SHORT COMMUNICATION

Serum ALT: LDH Ratio in Typhoid Fever and Acute Viral Hepatitis

S BALASUBRAMANIAN, K KAARTHIGEYAN, S SRINIVAS* AND R RAJESWARI

*From the Department of Pediatrics and *Pediatric Gastroenterology, Kanchi Kamakoti CHILDS Trust Hospital, Chennai, India.*

Correspondence to:
Dr S Balasubramanian, Senior Consultant Pediatrician, Kanchi Kamakoti CHILDS Trust Hospital, 12-A, Nageswara Road, Nungambakkam, Chennai 600 034, TN, India.
sbsped53@sify.com
Received: September 15, 2008; Initial review: October 18, 2008; Accepted: February 10, 2009.

In 100 consecutive children aged below 18 years with confirmed typhoid fever, 29 had moderate hepatitis. Serum alanine amino transferase: lactate dehydrogenase (ALT: LDH) ratios of these 29 children at the time of hospitalization were compared with that of 29 children with acute viral hepatitis. The serum ALT: LDH ratio levels (expressed in multiples of upper limit of normal) was found to be less than 9 in typhoid hepatitis and more than 9 in acute viral hepatitis. Serum ALT: LDH ratio helps to differentiate typhoid hepatitis from acute viral hepatitis.

Key words: *Acute viral hepatitis, Enteric fever, ALT: LDH ratio, Typhoid hepatitis.*

Published online: 2009. April 15. ***PII : S097475590800558-2***

Salmonella hepatitis is known to clinically mimic acute viral hepatitis(1,2). The differentiation between typhoid fever and evolving acute viral hepatitis in a child presenting with fever, hepatomegaly, elevated transaminases with or without jaundice assumes paramount significance in clinical practice in a country where both diseases are common, since the former has definitive treatment in the form of antimicrobials. We studied the profile of hepatobiliary involvement in children with typhoid fever and evaluated the significance of ALT: LDH ratio in differentiating typhoid hepatitis from acute viral hepatitis.

METHODS

A descriptive case control study was carried out at Kanchi Kamakoti Childs Trust Hospital, a tertiary care children's hospital at Chennai, India from March 2003 to March 2005. 100 consecutive children with confirmed typhoid fever (blood culture positive for *Salmonella typhi*) were evaluated with special reference to hepatobiliary manifestations. They were hospitalized and investigated with complete blood counts, abdominal sonogram, complete liver functions tests, serum lactate dehydrogenase (LDH), prothrombin time (PT) and activated partial thromboplastin time (aPTT). The children were classified as having mild, moderate and severe hepatitis based on serum alanine amino transferase levels: 2-3 times, 3-20 times and more than 20 times above the upper limit of normal, (40 IU/L), respectively. Children were followed up to detect any complication.

The controls consisted of 29 children with a clinical picture consistent with acute viral hepatitis and jaundice and IgM positive for Hepatitis A or E viruses. Their serum ALT levels, serum LDH levels and serum ALT: LDH ratio at hospitalization was compared with the subgroup of 29 children with typhoid having moderate to severe hepatitis.

Statistical analysis: Z- test was used to compare the significance of difference between arithmetic means and standard deviations of ALT and LDH in viral and typhoid hepatitis. The ratio analysis was carried over to find the upper and lower bounds of serum ALT: LDH ratios in typhoid and viral hepatitis. Fischer 'F' test was used to identify the existence of variability and consistency between ALT: LDH ratios in typhoid and viral hepatitis. Statistical analysis was done using SPSS version 11.0 and a *P* value <0.05 was considered significant.

RESULTS

Of the 100 children with enteric fever enrolled into the study (66 boys and 34 girls), 44 children were below 5 years of age and these included 7 infants. Hepatomegaly was noticed in 54% children, splenomegaly in 37% and hepatosplenomegaly in 36%. Icteric hepatitis was seen in 4% of typhoid patients whereas anicteric hepatitis was more common. Fifty-nine cases had elevated serum transaminases more than two times above the upper limit of normal (i.e. > 80 IU/L). Thirty children had mild hepatitis and 29 children had moderate hepatitis. Prolongation of PT/PTT was seen in 4% of patients and only one child had bleeding manifestations in the form of upper gastrointestinal bleeding.

