Case Study

ASSESSING THE ACCURACY OF THE JM-102 TRANSCUTANEOUS BILIRUBIN MEASUREMENT IN DARK SKIN JAUNDICED NEONATES. CASE OF UNIVERSITY TEACHING HOSPITAL, RWANDA

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ABSTRACT

Background: Clinical assessment of neonatal jaundice is inaccurate and results in a significant number of blood tests in otherwise well babies. The number of these blood tests could be reduced, with benefit to the neonates and potential cost savings by using a noninvasive transcutaneous bilirubinometer.
Objective: The aim of our study was to evaluate the accuracy of one of the birubinometer JM-102(Minolta/Hill-Rom Air-Shields ® JM-102), in dark skin term and preterm neonates old less than two weeks compared to the gold standard which is the measurement of serum bilirubin (SBR) and to identify the most informative value of transcutaneous bilirubinometer (TcB) in terms of sensitivity and specificity.
methods: The study included 275 jaundiced neonates who were less than 14 days and consulted neonatology unit of University teaching hospital during the study period. Neonates with severe conditions (hypothermia, respiratory distress, cardiovascular disorders, and neurological disorders) and/or with previous history of phototherapy were excluded from the study.
On these 275 newborns, the Minolta/Hill-Rom Air-Shields ® JM-102 was used to measure the transcutaneous bilirubin and SRB sampling was performed within 30 minutes. All newborns were black skin.
Results: The correlation of the gold standard and the measurements of the TcB Minolta/Hill-Rom Air-Shields ® JM-102 was 74.5 %. Comparing the gold standard with measurements of the TcB Minolta/Hill-Rom Air-Shields ® JM-102, we estimated the area under the Receiver Operating Curve (ROC) to be 0.887 classified as good and a p value of < 0.001 suggesting that the TcB measurement is far better than guessing.
Conclusion: The correlation between TcB measurement and the serum bilirubin measurement was good for the population studied. The TcB measurement using the Minolta/Hill-Rom Air Shields ® JM-102 was found to be useful in detecting infant with hyperbilirubinaemia in dark skin jaundiced neonates.The Minolta JM-102 device could be used as a screening instrument, leading to the avoidance of invasive blood samplings for term and preterm neonates. TcB measurements with the JM-102 bilirubinometer should obviate the need for serum bilirubin levels in dark skin jaundiced newborns, although serum bilirubin measurements are still required when treatment with phototherapy or exchange transfusion is being considered.

Keywords: Newborn - Neonatal jaundice - Neonatal hyperbilirubinemia -Transcutaneous bilirubin measurement - JM-102 bilirubinometer

RESUME

Introduction: L'évaluation visuelle de l'ictère néonatal est imprécise et conduit aux prélèvements sanguins inutiles pour dosage de la bilirubine chez les nouveau-nés qui de part ailleurs sont en bon état général. Le nombre et le coût de ces prélèvements pourraient être réduits par l'utilisation non invasive du bilirubinomètre transcutané.
Objectif: Le but de notre étude était d'évaluer l'utilité du bilirubinomètre JM-102(Minolta/Hill-Rom Air-Shields ® JM-102) chez les nouveau-nés à peau foncée âgés de moins de deux semaines de vie présentant un ictère néonatal. Les mesures fournis par le bilirubinomètre ont été comparés au gold standard qui est le dosage sérique de la bilirubine.
méthodes: L'étude a enrôlé 241 nouveau-nés âgés de moins de 2 semaines présentant un ictère néonatal et 34 nouveau-nés non ictériques. Les nouveau-nés qui étaient en mauvais état général (hypothermique, en détresse respiratoire, présentant des troubles hémodynamiques ou des troubles neurologiques) ou qui avaient été sous photothérapie ont été exclus de l'étude. Le bilirubinomètre transcutané JM-102(Minolta/Hill-Rom Air-Protections ® JM-102) a été appliqué au niveau frontal et sternal et le sang pour dosage de la bilirubine sérique a été prélevé dans les 30 minutes suivant la mesure transcutanée. Tous les nouveau-nés enrôlés dans l'étude étaient à peau foncée.
Résultats: La corrélation des résultats fournis par le bilirubinomètre transcutané et ceux obtenus par le dosage sérique de la bilirubine était de 74,5 %. L'aire en dessous de la courbe ROC (Receiver Operating Cuve) était de 0,887 avec une valeur p <0,001 suggérant que l'évaluation de l'ictère néonatal par le bilirubinomètre transcutané était de loin meilleur que l'évaluation visuelle.
Conclusion: La corrélation entre les résultats fournis par le bilirubinometre transcutané JM 102 et le dosage de la bilirubine sérique était bonne sur la population étudiée. Le bilirubinomètre Minolta JM-102 pourrait être utilisé pour identifier les nouveau-nés ictériques chez lesquels le dosage de la bilirubine sérique devrait être fait en vue d'une photothérapie ou exsanguino-transfusion éventuelle.

