

Liver Function Tests Abnormalities in Enteric Fever- A Recent Update

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Abstract: Introduction: Enteric fever is still a major health problem in developing countries. The term enteric fever includes typhoid and paratyphoid which is characterised by generalised infection of the reticuloendothelial system and intestinal lymphoid tissue accompanied by sustained fever and bacteremia. Hepatic involvement was known for a long time and it was first described by Osler in 1899 who documented cases of typhoid fever with jaundice and hepatomegaly. Aims and objectives: This study was undertaken to observe the hepatic manifestations and study the LFT abnormalities during the course of enteric fever and analyse their clinical significance.

Settings: A tertiary hospital based study

Patients And Methods: The present prospective study was conducted at M.S.Ramaiah Medical Teaching Hospital. 50 patients of enteric fever diagnosed on the basis of clinical history, physical examination, blood culture and Widal test were included in the study. A detailed evaluation of the patients was done with particular reference to hepatic dysfunction. A past history of fever was looked. A detailed clinical examination was carried out particularly for the presence of jaundice, pallor, hepatosplenomegaly, altered sensorium, perforation and bleeding tendencies. The investigations done were complete hemogram, Liver function tests which included total proteins, albumin, total and direct bilirubin, aspartate amino transferase, alanine amino transferase, alkaline phosphatase and prothrombin time. Urine for routine examination and presence of urobilinogen, bile salt and pigments. Routine blood tests for sugar, urea and creatinine, Blood Culture, Stool Culture, Urine culture, Widal Test, Chest X-ray, Peripheral smear for malaria parasite, Brucella agglutination test and Hepatitis B surface antigen. Bleeding and clotting times. Ultrasonography of abdomen were done in clinically indicated cases.

Results: In the present study age of the patients ranged from 14 yrs to 60 yrs with a mean age of 21.9 yrs and male:female ratio being 3.5:2. Analysis of Liver Function Tests: Serum AST was normal in 28 patients, elevated (More than 2 fold) in 22/50 (44%) patients and the range of AST is 4 U/L to 301 U/L. Out of 50 cases of enteric fever, elevated AST of more than two fold was seen in 2 cases in 1st week, 13 cases in 2nd week and 7 cases in 3rd week. There is statistically significant association between duration of fever and AST levels ($\chi^2 = 7.2219$; $df = 2$; $P < 0.05$). Serum ALT was normal in 29 patients, elevated (more than 2 fold) in 21/50 (42%) patients and the range of ALT is 3 U/L to 368 U/L was seen in 2 cases in 1st week, 12 cases in 2nd week and 7 cases in 3rd week. There is statistically significant association between duration of fever and ALT levels ($\chi^2 = 6.3557$; $df = 2$; $P < 0.05$). Serum Alkaline Phosphatase (ALP): ALP was normal in 31 patients, elevated to more than 2 fold in 19/50 (38%) patients and the range of ALP is 13 U/L to 628 U/L. Out of 50 cases of enteric fever, elevated ALP levels of more than two fold was seen in 2 cases in 1st week, 11 cases in 2nd week and 6 cases in 3rd week. There is statistically significant association between duration of fever and serum alkaline phosphatase. ($\chi^2 = 8.3882$; $df = 2$; $P < 0.05$). Serum Bilirubin level in the study group: Hyperbilirubinemia was found in 5/50 (10%) patients (>1.8 mg/dl) and the range of bilirubin in these patients is 1.8 to 5.6 mg/dl and predominantly had conjugated hyperbilirubinemia. Serum Albumin: Albumin levels of more than 3 gm/dl were seen in 32 patients, and levels less than 3 gm/d were seen in 18/50 (36%) patients. Prothrombin Time: Prothrombin time was done for patients who had total bilirubin >1.8 mg/dl. One patient had prothrombin time of more than 1.5 times of control.

Conclusion: Abnormal LFTs in enteric fever is seen more commonly in patients presenting in 2nd and 3rd week of illness. Hepatic dysfunction is common in enteric fever. Salmonella hepatitis was seen in patients with prolonged illness and inappropriate antibiotic use. It increases morbidity and prolongs hospital stay.

