact with those with respiratory illness (OR 3.01; 95% CI 1.35–6.68) were associated with higher risk. Malaysian hajj pilgrims with previous experienced of hajj (OR 0.26; 95% CI 0.15–0.46) were protected from ILI while those who suffered from bronchial asthma (OR 7.27; 95% CI 0.96–54.94) were found to be significantly associated with higher risk of getting ILI.

Conclusions: The prevalence of respiratory illness remains high among Malaysian hajj pilgrims despite having some practices of preventive measures. All preventive

measures which include hand hygiene, wearing face masks and influenza vaccination must be practiced together as bundle of care to reduce respiratory infections effectively.

Supervisor:
Professor Dr Zeehaida Mohamad

Co-Supervisor:
Dr Nabilah Ismail

A STUDY ON KNOWLEDGE, PERCEPTION AND PRACTICE (KPP) OF PREVENTIVE MEASURES AGAINST RESPIRATORY TRACT INFECTIONS, FACTORS ASSOCIATED WITH HAND HYGIENE PRACTICES AND THE EFFECT OF SUPPLYING HANDRUB AMONG MALAYSIAN HAJJ PILGRIMS 2013

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Introduction: Every year, approximately 2 million pilgrims from all over the world gathered in Mecca to participate in Hajj, one of the pillar of Islam. Extreme congestion of people and heat represent an important risk for local or widespread outbreak of infectious diseases. Acute respiratory infections (ARIs) are the most common cause of hospital admission during hajj. Respiratory illness refers to influenza-like illness (ILI) defined as the presence of fever and cough with and without other respiratory symptoms; nasal congestion, sore throat, sneezing or breathing problems.

Protective behaviors such as using facemask, frequent usage of handrub, cough etiquette, social distancing and contact avoidance have been used to prevent its spread. Previous studies showed that hajj pilgrims that engaged in the recommended protective behaviors particularly hand hygiene and social distancing to have lower rate of respiratory illness, less severe and shorter duration of illness compared with those who don't adhere to the recommended protective behaviors.

Objectives: The aim of this study is to determine the knowledge, perception and practice (KPP) of preventive measures against respiratory tract infections, factors associated with hand hygiene practices and the effect of supplying handrub among Malaysian hajj pilgrims 2013.

Materials and Methods: This is an open-label randomised controlled trial which was conducted to Malaysian hajj pilgrims who transit in Kompleks Tabung Haji Kelana Jaya, Malaysia from 15 to 19 September 2013. The hajj pilgrims were randomised according to the flight batch (KT). Intervention group was part of hajj pilgrims from KT 24, 25, 27, 30, 40, and 47. Control group was part of hajj pilgrims from KT 31, 33, 35, 36, 44, 57, 66. A total of 500 hajj pilgrims involved in this study (250 in intervention group and another 250 in control group). They were given two sets of self-administrated validated Knowledge, Perception and Practice of Respiratory Infection Preventive Measure Questionnaires

(KPP-PMQ) to be filled up before and during hajj to assess the baseline knowledge, attitude and practice of protective measures of acute respiratory infections (ARIs) and compared them with post intervention. This Knowledge, Perception and Practice of Respiratory Infection Preventive Measure Questionnaire consist of three (3) main domains and twenty-nine (29) items. Maximum score for knowledge, perception and practice scores were 24, 35 and 70 respectively. Each pilgrim in the intervention group was given four bottles of alcohol-free handrub (100 mLs per bottle), a pamphlet and demonstration on how to use the handrub. Each pilgrim in the control group was given a bottle of 100ml unmedicated hand lotion. Data on presence or absence of acute respiratory symptoms and influenza like illness were recorded. Both groups were followed-up in Mecca, Mina and Madinatul Hujjaj where lost questionnaires were replaced. The post-hajj questionnaire was collected at Mecca and by postage after coming back to Malaysia.

Results: Pre-hajj Knowledge, Perception and Practice of Respiratory Infection Preventive Measure Questionnaire were completed by all participants ($n = 500$). Post-hajj Knowledge, Perception and Practice of Respiratory Infection Preventive Measure Questionnaire were completed and returned by (37.6%) $n = 94$ participants in intervention group and (31.2%) $n = 78$ participants in control group. Socio-demographically, both groups were comparable.

There were reduction in percentage of frequent handrub practice (daily practice) 10.2% in intervention group and 9.1% in control group compared with pre-hajj handrub practice. There were significant association between influenza-like illness (ILI) occurrences with hand hygiene practices during hajj. Hajj pilgrims with infrequent handwash after in contact with personal belongings of infected pilgrims are at 2.56 higher odds of getting influenza-like illness (ILI) compared to frequent handwash. Besides, hajj pilgrims with infrequent handwash after in contact with hands of infected pilgrims are at 2.18 higher odds of getting ILI compared to frequent handwash. Hajj pilgrims with infrequent handrub practice using antiseptic handrub were at 3.63 higher odds of getting ILI compared to infrequent handrub.

The knowledge that ILI spread was fast was statistically significant ($P = 0.019$) between pre-hajj and post-hajj. Regarding the wearing of facemasks by infected people, there was a significant difference (P -value = 0.009) between pre- and post-hajj that perceived it as an effective precautionary method. However, regarding behavioural and humanity aspects, there was a significant reduction in those who perceived that doing more charity in Mecca (P -value: 0.009) and being calm in handling problems in Mecca (P -value: 0.014) were effective precautionary methods. The mean (SD) knowledge, perception and practice scores during hajj with ILI versus non-ILI were 20.6 (1.91) versus 20.8 (1.98), 28.7 (3.66) versus 29.9 (3.52), 51.6 (6.05) versus 50.7 (5.72), respectively. Only the mean difference of perception score was found to be significant with the presence of ILI ($P = 0.026$, 95% CI: -2.354, -0.150). There is no mean difference of knowledge and practice scores with the presence of ILI.

Conclusion: In conclusion, giving handrub has not resulted in better compliance. Hajj pilgrims perception during hajj does affect the presence of ILI. Infrequent hand hygiene practices were associated with higher risk of getting ILI. There are significant changes in knowledge and perceptions

of Malaysian hajj pilgrims pre- and post-hajj concerning the spread and preventative measures of influenza-like illnesses.

Supervisor:

Professor Dr Habsah Hasan

Co-Supervisor:

Dr Aniza Abdul Aziz

ASSESSMENT OF RELIABILITY AND VALIDITY OF THE MALAY VERSION PedsQLTM 3.0 CARDIAC MODULE

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Introduction: The improvement in medical and surgical treatment over the last decades has led to a dramatic increase in survival rates of patients with congenital heart disease (CHD). Hence, it is a very important to focus on HRQOL among children with CHD. Up to date, there is no assessment tool in *Bahasa Melayu* to measure HRQOL among children with heart disease. The validated tool is available in English and other languages. The PedsQLTM 3.0 Cardiac Module was chosen because it has been validated, developmentally appropriate for our subjects, disease specific, includes both self and proxy-report and covering a wider age group for children 5–18 years old and parent-proxy age 2–18 years old, it can be conducted within 15 minutes, the questionnaires also multidimensional and had minimal missing data.

Objective: To produce a reliable and validated Malay version of the PedsQLTM 3.0 Cardiac Module.

Patients and Methods: This is a cross sectional study involving children with CHD between 5–17 years old and parent of children with CHD aged 2–18 years old. A total of 528 participants were enrolled into this study when they presented to the pediatric cardiology clinic and echocardiography clinic at Hospital Raja Perempuan Zainab II and Hospital Universiti Sains Malaysia. The methods used including linguistic validations of Malay version of the PedsQLTM 3.0 Cardiac Module questionnaires.

Results: Most of 27 items in Malay version PedsQLTM 3.0 Cardiac Module questionnaires showed satisfactory internal consistency with Cronbach Alpha exceeding 0.7 and good correlation with intra-class correlation coefficient 0.76–0.98. The validity also showed all the domains are significantly correlated among each other. There were no missing data.

Conclusion: The result generally supports reliability and validity of Malay version PedsQLTM 3.0 Cardiac Module in assessing HRQOL among children with congenital heart disease.

Supervisor:

Associate Professor Dr Ariffin Nasir

Co-Supervisors:

Associate Professor Dr Norsarwany Mohamad
Professor Col (B) Dr Wan Pauzi

A PILOT STUDY ON VALIDATION OF THE INTERNATIONAL SOCIETY FOR THE PREVENTION OF CHILD ABUSE AND NEGLECT CHILD ABUSE SCREENING TOOL-CHILDREN'S VERSION (ICAST-CH)

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Background: Childhood maltreatments, which include all forms of abuse namely physical, sexual, emotional or psychological abuse and neglect undeniably is a very crucial problem across the continents, cultural and beliefs. Despite the alarming increasing in rates and prevalence of such maltreatments all over the world, the true extent of the problem remains a conundrum. There are multitudes of studies carried out in an attempt to explore this pressing problem, but the mysteries have yet to be solved. The International Society for the Prevention of Child Abuse and Neglect (ISPCAN), has developed an instrument ICAST-CH specifically designed for children. This instrument proved to be reliable in accessing the scope and prevalence of childhood maltreatment. Malaysia, in particular, has very limited tools to assess childhood experiences of maltreatment.

Objective: The study aimed at translating and validating Malay version of ISPCAN Child Abuse Screening Tool-Children's Version (ICAST-CH) among Malaysian children.

Methods: A two-phase study was conducted. In phase I, the ICAST-CH English Version was translated into Malay using forward and backward translation procedure and following that, the content validity was obtained. In phase II, 253 students, aged 13 to 17 years old were recruited by universal sampling method to examine internal consistency by mean of Cronbach's alpha and to explore construct validity by mean of exploratory factor analysis.

Results: Analysis of the study indicated that Malay version ICAST-CH-M had high total score internal consistency with Cronbach's alpha of 0.84, but low on subscale that ranged from 0.61–0.81.

Conclusion: This study failed to demonstrate satisfactory reliability and validity for ICAST-CH-M. Thus the recommendation to use ICAST-CH-M as an instrument to measure childhood maltreatment's among Malaysian children could not yet be concluded. Further study to explore the instrument is highly recommended.

CHILDREN WITH TRANSFUSION DEPENDENT THALASSAEMIA: THE STUDY OF PSYCHOLOGICAL DISTRESS AND COPING STRATEGIES AMONG CARETAKERS

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Introduction: Hemoglobin E beta thalassaemia is prevalent in Malaysia. Knowing thalassaemia is a chronic disease it is a lifelong burdens not only to the patient but also to the parent and other caretakers. Psychological distress is manifested in multiple ways and at different level of severity. Therefore coping strategies are developed in order to reduce the stress hence ascertain a high quality of life.

Objectives: The aim of this study were to determine the mean psychological distress level and brief COPE of caretakers, to compare mean psychological distress level with brief COPE and income status and to identify the associated factors for psychological distress and brief COPE, respectively.

Methodology: DASS 21 and brief COPE questionnaires.

Results: Depressive median score was (2.00, IQR 4.00). Anxiety mean score was (3.54, SD 3.54). Stress mean score was (4.25, SD 3.26). The highest mean score for brief COPE was religion (7.00, IQR 2.00). Depressive caretakers had significant score for substance use (4.50, IQR 3.00). Meanwhile anxious caretakers had significant score for denial (5.50, IQR 3.00), substance use (4.00, IQR 4.00) and behavior disengagement (4.00, IQR 3.00). There was no significant difference between psychological distress and income status. Age, gender, education, working and income status were identified to have association with brief COPE.

Conclusion: Majority of caretakers had utilised religion coping, meanwhile substance use, denial and behavioral disengagement were utilised by depressive and anxious caretakers. Scoring for DASS 21 showed no significant different between two groups of income. Brief COPE was associated with age, gender, education, working and income status.

Supervisor:

Associate Professor Dr Norsarwany Mohamad

Co-Supervisor:

Associate Professor Dr Azizah Othman

SURVIVAL RATE AND PROGNOSTIC FACTORS OF EWING FAMILY TUMOR IN PAEDIATRIC PATIENTS, (A 11-YEAR REVIEW) IN HOSPITAL USM FROM 2002–2012

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Introduction: Ewing Family Tumor (EFT) is a very malignant and aggressive tumor. It was very rare tumor especially in Asia compare to western countries. During the past three decades, the prognosis of patient with EFT had

improves considerably as shown in several clinical trials, mainly because of improved chemotherapy regimes. In our country, there is lack of reports in the treatment outcome and survival of children with EFT. There is no published study predicting the treatment outcome in Hospital USM at present.

Objectives: The objectives of this study were to evaluate the Overall Survival (OS) and Event Free Survival (EFS) rate of patients who were diagnosed with EFT. We want to evaluate the demographic data and identify the possible predictive factors that determine the EFS and OS rate of those children with EFT and treated in Hospital USM.

Patients and Methods: This is a retrospective record review of children aged 0–18 years with EFT. Children were identified from registration data in Oncology Unit and medical records from Record Office, Hospital USM. In case of uncontactable or deceased patients, a letter was sent to State Registry to obtain the end result/outcome of the patients. The associations of demographic and clinical factors with patient's outcome were determined by Cox regression. Survival curves were estimated by the Kaplan-Meier method and compared by the Log-rank test.

Results: There were 51 patients identified from the registration but then only 29 children were enrolled in this study, which full filled all the inclusion criteria. The mean duration follow up was 21 months. The OS rate at 1, 2, 3 and 5 years were 62.1%, 44.8%, 30.2% and 21.6%, respectively. The EFS rate at 1, 2, 3 and 5 years were 41.9%, 26.7%, 17.8% and 0%, respectively. Multivariate Cox regression analysis showed that presence of surgical intervention ($P = 0.030$) and major complications ($P = 0.045$) were significant prognostic factors to the survival of EFT in this study.

Conclusion: Survival rate among our patients was comparable to other developing countries. However we are far away if compared to developed countries as the survival rate only achieved almost half from their survival rate. We are able to identify two significant independent prognostic factors to the survival for EFT in our patients which were surgical intervention and presence of major complications.

Supervisor:

Associate Professor Dr Nik Zainal Nik Ismail

Co-Supervisors:

Associate Professor Dr Ariffin Nasir

Associate Professor Dr Norsarwany Mohamad

EFFECT OF MATERNAL VOICE ON PHYSIOLOGICAL AND BEHAVIORAL MEASURES IN PREMATURE INFANTS: A RANDOMISED CONTROLLED TRIAL

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Introduction: Preterm infants lose significant contact with their mothers during prenatal development and nursed

in hospital environment that exposed them to elevated stimulus from NICU environment. They are not only deprived from the protective properties of womb, they also remain in an enclosed incubator where touching and sensory stimulation are restricted which possibly a critical aspect for normal development, that is the mother's voice

Objective: The aim of this study is to determine the effect of maternal voice versus NICU environmental sounds on physiological and behavioral measures in premature infants.

Methods: This is a parallel randomised control trial conducted in NICU Hospital Sultanah Bahiyah, Alor Setar from June 2015 to November 2015. This study involved all premature infants with corrected gestational age 27–35 weeks who is already on full feeding and nursed in incubator. All subjects were randomised into two groups that are Intervention and Control. Their mother will be asked to sing appropriate lullabies that will be recorded for 10 minute duration. Infants were randomly assigned to one of two groups. Infants in the Control group received routine NICU nursing care. Infants in the Intervention group received routine NICU care as well as 10 minutes of exposure to their mothers recorded voice every day for 14 days. Infants in the two groups were evaluated and observed for 30 minutes every day for 14 days. Heart rates, respiratory rates and oxygen saturation levels as displayed on the monitor were recorded every minute for 30 minutes. Behavioral score (BIIP) was measured at every 10 minute. Weight gain was measured every other day by a standardised digital weight scale. Infants were evaluated during 3 phases: 10 minute baseline, 10 minute intervention and 10 minute post intervention.

