Trakia Journal of Sciences, Vol. 4, No. 2, pp23-27, 2006

Available online at:
http://www.uni-sz.bg

ISSN 1312-1723

Original Contribution

LIVER DISTURBANCES IN PATIENTS WITH SALMONELLOSIS

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ABSTRACT

Salmonellosis continues to be a serious health problem in many parts of the world. Liver disturbances in salmonellosis are not rare but have not been well studied. The aim of this study is to investigate the frequency and the clinical and laboratory features of liver disturbances in patients with salmonellosis. 361 patients with salmonellosis (aged 45days to 84 years) were carefully studied with regard to their liver condition. Hepatomegaly was established in 117 patients – 40 %. Splenomegaly was found in 78 patients (21.60 %) and jaundice – in 12 (3.32%). Elevated ALT level (up to 800UI) was seen in 78 cases – 7.76%. Other tests performed included: thymol test, serum fibrinogen and albumin. Anti HAV IgM and HBsAg were negative in all patients. On the basis of the accumulated evidence hepatosplenomegaly syndrome was found in 88 patients (24.37%), toxic hepatitis was diagnosed in 25 cases (6.92%), and cholangiohepatitis – in 5 (1.38%). Liver disturbances were associated with different salmonella serotypes and were more frequent in infants especially in those with serious underlying medical conditions.

Key words: salmonellosis, liver disturbances

INTRODUCTION

Salmonelloses are among the most common bacterial infections worldwide and still remain a major public health problem not only in underdeveloped but also in developed countries (1, 2, 3)

This fact is likely to be attributable to the growing incidence rate of the disease, the occurrence of epidemic outbursts and hospital acquired salmonella infections as well as to the possibility of severe clinical forms of the disease especially in early childhood and in immunocompromised patients (4, 5, 6).

Salmonella infection in humans usually presents as self-limiting gastroenteritis but septic and extra intestinal forms of the disease have also been described (5, 6, 7).

Clinical features of salmonellosis vary in character and in severity in different patients. Organ and systemic complications are likely and further contribute to the polymorphism of the clinical picture. According to some authors complications might be registered in 45%-52% of the cases and are frequently crucial to the clinical course and disease outcome (8).

Liver disturbances are not rare in salomonellosis but are not well studied. This study was focused on the frequency and the clinical features of liver disturbances in patients with salmonella infection.

PATIENTS AND METHODS

The study comprised 361 nonselected patients with culture proven non-typhoid salmonella infection. All of them received treatment at the Clinics of Infectious Diseases of St. George University Hospital, Plovdiv. Patients were prospectively studied in view of their liver condition. Their age ranged from 2 months to 84 years. Patients were assigned into two groups- group 1 – infants up to 1 year of age and group 2 – patients over 1 year of age. *Salmonella enterica* serotype Enteritidis was the causative agent in 53.46% of the cases, *Salmonella enterica* serotype Typhimurium – in 38.27% and group C salmonellae (Cotbus, Isangi, Virchow) in 8.31% of the cases respectively. 354 of the patients presented with gastrointestinal salmonellosis (98.06%). Septic infection was observed in 8 (1.93%).

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The course of salmonellosis was mild in 24.09% of the patients, moderate in 52.63% and severe in 23.28%.

Methods included: clinical examination, laboratory testing and abdominal US scanning when necessary. Identification of Salmonella serotypes was based on culture, biochemical and serological tests. Student's t test was used for statistical analysis.

CLINICAL CRITERIA AND DEFINITIONS

Septic infection was defined by the presence of salmonella bacteria in peripheral blood cultures and distinct clinical signs and symptoms. *Hepatosplenomegaly syndrome* was diagnosed in the presence of enlarged liver and spleen on examination and on US scanning in the absence of data for functional impairment. The diagnosis of *toxic hepatitis* was based on the presence of elevated levels of aminotransferases (AST and ALT), the positive thymol turbidity test, hypoalbuminaemia and occasionally jaundice as well as on the negative markers for viral hepatitis (HBsAg, antiHAV IgM). *Cholangiohepatitis* was characterised by enlarged and tender liver, prolonged fever, elevated leukocyte count with significant shift to the left and elevated bilirubin, alkaline phosphatase (AP) and γ-glutamyltranspeptidase levels.

RESULTS

The frequency of signs and symptoms indicating liver disturbance was compared between the two groups of patients (**Figure 1**).

