ORIGINAL ARTICLE

Study of Current Trends in Typhoid Fever: Risk of Hepatomegaly

HUMERA RAFIQ , RASHID ZIA, RAKSHAN KHURSHID, *IRFAN KHURSHID, AHMAD HAMEED, AMBREEN HAMEED, SAMINA NAEEM*

ABSTRACT

Objective: To characterize the clinical picture, biochemical features, and prognosis of typhoid hepatitis.

Material and methods: The present prospective randomized controlled parallel study was conducted on 100 children up to 12 years admitted in our hospital between April 2007-8 with clinical and/or laboratory diagnosis of typhoid fever admitted to the pediatric ward were reviewed for demographic data such as age, sex, clinical features, and results of laboratory tests.

Results: 08 were less than one year of age, while 34 were under the age of five years. Predominant symptoms, hepatomegaly, splenomegaly, fever, abdominal pain, vomiting and headache were noted. A febrile convulsion was the presenting symptom in 2 of the patients, all of whom were under the age of five years. Intestinal perforation was not present in any of the patients. Anemia was present in 61%, leukopenia in 31% and thrombocytopenia in 38%. Elevated serum alanine and aspartate aminotransferase (50 > /U/L) levels were observed in 28% of our patients.

Conclusion: Study suggested that in diagnosis of typhoid, hematological findings as well as the level of transaminases related to heptomegaly must be interrogated.

Key words: typhoid, transaminases, blood picture

INTRODUCTION

Typhoid fever is a distinctive acute multi-systemic febrile disease caused primarily by Salmonella typhi . It is recognized as a major cause of morbidity globally with over 21.6 million cases annually worldwide, and an estimated 216500 deaths[1]. Almost 80% of cases and deaths are in Asia. The attack rate as high as 1100 cases per 100000 populations have been documented in developing countries[2]. It remains a serious public health in developing countries[3].

Typhoid fever is often associated with abnormal liver biochemical tests, but severe hepatic involvement with a clinical feature of acute hepatitis is a rare complication[4]. Incidence of typhoid hepatitis varies from 0.4% - 6%. Several patient series have previously reported biochemical evidence of hepatic dysfunction in 23% - 60% of cases[3]

The possible associated factors for development of salmonella hepatitis are virulence of the organisms, delayed treatment and poor general health of the patients. The pathogenesis of severe hepatic involvement in salmonella infection may be multifactorial and includes endotoxin, local inflammatory and/or host immune reactions. Clinical jaundice in salmonella hepatitis usually occurs within the first 2 weeks of the febrile illness. Hepatomegaly and moderate elevation of transaminase levels are common findings. Extreme hepatic dysfunction with hepatic encephalopathy is a rare coexisting complication in salmonella hepatitis[4].

Besides, epidemiological pattern, clinical picture is also a trend noted in typhoid fever. Laboratory examination of blood revealed that anemia was noted in 25.8% cases and leucopenia in 31% cases[3].

Elevated serum enzyme values are often the earliest indicators of liver injury in asymptomatic patients. Abnormal AST and ALT point to a hepatocyte disorder. Selected case histories illustrate how these enzyme levels, in conjunction with the history and physical examination, can guide the rest of the workup[5].

Our aim was to characterize the clinical picture, biochemical features, and prognosis of typhoid hepatitis.

MATERIAL AND METHODS

The present prospective randomized controlled parallel study was conducted on 100 children up to 12 years admitted in our hospital between April 2007-8 with clinical and/or laboratory diagnosis of typhoid fever admitted to the pediatric ward were reviewed for demographic data such as age, sex, clinical features, and results of laboratory tests. Predominant symptoms were hepatomegaly, splenomegaly, fever, abdominal pain, vomiting and headache. A febrile convulsion was the presenting symptom in 2 of the patients, all of whom were under the age of five

---

Department of Pathology KE medical University Lahore
Correspondence to Dr. Humera Rafiq, Assistant Professor (0321-8440973)

years. Intestinal perforation was not present in any of the patients. Blood picture including hemoglobin, TLC and platecoutn was analyzed by autoanalyzer. Level of transaminases including AST and ALT were estimated by standard kit (Merck) method. Standard error of difference between means and p-value where applied to assess the probability and significance of the data using the computer Programm SPSS version.

