ADVISORY BOARD
Dr. KB Sharma (New Delhi), Dr. NK Ganguly (New Delhi), Dr. SP Thyagarajan (Chennai), Dr. R Sambasiva Rao (New Delhi), Dr. MK Lalitha (Chennai), Dr. PG Shivananda (Manipal)

Annual Subscription Rs 2,000/- US $ 150
Single Copy Rs 600/- US $ 75

Published by MEDKNOW PUBLICATIONS
A-109, Kanara Business Center, Off Link Rd, Ghatkopar (E), Mumbai - 400075, INDIA
Phone: 91-22-6649 1818/1816, Fax: 91-22-6649 1817 • E-mail: publishing@medknow.com, Web: www.medknow.com

The journal is printed on acid free paper.
CONTENTS

Guest Editorial
The Need for Control of Viral Illnesses in India: A Call for Action
C Lahariya, UK Baveja

Review Article
Immunobiology of Human Immunodeficiency Virus Infection
P Tripathi, S Agrawal

Special Articles
Serum Levels of Bel-2 and Cellular Oxidative Stress in Patients with Viral Hepatitis
HG Osman, OM Gabr, S Lotfy, S Gabr

Rapid Identification of Non-sporing Anaerobes using Nuclear Magnetic Resonance Spectroscopy and an Identification Strategy
S Menon, R Bharadwaj, AS Chowdhary, DV Kaundinya, DA Palande

Original Articles
Species Distribution and Physiological Characterization of Acinetobacter Genospecies from Healthy Human Skin of Tribal Population in India
SP Yavankar, KR Pardesi, BA Chopade

Extended-spectrum Beta-lactamases in Ceftazidine-resistant Escherichia coli and Klebsiella pneumoniae Isolates in Turkish Hospitals
S Hosoglu, S Gundeş, F Kolayli, A Karadenizli, K Demirdag, M Gunaydin, M Altindis, R Caylan, H Ucmak

Typhoid Myopathy or Typhoid Hepatitis: A Matter of Debate
M Mirsadraee, A Shirdel, F Roknee

Correlation Between in Vitro Susceptibility and Treatment Outcome with Azithromycin in Gonorrhoea: A Prospective Study
P Khaki, P Bhalla, A Sharma, V Kumar

Comparison of Radiorespirometric Buddemeyer Assay with ATP Assay and Mouse Foot Pad Test in Detecting Viable Mycobacterium leprae from Clinical Samples
VP Agrawal, VP Shetty

Detection of Mycoplasma Species in Cell Culture by PCR And RFLP Based Method: Effect of BM-cyclin to Cure Infections
V Gopalkrishna, H Verma, NS Kumbhar, RS Tomar, PR Patil

Page No.
309
311
323
330
336
346
351
354
358
364
Virulence Factors and Drug Resistance in *Escherichia coli* Isolated from Extraintestinal Infections

*S Sharma, GK Bhat, S Shenoy*

Antimicrobial Susceptibility Testing of *Helicobacter pylori* to Selected Agents by Agar Dilution Method in Shiraz-iran

*J Kohanteb, A Bazargani, M Saberi-Firouzi, A Mobasser*

Outbreak of Acute Viral Hepatitis due to Hepatitis E virus in Hyderabad

*P Sarguna, A Rao, KN Sudha Ramana*

A Comparative Study for the Detection of Mycobacteria by BACTEC MGIT 960, Lowenstein Jensen Media and Direct AFB Smear Examination

*S Rishi, P Sinha, B Malhotra, N Pal*

Cytokine Levels in Patients with Brucellosis and their Relations with the Treatment

*H Akbulut, I Celik, A Akbulut*

**Brief Communications**

Rapid Detection of Non-enterobacteriaceae Directly from Positive Blood Culture using Fluorescent **In Situ** Hybridization

*EH Wong, G Subramaniam, P Navaratnam, SD Sekaran*

Latex Particle Agglutination Test as an Adjunct to the Diagnosis of Bacterial Meningitis