Result: A total of 138 patients completed the study. There was significant reduction of mean heart rate over time [$F = 5.071$, $P < 0.05$] and median respiratory rate over time ($Z = -7.27$, $P < 0.01$) in the intervention group. There was significant difference in median respiratory rate in intervention group ($Z = -4.39, -4.23, -4.15$, $P < 0.01$) compared to control group. There was also significant increase of oxygen saturation in intervention group ($Z = -2.14, -2.39, -2.56$ $P < 0.05$). There was no significant difference in mean weight gain between intervention and control group [MD 0.30 (-1.9, 2.5), $P > 0.05$]. There was no significant changes of Behavioral Indicator of Infant Pain profile (BIIP) with regard to time [$Z = -0.31, -0.36, -0.65$ $P > 0.05$].

Conclusion: This study showed that exposure to mother's voice had positive effect on premature infant's heart rate, respiratory rate and oxygen saturation while no changes on mean weight gain and behavioral score with no adverse reaction noted during intervention.

Supervisor:

Dr Nor Rosidah Ibrahim

Co-Supervisors:

Associate Professor Ariffin Nasir

Dr Thiyagar Nadarajaw

ASSESSMENT OF VALIDITY AND RELIABILITY OF MALAY VERSION OF ASTHMA CONTROL TEST (ACT) QUESTIONNAIRE

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Introduction: The Asthma Insights and Reality in Asia Pacific (AIRIAP) study showed an under achievement of asthma control basically due to low awareness and underestimation of asthma severity either by caretaker or pediatricians and thus leading to poor quality of life of the patients. Asthma control test (ACT) questionnaire was developed to provide a more simplified assessment asthma control by not requiring FEV₁. As the translation of ACT questionnaire may influence the study outcome, validation of Malay version of ACT questionnaire is very important for its further utilization in assessing asthma control in Malaysia.

Objective: To validate the Malay version of ACT questionnaire for asthma children aged 12 to 18 years old.

Methods: Pilot test was administered as linguistic validation before proceeding with data collection. The participants completed the ACT questionnaire concurrently while performing the spirometry. Respiratory paediatricians who were blinded to ACT rated their asthma control based on Global Initiative for Asthma (GINA) guideline in order to evaluate validity and reliability of Malay version of ACT.

Results: A total of 60 patients were recruited with median age of 14 years old. The Malay version of ACT has good internal consistency; Cronbach's alpha 0.91. A significant difference was noted between the different groups of asthma control as grouped by the GINA-defined classification [$F(2,25) = 88.16$. There was good agreement of ACT with the specialist classification, kappa = 0.84. The study has good sensitivity and specificity for cut off 19 with 92% and 96%, respectively. It has fair correlation with FEV₁ and PEF ($r = 0.41-0.42$).

Conclusion: The Malay version of ACT is a valid and reliable test for asthma control assessment in pediatric asthma in Malaysia.

Supervisor:
Associate Professor Dr Ariffin Nasir

Co-Supervisors:
Dr Mariana Daud
Dr Wan Nor Ariffin Wan Mansor

AN OPEN LABEL RANDOMISED CONTROLLED TRIAL ON THE EFFICACY OF ADDING INTRANASAL FENTANYL TO INTRAVENOUS TRAMADOL IN PATIENTS WITH MODERATE TO SEVERE PAIN FOLLOWING ACUTE MUSCULOSKELETAL INJURIES

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Introduction: Intra-nasal fentanyl, as an alternative route of analgesic administration, has been shown to be effective particularly in pediatric population and in pre-hospital setting. Studies on such use among adult patients in emergency department are limited.

Objectives: The aim of this study was to compare intranasal fentanyl with intravenous tramadol as analgesia with intravenous tramadol.

Methods: An open-label study was conducted to evaluate the effectiveness of adding 1.5 mcg/kg intranasal fentanyl on top of 2 mg/kg intravenous tramadol (FENTANYL_TRAMADOL, $n = 10$) as compared to 2 mg/kg intravenous tramadol alone (TRAMADOL, $n = 10$) in adult patients with acute musculoskeletal injuries in moderate to severe pain.

Results: When analysed using independent t -test, the mean visual analog scale (VAS) difference between pre- and 10-minute post-intervention was found to be 29.8 mm (SD +/- 8.4 mm) in the FENTANYL_TRAMADOL arm and 19.6 mm (SD +/- 9.7 mm) in the TRAMADOL arm [$t(8) = 2.515$, $P = 0.022$, 95% confidence interval (CI) 1.68 to 18.72 mm]. A significantly greater albeit transient reduction in mean arterial pressure 10 minutes post-intervention was noted in the FENTANYL_TRAMADOL arm as compared to those in the TRAMADOL arm (13.35 mmHg versus 7.65 mmHg, using Mann-Whitney U test with U-value = 21.5; $P = 0.029$; $r = 0.48$). Patients in the FENTANYL_TRAMADOL arm also experienced a higher incidence of transient dizziness 10 minutes post-intervention.

Conclusion: Although effective, intra-nasal fentanyl in adult patients may not be ready for primetime as it may result in significant reduction in blood pressure.

Supervisor:
Dr Nik Arif Nik Mohamed

THE DEVELOPMENT AND VALIDATION OF THE CLINICIANS' ATTITUDES TOWARDS THE IMPACT OF COGNITIVE ERRORS (CATCHES) IN CLINICAL DECISION MAKING QUESTIONNAIRE TOOL

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Introduction: Despite their impact on diagnostic accuracy, there is a paucity of literature on questionnaire tool to assess the clinicians' attitudes toward cognitive errors. A validation study was conducted to develop a questionnaire tool to evaluate the Clinician's Attitude Towards the impact of Cognitive Errors (CATCHES) in clinical decision making.

Objectives: The aims of this study were to develop and validate a questionnaire tool to evaluate the Clinician's

Attitude Towards the impact of Cognitive Errors (CATChES) in clinical decision making.

Methods: This questionnaire is divided into two parts; Part A is to evaluate the clinicians' attitude towards cognitive errors in clinical decision making while Part B is to evaluate their attitude towards specific cognitive errors. For Part A, construct validation using exploratory factor analysis (EFA) was performed. For Part B, content validation using content validity index (i-CVI) and modified kappa was performed.

Results: For EFA of Part A shows a two-factor model with total variance extraction of 60%. Two items were deleted. The EFA was then repeated with all factor loadings above the cut-off value of > 0.5. The Cronbach's alpha for both factors were above 0.6.

For Part B, the content validity is acceptable with values of CVI of 0.89 and above in terms of their relevance. Modified kappa was shown to be 0.89 and above for all items and rated as "excellent".

Conclusion: The CATChES questionnaire tool is a valid questionnaire tool to evaluate the attitude among clinicians toward cognitive errors in clinical decision making.

Supervisor:

Dr Keng Sheng Chew

Co-Supervisor:

Dr Yee Cheng Kueh

RETROSPECTIVE STUDY ON THE DURATION OF STAY AMONG MOTOR VEHICLE CRASH PATIENTS IN HOSPITAL USM

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Background: Hospital University Sains Malaysia (HUSM) is a tertiary hospital, and receives referral from many district hospitals in Kelantan and part of Terengganu state. The current study was on referral traffic injury cases among all trauma patients those refer to EDHUSM.

Objectives: The aim of this study was to determine the length of stay among all motor vehicle crash patients in hospital and also to determine the factors associated with the length of stay such as age, sex, operative interference, capillary blood sugar (CBS) and injury severity score (ISS).

Methodology: It is retrospective cohort study carried out over one year period in EDHUSM among all motor vehicle crash patients, from 1st January, 2012 to 31 Dec. 2012 by reviewing medical records for the documented information of injury pattern, type of vehicle, ISS, CBS, operative interference and the length of hospital stay by using simple and multiple logistic test.

Result: Total of 111 road traffic injury patients were included in this study 79.3% were male and 20.7% were females. The main age was 29 years and 75.7% were motorcycle users. Injury to the extremities was the major type

of injury which has been seen in 38.7% of cases followed by head in 33.3%. The majority of patients 55% sustained minor trauma and the remaining 45% major trauma. While 64.9% of the patients stayed < 1 week and 35.1% more than 1 week, the multiple logistic regression test found that statistically there was association between ISS and length of stay in hospital (OR = (1.50, 15.36), $P < 0.022$). Also there was remarkable association between motor vehicle crash and the length of stay in hospital among trauma patients by using multiple logistic regression ($P < 0.004$).

Conclusion: There was higher incidence between motor vehicle crash and length of stay and therefore a significant relationship exist between motor vehicle crash and length of hospital stay.

Supervisor:

Associate Professor Nik Hishamuddin Nik Abdul Rahman

A PILOT STUDY OF STERILE SALINE VERSUS REVERSE OSMOSIS WATER IN TRAUMATIC LACERATION WOUND CLEANSING IN EMERGENCY DEPARTMENT IN HOSPITAL UNIVERSITI SAINS MALAYSIA, KELANTAN AND HOSPITAL TENGGU AMPUAN AFZAN, PAHANG

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Introduction: Traumatic laceration wound is a common reason for people seeking treatment in emergency care setting. As for current practice, sterile saline is still the most common agent used in cleansing or irrigating the wound in the emergency department. In overseas, there have been studies on alternative cleansing agent particularly tap water, which have showed equal or better outcomes in term of wound infection. There is no previous study been conducted on wound cleansing using Reverse Osmosis water.

Objective: To compare the rate of wound infection between sterile saline and reverse osmosis water cleansing for traumatic laceration wound.

Method: This study was a multicenter, prospective, randomised controlled trial conducted at two tertiary hospitals. Subjects were a convenience sample of adults presenting with acute simple traumatic laceration requiring wound cleansing. They were randomised using block randomisation method to irrigation with 'sterile saline' or 'reverse osmosis' water. Wounds were closed in the standard fashion. Follow-ups were done on day 5 and 14 after the intervention to assess for outcome or wound infection.

Results: A total of 48 patients ($n = 48$) were selected and randomised into RO water group ($n = 24$) and Saline group ($n = 20$) (4 patients withdrew). The infection rate for sterile saline cleansing was 5% (95% CI -4.55%, 14.55%) compared to RO cleansing which was 4.17% (95% CI -3.83%, 12.17%). Relative risk for RO water group was 0.834 (95%CI 0.056,

12.494) compare to saline group. Fisher's Exact test showed no significant effect on type of cleansing agent on wound infection.

Conclusion: There was no significant difference between reverse osmosis and saline on wound infection. Reverse osmosis water can be considered as alternative cleansing agent to sterile saline in acute uncomplicated traumatic laceration wounds.

Supervisor:

Dr Mohd Hashairi Hj Fauzi

THE EFFECTIVENESS OF INTRAVENOUS PARECOXIB SODIUM AS AN ANALGESIC ALTERNATIVE TO MORPHINE IN SUSPECTED ACUTE RENAL COLIC IN EMERGENCY DEPARTMENT HOSPITAL UNIVERSITI SAINS MALAYSIA

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Introduction: Patients with renal colic usually presented to Emergency Department with severe and excruciating pain. Emergency Physicians using numerous medications to treat the problem, however none of them had been proven to relieve the pain completely. This study aimed to compare the effectiveness of IV parecoxib versus IV morphine in suspected acute renal colic in Emergency Department.

Objectives: The objectives of this study were comparison between IV parecoxib sodium and morphine in Emergency Department, Hospital USM regarding pain score reduction among acute renal colic patient over time, mean pain score reduction by group over time and to compare the effectiveness of both analgesics (reduction by 2 pain scores) after 5 minutes of drug administration. The side effects of both drugs will be evaluated too.

Methods: A randomised, single-blinded study comparing IV parecoxib 40 mg versus IV morphine at 0.10 mg/kg was conducted in adult patients who presented with features suggestive of acute renal colic and NRS of 6 or more. Periodic assessment of vital signs and NRS were taken at 0, 5, 15 and 30 minutes as well as evaluation of side effects within 30 minutes after the administration of the study drugs. The primary outcome was the reduction of NRS. The data was analysed by repeated measures ANOVA analysis.

Results: There was no significant difference in the mean NRS between patients in IV parecoxib group and morphine group over time ($F(3,126) = 0.229, P = 0.876$). Comparison of the effectiveness at 5 minutes between the groups was not significant ($P = 0.498$). Dizziness, vomiting and nausea were experienced in 22.7%, 13.6% and 4.5% of patients respectively in IV morphine group as compared to parecoxib group 4.5% experienced of nausea only.

Conclusions: There was no significant difference in NRS between the groups over time, as well as in term of the

effectiveness at 5 minutes. Due to lack of IV parecoxib side effect compared to morphine, IV parecoxib seemed to be valuable in the future and can be used as analgesic alternative to morphine in acute renal colic as well as extended further to treat a variety of cases presented in ED HUSM.

Supervisor:

Associate Professor Dr Kamarul Aryffin bin Baharuddin

Co-Supervisor:

Dr Wan Nor Arifin Wan Mansor

POST-CONCUSSION SYNDROME FOLLOWING MILD TRAUMATIC BRAIN INJURY IN EMERGENCY DEPARTMENT HUSM

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Introduction: Post-concussion syndrome is a treatable yet debilitating complication that is frequently seen in patients who sustained mild traumatic brain injury. Proper defining, evaluating and managing these patients and its associating factors can alter clinical course and severity of the illness. Various clinical tools were developed to aid proper diagnosis and management of these patients.

Objective: To determine the incidence of post-concussion syndrome and its association risk factors in patients presenting with a mild traumatic brain injury to the Emergency and Trauma Department, Hospital USM.

Patients and Methods: In this prospective cohort study, we recruited patients with mild traumatic brain injury, who fulfilled the inclusion and exclusion criteria, admitted directly or referral from local clinics to the Emergency and Trauma Department, Hospital USM. Baseline interviews were conducted on those eligible consented patients to gather information on demographic data, type of injury and risk factors on the day of injury. Subsequent telephone interviews were carried out within 2 weeks after the initial presentation and post-concussion symptoms were documented using the Rivermead Post-Concussion Symptoms Questionnaires as the measurement tool. Present of three or more symptoms were considered as post-concussion syndrome. Statistical analyses were performed by using a simple and multiple logistic regressions. Adjusted OR and 95% CI were computed, and a P -value of less than 0.05 was set.

Results: A total of 113 patients with mild traumatic brain injury were included in this study, but only 80 patients have completed the study due to various reasons. 16.3% of the patients have three or more post-concussion symptoms at 2 weeks post mild TBI. The most common presenting symptoms were headache (30%), feeling of dizziness (28.7%), fatigue, tiring more easily (8.8%), nausea and/or vomiting (7.5%), and sleep disturbance (7.5%). Among the risk factors examined, previous history of concussion was statistically significant

for post-concussion syndrome. Patients with previous history of concussion are 4 times more likely to experience Post-Concussion Syndrome as compared to those without a previous history of concussion.

Conclusions: Our study suggested that the incidences of post-concussion syndrome among patients with mild TBI are high, with previous history of concussion as the predictive risk factors for the patients with mild TBI to develop post-concussion syndrome.

Supervisor:

Dr Shaik Farid Abdull Wahab

PSYCHOLOGICAL STATUS AMONG EMERGENCY DEPARTMENT PERSONNEL IN HOSPITAL UNIVERSITI SAINS MALAYSIA

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Objectives: The aims of this study are to determine the psychological status, particularly level of depression, anxiety and stress level among Emergency Department personnel in Hospital Universiti Sains Malaysia and its association to demographic factors.

Methods: This prospective cross-sectional study was conducted in Emergency Department (ED) Hospital Universiti Sains Malaysia from March to June 2014. A total of 122 personnel from the ED who fulfilled the inclusion criteria were included in the study. Each personnel was given a set of questionnaire consisting demographic background and the DASS 21 form. Demographic factors assessed were age, gender, race, profession and years of working experience.

Results: The results from 122 personnel showed a total of 2 personnel (2%) recorded score for moderate depression, 5 personnel (4%) recorded for moderate anxiety and 3 personnel (2%) recorded for severe anxiety. No personnel recorded for moderate-severe stress. Among the demographic factors tested, statistically significant associations were found between stress levels with age, profession and working experience of personnel. Significant associations were also found between depression levels with the gender of personnel.

Conclusion: The psychological status, particularly depression, anxiety and stress level among ED personnel were generally low. The stress level was noted to be most affected by demographic factors compared to depression and anxiety.