Mots clés: Nouveau-né - Ictère néonatal - Hyperbilirubinémie néonatale - Bilirubine par mesure transcutanée - Bilirubinomètre JM-102

INTRODUCTIO

About 50-60% of newborns are estimated to have an episode of jaundice in the first few days of life and six percent of newborns may develop hyperbilirubinemia (> 220 µmol/L); a potential cause of bilirubin encephalopathy: "kernicterus". Clinical evaluation of hyperbilirubinaemia involves visual estimation of jaundice, which is subjective and more inaccurate for several reasons [1,2] and may even be more difficult in black newborns. Serum bilirubin measurement (SBR) is the gold standard for detecting hyperbilirubinaemia. However, measuring SBR in newborns with a concentration below the treatment threshold involves unnecessary blood sampling [1-3] and

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skin puncture collection of blood exposes the neonate to trauma, pain, blood loss and risk of infection.
Bilirubin meters, devices which provide a non-invasive transcutaneous bilirubin measurement have proven as screening tools to be very useful providing a valid estimate of the total serum bilirubin level (TSB) and a recent literature review [4-10] indicate that this device provides measurements within 30–50 µmol/L of the TSB levels and can replace laboratory measurement specially when TSB levels are below 260 µmol/L. The interpretation of the measurements done by the bilirubinometer will vary in function of gestational age, postnatal age and birthweight. Each brand will provide cut off value for hyperbilirubinaemia. TcB can be used in the first 14 days of life. The use of bilirubinometer device may be interesting in neonates with dark skin colour, in whom the jaundice assessment is difficult and therefore delays the diagnosis making these newborns at high risk of kernicterus.
However, little is known about the cut off point for transcutaneous bilirubinometer in dark skin babies [1,11]. One of these devices is the " Minolta/Hill-Rom Air-Shields ® JM-103 ", whose accuracy was evaluated in different newborn race and found the correlation in black infants not as close as in other groups. This device is also available in version JM-102 in our hospital.
This study evaluated the accuracy of the " Minolta/Hill-Rom Air-Shields ® JM-102 " for the evaluation of bilirubin level in comparison with the gold standard in dark skin babies to assess sensitivity for different levels of cut off points.

RESEARCH OBJECTIVES

- Evaluate the accuracy of one of the birubinometer JM-102(Minolta/Hill-Rom Air-Shields ® JM-102), in dark skin term and preterm neonates old less than two weeks of postnatal age compared to the gold standard which is the measurement of serum bilirubin (SBR).

- Identify the most informative value of transcutaneous bilirubinometer (TcB) in terms of sensitivity and specificity.

- Estimate the magnitude of the reduction in SBR measurements in our hospital that we could achieve by adopting TcB with bilirubinometer JM-102 as a screening method in term babies with visually detectable jaundice.

METHODOLOGY

This prospective observational study was carried out in The neonatology Unit of University Teaching Hospital in Rwanda from June 2007 until February 2008.

Sample size calculation:

The number of babies needed to produce an adequate ROC curve was estimated using the Everard's calculations. Assuming the lowest acceptable sensitivity (SN) of 96%, and the specificity (SP) of 85% with confidence intervals of 5% for the sensitivity (W), patients in the study will have the target disorder - in this case; hyperbilirubinaemia - of 25 %
Using the Everard's calculations; the sample size for the sensitivity was 236 and for specificity 261. We finally included 275 neonatal babies in the study.

Inclusion criteria

All neonates:

- admitted in Neonatal Unit regardless of their gestational age less than 2 weeks of postnatal age

- who were not in critical conditions including: hypothermia, respiratory distress, cardiovascular disorders, and neurological disorders.

Newborns who had received phototherapy or exchange transfusion, were excluded.

All newborns were recruited with verbal consent from their parents when visual observation of jaundice raised concern for hyperbilirubinemia and necessitated the determination of the serum bilirubin.