*K Surinder, K Bineeta, M Megha*

Helminthic Infestation in Children of Kupwara District: A Prospective Study

*SA Wani, F Ahmad, SA Zargar, BA Fomda, Z Ahmad, P Ahmad*

Clinical and Mycological Profile of Cryptococcosis in a Tertiary Care Hospital

*MR Capoor, D Nair, M Deb, B Gupta, P Aggarwal*

*Candida* spp. other than *Candida albicans*: A Major Cause of Fungaemia in a Tertiary Care Centre

*S Shivaprkasha, K Radhakrishnan, PMS Karim*

**Case Reports**

*Enterobacter sakazakii* in Infants: Novel Phenomenon in India

*P Ray, A Das, V Gautam, N Jain, A Narang, M Sharma*

Ocular Toxocariasis in a Child: A Case Report from Kashmir, North India

*BA Fomda, Z Ahmad, NN Khan, S Tanveer, SA Wani*

Cutaneous Actinomycosis: A Rare Case

*SC Metgud, H Sumati, P Sheetal*

Fatal Haemophagocytic Syndrome and Hepatitis Associated with Visceral Leishmaniasis

*P Mathur, JC Samantaray, P Samanta*

A Rare Case of Mucormycosis of Median Sternotomy Wound Caused by *Rhizopus arrhizus*

*R Chawla, S Sehgal, S Ravindra Kumar, B Mishra*

*Mycobacterium fortuitum* Keratitis

*C Sanghvi*

**Correspondence**

Prevention of Parent-to-Child Transmission of HIV: An Experience in Rural Population

*N Nagdeo, VR Thombre*
Combining Vital Staining with Fast Plaque: TB Assay
D Rawat, MR Capoor, A Hasan, D Nair, M Deb, P Aggarwal

Disseminated Histoplasmosis
PK Maiti, MS Mathews

Authors’ Reply
RS Bharadwaj

Microwave Disinfection of Gauze Contaminated with Bacteria and Fungi
VH Cardoso, DL Gonçalves, E Angioletto, F Dal-Pizzol, EL Streck

Endoscope Reprocessing: Stand up and Take Notice!
A Das, P Ray, M Sharma

Prevalence of Toxoplasma gondii Infection amongst Pregnant Women in Assam, India
BJ Borkakoty, AK Borthakur, M Gohain

MR Capoor, D Rawat, D Nair, M Deb, P Aggarwal

Resurgence of Diphtheria in the Vaccination Era
N Khan, J Shastri, U Aigal, B Doctor

A Report of Pseudomonas aeruginosa Antibiotic Resistance from a Multicenter Study in Iran
MA Boroumand, P Esfahanifard, S Saadat, M Sheihkvatan, S Hekmatyazdi, M Saremi, L Nazemi

Trends of Antibiotic Resistance in Salmonella enterica Serovar Typhi Isolated from Hospitalized Patients from 1997 to 2004 in Lagos, Nigeria
KO Akinyemi, AO Coker

Book Review
Hospital-Acquired Infections: Power Strategies for Clinical Practice
Reba Kanungo

Title Index, 2007

Author Index, 2007

Scientific Reviewers, 2007

The copies of the journal to members of the association are sent by ordinary post. The editorial board, association or publisher will not be responsible for non-receipt of copies. If any of the members wish to receive the copies by registered post or courier, kindly contact the journal's / publisher's office. If a copy returns due to incomplete, incorrect or changed address of a member on two consecutive occasions, the names of such members will be deleted from the mailing list of the journal. Providing complete, correct and up-to-date address is the responsibility of the members. Copies are sent to subscribers and members directly from the publisher's address; it is illegal to acquire copies from any other source. If a copy is received for personal use as a member of the association/society, one cannot resale or give-away the copy for commercial or library use.
TYPHOID MYOPATHY OR TYPHOID HEPATITIS: A MATTER OF DEBATE