Supervisor:

Dr Sahik Farid Abdul Wahab

Co-Supervisors:

Dr Muhamad Saiful Bahri Yusoff

Dr Mohd Azhar Mohd Yasin

RETROSPECTIVE COHORT STUDY OF DECOMPRESSION ILLNESS IN LUMUT AND THE EFFECT OF EARLY TREATMENT

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Introduction: Decompression illness is a rare condition among divers, aviators and astronauts in which bubbles form in blood and tissues following a reduction in environmental pressure. It has wide clinical manifestation and gives a great challenge to Emergency Physician to differentiate decompression illness from other diving related injury. Early detection of decompression illness is crucial as this will determine the type of treatment based on the severity. Severe decompression illness is a denominator for poor prognosis and warrant a definitive treatment with hyperbaric oxygen therapy. Fast access to the treatment will be a good indicator for the recovery. This study aimed to determine recovery outcome in relation to the time to treatment from the onset of symptoms.

Objectives: The aim of this study were to determine the incidence of Decompression Illness, the risk factors that may contribute to the illness and recovery outcome based on time after the initiation of recompression therapy as the definitive treatment.

Methods: This was a retrospective cohort study of all patients diagnosed as decompression illness and treated with hyperbaric oxygen therapy in Hospital Angkatan Tentera Lumut since January 2000 to December 2010. Data was collected from registration book and medical records in the recompression hyperbaric chamber. All data entered into SPSS version 21.0.1 for further descriptive statistic and analysis. Chi square test, univariate and multiple logistic regressions was used to identify significant variables ($P \leq 0.25$) in comparison of complete recovery between early TTR group (within 6 hours) and delayed TTR group (more than 6 hours).

Results: A total of 96 cases reviewed and 16 patients (16.7%) were able to get early access for the recompression therapy whereas 80 patients (83.3%) had delayed treatment of more than 6 hours from symptoms onset after surfacing. All different times of treatment was tested and significantly found that early treatment of less than 6 hours had better recovery status in getting complete resolution of symptoms (OR 8.33, P -value 0.050).

Conclusion: Recompression should be administered early as it resulted in better outcome recovery by limiting disability in divers associated with DCI and prompt complete resolution of symptoms.

Supervisor:

Dr Abu Yazid Md Noh

DEVELOPMENT AND VALIDATION OF INVENTORY - "KNOWLEDGE AND CLINICAL REASONING OF ACUTE ASTHMA MANAGEMENT IN EMERGENCY DEPARTMENT (K-CRAMED)"

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Introduction: Asthma is one of the most common non-communicable and chronic respiratory illnesses that may affect any individuals of any age. Sub-optimal management of asthma will burden not only to individuals and communities; it will possibly restrict daily activities of affected individuals for a lifetime. An observational study was conducted in the Emergency Department (ED), Hospital Universiti Sains Malaysia (HUSM) in the middle of July 2013 and it was found that about 40% of asthmatic patients were managed without adhering to the recommended guidelines. The non-adherence was not a local issue, but an international issue with some other centres worldwide having the similar problem.

Objectives: The aims of this study are to develop and validate an inventory to assess knowledge and clinical reasoning of healthcare provider (HCP) regarding acute asthma management in ED.

Methods: This study was divided into two phases: 1) the development phase, and 2) the validation process. The development phase of this tool consists of domain identification, blue printing of each domain using Global Initiative of Asthma (GINA) guideline and British Thoracic Society (BTS) guideline, and item generation for each domain according to the specific component suggested for this tool which are knowledge and clinical reasoning. The initial validation phase of this tool used content validation index (CVI), face validation index (FVI) and intra-class correlation coefficient (ICC) for each domain.

Results: For relevancy scoring, CVI for domain of diagnosis showed scale-level content validity index, universal agreement method (S-CVI/UA) of 0.83 and scale-level content validity index, averaging method (S-CVI/Ave) of 0.91. CVI for domain of treatment showed S-CVI/UA of 0.85 and S-CVI/Ave of 0.85. CVI for domain of disposition showed S-CVI/UA of 0.89 and S-CVI/Ave of 0.89. FVI of clarity among doctors was 0.97 and FVI clarity among paramedics was 0.87. FVI for comprehension of the doctors was 0.97 and comprehension of the paramedics was 0.83. ICC scoring for average measure among expert panel chosen was 0.989 (CI 95% 0.982, 0.994, P -value = < 0.001).

Conclusion: As conclusion, this tool later referred as K-CRAMED (Knowledge and Clinical Reasoning of Acute Asthma Management in Emergency Department) can be used to assess the HCP that deal with asthma exacerbation patient. Further analysis should be conducted to strengthen the reliability and validity of this new tool.

Supervisor:
Associate Professor Dr Kamarul Aryffin bin Baharuddin

Co-Supervisor:
Dr Muhamad Saiful Bahri bin Yusoff

A SURVEY ON KNOWLEDGE, ATTITUDE AND CONFIDENCE LEVEL OF ADULT CARDIOPULMONARY RESUSCITATION (CPR) AMONG MEDICAL OFFICERS IN HEALTH CLINICS IN KELANTAN

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Introduction: Medical officers are defined as those who have already completed a two-year internship in hospital settings. They will be posted to any government health facilities including health clinics. Health clinics are considered out-of-hospital health facilities. Based on recent statistics, out-of-hospital cardiac arrests survival rates were very low as compared to in-hospital survival rates. Medical officers working in health clinics have long left the hospital settings. Are their knowledge, attitude and confidence level sufficient to deal with these cases of cardiac arrest? The aim of this study is to determine the level of knowledge, attitude and confidence of medical officers in health clinics in Kelantan and the factors associated with it.

Methodology: This was a cross-sectional study using simple random sampling. To validate and test the reliability of the questionnaire, a pre-test was previously done. All medical officers in health clinics in Kelantan were involved in this study. The questionnaire were posted to their workplace and then collected in a period of a few months. The data was entered and analysed by SPSS software version no 22.

Results: A total of 75 medical officers were involved in the study. The average age was 30.0 years with 73.4% of them had practiced medicine for more than two years, 58.7% of them had attended more than 5 cardiac arrest cases, 54.7% of them had last performed CPR for more than 12 months, 98.7% had attended BLS courses, 28% out of them had never attended ACLS courses, 40% of the subjects achieved good knowledge scoring and 100% of these subjects had positive attitude towards adult CPR. In the confidence domain, 53.3% of the subjects had poor confidence in dealing with resuscitation. 60% was not confident to perform endotracheal intubation, 49.3% was not confident to perform defibrillation, 48% was not confident in using resuscitation drugs and 41.3% was not confident to be the team leader in resuscitation. ACLS training was the most important factor that improved their confidence level in adult CPR.

Conclusion: Knowledge of adult CPR among medical officers in health clinics in Kelantan was only average but all of them had positive attitude. The majority had low confidence level. From the study, it was revealed that ACLS training improved both knowledge and confidence level of the doctors. The researcher's recommendation includes integration of life support courses in medical school's syllabus as well as frequent recertification of the courses for everyone. Better knowledge,

attitude and confidence level in cardiopulmonary resuscitation would lead to a better healthcare system in Malaysia.

Supervisor:

Dr Nik Arif Nik Mohamed

PROCEDURAL SEDATION ANALGESIA IN EMERGENCY DEPARTMENT: SURVEY ON KNOWLEDGE AND PRACTICE AMONG NON-ANAESTHETIC DOCTORS IN HOSPITAL UNIVERSITI SAINS MALAYSIA (HUSM)

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Introduction: Procedural Sedation and Analgesia refers to a technique of administering sedatives with or without analgesia to induce a state allowing patients to tolerate unpleasant procedures while being hemodynamically stable.

Objectives: This study intended to identify the level of knowledge and practice of procedural sedation and analgesia among two subgroups of non-anaesthetic doctors; medical and surgical based. By comparing the mean of knowledge and practice level between these two major sub-groups, demographic factors that influence the knowledge level will also be determined.

Patients and Methods: This is a prospective cross sectional study involving 144 non-anaesthetic doctors involved in procedural sedation and analgesia in the emergency department HUSM. A questionnaire survey were conducted among equally distributed respondents from two sub-groups which is medical and surgical based. This study was conducted from January 2013 to December 2014.

Results: The total of 144 respondents aged from 24 to 37 years old with mean age of 30 years old. Mean score of knowledge level in PSA for medical-based doctors is 8.06 compared to 6.60 marks of those in surgical based. There was no significant difference between knowledge level of PSA among medical-based (P -value 0.299) and surgical-based (P -value 0.233) non-anaesthetic doctors in HUSM. Medical based doctors displayed significantly better practices by being aware of protocol available, completing vital signs monitoring, and having formal teaching prior to handling drugs for PSA (P -value < 0.01). Age, level of education and service years gave positive correlation towards level of knowledge (0.5–0.64).

Conclusion: There was no significant difference of knowledge level between medical based and surgical based non-anaesthetic doctors in HUSM though both groups revealed more than average knowledge level. Medical based doctors displayed significant good practices in performing procedural sedation analgesia. Older age, higher level of education, and longer service years contributed to higher knowledge level in procedural sedation and analgesia.

Supervisor:

Dr Emil Fazliq Mohd

A SURVEY ON PEDIATRIC EMERGENCY PREPAREDNESS AMONG HEALTH CLINICS IN KELANTAN

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Introduction: Medical practitioner in health clinic or also known as primary care, as the first point of contact for most patients in the community need to be appropriately skilled and equipped to deal with the emergencies. Most of the previous studies showed that a substantial number of pediatric patients with potentially life-threatening emergencies presented to health clinics. However, the availability of basic emergency equipment and medication was sub-optimal. As a result, patient did not receive optimal treatment that results in morbidity and mortality. In order to address the problems, numbers of guideline were published and specific training being established to the staff. Thus, this study focused on the pediatric emergency preparedness and factors influencing the preparedness.

Objectives: Generally the objectives of this study were to assess paediatric emergency preparedness among health clinics in Kelantan. Specifically, to determine the characteristics of practitioners and practice those are related to preparedness for pediatric emergencies, to assess the availability of specific equipments and medications for pediatric emergencies and to study the factors that influence overall preparedness for pediatric emergencies.

Methods: This prospective, cross sectional study was conducted among all health clinics in Kelantan from 1 July 2015 to 31 August 2015. Only one medical officer in each health clinics was chosen to answer the questionnaire to avoid duplicate reporting of practice equipments and drugs.

Results: Responses were received from 74 respondents (92.5% response rate) including information regarding the availability of equipment and medication, practitioners, and practice characteristic. Three separate scores were calculated for each respondents; equipments score, medications score and overall preparedness score. A multiple regression analysis was used to investigate the relationship between overall preparedness score with the practitioner and practice characteristics. The mean for overall preparedness score was 87.22 of a possible 148 with standard deviation of 10.345 ($n = 74$). In multiple linear regression analysis, only 4 factors were found to have significant association with better preparedness score. They were age, basic life support provider, availability of family physician and paramedic or ambulance response time.

Conclusion: In conclusion, despite of few limitations in this study, it has shown that health clinics in Kelantan are not adequately prepared in terms of equipment and medication for pediatric emergency. There are correlation between few characteristics of practitioners and practice with the pediatric emergency preparedness among health clinics in Kelantan.

Supervisor:

Dr Abu Yazid Md. Noh

A STUDY ON KNOWLEDGE AND PRACTICE ON POST CARDIAC ARREST CARE AMONG HEALTHCARE PROVIDERS WORKING IN EMERGENCY DEPARTMENT IN KELANTAN

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Introduction: 2010 American Heart Association (AHA) guidelines on CPR and ECC had created the fifth link of the chain of survival which is integrated post cardiac arrest care. Since 2002 two landmark studies (HACA et al. and Bernard et al.) proved that therapeutic hypothermia in resuscitated patient with initial rhythm ventricular fibrillation improve their survival rate with good neurological outcome. (Passali, Pantazopoulos et al. 2011) found that nurses and doctors knowledge of basic and advanced life was sub-optimal and practice is varied (Nick Truman et al. 2015). Therapeutic hypothermia implementation is low (Abella, Rhee et al. 2005).

Objectives:

1. To determine the level of knowledge of post cardiac arrest care among healthcare personnel in Emergency Department in Kelantan
2. To determine the level of practice of post cardiac arrest care among healthcare personnel in Emergency Department in Kelantan
3. To compare the mean of knowledge and practice of post cardiac arrest care among general, district and university hospital
4. To determine factors associated with the level of knowledge and practice of post cardiac arrest care among healthcare personnel in Emergency Department in Kelantan.

Methodology: The questionnaire is created based on 2010 AHA guidelines on CPR and ECC which has 3 domains, demographic, knowledge and practice had been validated. The study was a cross sectional study conducted for six months period from Jun till November 2015 in whole tenth of Emergency Departments in Kelantan. Sample size calculated is 156 and the respond rate was 155, 99%. Data was entered and analyzed via SPSS version 22.

Result: We enrolled 155 people with age ranged from 24 to 57 years old. Male population (52.9%) are more than female (47.10%). The mean knowledge score is 5.25, while the mean practice score is 7.5. The median score of knowledge among workplace are different general hospital (6.0, Iqr 3) district hospital (5.0, Iqr 2) and university hospital (7.0, Iqr 3).

In this study we found that five variables were statistically significant with knowledge score which were ACLS trained, position, workplace, place of practice, and number of patient with ROSC attended before. We also found that median practice score of respondent attended ACLS course and service duration is significantly different.

Conclusion: Healthcare personnel working in emergency department in Kelantan had low knowledge and average practice of post cardiac arrest care. The score of knowledge between districts, university and general hospital are different, however practice score are not. Previously attended ACLS course was found to be a significant factor for better knowledge and practice score. Workplace, place of practice, number of cardiac arrest patient with ROSC attended before and position of healthcare personnel was found to be a significant factor affecting knowledge of post cardiac arrest care. Service duration was found to be a significant factor for practice score.

ADHERENCE TO TRIAGE PAIN SCORING AT EMERGENCY DEPARTMENT OF HOSPITAL UNIVERSITI SAINS MALAYSIA

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Introduction: Pain is the most common reason for presentation to the emergency department (ED), and it has been established that more than 70% of patients present with pain as their main symptom. Proper pain score documentation is important to alert the doctors and nurse that the patients might need early analgesia and need early attention.

Objectives: The aim of this study was to determine the level of adherence to triage pain scoring documentation at ED HUSM and to determine the associated factors that influence the adherence to triage pain score, so that actions can be made later to improve emergency services on evaluating pain and providing immediate analgesia to the patients in the future.

Patients and Methods: This study was a cross sectional study of a six months period from July 2014 until December 2014. A total of 334 samples included in the study. Information obtained from triage paper of those adult patients presented in pain and staffs who fulfil the inclusion criteria were documented on data collection sheets. All data were analysed using descriptive analysis, simple logistic regression and multiple logistic regression.

Results: Out of 334, only 94 (28.1%) sample showed adherence to documentation of pain score, while remaining 240 patients (71.9%) showed non adherence to triage pain score documentation. SN has about 4 times more likely compared to AMO to adhere to pain score documentation (95% CI: 2.11, 7.03; P -value = < 0.001). When number of patient increase by 1, ED triage staffs have about 1 time less likely to be adhered to pain score documentation (95% CI: 0.96, 0.99; P -value = < 0.001). When systolic BP of patient increase by 1mm/Hg, ED triage staffs have about 1 time less likely to be adhered to pain score documentation (95% CI: 0.976, 0.99; P -value = 0.004). Abdominal pain has 4 times more likely compared to trauma or limb pain, for ED triage staffs to adhere to pain score documentation (95% CI: 2.17, 8.44; P -value = < 0.001). Back pain has 4 times more likely compared to trauma or limb pain, for ED triage staffs to adhere to pain documentation (95% CI: 1.43, 9.71; P -value = 0.007).

Conclusion: There was poor adherence to triage pain score documentation at ED HUSM during the study period. Factors that influence the adherence to triage pain score documentation were position of staff, number of patients per shift, SBP, and sites of pain.