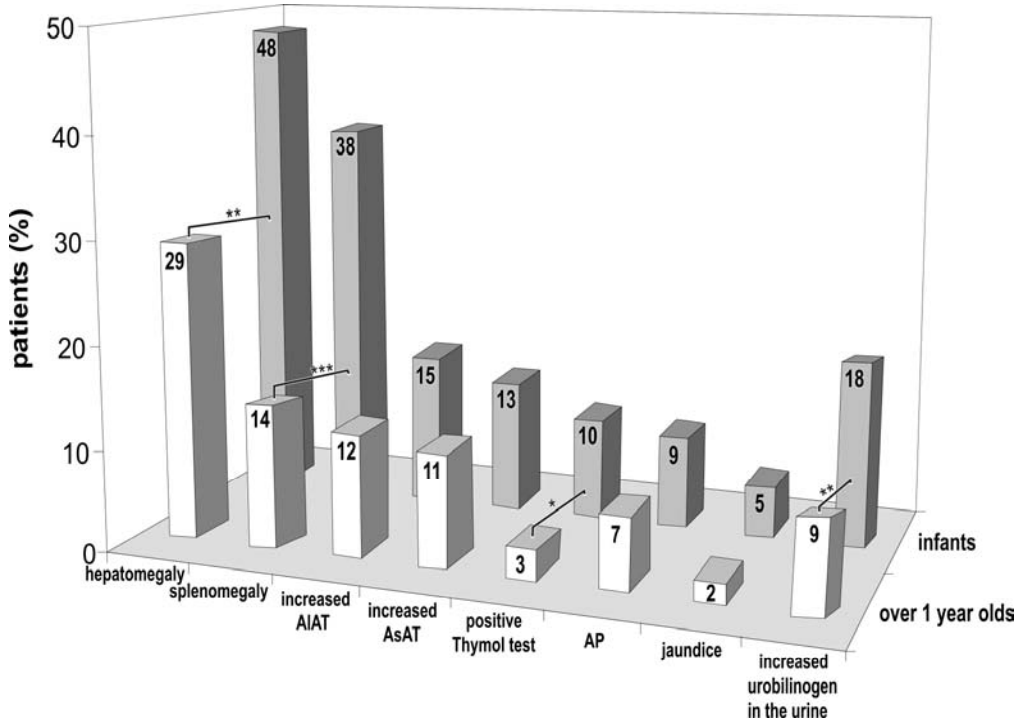

Figure 1. *Frequency rate (%) of liver disorders symptoms in patients with Salmonellosis.*

Significant differences are indicated as single ($p<0.05$), double (** $p<0.01$) or triple (*** $p<0.001$) asterisks.*

Enlarged liver and spleen, positive thymol turbidity test and increased urine urobilinogen were significantly more frequent in infants compared to patients over 1 year of age. Elevated AST and ALT levels, as well as jaundice, were also more frequent in patients from group 1 but the difference was not significant.

The incidence rate of liver disturbances was compared among patients infected with different salmonella serotypes (**Figure 2**). It was seen that the occurrence rate of hepatomegaly, splenomegaly and elevated transaminase activity was significantly higher in salmonellosis caused by *Salmonella enterica*, serotype Typhimurium and group C salmonellae than in salmonellosis caused by *Salmonella enterica* serotype Enteritidis. If other clinical symptoms were compared no difference was observed.

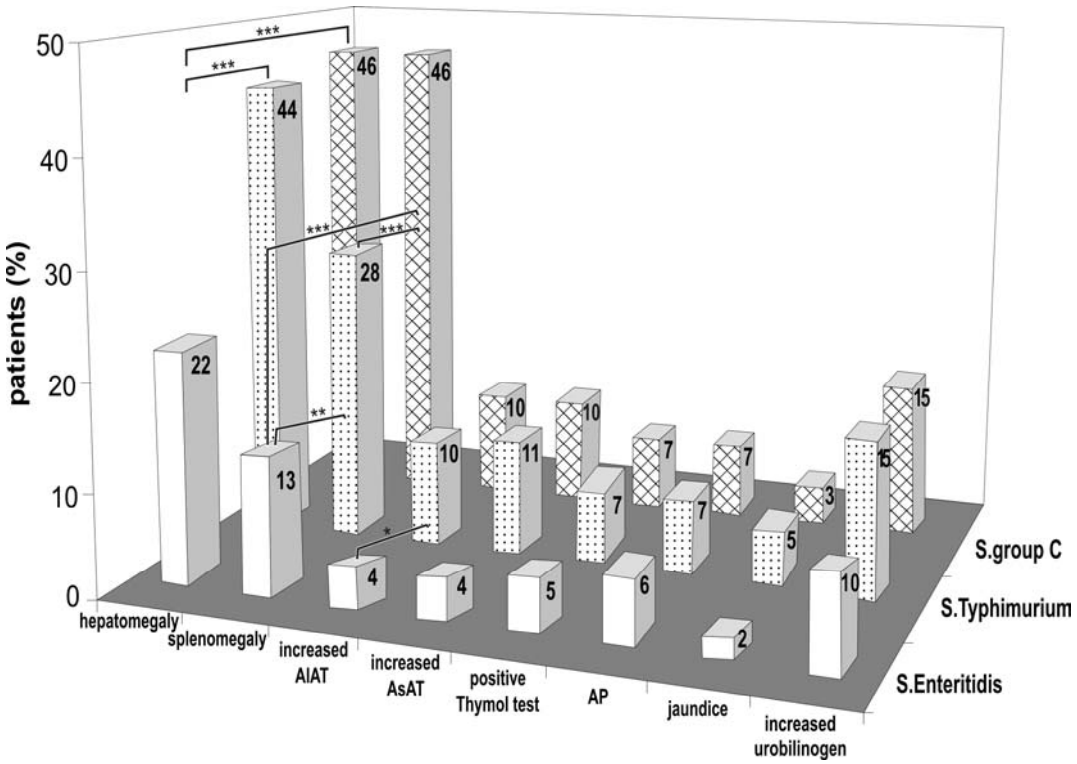

Figure 2. *Frequency rate (%) of liver disorders symptoms in patients with Salmonellosis due to different S.serotypes.*