Almost 80% (275/342) of the neonates admitted were jaundiced and had blood taken for SBR measurement to evaluate clinical jaundice.
34 non-jaundiced neonates were also included. Measurements from non-jaundiced babies were used to investigate the correlation between the two methods, but not for assessing the effectiveness of TcB as a screening test.
For each neonate enrolled, a clinical examination was done and a data collection form was filled. The specific age in hours at time of assessment were recorded, as well as the birth weight and gender.
All TcB measurements were performed by using the bilirubinometer JM-102 device manufactured by "Minolta/Hill-Rom Air-Shields ® ".
The measurements were obtained from the forehead and sternum areas of the neonates, while lying in a supine position in their bassinets. Gentle pressure was applied, and the mean values index obtained from the two sites was used according to the manufacturer's instructions.
The blood samples for SBR were performed by venous sampling within 30 minutes after TcB measurements.
Blood samples for CBC, CRP, and blood group were taken simultaneously.

Data analysis

Demographic data, TcB and TSB values were entered using Epi data and analysed using SPSS 16.0 and Stata 11.0

Classification of hyperbilirubinaemia was done using the Norwegian guidelines for neonates below 2500 grams of weight and the American Academy of Pediatrics subcommittee on Hyperbilirubinemia guidelines were used for neonates of more than 2500 grams of weight.
The correlation coefficient between TcB and TSB was determined using Pearson linear regression analysis.
The area under the receiver operator characteristic curve (ROC) was estimated. The sensitivity and specificity were calculated for different cut-off points.

RESULTS

A total of 275 TcB-TSB pair specimens were performed in this study, from June 2007 to February 2008.
All neonates were of black skin, 141 babies were males (51.27%), 134 newborns were females (48.73%). The male to female ratio was 1.05:1.
241 newborns were visual jaundiced (87.64%) and 34 were not visual jaundiced (12.36%).
The demographic characters by Weight (g), gestational age (WA), postnatal age when assessed (H) distribution of SRB (µmmol/l) and TcB (index) are shown in the following table.

Table 1: Characteristics of the sample

Characteristics	Number	Percentage
Total population	275	100
≤ 30 WA	15	5.45
31WA – 34 WA	56	20.36
≥35 WA	204	74.18
< 1000 g	1	0.36
1000 g – 1499 g	41	14.91
1500 g - 2499 g	93	33.82
≥ 2500 g	140	50.91
0 – 24 hrs (postnatal age)	58	21.09
25 hrs – 48 hrs (postnatal age)	43	15.64
49 hrs – 120 hrs (postnatal age)	136	49.45
> 120 hrs (postnatal age)	38	13.82

Table 2: Characteristics of the sample

	Mean	Std dev	95% Conf. Interval
Weight (g)	2550.7	869.0	[2447.5 - 2653.8]
Gestational age (WA)	36.7	3.1	[36.4 - 37.1]
Postnatal age (H)	72.1	44.1	[66.9 - 77.3]
SBR (µmol/L)	160.0	72.2	[151.4 - 168.6]
TcB (index)	22.0	4.1	[21.5 - 22.5]

Correlation between SBR and TcB

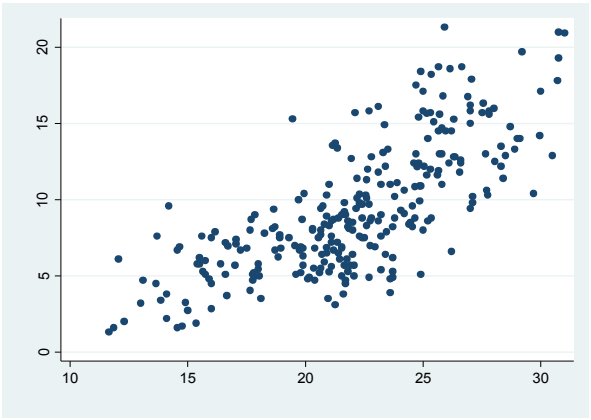

Fig 1: The correlation between the two measures is 74.5% N=275, R = 0.745

There was a significant correlation between SBR and TcB measurements (figure 1: r = 0.745 ; n = 275).
In 275 newborns in whom SBR was measured to evaluate clinically apparent jaundice, 53 had significant jaundice according to their gestational age and weight.