ADHERENCE TO INITIAL RESUSCITATION BUNDLE FOR SEVERE SEPSIS/SEPTIC SHOCK IN HOSPITAL UNIVERSITI SAINS MALAYSIA

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Introduction: Severe sepsis is devastating disease, associated with significant morbidity and mortality. The incidence of sepsis has increased dramatically and it has become one of the leading causes of mortality in patients admitted to the hospital. Started with simple sepsis which can be a self-limited disease process with the appropriate treatment; it can progress to severe sepsis, septic shock and eventually result in death if it is not treated appropriately. Initial Resuscitation Bundle has been shown to reduce mortality in patients with severe sepsis/septic shock. It has a set of goals to be completed within first six hours of treatments. Meeting these goals within this six hours is associated with reduced mortality in hospitalised patient.

Objectives: This study aimed to evaluate the adherence to Initial Resuscitation Bundle in patients with severe sepsis/septic shock. At the same time, the study intended to identify the associated patient-specific factors contributing to completion of Initial Resuscitation Bundle for severe sepsis/septic shock in Emergency Department, Hospital Universiti Sains Malaysia (Hospital USM).

Patients and Methods: This was a prospective cohort study of 102 patients presenting to Emergency Department, Hospital University Sains Malaysia (Hospital USM) from 15 November 2014 to 15 May 2015. All eligible patients specifically patients ≥ 18 years of age who met criteria for severe sepsis/septic shock that triggers the initiation of the Initial Resuscitation Bundle during the period of study were included. A standardised checklist form was used for each selected subject to evaluate the adherence to the Initial Resuscitation Bundle in managing the case. Subsequently, retrospective data collection were obtained from patient's medical record to determine the completion of the bundle and also the outcomes of the patients. All data entered into SPSS version 22.0 for further descriptive statistic and analysis. Multivariable Logistic Regression was used to adjust for potential confounding.

Results: The results from 102 patients showed a total of 27 patients had completed the Initial Resuscitation Bundle which reflecting the adherence to the Bundle. The three types of sepsis when the patients presented to Emergency Department, Hospital Universiti Sains Malaysia (Hospital USM) were identified to be the patient-specific factors associated with

adherence to the bundle. Those factors were sepsis-induced tissue hypoperfusion, severe sepsis and septic shock. The patient with sepsis-induced tissue hypoperfusion had the most significant association with adherence to the bundle after adjusted with other types of sepsis and gender. This group of patient had 4.80 times higher chance for adherence to the bundle as compared to patient who were not in sepsis-induced tissue hypoperfusion state, P -value = 0.010.

Conclusions: The study has revealed the adherence to the Initial Resuscitation Bundle at Emergency Department, Hospital USM was only 26.5%. The patient-specific factors associated with adherence to the bundle were identified from the study, with sepsis-induced tissue hypoperfusion found to be the most significant factor. Identifying these factors may help in recognising those patients at risk in order to initiate the Initial Resuscitation Bundle as early as possible.

Supervisor:

Prof Dr Nik Hisamuddin bin Nik Abdul Rahman

A RETROSPECTIVE STUDY ON FACTORS AFFECTING LENGTH OF STAY IN HOSPITAL UNIVERSITI SAINS MALAYSIA (HUSM) FOR DENGUE FEVER IN ADULT PATIENTS: A FIVE YEARS REVIEW

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Introduction: Dengue fever is caused by dengue virus (DEN), a flaviviridae and transmitted to human by mosquito vector, usually *Aedes aegypti*. Basic clinical features recorded in adult dengue patients on admission to the emergency room are fever, headache, myalgia, back pain, arthralgia, vomiting, rashes, lymphocytopenia and thrombocytopenia. Dengue fever is a common presentation in emergency and trauma department in Malaysia and results in large number of hospital admission. However, there is no published data found regarding factors affecting length of stay in dengue fever especially in our country. Therefore this study was done to describe the socio-demographic, clinical profiles, outcome, length of stay and associated factors affecting length of stay.

Objectives: The aims of this study were to describe the statistic of dengue patients and their demographic characteristics, clinical profiles and its outcome and to determine mean length of stay in dengue patients. Besides, this study was done to determine the association between clinical profiles of dengue patients with dengue serology and to determine the association between socio-demographic characteristics and clinical profiles of dengue patients with length of stay. Apart from that, the other aim of this study was to identify associated factors in demographic characteristics and clinical profile of dengue patients affecting length of stay.

Patients and Methods: A retrospective cross-sectional study was done from January 2007 to December 2011 on eligible patients suspected or confirmed dengue fever in

HUSM. Patients' medical records were traced from the record office, reviewed and the data were recorded using the data collection form. The socio-demographic characteristics, clinical profiles, outcome, length of stay, factors affecting length of stay and other parameters were analyzed using SPSS version 20.0.

Results: The mean age of the patients in this study was 33.95 (6.614) years old. 66.1% of patients were male, and the most common co-morbid diseases was hypertension (9.8%). All patients presented with fever, 95.3% had body ache and 58.8% had IgM positive. The mean length of stay was 3.98 (2.46) days. Symptom of rashes, diastolic blood pressure, shock index and haematocrit level were found to have significant association with dengue serology result. Patients with diabetes mellitus, hyperlipidaemia, symptom of rashes, pulse rate at emergency department, shock index in the ward, ascites and dengue serology result had significant association with length of stay. Patients with co-morbid diabetes mellitus, background of hyperlipidaemia, underlying bronchial asthma, symptom of fever, diastolic blood pressure reading at emergency department, temperature at emergency department and ascites were the significant associated factors affecting length of stay.

Conclusion: We concluded that socio-demographic as well as clinical profiles were the associated factors affecting length of stay in dengue fever. Diabetes mellitus, hyperlipidaemia, bronchial asthma, symptom of fever, diastolic blood pressure at emergency department, temperature at emergency department, and ascites were the significant associated factors affecting length of stay in dengue patients.

Supervisor:

Dr Shaik Farid Abdull Wahab

QUALITY PERFORMANCE MEASUREMENTS OF AMBULANCE SERVICES IN EAST COAST, MALAYSIA

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Introduction: East Coast Region states in Malaysia consists of Kelantan, Terengganu and Pahang. Similar to other states in Malaysia, ambulance services in this region are mainly provided by the government under Ministry of Health (MOH) and Ministry of Education (MOE) in the hospital-based emergency medical system (EMS). The service plays a significant role in public to provide fast and efficient healthcare services in the field as well as inside the ambulance. Therefore, the quality of services must be achieved according to international standard. This study is focused on evaluating the current performance of ambulance service in East Coast, Malaysia based on ambulance response time, ambulance crash and patients complaints as well as identifying the factors affecting the ambulance response time and also ambulance crash.

Objectives: The aim of this study were to evaluate the quality performance of ambulance services in government hospital in East Coast Malaysia based on ambulance response time, number of ambulance crash and number of patients' complaint and factors affecting its quality services.

Methods: This study was a cross-sectional study to evaluate the quality performance measurements of ambulance service in East Coast Region, Malaysia from January 2014 to December 2014. The data was obtained from questionnaires which was distributed to all the government hospitals in Kelantan, Terengganu and Pahang. Series of interviews with paramedics in-charged of ambulance services was done in selected hospitals to identify the factors contributed to its performance. It was conducted from November 2014 to March 2015. Statistical analysis was done using SPSS software version 22.0. Simple linear regression was used to determine the associated factors influencing the ambulance response time whereas simple logistic regression was used to determine factors associated with ambulance crash incident.

Results: A total of 22 hospitals out of 26 were involved in this study with 8 hospitals from Pahang, 8 hospitals from Kelantan and 6 hospitals from Terengganu. Majority ambulances were in charged by assistant medical officer (pembantu pegawai perubatan) level U32 and above. Among parameters used to measure the key performance index, the ambulance response time had been the highest (95.5%). The mean response time in 2014 for all hospitals in East Coast, Malaysia was 16.90 minutes (SD) of 5.94. The mean ambulance crash was 0.77 and the median was 1.00. Majority hospitals had none /unknown complaints regarding ambulance services in their centres (59.1%). Otherwise, 40.9% had less than 10 formal complaints. From this study, univariate linear regression analysis showed that there were no significant factors influenced the ambulance response time and univariate logistic regression showed that there were no factors significantly associated with ambulance crash.

Conclusion: Based on the study, we concluded that the quality of ambulance services in East Coast, Malaysia still not achieving the international standard. There were no significant factors which influenced ambulance response time and ambulance crash.

PSYCHOLOGICAL STATUS AMONG ACUTE CORONARY SYNDROME PATIENTS IN HOSPITAL UNIVERSITI SAINS MALAYSIA, KELANTAN AND HOSPITAL SULTANAH NUR ZAHIRAH, TERENGGANU

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Introduction: Coronary heart disease is the most common form of cardiovascular disease and frequently manifests as acute coronary syndrome (ACS) which includes a range of clinical conditions from angina pectoris, unstable angina, non-ST elevation myocardial infarction to ST

elevation myocardial infarction. The ACS is a common cause of emergency hospital admission and a major burden on health care resources in industrialised countries including Malaysia. Depression, anxiety and stress occur at high rates among patients suffering an ACS. The depression, anxiety and stress symptoms appear to adversely affect in-hospital and long term cardiac outcomes of post-ACS patients. Despite their high prevalence and serious impact, the psychological symptoms are commonly unrecognised and untreated in most ACS patients. This study was to investigate the psychological status of ACS patients and to establish the associated factors that contribute to it.

Objectives: To determine the prevalence and its associated factors of depression, anxiety and stress condition of acute coronary syndrome patients in Hospital Universiti Sains Malaysia and Hospital Sultanah Nur Zahirah.

Methodology: A cross-sectional prospective study for ten months duration was done from August 2014 until May 2015 on eligible subjects of ACS patients in Hospital USM and HSNZ. A questionnaire consists of two sections (socio-demographic data and Depression, Anxiety and Stress Scale 21) was used in this study. The questionnaire was distributed to all ACS patients admitted to wards. The prevalence of depression, anxiety and stress and their associated factors was analysed using SPSS software version 22 (IBM Corp, 2013).

Results: There were 400 patients enrolled into the study during the study period. The prevalence of depression, anxiety and stress were 80.3%, 85.8% and 58.5%, respectively. There were significant associations between gender, ischemic heart disease and other co-morbid with depression [$P = 0.000$, OR 2.545(1.525, 4.248); $P = 0.003$, OR 2.301(1.317, 4.021) and $P = 0.032$, OR 2.297(1.076, 4.904)]. There was significant association between ischemic heart disease and anxiety [$P = 0.013$, OR 2.202(1.185, 4.093)]. There was significant association between ischemic heart disease and stress [$P = 0.010$, OR 1.730 (1.139, 2.626)]. There were no statistically significant associations between other demographic factors with depression, anxiety or stress.

Conclusion: We concluded that the prevalence of depression, anxiety and stress were high in ACS patients. The recognised significant associated factors were gender, ischemic heart disease and other co-morbid. Subjects who had other co-morbid and female gender were more likely to have depression. Subjects with ischemic heart disease were more likely to have depression, anxiety and stress.

Supervisor:

Dr Mohd Hashairi bin Hj Fauzi

Co-Supervisor:

Dr Siti Azrin bt. Ab Hamid

DEPRESSION AMONG ELDERLY WITH TYPE 2 DIABETIS MELLITUS

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Introduction: The prevalence of Diabetes Mellitus in elderly is escalating. Depression although carries high mortality and morbidity is often under diagnosed and undertreated. Furthermore elderly with diabetes has higher chance to have depression compared to those who are not.

Objectives: To determine the proportion of depression and its associated factors among elderly with Type 2 Diabetes Mellitus in Sungai Petani, Kedah, Malaysia.

Methodology: A cross-sectional study involving 509 elderly with type 2 Diabetes Mellitus age 60 and more. Systematic random sampling 1:3 was applied to elderly patients attended Klinik Kesihatan Bandar, Sungai Petani, Kedah from November 2015 to January 2016. The inclusion criteria were patients who were diagnosed with Type 2 Diabetes Mellitus. The exclusion criteria were cognitive impairment, ECAQ score 5 and less, presence of organic brain syndrome, presence of severe mental disorder like schizophrenia, patients with mental retardation and patients who either deaf or mute. A self-administered questionnaire and participant's case note were used to obtain the information needed. Malay version of Geriatric Depression Scale (M-GDS-14) was used to assess the depressive symptoms. The data was analyzed using descriptive statistic and multiple logistic regressions.

Results: The median age of the respondents was 65 (8.0) years old. Half of respondents were male (54%) and 236 (46%) were female. Majority of respondent were Malays (63.3%) followed by Indians (27.3%) and Chinese (9.4%). Majority of respondents were married (76.8%), some were widows/divorced (21%) while the remaining were single (2.2%). More than half were retired (68.2%), 23.4% were never employed and only small numbers of them who were still working (8.4%). Only small number of respondents completed their tertiary education (16.3%), many had completed their secondary schools (39.7%), while the remaining only had their education at primary school level (34.8%) or they did not received formal education (9.2%). Majority of the respondents (67.4%) had household income of less than RM1000. The proportion of depression was 32.2%. Elderly living with children -1.62($P = 0.002$, 95% CI 0.07, 0.55), Elderly living with spouse, children, in law & grandchildren 1.08($P = 0.021$, 95% CI 1.18, 7.37), diabetic complication 4.68($P = 0.001$, 95% CI 2.63, 8.35) and HbA1c 1.23($P = < 0.001$, 95% CI 1.09, 1.39) are significantly associated with depression.

Conclusion: Depression is high among elderly with Type 2 Diabetes Mellitus. Living arrangement, diabetic complication and HbA1c were significantly associated with depression.

Supervisor:

Dr Nani Draman

Co-Supervisor:

Dr Siti Suhaila Mohd Yusoff

CONTROLLED TRIAL OF ORAL *Channa striatus* EXTRACT AND GLUCOSAMINE SULPHATE AMONG PRIMARY KNEE OSTEOARTHRITIS PATIENTS

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Introduction: Knee osteoarthritis is the commonest form of arthritis worldwide with significant impact on the health-related quality of life. Complementary and alternative medicine use in osteoarthritis is gaining popularity. *Channa striatus*, an indigenous fresh water fish in Malaysia is well-known for its nutritional and medicinal value in traditional medicine. The current evidences support its therapeutic potential in treating primary knee osteoarthritis patients.

Objectives: The aim of the study was to compare the effectiveness of oral *Channa striatus* extract and glucosamine sulphate in improving knee symptoms and physical function, as well as in rescue analgesic consumption among primary knee osteoarthritis patients.

Methods: Seventy eight patients with primary knee osteoarthritis were enrolled into this double-blind randomised controlled trial and assigned to receive either *Channa striatus* 500 mg/day ($n = 39$) or Glucosamine sulphate 1500 mg/day ($n = 39$) for six months. The efficacy outcome measures were Western Ontario and Mc Master Osteoarthritis Index WOMAC index for pain, stiffness and physical function, Visual Analogue Scale for pain during movement and Analgesic score for rescue analgesia consumption. These outcomes measures were assessed using an intention-to-treat analysis. All patients were evaluated at baseline, 3 and 6 months post-randomisation.

Results: All the baseline characteristics were comparable between *Channa striatus* and glucosamine sulphate group. Of 78 patients randomised, 73 completed the study (*Channa striatus*, $n = 36$ and Glucosamine sulphate, $n = 37$). There were no statistically significant difference between these two groups in WOMAC index, Visual Analogue scale and Analgesic score after 6 months of intervention. However, there were statistically significant improvement in all the domains of WOMAC index based on time for *Channa striatus* group from baseline to 3 months up to 6 months. Although there were improvement observed from 3 to 6 months of treatment, they were not statistically significant. All the safety profile parameters were normal for both groups before and after the intervention.

Conclusions: *Channa striatus* 500 mg/day is comparable to glucosamine sulphate 1500 mg/day in improving pain, stiffness and physical function in patients with primary knee osteoarthritis. It could be a new alternative treatment with good safety profile for medium to long term management of knee osteoarthritis.

Supervisor:
Dr Azlina Ishak

Co-Supervisor:
Dr Rosnani bt Zakaria

A CASE – CONTROL STUDY ON RISK FACTORS FOR FALLS AMONG OLDER ADULTS ATTENDING KLINIK RAWATAN KELUARGA IN HOSPITAL SAINS MALAYSIA

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Background: Falls is an important geriatric problem due to its potential negative impacts on the affected older adults. But, little is known about the risk factors for falls among older adults who attend the health clinics.