Table 1: Clinical symptoms & signs of patients at admission

Symptoms	(%) of Patients
Fever	95
Abdominal pain	66
Vomiting	44
Headache	38
Diarrhea	23
Constipation	8
Cough	15
Anorexia	39
Weakness	37
Nausea	23
Hepatomegaly	09
Splenomegaly	13
Abdominal tenderness	08
Rose spots	01
Relative bradycardia	02
Cervical lymphadenopathy	06

Table 2: Haematological parameters in patients suffering from typhoid fever
No of cases in parenthesis

Hb(g/dl)	TLC	Platelets
13.5±2 (39)	<4000x10^9/l (31)	150,000-45000/mm^3 (62)
10±1.5 (30)	4000-11000x10^9/l (59)	>150,000/mm^3 (38)
<8.5 (31)	>11,000x10^9/l (10)	-

Table 3: Level of transaminase in patients
No of cases in parenthesis.

AST	>50 Iu/l (28)
	<50 Iu/l (72)
ALT	>50 Iu/l (29)
	<50 Iu/l (71)

RESULTS

Table 1 shows the clinical features of the children on admission. The predominant symptoms were fever (95%), abdominal pain (66%), vomiting (44%), and headache (38%). Fever, vomiting, abdominal pain, loss of appetite, diarrhea and cough were the predominant symptoms. Hepatomegaly was detected in 9(9%), splenomegaly in 13(13%) patients. Patients included into this study with clinically suspected typhoid fever had typhi dot positive, Widal's agglutination titers of at least 62 were positive.

Hematological findings include hemoglobin, total leukocyte count and platelet count of children suffered with typhoid were tabulated (Table 2). It is observed that 31% patients have very low level of hemoglobin indicate server anemia, while 30% have moderate type of anemia and only 39% have normal level of hemoglobin. Total leukocyte count with normal value was observed in most of the patients while leucopenia was observed in 31% cases and only 10% cased showed the high level of leukocytes count. Low level of platelet count was only observed in 38% cases indicate thrombocytopenia while most of the patients have normal level of platelet counts.

Level of ALT and AST were also tabulated (Table 3). It was observed that the level of both transaminases ALT & AST were raised only in 28-29% cases respectively. On the other hand the level of these hormones were within the normal range in 70-71% cases.

DISCUSSION

Liver involvement is commonly observed in patients with typhoid fever. However, a hepatitis-like picture with fever and jaundice is unusual and infrequently reported in the paediatric literature [6,7].

Fever was the commonest presentation in all the cases. It was observed in 95% of cases. Our study is in accord to most of the studies by other authors[8,9,10].

Significant incidences of gastrointestinal complaints - abdominal pain, nausea, vomiitting, diarrhea, anorexia etc were noted in children. Our study is in accord to various stuty who observed the same complains[11,12,13] . However no study observed the GIT bleeding as by one of study[13].

Hepatomegaly was seen in only 09% cases in this study. However our study is incontrast to various studies who observed a high percentage of i.e. these studydies observed 88% and 33% of hepatomegaly[14, 8,13]. Splenomegaly was seen in 13% of cases in our study which was again in contrast to that reported[15]. In conjunction with the spleen, liver is involved in the destruction of spent red blood cells and the reclamation of their constituents[16].

Most of the patients in this study have low hemolglobin level or having anemia. Our study is inaccord with a study who also reported that in typhoid, blood picture revealed anaemia, within normal white blood count and thrombocytopenia[17]

Most of the patients in this study had normal leukocyte count although leucopenia is said to be the common hematological finding in typhoid fever. Leucopenia was seen in 31% cases, continuing the observation of others[8,13]. However, a study reported

the characteristic changes of the differential blood picture, such as lymphomonocytosis. Study suggested that in diagnosis of this disease hematological findings must be questioned[18].

In Thi S study, hepatomegaly was found during the 2nd or 3rd wk more often than in the 1st wk (36% vs. 11%). AST, and ALT were mild to moderately raised in 28%, 29% cases, respectively, during the 2nd and 3rd wk. Our study is in accord to a study who observed the same results. This study showed that, although the clinical picture of hepatitis is unusual, liver involvement is invariably present after the 1st wk, and should not be considered as a complication, but as a feature of the disease[19]. According to a study hepatomegaly and moderate elevation of transaminase levels are common findings. Extreme hepatic dysfunction with hepatic encephalopathy is a rare coexisting complication in salmonella hepatitis[4]. Another study also observed elevated serum levels of transaminases that usually indicate hepatocellular damage. ALT elevations, however, can also be of extrahepatic origin[20]. A group of workers reported that as many as 2.5% of normal patients have "abnormal" aminotransferase levels liver enzymes are commonly reflect hepatocyte integrity[16]. However a study found that 60% of cases of elevated hepatic AST levels can be attributed to ischemic or toxic liver injury[21].