The area under the ROC curve was 0.88 (fig 2).

The area under the receiver operator characteristic curve (ROC) is good and significant

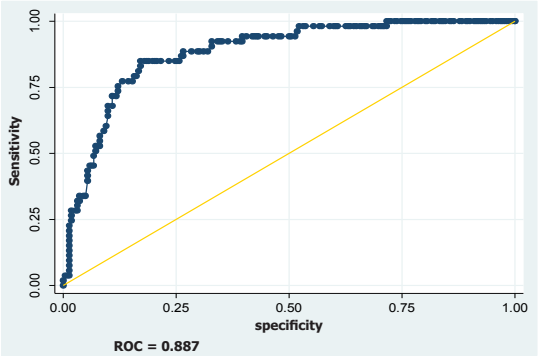

Fig 2: The area under the receiver operator characteristic curve (ROC) is good and significant ROC : 88.7 CI [84.3 – 93.1] , p value : < 0.0001.

Analysis of the ROC curve showed the TcB value that detected significant jaundice with the greatest predictive value of 22.1. This gave a sensitivity of 94.34 % and a specificity of 60.36% [table 3].

Table 3 : Cut-off point : Sensitivity analysis

Population	Cut off point	Sensitivity	Specificity	ROC	95% Conf. Interval
Overall	22.10	94.34	60.36	0.88	0.83 - 0.93
>= 35 WA	21.25	96.00	52.00	0.85	0.77 - 0.92
< 35 WA	24.60	96.43	69.77	0.89	0.81 - 0.96
0 H - 48 H	21.25	95.45	72.15	0.91	0.85 - 0.97
49 H - 120 H	24.60	96.77	74.83	0.92	0.88 - 0.96
< 2500 g	23.40	95.00	65.17	0.91	0.87 - 0.96
>= 2500 g	21.25	92.31	54.89	0.79	0.67 - 0.91
No neonatal infection	24.65	92.31	84.13	0.88	0.78 - 0.98
Neonatal infection suspected	22.10	95.00	63.52	0.88	0.83 - 0.93

However, for clinical purposes, this is unsatisfactory as a sensitivity of 100% is needed.
The TcB value that gave 100% sensitivity was 19.45, had a specificity of 28.38% [table 4].

Table 4 : Data analysis

Population	Cut off point	Sensitivity	Specificity
Overall	19.45	100	28.38
>= 35 WA	19.45	100	30.17
< 35 WA	22.70	100	48.80
0 H - 48 H	19.45	100	56.96
> 48 H	23.30	100	65.00
< 2500 g	22.70	100	60.00
>= 2500 g	19.45	100	36.09
No neonatal infection	21.35	100	34.92
Neonatal infection suspected	19.45	100	94.92

Table 5 : Data analysis

Population	Cut off point	Blood test prevented
Overall	19.45	63/275 (22.90%)
>= 35 WA	22.70	21/71 (29.57%)
< 35 WA	19.45	54/204 (26.47%)
0 H - 48 H	19.45	45/101 (44.55%)
> 48 H	23.30	83/174 (47.70%)
< 2500 g	22.70	54/129 (41.86%)
>= 2500 g	19.45	48/146 (32.87%)

In our cohort of 275 newborns having blood tests to evaluate their jaundice, if we had taken blood from only newborns with a bilirubinometer reading of 19.45 or more, we would have prevented 63 blood tests, a reduction of 22.90% [table 5].
In terms of sensitivity and specificity, at a cut off point of 22.7 in premature newborns less than 35 WA, 29.57% of blood test could be prevented and 26.47% of blood test could be prevented in newborns with more than 35 WA at a cut off point of 19.45.
In terms of birth weight, in low birth weight (2500g), at a cut off point of 22.7, 41.86 % of blood test could be prevented and 32.87 % of blood test could be prevented in more than 2500g at cut off point of 19.45.