Objectives: The objective of the study was to identify the associated factors for falls among older adults attending Klinik Rawatan Keluarga (KRK) of Hospital Universiti Sains Malaysia (USM).

Methods: An unmatched case-control study was conducted among 60 older adults with self-reported falls and 60 “normal controls”. Both cases and controls were recruited from the KRK, Hospital USM via convenient sampling from December 2014 to June 2015. All participants completed a questionnaire regarding sociodemographic and other health risk factors. Logistic regression analysis was used for obtaining the odds ratio (OR) for associated factors.

Results: Independent associated factors observed for falls were female sex (adjusted OR: 5.72, 95% CI: 2.50, 13.07, $P < 0.001$) and impaired physical function capacity (adjusted OR: 4.33, 95% CI: 1.67, 11.28, $P = 0.003$).

Conclusions: Female older adults and older adults with impaired physical function capacity were significant associated factors for falls among older adults attending KRK, Hospital USM.

Supervisor:
Professor Shaiful Bahari Ismail

Co-Supervisor:
Dr Faridah Mohd. Zin

KNOWLEDGE AND ATTITUDES ON HUMAN PAPILLOMAVIRUS (HPV) INFECTION AND HPV VACCINATION AMONG HEALTH CLINIC NURSES IN THE STATE OF KELANTAN

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Introduction: Cervical cancer, though preventable, is still the leading cause of cancer death among women in Malaysia second to breast cancer. Persistent infection with HPV has been causally linked to cervical cancer. The school-based HPV vaccination program was introduced in late 2010. Nurses' support is imperative for the success of this program; however, it has not been assessed yet. This study aims to determine factors associated with their knowledge score.

Methods: A survey was conducted from June till July 2014 at health clinics in Kelantan. The nurses were selected through the multistage random sampling process, and self-administered questionnaires were distributed to 352 nurses. Data were analysed using SPSS version 22. Multiple linear regression models were used to determine the variables associated with the nurses' knowledge score.

Results: A total of 330 completed questionnaires were analysed and showed that: 32.4% nurses participated from the outpatient unit and 67.6% from maternal and child health unit. The mean knowledge score (SD) was 5.3 (1.7) out of 11. Only, 24% knew that HPV is the most common sexually transmitted virus; 67% knew that Gardasil protects against four types of HPV and 29% correctly answered the target age of vaccination. Nursing qualification ($P < 0.001$) was the only factor that significantly associated with knowledge score. HPV-related work experience, having children in vaccination age group and reading resources showed no influence in knowledge score.

Conclusion: This is the first study done in Kelantan to assess nurses' knowledge in this regard. Findings from this study indicate nurses have favorable attitudes toward HPV vaccination, but they are in urgent need of improving HPV-related knowledge and its actual vaccination. Similar studies need to be conducted in other states, to have a broad estimation and to make a nationally based education program to increase nurses' knowledge in this matter.

COGNITIVE IMPAIRMENT AND DIABETIC CONTROL ASSOCIATION AMONG ELDERLY TYPE II DIABETES MELLITUS IN HOSPITAL UNIVERSITI SAINS MALAYSIA

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Introduction: This study aims to look at the proportion of diabetic control and cognitive impairment, and its association among elderly Type II diabetes Mellitus in HUSM. As the elderly population in our country and diabetes keep increasing to determine proportion and its associations is important to see our population disease trend. Increase number of ageing people with diabetes will increase our health care burden, thus hopefully it will help in managing geriatric with diabetes population.

Objectives: This is a cross sectional study to determine the proportion of cognitive impairment and diabetes control and their association among elderly diabetes in HUSM

Methods: It's involved 403 patient type 2 DM who attending *Klinik Rawatan Keluarga* HUSM, aged more than 60. This study was conducted from August 2013 until May 2014. Self-administrated questionnaire were given for data collection. Patients were screen for depression then they were put into systematic random sampling 1 in 2. The questionnaires that were used in this study consist of socio-demographic data, and Malay version Diabetes Knowledge questionnaire. Hba1c 7 and below was used to determine diabetes control and Mini Mental State Examination Malay version was used to asses cognitive impairment.

Results: The proportion of diabetic control in this study based on Hba1c level 7% and below was 25% and 4.0% found to have cognitive impairment. There is no association between cognitive impairment and diabetes control. The mean score of diabetes knowledge questionnaire is 12.9.

Conclusion: From this study, the diabetes control was quiet good compared to other study in this country, but still below national standard and low proportion of cognitive impairment. There is no association between cognitive impairment and diabetes control may due to low proportion of cognitive impairment.

Supervisor:
Associate Professor Dr Juwita Shaaban

Co-Supervisors:
Dr Razlina Abdul Rahman
Associate Professor Dr Azidah Abdul Kadir

A STUDY ON KNOWLEDGE, DECISION MAKING AND ACCEPTANCE OF HUMAN PAPILLOMA VIRUS VACCINATION AMONG PARENTS OF PRIMARY SCHOOL STUDENTS IN KOTA BHARU

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Introduction: Cervical cancer is the second most common cancer in women and fifth most common cancer in the entire general population in Malaysia. The ultimate cause of cervical cancer is Human Papilloma Virus. Malaysia is the first country in South East Asia implements school based vaccination, which is free vaccine to 13 years old girls in government and private schools starting in 2010. However it is a voluntary HPV immunisation program, which required parental written consent. Therefore children rely on parents not only for the consent even for the guidance and information about the vaccines.

Objectives: The study to determine parental knowledge, decision making, acceptance of HPV vaccination, and factors associated with acceptance.

Methods: This cross sectional study was conducted among 280 parents of primary school students in Kota Bharu from January until May 2015. Systemic random sampling and

a validated self administered questionnaire was used to assess knowledge of HPV vaccination. Data was analysed using SPSS ver 22.

Results: Parents with good knowledge in Kota Bharu was 38% and 62% was poor. Most decision regarding vaccination was a shared decision, 72%. The proportion of acceptance was 63%. Our results showed that the acceptance increases more amongst older age and good knowledge groups of parents.

Conclusion: Parent's level of knowledge is poor despite the implementation of the HPV vaccine since 2010. The identified factors that associated with acceptance on HPV vaccination were age and knowledge. Parents play an important role in determining the success of HPV vaccine program. The trend of decision making has changed in Malaysian family as most couples make joint decisions in allowing vaccinations on their child as compared to traditionally decision making by the father.

Supervisor:

Associate Professor Dr Juwita binti Shaaban

Co-Supervisor:

Dr Siti Suhaila binti Mohd Yusoff

AN OPEN LABELLED RANDOMISED CLINICAL TRIAL OF FLUOXETINE VERSUS DAPOXETINE TREATMENT AMONG MEN WITH PREMATURE EJACULATION AND ITS EFFECT ON MARITAL SATISFACTION

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MMed (Family Medicine)

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Introduction: Premature ejaculation (PE) causes reduced sexual satisfaction and quality of life. Both Selective Serotonin Re-uptake Inhibitor Fluoxetine and Dapoxetine have been used in treatment of PE. Fluoxetine is used as off-label treatment meanwhile Dapoxetine is the first SSRI specifically designed for PE that has a short half-life and few side effects.

Objectives: To compare the PE symptoms score and marital satisfaction score between Fluoxetine and Dapoxetine groups.

Methods: In this open labelled randomized clinical trial, 44 participants aged between 18 and 64 with PEDT score of ≥ 9 from the Primary Care clinic of Hospital USM, Kelantan Malaysia were recruited and randomised into two groups; Fluoxetine Group (FG) and Dapoxetine Group (DG). They were prescribed with either daily oral Fluoxetine 20mg or Dapoxetine 30mg on demand twice weekly for 8 weeks. PE symptoms were measured using the Premature Ejaculation Diagnostics Tool (PEDT) score and marital satisfaction score were measured using the Dyadic Satisfaction-Dyadic Adjustment Scale (DS-DAS) score. Measurements were made at baseline and at the 8th week (post-intervention).

Results: In FG and DG, 22 and 21 participants completed the study, respectively. PEDT scores reduced significantly within both groups [from 11.41 to 5.45 ($P < 0.001$) within FG and from 13.43 to 3.10 ($P < 0.001$) within the DG]. At the 8th week follow-up, PEDT scores was observed to be lower in DG (6.03 versus 2.49, $P < 0.001$) after adjustment of the baseline PEDT score. Significantly increased DS-DAS scores were observed in both groups [from 34.50 to 40.68 ($P < 0.001$) within FG and from 36.57 to 44.33, ($P < 0.001$) within DG] with no significant difference in DS-DAS scores at the end of study (41.13 versus 43.86, $P = 0.055$) after adjustment of the baseline DS-DAS score.

Conclusions: Reduction in PE symptoms was observed for both groups. At 8 weeks, PE symptoms among participants on Dapoxetine were significantly lower compared to the participants on Fluoxetine group at 8 weeks. Treatment of PE with either Fluoxetine or Dapoxetine reduces symptoms of PE and improves marital satisfaction.

Supervisor:

Dr Faridah binti Mohd Zin

Co-Supervisors:

Professor Dr Shaiful Bahari bin Ismail

Dr Najib Majdi bin Yaacob

USE OF TRADITIONAL AND COMPLEMENTARY MEDICINE AND ITS ASSOCIATED FACTORS AMONG KNEE OSTEOARTHRITIS PATIENTS IN OUTPATIENT CLINIC, HOSPITAL UNIVERSITI SAINS MALAYSIA

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Mmed (Family Medicine)

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Introduction: Osteoarthritis is the commonest arthritis worldwide especially in elderly. It ranks among the top ten causes of disability worldwide. The current management of Osteoarthritis does not provide definitive cure, however it was able to control pain, improved function and overall quality of life. Other than conventional treatment, some patients opted for traditional and complementary medicine (TCM) to treat the disease. Some of them use it alone however most of the patient combine both the conventional and TCM. Even though TCM is widely used, many of its marketed products were questionable in term of quality, efficacy, content and safety. There are many unregistered product which found to be contaminated with controlled drugs and poisons such as steroid, hormones, antihistamine and heavy metal which can cause a lot of unwanted effect and complication.

Objectives: To determine the proportion of knee Osteoarthritis patient at HUSM outpatient clinic who uses traditional and complementary medicine (TCM) for their knee Osteoarthritis and its associated factors.

Methodology: This study is a cross sectional study. A total of 214 patients were involved in this survey. Convenience sampling method was applied to select participants who attended outpatient clinic in HUSM (*Klinik Rawatan Keluarga*) from May 2013 to October 2013. First, participants were interviewed to get the sociodemographic characteristics, clinical history and history of TCM use for knee osteoarthritis. After that, patients were given a questionnaire which is validated Malay version of Western Ontario and McMaster Universities Arthritis Index (WOMAC) to be self-administered. This questionnaire was used to assess the severity of knee osteoarthritis in term of pain, stiffness and disturbances in daily activity. The data was analysed using the descriptive statistic and multiple logistic regressions.

Result: This study showed that the proportion of knee Osteoarthritis patient attended HUSM out-patient clinic that practice traditional and complementary medicine was 57.9%. Factors associated with TCM use in this study population was male (OR; 2.47, 95% CI: 1.28, 4.77), duration of knee Osteoarthritis (OR; 1.51, 95% CI: 1.03, 2.23) and severity of knee pain (OR; 2.57, 95% CI: 1.71, 3.86).

Conclusion: The proportion of TCM use for knee Osteoarthritis in this population study was high. Clinicians should aware of its high usage. They should identify patients by asking them regarding use of TCM so further discussion and shared decision can be undertaken.

Supervisor:

Dr Lili Husniati bt Yaacob

Co-Supervisor:

Dr Azlina binti Ishak

DIABETES SELF-CARE AND ITS ASSOCIATED FACTORS AMONG ELDERLY DIABETES PATIENT IN THE OUTPATIENT DEPARTMENT HOSPITAL UNIVERSITI SAINS MALAYSIA

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Introduction: The world population is ageing and diabetes mellitus is one of the most prevalent diseases that afflict senior citizens. One of the reason of suboptimal glycemic control and diabetes complications is lack of self-care by those with diabetes.

Objectives: To describe diabetes self-care among elderly diabetic in the KRK, HUSM and to determine the associated factors.

Material and Method: A cross sectional study was conducted among elderly type 2 diabetes patients attending KRK, HUSM, Kelantan. Diabetes self-care was assessed using interview-based questionnaire the Malay Elderly Diabetes Self-Care Questionnaire (MEDSCaQ).

Result: A total of 143 patients responded giving a response rate of 91.7%. The mean of total diabetes self-care score was 26.5 (SD 8.0), with minimum score of 1 and maximum score of 40. The factors with positive impact on diabetes self-care were being non-Malay ($\beta = 5.275$, $P = 0.002$), taken care by family during sick ($\beta = 8.995$, $P = 0.004$), higher family support ($\beta = 0.159$, $P = 0.042$), without neuropathy ($\beta = 3.261$, $P = 0.016$), acceptable knowledge in diabetes ($\beta = 4.375$, $P = 0.001$) and good knowledge in diabetes ($\beta = 5.893$, $P = 0.004$). However, having no CKD lowered diabetes self-care ($\beta = -4.053$, $P = 0.003$).

Conclusion: Race, care-taker during sick, family support, diabetes knowledge, neuropathy and CKD were significantly associated with diabetes self-care in elderly. These factors should be taken in account in planning future diabetes self-management programs among the elderly.

Supervisor:

Dr Siti Suhaila Mohd Yusoff

Co-supervisors:

Associate Professor Dr Azidah Abdul Kadir

Dr Razlina Abd Rahman

PREVALENCE OF DEPRESSION, ANXIETY AND STRESS AMONG OBESE PATIENTS WITH CHRONIC MEDICAL ILLNESS IN KLINIK RAWATAN KELUARGA, HOSPITAL UNIVERSITI SAINS MALAYSIA (HUSM) AND ITS ASSOCIATED FACTORS

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MMed (Family Medicine)

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Introduction: Obesity and depression are two prevalent disorders that are costly to both individuals and society especially in patients with chronic medical illness. Depression usually co-exists with anxiety and stress. The aim of this study is to determine the prevalence and the factors associated with depression, anxiety and stress in obese patients with chronic medical illness attending *Klinik Rawatan Keluarga*.

Methods: The study was cross sectional in design and was carried out in HUSM. A total of 274 eligible consenting respondents participated in the study. The Depression, Anxiety and Stress Scale (DASS21) questionnaire was used for measurement of depression, anxiety and stress among the respondents. Data was analysed using the SPSS version 21 software using both descriptive and inferential statistics (single and multiple logistic regression).

Objectives: The aims of this study is to determine the prevalence and associated factors of depression, anxiety and stress among obese patients with chronic illnesses attending *Klinik Rawatan Keluarga, Hospital USM*.

Results: The prevalence of depression, anxiety and stress among obese patients with chronic medical illness were 13.9%, 23.4%, and 10.9% respectively. Using multiple logistic

regression, age ($P = 0.003$, OR: 0.96, 95% CI: 0.91,0.98), occupation (not working) ($P = 0.013$, OR:3.65, 95% CI:1.32,10.09,) and current smoker ($P = 0.022$, OR:3.18, 95% CI:1.18,8.55) were associated with depression. For anxiety, the associated factors were no formal education ($P = 0.011$, OR:5.70, 95% CI: 1.49, 21.89), BMI ($P = 0.029$, OR:1.07, 95% CI:1.01,1.13) and family history of mental illness ($P = 0.018$, OR:5.10, 95% CI: 1.33, 19.56). Stress was strongly associated with female gender (OR 5.06, 95% CI 1.70–15.13) and current smoking status (OR 6.49, 95% CI 2.03–20.70).

Conclusion: Prevalence of depression, anxiety and stress symptoms in obese patients with chronic medical illness were 13.9%, 23.4% and 10.9% respectively. The significant associated factors were age, not working, BMI, current smoker, no education, family history of mental illness and gender. Screening of obese patients with chronic illness for depression, anxiety and stress at primary care setting is recommended hence early intervention can be offered.