Keywords: Liver function tests, salmonella hepatitis, enteric fever course

I. Introduction

Enteric fever is an acute systemic febrile disease caused by ingestion of food and water contaminated with gram negative bacilli salmonella typhi and salmonella paratyphi. The incidence of enteric fever has gradually decreased in developed countries due to improvised sanitation, but in developing countries it is still a major health problem. Nowadays the classical disease presentation is not seen due to injudicious use of

antibiotics in the first week of the disease and advent of multidrug resistant salmonella^{1,2} So it is important to be aware of the unusual presentation of enteric fever.

Hepatic manifestations are not uncommon in enteric fever and can be easily confused with other entities. This condition was previously called as “hepatitis typhosa” and now termed as “typhoid hepatitis”. Hepatic involvement in enteric fever was first described by Osler³ in 1899 and Stuart and Pullen in 1946. Most authors in their study have taken hepatomegaly, jaundice with abnormal liver function tests as criteria for hepatitis in enteric fever⁴.

Diagnosis of Salmonella hepatitis:

A routine practice of obtaining blood culture and other modes of investigations mentioned above are helpful in establishing the diagnosis.

Criteria for the diagnosis of Salmonella hepatitis⁴:

Clinical Jaundice or total bilirubin ≥ 1.8 mg/dl.

Hepatomegaly (liver span more than 14 cm).

Elevated transaminases (more than two fold) or increase in the prothrombin time (1.5 times of the control).

Abnormal liver pathology.

This study is undertaken in order to observe the hepatic manifestations during the course of enteric fever and study their clinical significance.

II. Aims And Objectives

- 1) To study the liver function test abnormalities in enteric fever.
- 2) To correlate liver function test abnormalities with clinical features of enteric fever.

III. Materials And Methods

The present prospective study was conducted at M.S.Ramaiah Medical Teaching Hospital.

Inclusion Criteria: 50 patients of enteric fever diagnosed on the basis of clinical history, physical examination, blood culture and Widal test were included in the study.

Exclusion Criteria

- Pediatric patients with enteric fever.
- History of alcohol consumption.
- History of hepatotoxic drug abuse.
- Positivity for markers of hepatitis viruses.
- History or clinical evidence of chronic liver disease, gall stones and coexistent disease.

Evaluation: A detailed evaluation of the patients was done with particular reference to hepatic dysfunction. The data was collected on the basis of proforma. The data collection included a detailed clinical history, examination, investigations, follow up, the treatment given and complications observed. A past history of fever was looked. A detailed clinical examination was carried out particularly for the presence of jaundice, pallor, hepatosplenomegaly, altered sensorium, perforation and bleeding tendencies.

- **The Investigations done included:** Liver function test which included total proteins, albumin, total and direct bilirubin, aspartate amino transferase, alanine amino transferase, alkaline phosphatase and prothrombin time. Blood Culture, Stool Culture, Urine culture.
- Widal Test (rising titres), Chest X-ray, Peripheral smear for malaria parasite, and Hepatitis B surface antigen.
- Complete haemogram. Urine for routine examination and presence of urobilinogen, bile salt and pigments. Routine blood tests for sugar, urea and creatinine. Ultrasonography of abdomen were done in clinically indicated cases.

Criteria for Salmonella hepatitis

1. Jaundice present either clinically or total bilirubin more than 1.8 mg/dl.
 2. Hepatomegaly (Liver span > 14 cm) either clinically or by ultrasound examination.
 3. Elevated liver transaminases more than two times or prolonged prothrombin time.
 4. Abnormal liver pathology.
- Any 3 of the 4 criteria should be fulfilled for making the diagnosis of salmonella hepatitis.

IV. Results

After satisfying the inclusion and exclusion criteria 50 cases of enteric fever were included in the study. In 18 cases salmonella typhi and in 4 cases paratyphi were isolated from blood. Other cases were included on the basis of positive widal reaction with rising titre. Patients were examined and investigated methodically for evidence of hepatic dysfunction.