Table 6: Characteristics of newborns with pathologic jaundice

Variables	Serum bilirubin: Gold standard			Chi-square	p value
	No Jaundice	Jaundice	Total		
Gastational age					
< 35 Weeks	43 (61%)	28 (39%)	71		
>= 35 Weeks	179 (88%)	25 (12%)	204	25.012	**0.000**
Total	222 (81%)	53 (19%)	275		
Weight					
>= 2500 g	133 (91%)	13 (9%)	146		
< 2500 g	89 (69%)	40 (31%)	129	21.507	**0.000**
Total	222 (81%)	53 (19%)	275		
Sex					
Male	109 (77%)	32 (22%)	141		
Female	113 (84%)	21 (15%)	134	2.178	0.140
Total	222 (81%)	53 (19%)	257		

Table 7: Characteristics of newborns with pathologic jaundice (cont)

Variables	Serum bilirubin: Gold standard			Chi-square	p value
	No Jaundice	Jaundice	Total		
Mother and baby blood group					
Others	177 (83.8%)	34 (16.1%)	211		
Mother with blood group O with baby A or B	45 (70.0%)	19 (29.0%)	64	5.8152	**0.016**
Total	222 (81.0%)	53 (19.0%)	275		
Neonatal infection					
No	63 (83.0%)	13 (17.0%)	76		
Yes	159 (69.0%)	40 (31.0%)	199	0.3171	0.573
Total	222 (81.0%)	53 (19.0%)	275		

Characteristics of newborns with pathologic jaundice were shown in table 6 and 7. The risk factors for pathologic jaundice in our study were the gestational age < 35 WA, birth weight < 2500g, and newborns with blood groups of A or B born from a mother with blood group O.

DISCUSSION

A noninvasive transcutaneous bilirubin measurement has been advocated because of its objectivity when compared to visual estimation of jaundice in a number of studies. Data suggest transcutaneous bilirubinometry has the potential to reduce the number of blood samples significantly [1,2,4,6,7,8,9,10].

Results are achieved with no trauma to the patient, no risk of infection, and potentially reduced cost of monitoring serum bilirubin by minimizing the use of hospital personnel and supplies.
In recent studies, the mostly used transcutaneous bilirubinometer are BiliCheck, Minolta JM-103, Bilimed. That particular device was not available in our setting and little is known about its cut off point in dark skin babies [1 ,2,4,5,6,7,8,9,10,11,12,13,31].

In our study, we used Minolta JM-102 and all neonates were black. According to previous study, Minolta JM-102 was found to be a reliable bilirubin measurement device in very low birth weight newborns, enabling reduction in the need for plasma bilirubin measurements without missing true hyperbilirubinemia.

The Jaundice Meter JM-102 (Minolta/Hill-Rom Air-Shields) is based upon two-wave length analysis and reported the result in form of Transcutaneous Bilirubin Index (TcBI). The TcBI can be converted into bilirubin values in mg/dl or umol/lL by using different multiplication factors for different populations.

However, the biliribinometer JM 102 has some major disadvantages. First, there are significant variations in the readings produced by differences in skin pigmentation. Furthermore, the displayed value is not a serum bilirubin level but is an index that must be converted to a serum bilirubin level in each hospital (11).

The major skin components which influence the spectral reflectance in neonate are melanin, dermal maturity, hemoglobin, and bilirubin (1).

In our study, we found that in the group of preterm newborns less than 35 WA and in the group of low birthweight, higher percentage of blood test would have prevented using Minolta JM-102 screening at cut off 22.7. Thus, significant underestimation of TSB values in these infants was very unlikely at a cut off of 19.45 as it was for the whole population of our study. At the 20.0 cut of point provided in the "Minolta/Hill-Rom Air-Shields® JM-102 notice", we found a sensibility of 98.1 % and a specificity of 35.1%.
The Minolta JM-102 device could be used as a screening instrument, leading to the avoidance of invasive blood samplings for term and preterm neonates.

Conclusion:

The correlation between TcB measurement and the serum bilirubin measurement was good in our sample of 275 dark skin newborns. Although there is a close correlation between TcB by "Minolta/Hill-Rom Air-Shields ® JM-102 device" and SBR measurements, the prediction interval for SBR from TcB is wide, and TcB cannot be the unique method to measure SBR. However, the correlation showed between TcB values and SBR indicate TcB might be used as a screening tool for babies requiring SBR measurement. The treatment of jaundice will remain a common intervention in neonatal medicine, and this will be based on SBR measurements.

Clinical assessment of jaundice is inaccurate and results in a significant number of blood tests in otherwise well newborns. The number of these blood tests could be reduced, with benefit to newborns and potential cost savings, by using TcB minolta JM102 as a screening tool.
In our study, if TcB measurements were used to determine the need for SBR measurements in newborns in whom there is clinical concern about significant jaundice, then the number of blood tests would be reduced by 22.90% (TcB: 19.45) in the whole group.