Serum ALT was elevated to a greater extent in viral hepatitis than in typhoid hepatitis; while serum LDH was elevated to a greater extent in typhoid hepatitis than in viral hepatitis (***Table* 1**) and these differences were statistically significant. Serum ALT: LDH ratio at the time of hospitalization, when levels of the enzymes were expressed in multiples of the upper limit of normal, was found to be more than 9 in acute viral hepatitis and less than 9 in typhoid hepatitis (***Fig.*1**).

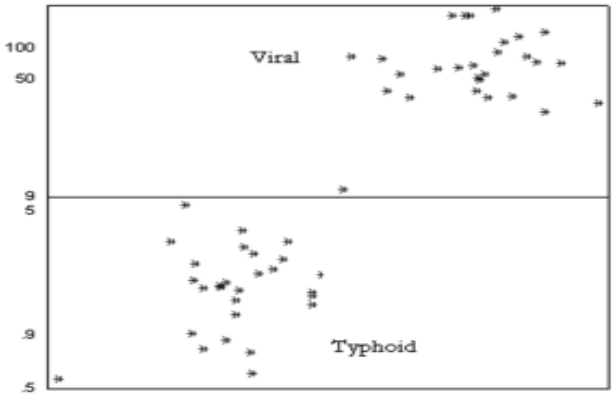

FIG.1 *Scatter diagram showing ALT/LDH ratios in typhoid and acute viral hepatitis.*

DISCUSSION

The spectrum of hepatic injury in typhoid has been well studied in adults and the liver is always affected in typhoid, although clinical jaundice is rare(3). In our study, the incidence of typhoid hepatitis was 59% versus only 19% documented in an earlier study in Malaysian children(4). The incidence of clinical jaundice in typhoid was low (4%) in our study and all 4 children with icteric typhoid hepatitis had serum transaminases levels between 5-12 times the upper limits of normal.

This is the first study on Indian children with culture proven typhoid to evaluate the serum LDH in differentiating typhoid hepatitis from acute viral hepatitis. The rise in serum LDH in typhoid occurs early during the disease and is attributed to cell necrosis of intestinal lymphatic tissue(5). Serum LDH could serve as an additional clue in the diagnosis of typhoid hepatitis apart from clinical pointers to typhoid, like fever persisting beyond the 1st week and a lower incidence as well as milder degree of jaundice, and lower levels of elevation of

TABLE 1 SERUM ALT AND LDH IN TYPHOID AND ACUTE VIRAL HEPATITIS

	Serum ALT (IU/L)			Serum LDH (IU/L)			ALT: LDH Ratio		
	Range	Mean±SD	*P* value	Range	Mean±SD	*P* value	Range	Mean±SD	*P* value
Typhoid hepatitis	120-428	188 ±78		348-2976	1103 ± 668		0.58-7.48	2 ± 2	
			<0.001			<0.001[+]			<0.001[†]
Viral hepatitis	1320-8678	4689 ± 1883		245-874	582 ± 165		10.33-192.81	86 ± 45	

[+]*Student's t-test,* [†]*Mann-Whitney U test.*

WHAT THIS STUDY ADDS?

- Serum ALT: LDH ratio is less than 9 in typhoid hepatitis and more than 9 in acute viral hepatitis in children.

serum transaminases than in acute viral hepatitis. Thus the combination of lower levels of serum ALT and higher levels of serum LDH in typhoid combine to give a lower serum ALT: LDH ratio than in acute viral hepatitis. Serum ALT: LDH ratio has been studied earlier in adults and suggested as a useful point in differentiating typhoid hepatitis from acute viral hepatitis(1,6). All cases of typhoid hepatitis had admission ALT: LDH ratio less than 4 and all cases of acute viral hepatitis had values above 5 in the study(1). In our study, all cases of typhoid hepatitis had admission ALT: LDH values below 9 and all cases of acute viral hepatitis had values above 9. If a cut-off value of 4 had been used in our study, typhoid hepatitis could be misclassified as viral hepatitis. Since there is no overlap between the cut-offs, construction of an ROC curve is not possible and sensitivities and specificities of different cut-offs were not calculated.

Serum LDH may also be elevated in other conditions like toxic and ischemic hepatitis(7). Our study has not evaluated serum LDH in other common febrile conditions with mild to moderate hepatitis like malaria, dengue hemorrhagic fever and leptospirosis.

Contributors: SBS designed the study and will act as a guarantor. SS and KK analyzed data. SBS and KK were involved in review of literature and preparation of manuscript. RR collected data and carried out clinical examination.

Funding: None.

Competing interests: None stated.

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