*M Mirsadraee, A Shirdel, F Roknee

Abstract

Purpose: The aim of the present study was to evaluate the major source of increased serum enzyme level in typhoid fever and to determine the most relevant clinical entity, hepatitis or myopathy, during typhoid fever. Methods: A total of 118 subjects proved to have typhoid fever were evaluated for serum enzymes such as transaminases, alkaline phosphatase, lactate dehydrogenase (LDH) and creatinine kinase (CK); and their relation with each other, clinical symptoms and serum bilirubin were evaluated by regression methods. Results: Hepatomegaly was revealed in 14% of the cases and was correlated with elevated serum bilirubin (5.05 ± 13.03 mg/dL in hepatomegalic subjects). Alanine aminotransferase (ALT) and CK were elevated in 22 and 60% of the cases, respectively. Correlation coefficient of CK with aspartate aminotransferase (AST) and LDH was \( R^2 = 0.68 \) and 0.75, respectively, which were higher than that of ALT with that two enzymes. Conclusions: In conclusion, elevation of serum enzymes in typhoid is mostly of muscular origin. Key words: Creatinine kinase, hepatitis, myopathy, transaminase, typhoid fever

Typhoid fever is yet claiming many lives in developing countries. Ramachandran described typhoid hepatitis and its histopathology in 1974. The hepatic manifestations of typhoid fall into three categories: i) patients with no evidence of hepatic enlargement or abnormalities in hepatic function; ii) patients with evidence of hepatic involvement, either hepatomegaly or abnormal liver function tests, in whom hepatic involvement was of no great clinical importance and occurred as an incidental feature of the illness; and iii) patients with hepatic manifestations as the dominant feature of the illness and often the mode of presentation of the disease. Elevated serum enzyme level related to hepatic damage was reported in 50-100% of typhoid patients.

Myopathy during the course of typhoid fever is reported increasingly. Both clinical entities, myopathy and hepatitis, are usually diagnosed by serum enzymes such as aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), lactate dehydrogenase (LDH) and creatinine phosphokinase (CK). AST and LDH are elevated in myopathy as well as hepatitis, whereas ALT and CK are relatively specific for liver and muscle, respectively. According to the original definition of typhoid hepatitis, it is possible that an overdiagnosis for typhoid hepatitis occurred and typhoid myopathy was missed.

The aim of the present study was to evaluate the major source of increased serum enzyme level in typhoid fever and to determine the most relevant clinical entity, hepatitis or myopathy, during typhoid fever.

Materials and Methods

The present study was conducted in patients with typhoid fever, who were admitted to Montaserieh University Hospital, Mashhad, Iran. The study design was cross-sectional and prospective. Diagnosis was confirmed by a positive culture of blood and/or bone marrow or fourfold rise in Widal titer. All subjects with proved typhoid fever were included in the present study regardless of their age. Patients with paratyphoid fever were not included in this study. Demographic data and clinical findings of liver and spleen involvement were mentioned in a questionnaire. Laboratory evaluation included serum enzyme activities (AST, ALT, ALP, LDH and CK: all evaluated by Technicon RA-1000), total and direct bilirubin, haematological assessment and urinalysis. The blood sample was drained on the first day of management at the same time with blood culture sample collection. For the determination of liver involvement, the enzymes were correlated with ALT and bilirubin (total and direct) and for the evaluation of muscular enzyme release, serum enzymes were correlated with CK. Due to the ethical considerations, tissue biopsy from liver and muscle was not performed. This study was approved by the Ethical Committee of Islamic Azad University of Mashhad (Iran).

Statistical analysis

Sample size was 110 subjects according to 0.05 alpha risk and 80% potency. Descriptive statistics was performed to generate descriptive data. In addition, correlation between the levels of different serum enzymes was calculated by regression analysis and \( F \)-statistics. Comparison of variables were tested by Chi-square and Student’s \( t \)-test. A two-sided or one-sided (depended on the test) \( P \)-value of 0.05 was
the criterion for statistical significance. Normal distribution of results was assessed by Kolmogorov-Smirnov test. All analyses were performed by statistical softwares EPI INFO 2000 and SPSS, version 12.0.