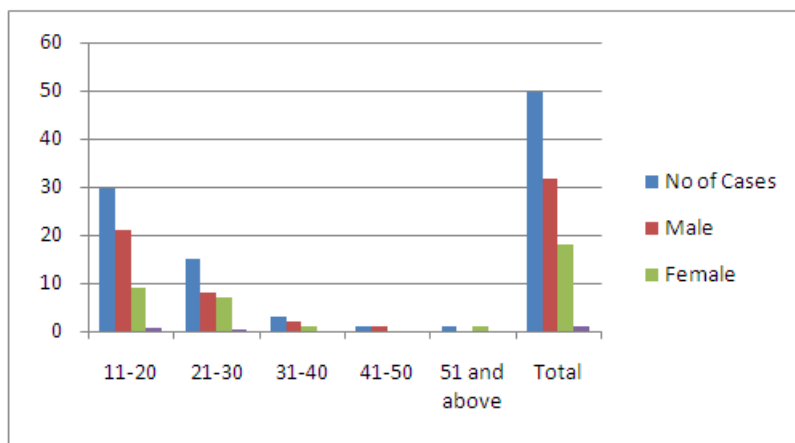
Table –1: Typhoid and paratyphoid cases of study group.

	No of Cases	Percentage
Typhoid	45	90%
Paratyphoid	5	10%

Age and Sex Distribution of Study Group

In the present study, the age of the patients ranged from 14 years to 60 years with a mean age of 21.9 years. Most of the patients in the study group were in the 2nd and 3rd decade.

Sex distribution :More in males(32) than females(18).M:F=3.5:2



No.3 : Typhoid and Paratyphoid cases of Study group

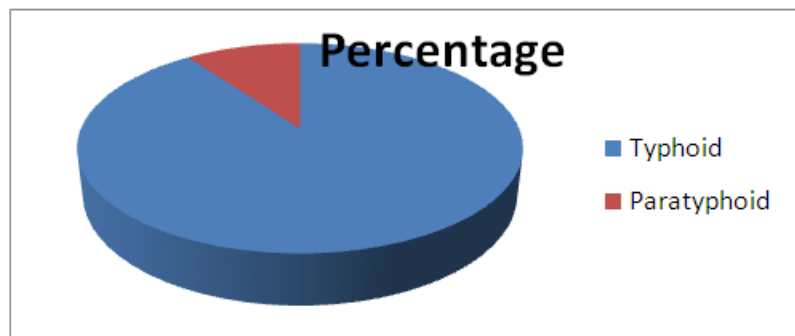


Table – 2Analysis of Symptoms of Enteric Fever

Symptoms	No. of Cases	Percentage
Fever with Chills	50	100%
Pain Abdomen	21	42%
Headache	17	34%
Vomiting	9	18%
Loose Stool	8	16%
Cough	8	16%
Altered Sensorium	2	4%
Jaundice	2	4%

Physical Signs: All patients had pyrexia, 47 patients (94%) were toxic, 34 patients (68%) had central coating of tongue. 21 patients (42%) had abdominal tenderness, 5 patients (10%) had relative bradycardia, 2 patients (4%) had Jaundice, 2 patients (4%) had altered Consciousness and 1 patient (2%) had signs of perfection. 23 patients (46%) had splenomegaly and 22 patients (44%) had hepatomegaly.

Table – 3: Analysis of physical signs of enteric fever:

Signs	Cases	Percentage
Pyrexia	50	100%
Toxic	47	94%
Coated Tongue	34	68%
Relative bradycardia	5	10%
Icterus	2	4%
Abdominal tenderness	21	42%
Splenomegaly	23	46%
Hepatomegaly	22	44%
Altered Consciousness	2	4%
Signs of Pneumonia	1	2%
Signs of Perforation	1	2%

Hematological Profile

Table – 4Haematological Profile in the present Study

Finding	Cases	Percentage
Anemia (<10gm%)	10	20%
Leucopenia (<4000 cells /Cu mm)	5	10%
Thrombocytopenia (<1 lakh/Cu mm)	3	6%
Elevated ESR	47	94%

Anemia was observed in 10 Cases (20%), Leucopenia in 5 cases (10%), Thrombocytopenia in 3 cases (6%) and ESR was elevated in 47 cases (94%).