CONCLUSION

Study suggested that in diagnosis of typhoid, hematological findings as well as the level of transaminases related to heptomegaly must be interrogated.

REFERENCE

1. Wasfy MO, Oyofo BA, David JC et al. Isolations and antibiotic susceptibility of Salmonella , Shigella , and Campylobacter from acute enteric infections in Egypt. J Health Popul Nutr 2000; 18: 33-38
2. Ivanoff B, Levine MM, Lambert PH. Vaccination against typhoid fever: present status. Bull World Health Organ 1994; 72 : 957-971.
3. Rajiv K, Nomeeta G, Shalini. Multidrug - resistant typhoid fever. Rev Infec Dis 2007; 18: 873-879.
4. Pramoolsinsap, Chutima; Viranuvatti & Vikit. Salmonella hepatitis. Journal of Gastroenterology & Hepatology. 13(7):745-750, July 1998. Herlong HFApproach to the patient with abnormal liver enzymes. Hosp Pract (Off Ed). 1994 Nov 15;29(11):32-8.
5. Ozen H, Seçmeer G, Kanra G, Ecevit Z, Ceyhan M, Dursun A, Anlar Y. Typhoid fever with very high transaminase levelsTurk J Pediatr. 1995 Apr-Jun;37(2):169-71.
6. Shetty AK, Mital SR, Bahrainwala AHT, Khubchandani RP and Kumta NB Typhoid hepatitis in children Journal **of** Tropical Pediatrics 1999 45(5):287-290;
7. Bhutta ZA, Naqvi SH, Razzaq ZA et al. Mutidrug-resistant typhoid in children: Presentation and Clinical features. Rev Infect Dis 1991; 13: 832-836.
8. Kabra S K, Kabra M, Talati A, Soni N, Patel S, Modi R R. Multidrug-resistant typhoid fever. Trop Doct 2000; 30: 195-197
9. Wongsawat J, Pancharoen C, Thisyakorn U. Typhoid fever in children: Experience in King Chulalongkorn Memorial Hospital. J Med Assoc Thai 2002; 85: 1247-1250
10. Agarwal K S, Singh S K, Kumar N et al. A study of current trends in enteric fever. J Commun Dis 1998; 30(3): 17174
11. Rasaily R, Dutta P, Saha MR, Mitra U et al. Multidrug-resistant typhoid fever in hospitalized children: clinical, bacteriological and epidemiological profiles. Eur J Epidemiol 1994; 10: 41-47
12. Koul P B, Murali M V, Sharma P P, Ghai O P, et al. Multidrug-resistant Salmonella typhi infection: clinical profile and therapy. Indian Pediatr 1991; 28: 352-356
13. Chandra R, Srinivasan S, Nalini P, Rao RS. Multidrug-resistant enteric fever. J Trop Med Hyg 1992; 95: 284-87
14. Garg K, Mangal N, Mathur HC. Clinical profile of multidrug-resistant typhoid fever in Jaipur city. Indian Pediatr 1994; 31: 191-193
15. Giannini EG, Testa R, Savarino V. Liver enzyme alteration: a guide for clinicians. CMAJ. 2005 Feb 1;172(3):367-79
16. Abdel Wahab MF, el-Gindy IM, Sultan Y, el-Naby HMComparative study on different recent diagnostic and therapeutic regimens in acute typhoid fever. J Egypt Public Health Assoc. 1999;74(1-2):193-205.
17. Sević S. [Serologic diagnosis of acute infectious mononucleosis] Med Pregl. 1997 Sep-Oct;50(9-10):403-8.
18. Morgenstern R, Hayes PC. The liver in typhoid fever: always affected, not just a complication. Am J Gastroenterol. 1991 Sep;86(9):1235-9
19. Renner EL, Dällenbach A [Increased liver enzymes: what should be done?] Ther Umsch. 1992 May;49(5):281-6.
20. Whitehead MW, Hawkes ND, Hainsworth I, Kingham JGC. A prospective study of the causes of notably raised aspartate aminotransferase of liver origin. *Gut* 1999;45(1):129-33