Results

One hundred eighteen patients with an age range of 2-53 years (23.1 ± 12.3) were enrolled in the study. The diagnosis was based on positive blood culture, bone marrow culture and fourfold rise in Widal titer of typhoid fever in 94, 12 and 12 cases, respectively. The men were affected more than the women (M/F = 2/1). Fever and chill were the most prevalent symptoms (100 and 98%, respectively) followed by headache and abdominal pain (77 and 63%, respectively). Hepatomegaly and splenomegaly were found in 16 (14%) and 28 (26%) cases, respectively. There was no significant association between hepatomegaly and the increased level of AST, ALT and ALP (Table 1) although serum bilirubin level in patients with hepatomegaly was significantly higher than subjects with normal liver (5.05 ± 13.03 mg/dL in hepatomegalic subjects vs. 0.73 ± 0.84 mg/dL, \( t = 2.28, P < 0.001 \) (Table 1). Summary of descriptive analysis of serum enzyme levels is showed in Table 2. Laboratory tests that point towards liver disease, such as ALT, ALP and bilirubin were not elevated in more than 22% of the cases; but CK, as diagnostic test for muscular disease, was increased in 60% of the cases. AST and LDH that are commonly increased in both conditions were elevated in a majority of the subjects (Table 2). Correlation of serum enzyme levels revealed that CK and LDH and also CK and AST showed the greatest association (\( F \)-statistics 40 and 62.4, respectively) (Table 3; Figure), in favour of muscular origin of serum enzymes in typhoid fever. Correlation of AST with ALT and LDH was significant but to a lesser degree (\( F \)-statistics 34.9 and 10, respectively) (Table 3).

Table 1: Comparison of Mean ± SD of serum enzymes and bilirubin in patients with typhoid fever (with or without hepatomegaly)

<table>
<thead>
<tr>
<th></th>
<th>With hepatomegaly</th>
<th>Without hepatomegaly</th>
<th>T-test</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AST (IU)</td>
<td>184.5 ± 191.80</td>
<td>229.16 ± 367.20</td>
<td>0.570</td>
<td>0.57</td>
</tr>
<tr>
<td>ALT (IU)</td>
<td>101.2 ± 89.30</td>
<td>93.7 ± 82.70</td>
<td>0.244</td>
<td>0.81</td>
</tr>
<tr>
<td>ALP (IU)</td>
<td>150.6 ± 136.08</td>
<td>104.56 ± 71.24</td>
<td>1.04</td>
<td>0.32</td>
</tr>
<tr>
<td>LDH (IU)</td>
<td>1243.00 ± 423.87</td>
<td>1477.19 ± 1250.80</td>
<td>0.934</td>
<td>0.35</td>
</tr>
<tr>
<td>CK (IU)</td>
<td>297.00 ± 261.64</td>
<td>1320.21 ± 2421.77</td>
<td>1.80</td>
<td>0.87</td>
</tr>
<tr>
<td>Bilirubin total (mg/dL)</td>
<td>5.05 ± 13.03</td>
<td>0.73 ± 0.84</td>
<td>2.28</td>
<td>0.00</td>
</tr>
</tbody>
</table>

Table 2: Summary of descriptive analysis of serum enzymes level in patients with typhoid fever

<table>
<thead>
<tr>
<th>Serum enzymes</th>
<th>Mean</th>
<th>SD</th>
<th>Min.</th>
<th>Max.</th>
<th>Frequency of subjects above normal (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AST (IU)</td>
<td>239</td>
<td>373.7</td>
<td>20</td>
<td>2446</td>
<td>84</td>
</tr>
<tr>
<td>ALT (IU)</td>
<td>92.1</td>
<td>74.2</td>
<td>5</td>
<td>411</td>
<td>22</td>
</tr>
<tr>
<td>ALP (IU)</td>
<td>117.9</td>
<td>86.8</td>
<td>5</td>
<td>494</td>
<td>4</td>
</tr>
<tr>
<td>LDH (IU)</td>
<td>1501</td>
<td>1381</td>
<td>75</td>
<td>7070</td>
<td>92</td>
</tr>
<tr>
<td>CK (IU)</td>
<td>1356</td>
<td>2413</td>
<td>40</td>
<td>9900</td>
<td>60</td>
</tr>
<tr>
<td>Bilirubin total (mg/dL)</td>
<td>1.5</td>
<td>5.36</td>
<td>0.1</td>
<td>39.8</td>
<td>5</td>
</tr>
<tr>
<td>Bilirubin direct (mg/dL)</td>
<td>0.8</td>
<td>4</td>
<td>0.1</td>
<td>30</td>
<td>3</td>
</tr>
</tbody>
</table>