Analysis of Liver Function Tests

Serum Aspartate Aminotransferase (AST,SGOT) (Normal Range 0-40 U/L)

Table-5Serum AST Level in the Study Group

AST Level	No of Patients	Percentage
Normal	28	56%
Elevated	22	44%

Serum AST was normal in 28 patients, elevated (More than 2 fold) in 22 patients and the range of AST is 4 U/L to 301 U/L.

Table – 6Relation between duration of fever to serum AST level

Fever Duration	Normal AST	Elevated AST
1 st Week	12	2
2 nd Week	10	13
3 rd Week	6	7
Total	28	22

($X^2 = 7.2219$; $df = 2$; $P < 0.05$)

Out of 50 cases of enteric fever, elevated AST of more than two fold was seen in 2 cases in 1st week, 13 cases in 2nd week and 7 cases in 3rd week. There is statistically significant association between duration of fever and AST levels. ($X^2 = 7.2219$; $df = 2$; $P < 0.05$)

Serum Alanine Aminotransferase (ALT.SGPT) (Normal Range 0-40 U/L):

Table – 7Serum ALT level in the study group

ALT Level	No of Patients	Percentage
Normal	29	58%
Elevated	21	42%

Serum ALT was normal in 29 patients, elevated (more than 2 fold) in 21 patients and the range of ALT is 3 U/L to 368 U/L

Table –8Relation between duration of fever to serum ALT Level

Fever Duration	Normal ALT	Elevated ALT
1 st Week	12	2
2 nd Week	11	12
3 rd Week	6	7
Total	29	21

Out of 50 cases of enteric fever, elevated ALT levels of more than 2 fold was seen in 2 cases in 1st week, 12 cases in 2nd week and 7 cases in 3rd week. There is statistically significant associated between duration of fever and ALT levels ($\chi^2 = 6.3557$; df -2 ; P < 0.05).

Serum Alkaline Phosphatase (ALP) (Normal Range 30-120 U/L)

Table – 9 Serum ALP level in the study group:

ALP Level	No of Patients	Percentage
Normal	31	62%
Elevated	19	38%

ALP was normal in 31 patients, elevated to more than 2 fold in 19 patients and the range of ALP in 13 U/L to 628 U/L.

Table – 10 -Relation between duration of fever and serum ALP level:

Duration of Fever	Normal ALP	Elevated ALP
1 st Week	12	2
2 nd Week	12	11
3 rd Week	7	6
Total	31	19

($\chi^2 = 8.3882$; df – 2; P<0.05)

Out of 50 cases of enteric fever, elevated ALP levels of more than two fold was seen in 2 cases in 1st week, 11 cases in 2nd week and 6 cases in 3rd week. There is statistically significant association between duration of fever and serum alkaline phosphatase. ($\chi^2 = 8.3882$; df-2 ; P<005)

Table-11-Serum Bilirubin level in the study group:

Bilirubin Level	No of Patients	Percentage
Normal	45	90%
Elevated (>1.8 mg/dl)	5	10%

Hyperbilirubinemia was found in 5 patients (>1.8mg/dl) and the range of bilirubin in these patients is 1.8 to 5.6 mg/dl. All patients had predominantly conjugated hyperbilirubinemia. Two patients who had presented with jaundice had bilirubin values of 5.6 mg/dl and 3mg/dl.

Table – 12Relation between duration of fever and serum bilirubin level:

Duration of Fever	Normal Bilirubin	Elevated Bilirubin > 1.8mg/dl
1 st Week	14	0
2 nd Week	19	4
3 rd Week	12	1
Total	45	5

Out of 50 cases of enteric fever, 5 patients had elevated bilirubin levels of >1.8mg/dl. 4 patients presented in 2nd week and 1 patient present in the 3rd week of the illness.

Serum Albumin

Table – 13Serum Albumin levels in the study group:

Albumin Levels	No. of Patients	Percentage
More than 3 gm/dl	32	64%
Less than 3 gm/dl	18	36%

Albumin levels of more than 3 gm/dl were seen in 32 patients, and levels less than 3 gm/d were seen in 18 patients.