Supervisor:

Dr Imran Ahmad

Co-Supervisor:

Dr Siti Suhaila Mohd Yusoff

PREVALANCE AND MOLECULAR EPIDEMIOLOGY OF *Clostridium difficile* INFECTION IN HOSPITAL UNIVERSITI SAINS MALAYSIA PATIENTS AND ELDERLY COMMUNITY SUBJECTS IN KELANTAN

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Introduction: An increase in the incidence of *Clostridium difficile* infection (CDI) in Western countries has come to prominence over the last 15 years. However awareness and surveillance of CDI in Asia remained poor with epidemiological data being scanty in Asia and in particular Malaysia. CDI is commonly associated with nosocomial infections, but community acquired CDI has been reported with increasing frequency lately. Despite the increase in incidence and severity of CDI, a recent survey found awareness of CDI being poor, with underestimation of its contribution to antibiotic-associated disease and recurrence rates.

Objectives: The aims of this study were to explore the prevalence and associated risk factors of CDI in hospitalised patients in HUSM, to explore the carriage rate among the elderly in the community in Kelantan, and to determine the level of awareness of CDI among staff and students in HUSM.

Patients and Methods: This study was divided into 3 arms: 1) the hospital arm, a prospective cross sectional study of CDI prevalence among hospitalized patients in HUSM, 2) the community arm, a cross sectional study of *C. difficile* carrier prevalence among elderly community in Kelantan, and 3) awareness survey, a cross sectional study of *C. difficile*

awareness among healthcare personnel in a university campus. For hospital and community arms, stools were tested for *C. difficile* antigen and toxin detection using *C. DIFF QUIK CHEK COMPLETE®* prior to be sent to Western Australia for culture and PCR for toxin genes and ribotyping for molecular epidemiology. For awareness survey, data was obtained thru a self-administered questionnaire which was based from a previous international internet-based awareness study.

Result: For the hospital arm, 20 samples (26.3%) were positive for *C. difficile* antigen (CDifAg), 7 samples (9.2%) were positive for *C. difficile* toxin (CDifToxin) and 19 samples (25%) were positive from direct culture. Significant ribotype diversity with six distinct ribotype groups (QX001, UK 017, QX 002, QX 107, QX 117 and QX 463) were identified. Independent risk factors based on Multiple Logistic Regression were age, duration of hospitalization and use of antibiotics (P -value < 0.05). For the community arm, 2 samples (1.6%) were positive for both CDifAg and direct culture while negative for CDifToxin. Ribotyping of the 2 samples showed unknown strain. From the study, it was found that the study population did not have high PPI and antibiotics use which were known CDI risk factors. For awareness study arm, there was a low level of awareness on CDI with only 2.6% of 154 respondents able to correctly answer all questions correctly. Ironically a large proportion of the participants ($n = 73$; 47.4%) considered *C. difficile* to be overestimated in their current practise. There was no significant association between level of awareness on CDI with age, gender and occupation i.e. being a clinician.

Conclusion: This study demonstrated that the prevalence rate for CDI in hospitalised patients in HUSM were 26.3% for CDifAg, 9.2% for CDifToxin and 25% for direct culture with 6 distinct ribotype strains; QX001, UK 017, QX 002, QX 107, QX 117 and QX 463 identified. Independent risk factors for CDI were age, duration of hospitalisation and use of antibiotics. The carrier rate for *C. difficile* was 1.6% among the elderly in the community with unknown strain identified from PCR ribotyping. Low usage of PPI and antibiotics were seen in our study population and could explain the low prevalence rate of CDI in our study population. Low awareness on CDI was seen among healthcare professionals in HUSM which was also seen internationally. Therefore CDI being an underdiagnosed and under recognised issue in the healthcare system is an issue that needs to be addressed by all parties.

AGREEMENT BETWEEN COMBINATION OF GALACTOMANNAN WITH CT THORAX AND POLYMERASE CHAIN REACTION WITH CT THORAX AS A DIAGNOSTIC TOOL FOR INVASIVE ASPERGILLOSIS IN FEBRILE NEUTROPENIA

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Introduction: Invasive infections due to *Aspergillus* species, mainly *Aspergillus fumigatus*, are an important

cause of morbidity and mortality in patients with hematologic malignancies. Successful outcome with treatment is linked to early diagnosis. The utility of classic diagnostic methods, however, is limited.

Objectives: The primary objective of this research was to study on agreement between galactomannan and *Aspergillus*-specific PCR as a diagnostic tool for invasive aspergillosis in febrile neutropenic patient. The secondary objective was to determine the association between CT thorax and both non-culture based biomarkers.

Patients and Methods: We performed a prospective study involving adult haematological patients with persistent febrile neutropenia from May 2015 to November 2015 in Hospital Universiti Sains Malaysia.

Results: A total of 14 haematological patients were recruited in the study. There was no agreement between Galactomannan with polymerase chain reaction with k value was -0.324 (95% CI: $-0.124, 0.127$). 21.4% patients had positive galactomannan and only one of them had positive result in 2 consecutive samples. We demonstrated three patients with positive result for aspergillus-specific PCR and there was no significant association between positive PCR with final diagnosis of probable IPA ($P = 1.000$). There was no association between galactomannan and CT thorax (P -value = 1.00, by Fisher's exact test). Analysis also showed no significant association between PCR with CT thorax (P -value = 1.000, by Fisher's exact test)

Conclusion: The data from this study demonstrate a disagreement between both two non-cultures based biomarkers in diagnosis of invasive aspergillosis. But both of the tests can assist in pre-emptive strategy of treating invasive pulmonary aspergillosis.

Supervisor:
Dr Azlan Husin

Co-Supervisors:
Associate Professor Dr Azian Harun
Dr Juhara Yaacob

PNEUMONIA IN CHRONIC KIDNEY DISEASE PATIENT: A STUDY OF CLINICAL FEATURES AND OUTCOMES

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Introduction: Chronic kidney disease (CKD) patient is recognised as group of patients prone for various infection with poorer prognosis. However, not many studies have been done for this group of patients to determine their clinical features and to ascertain their outcomes in pneumonia.

Methods: All patients admitted for community acquired pneumonia from January 2014 to May 2016 in Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan were screened for the eligibility to enroll in this study. Eligible

subjects case notes were then extracted from the record office and reviewed.

Result: During the study period, a total of 398 subject's medical records were extracted from the record office, and were divided to 1:1 ratio between CKD and non-CKD subjects. CKD patient was noted significantly older (Mean age 64 versus 56, with P -value < 0.05), having more co-morbidity, more smoker and less vaccinated. They did present as more in septicemia shock and altered mental status (46% versus 23%, $P < 0.05$ and 56% versus 26%, $P < 0.05$) with more severe chest radiograph (54% versus 29%, $P < 0.05$) and more in high PSI score group (52% versus 20%, $P < 0.05$) than were other patients without CKD. Patient with chronic kidney disease was also noted to have more unfavorable outcomes, higher mortality (35% versus 12.7%, $P < 0.05$), higher HDW/ICU admission rate (50.2% versus 22%, $P < 0.05$), longer median length of stay (LOS) (9 days versus 6 days, $P < 0.05$), and more subjects required mechanical ventilation (37% versus 19.6%, $P < 0.05$) as compared to subjects without Chronic kidney disease.

Conclusion: We concluded that in overall picture CKD patient did come with higher prevalence with risk factor that can contribute to poorer prognosis. However, we did found that mortality in our subjects merely involved subjects that develop complication especially a nosocomial infection. This fact auspiciously provides us with a guide to further reduced mortality in CKD subjects with community acquired pneumonia

Supervisor:
Dr Alwi bin Muhd Baseri@Hashim

FACTORS ASSOCIATED WITH LEVEL OF SPIRITUAL WELL-BEING IN FEMALE CANCER PATIENTS IN CLINICAL REMISSION IN HOSPITAL UNIVERSITI SAINS MALAYSIA

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Introduction: Spiritual well-being (SWB) is believed to be an important component in ensuring better quality of life in cancer patient and incorporating SWB into clinical practice has been given more emphasis in recent years.

Objectives: This study examines the relationship between anxiety and depression with SWB and its domains, and other associated factors, among female cancer patients who are in remission.

Methods: A total of 150 female cancer patients who are in remission for at least 6 months, were recruited from the outpatient oncology clinic of Hospital Universiti Sains Malaysia (HUSM). Anxiety and depression, and level of spiritual well-being were assessed using the Hospital Anxiety and Depression Scale (HADS)–Malay Version and the Spiritual Well-Being Scale (SWBS)–Malay version, respectively. Other possible associated demographic and clinical factors data

were obtained using the Patient's Data Sheet. The relationship between level of SWB and associated factors were analysed using the Multiple Linear Regression (MLR), controlling possible confounding factors.

Results: One hundred and fifty complete data sets were obtained. There is a significant negative correlation between anxiety score and overall SWB score ($P = 0.200$) and EWB ($P < 0.001$), but no significant correlation with RWB. Employment showed a significant positive correlation with overall SWB ($P < 0.001$), EWB ($P < 0.001$) and RWB ($P < 0.001$). However, there were no significant correlation found between depression score and other demographic factor.

Conclusion: This study found that anxiety and employment is significantly associated with spiritual well-being but depression and other demographic factors has no impact on the spiritual well-being of female cancer patients who are in remission.

Supervisor:

Professor Dr Hasanah Che Ismaili

Co-Supervisors:

Associate Professor Dr Asrenee Ab Razak

Dr Venkata Murali Krishna Bhavaraju

CORRELATION OF VASCULAR STENOSIS WITH HEMODIALYSIS PARAMETERS IN NATIVE ARTERIO-VEIN FISTULA (AVF), PRE AND POST PERCUTANEOUS TRANSLUMINAL ANGIOPLASTY

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Introduction: Stenosis and thrombosis of Arterio-Venous Fistula (AVF) has been an ongoing problem in hemodialysis patients. Early treatment by Percutaneous Transluminal Angioplasty (PTA) helps in maintaining AVF patency. However, how much PTA would improve the hemodialysis function was still questionable and only few literatures discussed on this matter. Hence, we performed a study on "Correlation of Vascular Stenosis with Hemodialysis Parameters in Native Arteriovenous Fistula (AVF), Pre and Post Percutaneous Transluminal Angioplasty".

Objective: To determine association between percentage of residual stenosis with hemodialysis success.

Methodology: A total of 47 patients underwent Percutaneous Transluminal Angioplasty (PTA) in AMIEN Unit HUSM from June 2014 till October 2015; 14 were excluded and 19 lost to follow up leaving 14 subjects to study. All measurements of stenosis diameter were made from the PACS system whereas hemodialysis parameters were gathered through phone call to the subjects' regular hemodialysis centre.

Results: This study has revealed a weak correlation between percentage of stenosis with blood pump flow rate (Qb) in pre and post PTA. No correlation between percentage of stenosis with venous dialysis pressure (Vp) in pre and post PTA. The achieved technical success was 57.1% ($P = 0.001$).

Conclusion: There is weak correlation between degree of stenosis with blood pump flow rate (Qb) but not observed in venous dialysis pressure (Vp).

Supervisor:

Dr Juhara Haron

Co-Supervisor:

Associate Professor Dr Azreen Syazril

THE APPENDICEAL INTRALUMINAL DIAMETER-COMPARISON WITH OTHER ESTABLISHED PARAMETERS IN CT SCAN ABDOMEN OF ACUTE APPENDICITIS

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MMed (Radiology)

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Introduction: Acute appendicitis is one of the commonest acute surgical emergency in Malaysia. Due to unpredictable clinical course of appendicitis, CT scan of abdomen is indicated in equivocal case. However, there are some false positive cases documented in CT scan of abdomen to diagnose appendicitis.

Objective: The purpose of this study was to assess the usefulness of appendiceal intraluminal diameter in diagnosing acute appendicitis based on Computed Tomography (CT) of Abdomen.

Patients and Methods: We retrospectively identified 36 patients with histopathological examination proven appendicitis as appendicitis group and 36 patients who underwent CT abdomen without appendicitis as control group. We measured CT findings of the appendiceal intraluminal (inner wall-to-inner wall) diameter, appendiceal outer wall to outer wall diameter, appendiceal intraluminal maximum fluid depth and appendiceal intraluminal air.

Results: There was statistically significant difference in the measurement of intraluminal appendiceal diameter at 5 mm from the appendiceal tip, at mid appendix and at the base of the appendix in two groups ($P < 0.001$). There is statistically significant difference in the measurement of maximum intraluminal appendiceal fluid depth in both groups ($P < 0.001$). There was no statistically significant difference in the measurement of intraluminal appendiceal air in both groups ($P > 0.05$). There was excellent direct correlation between intraluminal appendiceal diameter at the mid part and appendiceal outer wall diameter in the appendicitis group ($P < 0.05$). There was excellent correlation between intraluminal appendiceal maximum fluid depth and appendiceal outer wall diameter in appendicitis group ($P < 0.05$). ROC analysis showed appendiceal intraluminal diameter to diagnose

appendicitis was more than 1.70 mm at 5 mm from the appendiceal tip, 1.95 mm at mid portion of appendix and 1.75 mm at the base of appendix. There was excellent correlation between the intraluminal appendiceal diameter (inner-to-inner wall) with intraluminal appendiceal maximum fluid depth in HPE proven appendicitis group ($P < 0.05$).

Conclusion: The appendiceal intraluminal diameter measurement is a useful diagnostic CT values in diagnosing appendicitis.

Supervisor:

Dr Norzila Tendot Abu Bakar

Co-Supervisors:

Dato Dr Hj Sahwah bt Hashim

Dr Phuah Hooi Fang

INNER EAR MORPHOMETRY ON HIGH RESOLUTION COMPUTED TOMOGRAPHY IN PATIENTS WITH SENSORINEURAL HEARING LOSS

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Introduction: Structural abnormality of inner ear structures found in high resolution CT scan in the patient with sensorineural hearing loss (SNHL) is well known, however this abnormalities only seen in 25% of the patients. Recent developments in CT image acquisition raised the hypothesis that subtle different in the size of inner ear structures can be detected by measuring this structures on High resolution CT image. This can help the physicians in early diagnosis of SNHL.

Objectives: To compare the cochlear, vestibular and lateral semicircular canal measurements between patients with sensorineural hearing loss (SNHL) patient and normal subjects using high resolution Computed Tomography (HRCT).

Materials and Methods: A retrospective study was conducted from May 2012 till August 2015 in the Department of Radiology, Hospital Universiti Sains Malaysia. Patients with sensorineural hearing loss who was referred for computed tomography of the temporal bone were selected in the study group. All scans were performed on Siemens 128-slices CT scanner Somatom Definition 128-slice with high-resolution scanning protocol. All the images were reconstructed to bone window. Patient who had computed tomography of the temporal bone for other indications with normal contralateral ear were taken as a control group. Three inner ear structures (vestibular width, cochlear basal turn and lateral semicircular canal bony island width) were measured on axial image on diagnostic workstation). The measurements were repeated three times and average of these measurements were taken. Measurements were randomly selected and validated by an experienced radiologist to minimize bias.

Results: Fifty ears from 28 patients with SNHL (22 patients with bilateral disease and 6 patients with unilateral) were included in this study. Gross abnormality of inner ear detected on HRCT in 5 ears (3 patients) of SNHL were excluded. A total of 45 ears were selected in both study and control groups. Twenty-five ears from patients with SNHL were male patient and 20 ears were female, same as control group. Age range for patients with SNHL was 2 to 23 years old with mean of 9.98 years old. The age range for control group was 2 to 76 years old with mean of 29.55 years. The mean (standard deviation) width of cochlear was 0.190 cm (0.017 cm), vestibular was 0.330 cm (0.039 cm) and lateral semicircular bone island width was 0.362cm (0.566 cm) of patients with SNHL. There were no significantly different of mean of these measurements with control group (P -value > 0.05).

Conclusions: The morphometry of cochlear, vestibular and lateral semicircular bone island width are not reliably differentiating between SNHL and non-SNHL patients.

Supervisor:

Associate Professor Dr Mohd Ezane Aziz

MRI EVALUATION OF THE EFFECT OF TUALANG HONEY IN BREAST TISSUE AMONG POST-MENOPAUSAL BREAST CANCER PATIENT TREATED WITH ANASTROZOLE IN HUSM

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Introduction: Adjuvant treatments with anastrozole or letrozole are not only associated with side effects but also cause a decrease in background parenchymal enhancement (BPE) among postmenopausal breast cancer survivors. Tualang honey (TH) is reported to ameliorate the toxic effects of carcinogens.