In preterm newborns below 35 WA, 29.57 % (TcB: 22.7) blood tests would be reduced, and in newborns with more than 35 WA, 26.47 % (TcB: 19.45) blood tests would be reduced.

The cut off point was high in group of neonates with postnatal age greater than 48 hours.
Babies with gestational age less than 35 weeks are more likely jaundiced than those with equal or more than 35 weeks.

Babies born with less than 2500 g are more likely jaundiced than those born with more than 2500 g.
Furthermore large scale studies are needed to test other available biliribunometers in dark skin babies.

REFERENCES

1. Bhutani VK, Gourley GR, Adler S, Kreamer B, Dalin C,Johnson LH. Noninvasive measurement of total serum bilirubin in a multiracial predischarge newborn population to assess the risk of severe hyperbilirubinemia. Pediatrics 2000; 106: 17-26.

2. Tanja Karen, Hans Ulrich Bucherand Jean-Claude Fauchère. Comparison of a new transcutaneous bilirubinometer (Bilimed®) with serum bilirubin measurements in preterm and full-term infants. BMC Pediatrics 2009, 9:70doi:10.1186/1471-2431-9-70

3. Suwimol Sanpavat, Issarang Nuchprayoon, Comparison of two transcutaeous biliribinometers – Minolta airshields jaundice meter JM103 and Spectrx Bilicheck – In Thai neonates. Southeast Asian J Trop Med Public Health 2005; 6:1533 – 1537.

4. H T Ho, T K Ng, K C Tsui,Y C Lo, Evaluation of a new transcutaneous bilirubinometer in Chinese newborns, Arch Dis Child Fetal Neonatal Ed 2006;91:F434-F438 doi:10.1136/adc.2005.090217

5. John R. Petersen, Anthony O. Okorodudu,1 Amin A. Mohammad, Amarasiri Fernando, and Karen E. Shattuck. Association of Transcutaneous Bilirubin Testing in Hospital with Decreased Readmission Rate for Hyperbilirubinemia, Clinical Chemistry2005 ; 51:3 540–544

6. L Briscoe, S Clark, C W Yoxall. Can transcutaneous bilirubinometry reduce the need for blood tests in jaundiced full term babies?,Arch Dis Child Fetal Neonatal Ed 2002;86:F190–F192

7. F Ebbesen, LM Rasmussen1 and PD Wimberley. A new transcutaneous bilirubinometer, BiliCheck, used in the neonatal intensive care unit and the maternity ward, Acta Pediatr 2002; 91: 203 - 211.

8. M Knupfer, F Pulzer, L Braun, A Heilmann, E Robel-Tillig, C Vogtmann. Transcutaneous bilirubinometry in preterm infants, Acta Pediatr 2001 90: 899 - 903.

9. Alex Robertson, Steve Kazmierczak, Paul Vos. Improved Transcutaneous Bilirubinometry:Comparison of SpectRX BiliCheck and Minolta Jaundice Meter JM-102 for Estimating Total Serum Bilirubin in a Normal Newborn Population, Journal of Perinatology 2002; 22:12 – 14

10. Firmino F. Rubaltelli, Glenn R. Gourley, Norbert Loskamp, Neena Modi, Matthias Roth-Kleiner, Alfred Sender et al. Transcutaneous Bilirubin Measurement: A Multicenter Evaluation of a New Device,Pediatrics 2001; 107 :6 1264 – 1271

11. M. Jeffrey Maisels, Enrique M. Ostrea, Suzanne Touch; Sarah E. Clune ;Eugene Cepeda; Elizabeth Kring et al. Evaluation of a New Transcutaneous Bilirubinometer, Pediatrics 2004;113;1628-1635

12. Lucia Stillova, Katarina Matasova, Tatiana Mikitova, Juraj Stilla,Hana Kolarovszka, Mirko Zibolen; Evaluation of transcutaneous bilirubinometry in preterm,Evaluation of transcutaneous bilirubinometry in preterm infants of gestational age 32 – 34 weeks ,Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2007, 151(2):267–271.

13. L Stillova, K Matasova, M Zibolen, J Stilla and H Kolarovszka; Transcutaneous Bilirubinometry in Preterm Neonates, 2009

14. American Academy of Pediatrics. Subcommittee of Hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics 2004; 114:297–316.

15. Norwegian guidelines for management of neonatal jaundice. 2006