Significant differences are indicated as single (p<0.05), double (** p<0.01) or triple (*** p<0.001) asterisks.*

According to the clinical symptoms and laboratory findings hepatic disturbances were classified as: hepatospenomegaly syndrome, toxic hepatitis and cholangiohepatitis. Their incidence rate was compared between the two groups of patients and among patients infected with different salmonella serotypes (**Table 1**). Hepatosplenomegaly was significantly higher in infants compared to patients over 1 year of age but difference was significant only in cases with Salmonella enterica serotype Typhimurium infections.

Table 1. *Frequency rate (%) of liver complications syndromes in patients with Salmonellosis; (■) – infants, (□) – over 1 year old*

Causative agent syndrom	*Enteritidis*		*Salmonella enterica Typhimurium*		*Group C*	
	n=21	*n=171*	*n=92*	*n=46*	*n=15*	*n=16*
Hepato-splenomegaly	23.80%	11.69%	38% *p<*	8.69% *0.001*	53.33%	37.5%
Hepatitis toxica	9.52%	3.51%	10.86%	8.69%	13.33%	6.25%
Cholangio hapatitis			2.17%	2.17%	6.66%	6.25%

Toxic hepatitis was significantly more common in patients infected with serotype Typhimurium than in those infected with serotype Enteritidis (p>0.05). Its incidence was similar in both age groups. The course of salmonellosis complicated with toxic hepatitis was severe in 38% of the patients, moderate - in 58% and mild – in 4% of the cases. One third of the patients with toxic hepatitis developed other complications, such as: paralytic intestinal obstruction, acute renal failure, shock, neurotoxicosis etc. Nearly 48% of them had preceding underlying medical conditions (malnutrition, pneumonia, bronchitis etc).

Cholangiohepatitis was due to

Salmonella enterica Typhimurium and *S. isangi* infections without difference between the age groups.

DISCUSSION

Results from this study showed that hepatospenomegaly was most frequent liver disturbance in patients with salmonellosis (21.8%), followed by hepatitis toxica (6.92%) and cholangiohepatititis (1.38%). Our data on the incidence rate of toxic hepatitis is consistent with the data presented by other authors (2, 8). In the literature, there is paucity of data on the incidence rate of cholangiohepatitis (9).

Two pathogenic mechanisms are likely to be involved in liver damage in salmonellosis – salmonella bacteria and the endotoxin released in the process of bacteriolysis. It is well known that salmonella bacteria tend to damage the hepatobilliary system and hepatic Kupffer cells are targets for the salmonella endotoxin (10, 11). The problem whether the macro organism reactivity or the aetiological agents involved are the determinants of liver damage severity still remains a matter of discussion. Which are the key factors for the clinical polymorphism of salmonella infections? More than 2000 salmonella serotypes might cause infection in humans. All of them have different adaptation capacity to the human organism, different level of virulence and resistance to the environmental factors (10, 11, 12). On the other hand, it has been established that both humoral and cell mediated immunity (local and systemic) are involved in the organism defence against salmonella infection (5). Our data showed that hapatospenomegaly in infants is significantly higher compared to that of patients over 1 year of age. This finding is consistent with the findings of other authors and might be explained by the fact that infants are particularly prone to generalization of the infectious process (1, 2).

The higher incidence of hepatosplenomegaly in infections caused by *S. enterica* serotype Typhimurium and group *C salmonellae* is likely to be attributable to the following: (i) these agents were more frequently found in infants and (ii) these serotypes tend to cause invasive disease.

Interestingly, it was established that toxic hepatitis occurred with similar frequency in infants and in patients over 1 year of age regardless of the causative agent.

Recent findings suggest plasmid mediated virulence in *S. enteritidis* and this serotype may cause systemic infections too (5, 12). Our data are consistent with the data of Galofre et al. who established that the incidence rate of toxic hepatitis was related to the course of salmonella infection as well as to the presence of underlying and concomitant medical conditions (13). Our data supported the view that overall patients' reactivity is more important for the development of toxic hepatitis rather than the salmonella serotype differences (14).

CONCLUSIONS

Liver disturbances are not uncommon in salmonellosis, especially in severe clinical forms of the disease. Liver function monitoring is necessary for early diagnosis and adequate treatment of liver damage in patients with salmonella infections.

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