Objective: To investigate whether the combination treatment with Tualang honey (TH) influences the background parenchymal enhancement (BPE) at breast magnetic resonance imaging (MRI) in post-menopausal women with history of breast cancer treated with anastrozole.

Methodology: A total of 22 patients were recruited from the Oncology Clinic, Hospital Universiti Sains Malaysia, Kelantan. The patients were divided into the control (anastrozole 1 mg daily) and intervention (anastrozole 1 mg daily + TH 20 mg daily) groups. The inclusion criteria were postmenopausal women with stage I, II, or III unilateral breast cancer; with estrogen receptor (ER)-positive and/or progesterone receptor (PgR)-positive disease; and who received anastrozole treatment for one year or less. The BPE of the contralateral breast before and six months following treatment was compared using the sign test.

Results: There was a decrease in BPE in 10% of the women ($P = 0.317$) who received only anastrozole, which

resulted in a change of BPE category from moderate to mild. However, the combination of anastrozole and TH evoked a decrease in BPE in 42% of the patients ($P = 0.034$), among which BPE decreased by one category of assessment in four women and by two categories of assessment in one woman.

Conclusions: The combination of TH and anastrozole is more efficacious than anastrozole alone in decreasing breast BPE of postmenopausal women with ERpositive breast cancer. These findings support the medicinal value of TH as an adjuvant treatment to anastrozole.

Supervisor:

Dr Juhara Haron

Former Supervisor:

Dr Nik Munirah Nik Mahdi

Co-Supervisor:

Professor Gan Siew Hua

RIGHT AND LEFT VENTRICULAR DIMENSIONS WITH 3 TESLA CARDIAC MAGNETIC RESONANCE IMAGING IN HEALTHY VOLUNTEERS: AN EXPLORATORY PILOT STUDY

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MMed (Radiology)

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Introduction: Cardiac magnetic resonance imaging (CMR) is a rapidly evolving field in medicine and it has a very promising future. Cardiac diseases are known to alter the cardiac dimensions such as chamber size, ventricular wall thickness, mass, contractility as well as ejection fraction. Studies on the cardiac dimensions are very important since they provide reference values for clinicians which facilitate the management of their patients. Among the current imaging modalities, MRI appears to be the best option for cardiac dimension assessment. Many international studies have been able to produce database on cardiac dimensions in relation to age, gender and risk factors using 1.5-Tesla (1.5 T) CMR. However, no studies have presented normal data at 3 Tesla scanner.

Objective: To evaluate the right and left cardiac ventricular dimensions in healthy volunteers with 3-Tesla magnetic resonance imaging.

Patients and Methods: A total of 50 volunteers (25 males, 25 females) without cardiovascular diseases were evaluated with 3T magnetic resonance scanner, using a steady-state free precession sequence (balanced turbo field-echo).

Results: Mean age was 28.04 for male and 30.12 for female. Right and left ventricular volumes and mass were larger in males than females. RV EDV 153.83 ± 22.67 mL versus 144.46 ± 14.92 mL, RV ESV 67.58 ± 14.44 mL versus 47.58 ± 9.49 mL, RV SV 86.24 ± 11.74 mL versus 66.97 ± 8.57 mL, RV mass 35.88 ± 8.18 g versus 26.29 ± 5.26 g. LV EDV

129.05 ± 18.3 mL versus 105.44 ± 13.91 mL, LV ESV 46.65 ± 9.56 mL versus 37.92 ± 8.39 mL, LV SV 82.42 ± 12.02 mL versus 67.52 ± 8.33 mL, LV mass 107.04 ± 16.55 g versus 65.92 ± 8.49 g; ($P < 0.05$ for all). There was no difference in ejection fraction of right and left ventricles between the genders. Males showed significant decrease in volume indices for both ventricles with age, while female values demonstrated no significant correlation.

Conclusion: We have produced the local database for right and left ventricular dimensions in accordance with gender and age using 3T magnetic resonance imaging.

Supervisor:

Dr Khairil Amir Sayuti

Co-Supervisors:

Associate Professor Dr Mohd Shafie Abdullah

Dr Wan Yus Haniff

THE ASSOCIATION BETWEEN INTRACRANIAL HAEMORRHAGE AND SKULL FRACTURE IN TRAUMA PATIENTS AT THE HOSPITAL UNIVERSITI SAINS MALAYSIA (HUSM)

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MMed (Radiology)

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Introduction: Majority of fatal trauma cases are caused by head injury. The most common cause of head injury is motor vehicle accident. Other causes include assault and fall from height. Skull fracture may or may not be accompanied by brain injury. Not all head injuries are life threatening. Some fatal head injuries may occur without the presence of skull fractures. Previous studies showed that the incidence of intracranial haemorrhage was high in patients with skull fracture compared to patients without skull fracture.

Objective: The main objective of this research is to study the association between skull fracture and intracranial haemorrhage in trauma patients and the association between types of skull fracture and types of intracranial haemorrhage.

Methodology: This was a retrospective study on the CT scan for head trauma performed between June 2014 until December 2014. A total of 151 patients with head injury aged 18 years old and above were included in this study. Ethical approval was obtained from The Human Research Ethics Committee of Universiti Sains Malaysia (JEPeM). Plain CT brain images were assessed using Picture Archiving Communication System (PACS). The findings of skull fracture and intracranial haemorrhage were documented. The statistical analysis was performed using SPSS statistical program (ISM SPSS software version 21).

Result: Out of 151 patients, 112 (74.2%) were male and 39 (25.8%) were female. Majority of the head trauma cases were caused by motor vehicle accident [$n = 126$ (83.4%)]. Intracranial haemorrhage was found in 64 (98.5%) of the 65

patients with skull fracture, compared with 26 (30.2%) of the 86 patients without skull fracture. There was significant association between skull fracture and intracranial haemorrhage (P-value < 0.001). The most common type of fracture was linear fracture. There was significant association between linear skull fracture and extradural haemorrhage (P-value = 0.011) and between comminuted skull fracture and subdural haemorrhage (P-value = 0.001).

Conclusion: There was significant association between skull fracture and intracranial haemorrhage, linear skull fracture and extradural haemorrhage and comminuted skull fracture and subdural haemorrhage.

Supervisor:

Dr Win Mar @ Salmah Jalaluddin

Co-Supervisor:

Associate Professor Dr Mohd Shafie Abdullah

DIAGNOSTIC PERFORMANCE OF SOLID BREAST LESIONS SHEARWAVE ELASTOGRAPHY WITH HISTOPATHOLOGICAL CORRELATION

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MMed (Radiology)

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Introduction: Shearwave elastography (SWE) is an emerging technique of obtaining quantitative tissue elasticity data during breast ultrasound examinations.

Objectives: The aim of this study were (1) to determine the mean of maximum SWE value of malignant and benign breast lesions (2) to determine the sensitivity and specificity of SWE correlating with histopathology (3) to determine the agreement between SWE and greyscale ultrasound in differentiating malignant and benign breast lesions.

Methodology: Using the Aixplorer® ultrasound system 174 solid breast lesions were identified using us. For each lesion, quantitative elasticity was measured and BI-RADS categories assessed with greyscale. SWE maximum value was calculated and compared with the previously published cut-off value (COV). SWE measurements were correlated with histology results. Greyscale images according to the American College of Radiology Breast Imaging Reporting and Data System (BI-RADS) categories 1–3 were taken as benign while categories 4–6 were classified as malignant.

Results: Of the 174 breast lesions, 149 (85.6 %) were benign and 25 (14.4%) were malignant revealed by histology. The mean of maximum elasticity values were significantly higher in malignant lesions (98.00 kPa ± 50.39) than benign lesions (28.16 kPa ± 17.22), ($P < 0.001$). The optimal SWE cut-off value was 42.58 kPa with sensitivity and specificity of SWE were 84.0% and 81.0%, positive predictive value (PPV) and negative predictive value (NPV) were 42.0% and 97.0% respectively. The AUC of ROC curve was 0.864 for greyscale ultrasound, 0.824 for SWE, and 0.773 for combined greyscale

and SWE. There was moderate agreement between results from BI-RADS with COV of 3.5 and SWE of the three COVs. The Kappa agreement between BI-RADS and SWE was increased from 0.458 to 0.550, as the SWE COV increased from 42.58 kPa to 50.0 kPa and 80.0 kPa. Overall, the highest agreement was obtained between BIRADS (COV = 3.5) and SWE (COV = 80 kPa).

Conclusions: Malignant breast lesions have higher maximum SWE value compared to benign lesions. The overall diagnostic performance of combination grey scale ultrasound and SWE was not significantly better than that of ultrasound alone. The optimum COV of SWE obtained from this study was lower than the previous studies, however one might choose higher COV in order to increase the specificity of this potential adjunct screening and diagnostic tool particularly in BI-RADS III or IV breast lesion.

HEIGHT ESTIMATION USING 2ND & 3RD METACARPAL BONE AMONG ADULT MALAY POPULATION ATTENDING HOSPITAL UNIVERSITI SAINS MALAYSIA (HUSM)

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Background: Estimation of individual's stature is an important parameter in forensic examination. Problems encountered in cases of mass disaster or assaults where the body was dismembered. Many studies have been encountered to determine stature by taking measurement of the long bones. The relationship between specific bone and proportion can be used to help in the process for identification in the absence of complete skeleton from a crime scene. In general, there is a scarcity of literature regarding the estimation of stature (height) among Malaysia population. Up to date there was no published study regarding height estimation among Malay population in Kelantan using metacarpal bone parameters. The regression formulae are population specific. Therefore, the aim of the present study was to set a general formula of stature estimation for both adult males and females using anthropometrical measurements of second and third metacarpal bones using AP hand radiograph among Malay adults attending Hospital Universiti Sains Malaysia.

Objectives: The general objective of this study was to estimate stature from the morphology of left hand radiograph among adult Malay population attending Hospital Universiti Sains Malaysia.

Patients and Methods: This was a cross-sectional study among adult Malay Kelantan population attended HUSM for posterior anterior (PA) view radiograph of left hand. A total of 124 subjects with age ranged from 19 to 60 years old were included. The length and width of the normal 2nd and 3rd metacarpal bones together with their heights were measured. Data entry and analysis were performed using Statistical Package for Social Sciences (SPSS version 22) software programme. The descriptive demographic data were

measured using independent *t*-test. The correlation between stature and parameters of metacarpal bones were performed using Pearson Correlation. The prediction of stature from the parameters of metacarpal bone were using simple linear regression and multiple (stepwise) regression analysis.

Results: Statistical analysis revealed that parameters formale subjects were higher than the female subjects ($P < 0.001$). There was significant correlation between all the parameters of second and third metacarpal bones in female subjects (P value < 0.001 and P value 0.05). For male subjects, significant correlation noted between stature and the length of second and third metacarpal bone (P value < 0.001). Using simple linear regression analysis, the standard error of estimate (SEE) ranged from ± 3.94 cm to ± 4.97 cm for males and ± 3.92 cm to ± 4.55 cm for females. From the simple linear regression analysis, four regression equations were established for each gender. The multiple linear regression analysis revealed smallest SEE from the second metacarpal bone length for male (SEE ± 3.94). For female subject the multiple linear regression analysis revealed smallest SEE revealed from the second metacarpal bone length and width (SEE ± 3.78 cm). Therefore, one multiple regression equation was established for each gender using the second metacarpal bone parameter.

Conclusion: It was concluded that stature can be determined successfully using 2nd metacarpal bone parameters which were the length for male and both length and width for female among adult Malay population in Kelantan.

CORRELATION OF LIVER ELASTOGRAPHY WITH LIPID PROFILE, LIVER FUNCTION TEST, AND HbA1c IN TYPE II DIABETES IN HOSPITAL UNIVERSITI SAINS MALAYSIA

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is a range of liver disorders which ranges from simple accumulation of fat in the hepatocytes (steatosis) to macrovesicular steatosis, periportal and lobular inflammation (steatohepatitis). The current gold standard to diagnose liver diseases is biopsy, however this has two major problems: it is dependent on the sampling area, which may cause an evaluation error in the case of mild fatty liver, and it is an invasive technique which carries a morbidity rate of 1%–5% and a mortality rate of 0.01%–0.1%. Non-invasive imaging tools such as shear wave elastography has been proven to be useful for screening and categorising of chronic liver disease, however, further evaluation of this tool is needed in different population.

Objectives: This study aimed to assess the associations among liver elastography, lipid profile, liver function test and HbA1c among type II diabetic patient in Hospital Universiti Sains Malaysia, in which (i) the prevalence and incidence rate of NAFLD and liver fibrosis/cirrhosis among type II diabetic

patient in Hospital Universiti Sains Malaysia was determined, respectively; (ii) the mean values of the blood lipid profile, liver functions test and HbA1c among patient with and without NAFLD were compared; and (iii) the associations between degree of liver elasticity; and blood lipid profil, liver function test and HbA1c were investigated.

Patients and Methods: Patients were recruited from Diabetic Clinic, HUSM. Only patients who fulfilled the selection criteria and provided written consent were enrolled into this study. The Medical record of the patient was provided by the clinic. Liver elastography was performed in Radiology Department, HUSM by Supersonic Imagine Using Shear Wave Elastography (Siemens Acuson Antares-Premium Edition, Camberley, UK), equipped with Aixplorer Multiwave. Data were recorded and analysed using SPSS version 22.0.

Results: The prevalence of NAFLD among participant with DM type II was 87%, while the incidence rate of liver fibrosis among the patients with NAFLD was 11.7% (8/68). The distribution of METAVIR score among T2DM patients were F0 (60/68), F1 (7/68), and F2 (1/68). The result revealed very poor correlation between SWE values and part of the study parameters, which includes HDL, LDL, TG, AST and HbA1c ($P > 0.05$). However, there were two parameters showed significant weak association between SWE values; TC ($r = 0.283$; $P = 0.019$) and ALT ($r = 0.252$; $P = 0.038$).

Conclusion: This study had determined to the prevalence of NAFLD and incidence rate of liver fibrosis among T2DM patients admitted to HUSM. The prevalence of NAFLD was higher but the incidence rate of liver fibrosis was lower compared to previous study. Further research with inclusion of parameters like race, AST/ALT ratio and advanced fibrosis patients to strengthen the finding of current conclusion.

SEX AND HEIGHT DETERMINATION BY FORAMEN MAGNUM MORPHOMETRY USING MULTIPLANAR RECONSTRUCTION (MPR) CT SKULL IMAGES

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Introduction: Radiological forensic is a specialised area of medical imaging using radiological technique for identification of human and also for ante or post mortem purposes. Radiological imaging of human remains become important in forensic field in determining sex, age, ethnicity, stature and in fact, cause of death.

Objective: The aim of this study is to determine the relationship between sex and height with foramen magnum (FM) morphology using multiplanar reconstruction (MPR) computed tomography (CT) scan of the skull.

Material and Method: Total of 104 CT scan of the skull were selected using randomised sampling, i.e. 52 samples for each gender. Images were analysed using PACS viewing application on grey-scale monitor. Seven variables of FM

morphology were measured on MPR skull images. Comparison between FM morphology and sex, and correlation with height were analysed using statistical test.

Results: There is statistically significant difference between males and females for all measurements, with P -value < 0.05 . The males have larger value than female, in all FM measurements. However, fair degree of correlation between FM parameters and height ($0.257 < r < 0.495$; $P < 0.05$) was observed in this study.

Conclusion: FM measurements are very useful in studying sexual dimorphism in forensic investigations, but less helpful to determine height of an individual.

Supervisor/Co-Researcher:

Associate Professor Dr Mohd Ezane bin Aziz

GRADING OF SUPRATENTORIAL GLIOMAS USING MR DIFFUSION TENSOR IMAGING

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Introduction: Gliomas, being the most common primary brain tumours are usually located at the supratentorial regions in adults. They are classified into low grade (grade I and II) and high grade (grade III and IV) based on WHO classification. Conventional MR imaging is essential to characterise the tumour morphology but lack accuracy in determining the grade of tumours. Advanced MRI technique such as DTI has emerged over the past decades as an additional method to further evaluate the brain tumours at the microstructural and physiological levels. Accurate grading of gliomas is important to determine the mode of treatment and sequences of management for patients.