IU - International unit; AST - Aspartate aminotransferase, ALT - Alanine aminotransferase, ALP - Alkaline phosphatase, LDH - Lactate dehydrogenase, CK - Creatinine phosphokinase

Figure: Relationship between aspartate aminotransferase (AST) and creatinine phosphokinase (CK) in patients with typhoid fever is shown in linear regression graph
Two serum enzymes compared

<table>
<thead>
<tr>
<th></th>
<th>R</th>
<th>R²</th>
<th>F-statistics</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AST and ALT</td>
<td>0.59</td>
<td>0.35</td>
<td>34.9</td>
<td>0.001</td>
</tr>
<tr>
<td>AST and LDH</td>
<td>0.42</td>
<td>0.18</td>
<td>10</td>
<td>0.002</td>
</tr>
<tr>
<td>AST and CK</td>
<td>0.81</td>
<td>0.68</td>
<td>40</td>
<td>0.001</td>
</tr>
<tr>
<td>ALT and LDH</td>
<td>0.39</td>
<td>0.15</td>
<td>8.83</td>
<td>0.005</td>
</tr>
<tr>
<td>LDH and CK</td>
<td>0.87</td>
<td>0.75</td>
<td>62.4</td>
<td>0.0001</td>
</tr>
<tr>
<td>ALT and CK</td>
<td>0.56</td>
<td>0.31</td>
<td>9.7</td>
<td>0.005</td>
</tr>
<tr>
<td>ALT and bilirubin</td>
<td>0.177</td>
<td>0.031</td>
<td>1.88</td>
<td>0.175</td>
</tr>
</tbody>
</table>

AST - Aspartate aminotransferase, ALT - Alanine aminotransferase, ALP - Alkaline phosphatase, LDH - Lactate dehydrogenase, CK - Creatinine phosphokinase

Discussion

Classically, typhoid fever presents with continuous fever, abdominal pain, constipation, rose spot and relative bradycardia; but some variations in clinical findings such as diarrhoea and leukocytosis have been reported. Many organs other than gastrointestinal tract may be involved in typhoid fever. Hepatic involvement is one of the earliest reported complications of typhoid fever, which can cause hepatomegaly, jaundice and coma, but its course with administration of treatment is favourable. As abnormal AST and ALT in combination are indicative of a hepatocyte disorder, many investigators used these enzymes for evaluation of hepatic involvement during typhoid fever. The frequency of elevated serum enzyme in two previous reports was 52 and 100%, respectively. But in our series, hepatomegaly was observed in 14% and ALT as the hallmark of liver damage was elevated in 22% of the cases.

As a different point of view, Scheig reported that the prothrombin time and serum albumin level are excellent measures of hepatic protein synthesis ability, whereas the bilirubin level is probably the best marker of overall liver function. Khan et al., reported jaundice as a main predictor of severe liver injury in 36% of typhoid fever. Jaundice was only present in 5% of our patients but it was significantly associated with hepatomegaly (Table 1).

The invasion of intestinal lymphatic tissue is suggested to result in a host reaction with hyperplasia of the liver reticuloendothelial system and infiltration of portal spaces as well as the reduction of the microcirculation causing necrosis. Hepatic damage by Salmonella typhi appears to be mediated by bacterial endotoxin. The presence of intact bacilli has been demonstrated in the hepatic tissue that may be related to presence of Salmonella bacteria in reticuloendothelial system and hyperplasia of Kupffer cells (typhoid nodule), without significant liver injury.

Myopathy is another reported complication of typhoid fever, which can cause severe myoglobinuria and elevated CK. In the present study, the pattern of serum enzymes is more comparable to what is found in myopathy (60%) rather than liver disease (22%), as the association of AST and CK is stronger than AST and liver enzymes (Table 3).

In conclusion, liver is involved in 14% of typhoid patients manifesting with hepatomegaly and elevated bilirubin. Elevation of serum enzymes in typhoid fever is presumably of a muscular origin, while elevation of liver enzyme is relatively less common.

References


Source of Support: Nil, Conflict of Interest: None declared.