Prothrombin Time: Prothrombin time was done for patients who had million >1.8mg/dl. One patient had prothrombin time of more than 1.5 times of control.

Complications

Table – 14Complications observed in study group:

Complications	No. of Patients	Percentage
Hepatitis	5	10%
Encephalopathy	2	4%
Perforation	1	2%
Pneumonia	1	2%

Out of 50 patients, 5 had hepatitis (10%), 2 had encephalopathy (4%), 1 had perforation (2%) and 1 had pneumonia (2%). Pure hepatitis was observed in 3 patients other 2 had associated complications of encephalopathy and pneumonia. Hepatitis was not observed in patients with perforation.

Characteristics of Patients with Salmonella Hepatitis

5 of the 50 patients of enteric fever had salmonella hepatitis, of which all the patients were males. Salmonella typhi was isolated in 4 patients and widal was positive in 5 cases. The mean age of these patients was 25.4 years with a range of 18 to 34 years. Two patients had presented with fever and Jaundice (4%).

V. Discussion

Osler described first reports of hepatitis in enteric fever in the year 1899. In a series of cases of enteric fever, Osler noticed Jaundice and hepatomegaly in 8 cases³.

Incidence of Salmonella Hepatitis

In our study we found 5 cases of salmonella hepatitis in a group of 50 cases of enteric fever corresponding to 10%

Table – 15: Incidence of Salmonella hepatitis reported in various studies.

Authors	Percentage of Salmonella Hepatitis
Khosla S N et al (1988) ⁵	8%
Khosla S.N. et al (1990) ⁴	4.8%
Ricrdo Morgenstern et al (1991) ⁶	9%
CalvaJ.J et al ⁷	11.6%
Present study	10%

The present study is comparable and near to most of the studies.

Most of the patients in the study group came to our hospital in the 2nd and 3rd week of the illness because of poor response to antibiotics. The prolonged morbidity in our study group may be the one reason for the high incidence of salmonella hepatitis. This finding was consistent with reports in literature about the salmonella hepatitis where the incidence was found to be in patients with prolonged illness with inappropriate treatment⁸.

Age of the Patients: The mean age of the patient with enteric fever was 27.1 years, whereas patients with hepatitis had a mean age of 24.4 years. In both the groups majority of patients were in the 3rd decade. No special predilection was found for hepatitis in the elderly or in the children. The age distribution of salmonella hepatitis is consistent with various studies, where it is common in 3rd and 4th decade.

Sex Distribution: Among the patients with only enteric fever (M : F = 3.5 : 2) and with hepatitis (M: F = 5:0). The sex distribution of salmonella hepatitis in our study is consistent with other studies where reported incidence was more in adult males⁹.

Duration of Fever

Patients without hepatitis had an average duration of 10.3 days, where as patient with hepatitis had an average duration of 11.6 days There was no significant difference between the two groups in the duration of illness. Patients with hepatitis presented mostly in the 2nd and 3rd week of their illness. The incidence of hepatitis in enteric fever reported was more during the 2nd to 4th week of illness particularly in untreated and under treated cases⁸. This finding was consistent with what we noticed in our study. Anemia and malnourishment were described as predisposing factors for hepatitis in enteric fever^{10,5}.

Clinical and Biochemical Parameters of Hepatic Manifestations

Table –16 Comparison of clinical and biochemical parameters in different study:

Parameters	Khosal S N et al (1988)	Ricardo Morgenstern et al (1991)	Sivaram et al (2000)	Present Study
Clinical Jaundice	8%	9%	7.5%	4%
Hepatomegaly	55%	25%	50%	44%
Raised Bilirubin (>1.8mg/dl)	17%	15 [^]	11.6%	10%
Raised AST	55%	100%	55%	44%
Raised ALT	52%	91%	44%	42%
Raised ALP	27%	100%	36%	38%

Presentation with Jaundice

In our study, 2 out of 50 patients (4%) presented with jaundice in the second week of illness. Early appearance of jaundice is rare in enteric fever¹¹ although abnormal liver function tests suggestive of hepatic involvement is common in the 1st week of illness. Reported incidence of jaundice in enteric fever in literature was 0.5 to 7.6%¹².