Objectives: This study aims at retrospectively determines whether FA or ADC values at 3-Tesla MR DTI are significantly different between low grade and high grade supratentorial gliomas. FA and ADC values between the gliomas and normal cerebral hemisphere are also being compared.

Patients and Methods: Sixteen patients aged 18 years old and above with newly diagnosed supratentorial gliomas with histopathological results were included. Their MRI with DTI sequence were retrieved from PACS into extended MR workspace for data analysis. DTI data was co-registered with post-gadolinium T1 weighted images. Four ROIs were drawn at the anterior, posterior, lateral and medial margins of tumours. ROIs were also placed at the contralateral NAWM of the opposite lobe. Comparison of FA and ADC values between low grade and high grade gliomas, and between gliomas with contralateral NAWM was performed using Mann-Whitney U test and Wilcoxon signed ranks test respectively.

Results: There was significant difference between FA of low grade and high gliomas, and between FA and ADC of gliomas and contralateral NAWM ($P < 0.05$). No statistical significant difference was found between the ADC of low grade and high grade gliomas ($P = 0.129$).

Conclusion: FA values generated from DTI can be used to grade gliomas. ADC values of low grade gliomas are higher than that of high grade gliomas but are not statistical significantly different.

Supervisor:

Dr Win Mar @ Salmah Jalaluddin

CORRELATION OF RISK FACTORS AND ASPECT SCORES IN PATIENTS WITH MIDDLE CEREBRAL ARTERY ISCHAEMIC STROKE IN HUSM

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Introduction: Stroke has becoming a leading cause of death in recent years. As the population ages, its incidence grows. Studying relationship between various risk factors and severity of stroke by using ASPECTS would be helpful in predicting patients' outcome after suffering a stroke. By realising the risk factors that contribute to severe stroke, the prevention of these risk factors or their control is of upmost important in management of stroke in primary care. ASPECTS has been shown as a more accurate, reliable, reproducible and objective measures in quantifying the severity of stroke.

Objectives: The aims of this study were to correlate between GCS and ASPECTS. Besides, this study also aims to correlate the risk factors (age, gender, fasting blood sugar level and fasting lipid profile) of acute stroke patients with ASPECTS.

Patients and methods: Patients who were admitted for stroke were identified from medical wards. Their admission GCS, fasting blood sugar, fasting lipid profile and ASPECTS were traced and documented.

Results: There was good positive correlation between GCS and ASPECTS ($r = 0.615$, $P < 0.001$). On univariate analysis, only GCS was statistically significant (OR 0.076; 95%CI 0.011 to 0.515, $r^2 = -2.58$, $P < 0.05$). One unit increment in GCS has 92.4% lesser odds to have worse ASPECTS when other confounders were not adjusted. However, multivariate analysis showed none of the variables was statistically significant.

Conclusion: This study provided a local data regarding stroke in this region of our nation. All risk factors included in this study (age, gender, fasting blood sugar level and fasting lipid profile), showed no correlation with severity of stroke. However, the prevalence of high fasting blood sugar, total cholesterol and LDL level were high among the stroke patients.

Supervisor:

Dr Salmah @ Win Mar

Co-Supervisor:

Dr Sanisah Abdul Halim

ASSOCIATION BETWEEN RISK FACTORS OF LOWER LIMB ARTERIAL STENOSIS WITH OUTCOME OF ANGIOPLASTY IN HOSPITAL UNIVERSITI SAINS MALAYSIA (HUSM)

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Purpose: To evaluate mean Bollinger score for lower limb among patients underwent angioplasty for peripheral arterial disease in Advanced Minimally Invasive Endovascular and Neurointervention Unit (AMIEN) HUSM and to determine the association between overall Bollinger score and other factors (underlying hyperlipidaemia, underlying hypertension, smoking) and outcome of angioplasty.

Method: Retrospective study on 35 patients who underwent angioplasty of the lower limbs in Advanced Minimally Invasive Endovascular and Neurointervention Unit (AMIEN) HUSM from January 2011 until May 2015. Pre-angioplasty images were scored using the Bollinger score and the outcome of angioplasty was categorised into successful and failed. Medical history of hypertension, hyperlipidaemia, and smoking were obtained from the medical record. Data were analysed using ISM SPSS software version 21 by using descriptive analysis for demographic data and Fisher exact test as statistical analysis.

Result: A total of 35 patients were included in our study and 21 (60%) were females. Twenty eight (80%) were hypertensive while 18 (51.4%) was diagnosed as having hyperlipidaemia. Only 8 (22.9%) patients were smokers. Mean Bollinger scores were higher for infrapopliteal arteries in comparison with superficial femoral artery. However, there was no statistical significant association between outcome of angioplasty with Bollinger score ($P = 0.156$), hypertension ($P > 0.95$), hyperlipidaemia ($P > 0.95$) and smoking ($P = 0.140$).

Conclusion: The infrapopliteal arteries were worse affected in peripheral arterial disease. There is no correlation of hypertension, hyperlipidaemia and smoking with outcome of angioplasty.

Supervisor:
Associate Professor Dr Mohd Shafie Abdullah

Plastic Surgery

PALATAL CLEFT DIMENSION IN PATIENTS WITH UNILATERAL CLEFT LIP AND PALATE AMONG ETHNIC MALAYS: AN IMPLICATION ON SURGICAL OUTCOMES

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Introduction: Comparative studies in cleft lip and palate patients between different countries have been difficult due to regional variations of cases, different management protocols, and racial and ethnic variation that is intrinsic to the population. In the state of Kelantan, which is largely populated by ethnic Malay, it has higher than average national incidence of patients with cleft lip and palate. This presented our centre a unique opportunity to characterise this population patient group, and investigate their cleft severity based on palatal fistula incidence and velopharyngeal insufficiency.

Objectives: A retrospective study was designed to assess and evaluate the demographic factors that may contribute to their clefts' incidence and severity using cleft anthropometric measurements.

Methods and Patients: The cleft anthropometric data was analysed to assess its effect on cleft treatment outcomes. A total of 100 patients who had palatoplasty between 2000 and 2012 were recruited and their record was reviewed.

Results: Our results revealed that age and weight at palatoplasty, gender, cleft sidedness and family history did not significantly influence the cleft severity in our population. Using cleft anthropology, we found that the rate of palatal fistula incidence was significantly affected by posterior palatal arch width (> 35 mm) whereas the presence of velopharyngeal insufficiency was significantly affected by posterior cleft width (≥ 12 mm) and the relative width of palatal shelves.

Conclusions: Therefore, cleft anthropometric measurement is essential to accurately determine cleft severity and thus, their treatment outcomes. The data obtained from this study forms invaluable information to improve the local cleft team's understanding, and advances their management of cleft patients in this region.

Supervisor:
Dr Wan Azman Wan Sulaiman

Co-Supervisor:
Sarina bt Ahmad

EIGHT YEARS COHORT STUDY ON SHORT TERM OUTCOME OF SUTURELESS THYROIDECTOMY IN HOSPITAL RAJA PEREMPUAN ZAINAB II

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Introduction: Thyroid surgery is one of the most common surgery performed now days with very low complication rates. The introduction of vessel sealing technology have assisted surgeon in securing hemostasis in limited operative field and shortened the operative time. However, surgeons are still skeptical in using this technology as there are many

important structures in close proximity to the thyroid gland. Therefore, this study is performed to evaluate the outcome of sutureless thyroidectomy as compared to conventional knot tying technique.

Objective: The aim of this study is to evaluate the feasibility and safety of using sutureless technique in performing thyroidectomy over conventional thyroidectomy.

Methods: This is a retrospective cohort study of case record of patients who underwent total thyroidectomy from 1 January 2007 to 31 December 2014 in Hospital Raja Perempuan Zainab II, Kota Bharu, Kelantan. Those who met the inclusion criteria will be recruited in the study. Patients were divided into two groups based on conventional or sutureless thyroidectomy. The short term outcome post thyroidectomy were studied. The data were analysed using Statistical Package for the Social Sciences (SPSS).

Results: Total of 495 patients were included in this study aged between 8 and 76 years old with mean age of 44.7 (13.29) years. It comprises 70 males and 425 female. Majority were Malays (96.6%), followed by Chinese (2.2%) and Indian (0.4%). From the total of 495 patients, 71 of them underwent sutureless thyroidectomy and 424 patients underwent conventional thyroidectomy. The mean operative time was significantly lower in the sutureless group (100.71 versus 121.73 min, $P < 0.01$). There were no significant difference in the post-operative outcome of sutureless thyroidectomy compared to conventional thyroidectomy in term of transient hypocalcemia (21.1% versus 25.7%), permanent hypocalcemia (0% versus 3.1%), transient recurrent laryngeal nerve injury (0% versus 2.8%), permanent recurrent laryngeal nerve injury (0% versus 1.4%), hematoma (0% versus 1.2%), reoperation (0% versus 0.2%), surgical site infection (0% versus 0.5%) and tracheostomy (0% versus 0.2%). There were no statistical significant comparing the post-operative length of stay between these 2 groups.

Conclusion: Post-operative complications in sutureless thyroidectomy were similar if not better than conventional thyroidectomy. Therefore, sutureless thyroidectomy can be safely practiced as it have the advantage of shorter operative time thus indirectly improving the operating room efficiency.

Supervisor:

Miss Wan Zainira bt Wan Zain

Co-Supervisors:

Mr Imisairi bin Ab Hadi

Dr Wan Nor Arifin Wan Mansor

A RETROSPECTIVE STUDY OF RISK FACTORS FOR PROLONGED MECHANICAL VENTILATION AFTER CORONARY ARTERY BYPASS GRAFTING (CABG) SURGERY IN HOSPITAL UNIVERSITI SAINS MALAYSIA KUBANG KERIAN KELANTAN

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Introduction: Prolonged mechanical ventilation (PMV) after CABG surgery increases airway and lung trauma ultimately increases hospitalisation costs. Many has attempted in promoting early extubation as a mean to reducing intensive care and hospitalisation costs. A few models have been developed aim to identify patients at risks of PMV but none of the studies had a local data. We studied the characteristics and variables in a relatively small cardiothoracic unit whereby patients population were more homogenous and operated by a single surgeon at Hospital Universiti Sains Malaysia (HUSM) and compare previously considered risk factors.

Objective: The main objective of this study is to identify patient characteristics and operative variable risk factors that predict PMV in patients undergoing coronary artery bypass grafting (CABG) in Hospital Universiti Sains Malaysia from January 2009 to December 2013.

Patients and Methods: Patients were divided into normal ventilation and PMV groups. Perioperative characteristics and variables were retrospectively analysed. Elapsed time between CABG and extubation of more than 24 hours was defined as prolonged mechanical ventilation. Risk factors affecting the duration of intubation will be included in univariate analysis and subsequently run into logistic regression model.

Results: There were 140 patients enrolled, only twenty four (17.1%) patients required prolonged mechanical ventilation (PMV) of more than 24 hours. Through univariate and logistic regression analysis, the independent risk factors for prolonged mechanical ventilation after CABG were renal dysfunction (OR = 12.90; 95% CI 1.33–124.99), NYHA class IV (OR = 7.10; 95% CI 1.33–37.93), recent myocardial infarction (OR = 8.12; 95% CI 1.81–36.38) and post-operative hemorrhage (OR = 25.1; 95% CI 4.73–132.76). The study also demonstrates significant higher length of hospital stay in PMV group. For 1 day additional hospital stay, it increases the risk of PMV by 1.18 times (95% CI 1.05–1.31) when adjusted to other factors.

Conclusion: Renal dysfunction, NYHA class IV, recent MI and post-operative hemorrhage were identified as the 4 independent risk factors for PMV after CABG surgery. Every one day of PMV predisposed patients to an increase day of hospital stay.

Supervisor:

Dr Mohd Nor Gohar

Co-Supervisor:

Professor Dr Mohamad Ziyadi Haji Ghazali

THE RELATIONSHIP OF P53 GENE MUTATION WITH CLINICOPATHOLOGICAL CHARACTERISTIC IN BREAST CANCER

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Introduction: P53 is a tumour suppressor gene. In breast cancer, p53 gene mutation were noted with frequency of about 30% (ranged 15%–71%) and associated with poor prognosis. This study was performed to determine p53 mutation association with clinicopathological characteristic in breast cancer and to assess the suitability of patients' serum to detect p53 auto-antibody.

Objectives: The aims of this study are to determine p53 mutation association with clinicopathological characteristic in breast cancer and to assess accuracy of patients' serum in detecting p53 auto-antibody.

Methods: This study conducted in Hospital Seberang Jaya and Institut Perubatan dan Pergigian Termaju, Universiti Sains Malaysia. Sixty four breast cancer patients with available fresh breast cancer tissue that been kept under -80 °C and with complete clinicopathological data involve in this study. These fresh breast tissues DNA extracted and 10 samples sent for DNA sequencing. The remaining 54 samples proceeded with Polymerase Chains Reaction analysis based on the result from DNA sequencing. The serum of these patients was also taken for p53 auto-antibody study using ELISA method.

Results: The mean age of the patients in this study was 52.45±9.51 years. Most of the patients were Malay with 67.2% followed by Indian and Chinese with 17.2% and 15.6% respectively. About 51.6% of these patients undergone CT scan staging and 14.1% has distant metastases. p53 gene mutation prevalence showed rs1042522 only has 15.7% mutation. There was 54.7% Deletion A and 45.3% Wild Type A detected in rs59758982, 87.5% Deletion A and 12.5% Wild Type A in rs35069695 and 92.2% recorded for Deletion GAA in rs376546152. There was no significant result between these mutation with breast cancer molecular classification and breast cancer aggressiveness except for rs59758982 shows significant result with P -value 0.04 ($P < 0.05$). In regards on for p53 serum auto antibodies, 20.3% of the patients noted to be positive but it has no significant association with p53 gene mutations.

Conclusion: In this study, tissue p53 genetic mutation has no significant association with clinicopathological characteristic of breast cancer and the use of serum p53 auto antibody as biomarkers is inconclusive.

Supervisor:

Dato' Dr Imran Abd Khalid

Co-Supervisors:

Dr Mohd Nor Gohar Rahman

Associate Professor Dr Badrul Yahaya Hisyam

A 10 YEAR RETROSPECTIVE EVALUATION OF BOEY SCORE IN PATIENTS WITH PERFORATED PEPTIC ULCER IN HOSPITAL UNIVERSITY SAINS MALAYSIA (JANUARY 2004–DECEMBER 2014)

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Introduction: For decades, perforated peptic ulcer (PPU) was treated without any risk stratifications though it carries high risk of mortality. Risk stratification is appropriate and imperative to study independent risk factors belonging to patients with particular disease and predict morbidity or mortality.

Objective: The aim of this study is to evaluate the Boey Scores in determining mortality outcome of patients presented with PPU in Hospital Universiti Sains Malaysia, Health Campus, Kelantan.

Patients and Methods: The study population consisted of patients who underwent surgery for PPU during the period of January 2004 until December 2014. The number of patients involved in the study were 82. The medical records were traced from the hospital records department after it was permitted by the Director of the hospital. The relevant socio-demographic, clinical, operative notes and survival status were entered into proforma form. All the data recorded were transferred into SPSS software version 21 and analyzed. Pearson chi-square was used as a statistical test. Significant differences were taken into account if the probability or P -value is equal or less than 0.05.

Results: The mean age of the PPU patients in this study was 68.5. Malays were the predominant race treated for perforated peptic ulcer. Male patients were higher compared to female with a ratio of 2:1. All the risk factors in Boey scores appeared to be statistically significant in predicting mortality except for the delayed treatment with the range of more or less than 24 hours. Apart from these variables, statistics shows age proven to be a significant risk factor in predicting mortality with the p value of 0.02. Statistically, Boey scores were highly significant in predicting mortality with the P -value of < 0.001 . This study recorded patients with risk score of zero, one, two, and three has mortality of 0%, 24%, 44% and 32%, respectively.

Conclusion: Boey scores would be a good scoring system to be used for risk stratification in patients with PPU. Apart from its simplicity, this score statistically proved to be significant in predicting mortality. Age appears to be another statistically proven independent risk factor in this study. However, further studies are needed to study actual outcome in detail.