Hepatomegaly

Hepatomegaly is a common feature in enteric fever. The incidence of hepatomegaly ranges from 13 – 65%^{13,14}. In our study 22 patients (44%) had clinical and ultrasound evidence of liver enlargement. The liver in most of these cases were more than 2 cms with liver span more than 14 cms. All the patients with hepatitis had palpable liver and in one patient liver was tender. In literature few cases of salmonella hepatitis were reported without hepatomegaly⁵. All the 5 cases of hepatitis were seen with typhoid and there were no paratyphoid fever with hepatitis.

Splenomegaly

Splenomegaly was seen in 23 patients (46%) in our study. 4 of 5 patients in the hepatitis group had splenomegaly.

Liver Function Test

Abnormal liver function tests suggesting hepatic involvement has been reported as 23-60% by various authors^{5,12,14}. Few studies report incidence of elevated transaminases and alkaline phosphatase significantly in all the cases in 2nd and 3rd week of illness and mild elevations in enzyme levels in first week⁶. In our study we observed abnormal liver function tests suggesting hepatic involvement in 44%. AST was elevated to twice more than normal in 44% of patients. Similarly ALT was elevated to twice more than normal in 42% of the patients. Highest levels of AST and ALT observed were 301 and 368 U/L respectively. Usually transaminase elevation will be more than 1000 U/L with the elevated bilirubin levels in patients with viral hepatitis. These features can readily differentiate salmonella hepatitis from viral hepatitis. The transaminase levels will be less than 10 times the normal in most cases of salmonella hepatitis where as transaminase levels are in thousands in viral hepatitis^{16,17}. Alkaline phosphatase was elevated to twice the normal in 38% of the patients in our study. The rise in transaminase along with alkaline phosphates indicates involvement of hepatobiliary system, which may be secondary to endotoxic effect on hepatic parenchyma causing edema and biliary stasis⁵.

Bilirubin levels ≥ 1.8 mg/dl was found in 5 patients (10%) of which all the patients had conjugated hyperbilirubinemia indicating hepatic dysfunction as the cause for jaundice. Elevated ALP and conjugated hyperbilirubinemia in a patient with severe jaundice indicates cholestasis. So it has to be differentiated from cholangitis, acute cholecystitis¹⁸ and cholestatic phase of viral hepatitis, where patient presents with fever and jaundice. None of our patients manifested with bleeding tendencies, although two patients were having thrombocytopenia and one patient had prolonged prothrombin time in the salmonella hepatitis group. The increased incidence of thrombocytopenia was more common in severe cases of enteric fever. Whereas the prolonged prothrombin time indicates significant involvement of liver, suggesting interference in the synthetic functions of liver^{5,10}.

Complications: Complications of enteric fever were present in 6 patients. Hepatitis (10%) was the commonest followed by encephalopathy (4%) pneumonia (2%) and perforation (2%), 3 patients had pure hepatitis where as others had associated complications of typhoid fever.

Though association of salmonella hepatitis was reported with other complications particularly encephalopathy, bleeding diathesis and acute renal failure^{14,19,20}, no mention as made about the hepatitis in studies done on major complications of typhoid fever like intestinal haemorrhage and perforation^{4,14}. In our study hepatitis was not seen in a patient with perforation.

Out of five patients with hepatitis two patients had encephalopathy. One patient was diagnosed as hepatic encephalopathy due to viral hepatitis and was started on anticomma measures. But later diagnosing it as salmonella hepatitis, this patient was treated with antibiotics. In literature encephalopathy was reported with salmonella hepatitis but the mechanism of encephalopathy was not clear whether it was secondary to hepatic dysfunction or to enteric fever toxemia itself⁴.

Treatment: There was no significant difference between enteric fever group and hepatitis group as far as antibiotic sensitivity was concerned. Most of the patients were treated with ceftriaxone in anticipation of antibiotic resistance. In all the patients with hepatitis liver function tests returned to normal following the treatment of enteric fever. On follow up no residual liver function abnormalities were noticed in these patients.

VI. Conclusion

Abnormal LFT S in enteric fever is seen more commonly in patients presenting in 2nd and 3rd week of illness. Hepatic dysfunction is common in enteric fever. Salmonella hepatitis was seen in patients with prolonged illness and inappropriate antibiotic use. It increases morbidity and prolongs hospital stay.

References

- [1]. Gulati PD, Sexana SN, Gupta PS, et al. Changing pattern of typhoid fever. *Am J. Med* 1968; 45: 444-448.
- [2]. Wicks ABC, Holmes GS, Davidson L. Endemic typhoid fever. *Q.J Med* 1971; 40: 341-354.
- [3]. Osler W. Heptic complications of typhoid fever. *Johns Hopkins. Hosp. Rep.* 1899; 8: 373 – 377.
- [4]. Khosla SN. Typhoid hepatitis. *Postgrad Med J* 1990; 66: 923-925
- [5]. Khosla SN, Singh R, Singh GP, et al. The spectrum of hepatic injury in enteric fever. *Am J Gastroenterol* 1988; 83: 413-416.
- [6]. Ricardo Morgenstern, Peter C Hyes. The Liver in Typhoid Fever : Always affected, not just a complication. *Am J Gastroenterol*, 1991; 86 : 1235-1239.
- [7]. CalvaJJ,RuizPalacios GM Salmonella Hepatitis-Detection of Salmonella Antigen in Liver patients with Typhoid Fever.*J Infect Dis* 1986;54;373-374.
- [8]. De Brito T, Trench-Vieira W, D Agostino-Dias. Jaundice in typhoidhepatitis; A light and electron microscopy study based onbiopsies. *ActaHepatoGastroenterol* 1977; 24: 426 – 433.
- [9]. Parmoolsinsap C, Viranavatriv V. Salmonella hepatitis. *J gastroenterolHepato* 1998; 13: 45-5010.
- [10]. Christopher C Kibbler. Bacterial Infections and Liver. *Salmonella Spp. Oxford Text Book of Hepatology*. 2nd edition, 1999; Vol-1: 1001.
- [11]. Pias P. A hepatitis like picture in typhoid fever. *BMJ* 1984 ; 289 : 225 – 226.
- [12]. Ramachandran S, Godfery JJ, Perera MVF. Typhoid hepatitis. *JAMA* 1974 ; 230 : 236 – 240.
- [13]. Butler T, Williams R and Bell JL, et al. Typhoid fever studies of blood coagulation, bacteremia and endotoxemia. *Arch Intern Med* 1978; 138: 407-410
- [14]. Stuart BM, Pullen RI. Typhoid clinical analysis of 360 cases. *Arch Int. Med* 1946; 78 : 629-667.
- [15]. Nasralla SM NassarVH. Enteric fever .*Am J Gastroenterol*,1978;69:63-69
- [16]. El – Newihi HM, alamy ME, Reynolds TB. Salmonella hepatitis. Analysis of 27 cases and comparison with acute viral hepatitis. *Hepatology* 1996; 24; 516-519.
- [17]. Norman Gitlin. Bacterial and Systemic Infections. Samonella induced liver disease. *Schiffs Disease of Liver*. 8th edition, 1999; Vol. 2: 1552-1553.
- [18]. Holdstock, Blanchard T, Robertson DAF, et al., Liver in infection. *Wrights Liver and Biliary Disease*. 3rd edition 1992 : 1406.
- [19]. Faierman D, Ross FA, Seckler SG. Typhoid Fever Complicated by Heptatis, Nephritis and Thrombocytopenia. *JAMA* 1972; 221:60-61.
- [20]. Rao PN, Bhusnurmath SR, Naik SR. Typhoid fever manifesting with hematemesis. Hepatitisand hemolysis. *J Trop Med Hyg* 1978; 81: 146-150.
- [21]. Olubodun JO, Kuti JA, Adefuya BO, et al. Typhoid fever associated with severe hepatitis. *Cent Afr J Med* 1994; 40: 262-264.
- [22]. Ozen H, Secmeer G, Kanava G, et al. Typhoid fever with high transaminase levels. *Turkish J Paediatr* 1995; 37 : 169-171.