



## Significance of Alanine Transaminase in Determining Drug Efficacy in Typhoid Hepatitis

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### ABSTRACT

**Objectives:** Abnormal liver enzyme levels might be observed with typhoid fever indicating liver involvement. Although, jaundice is unusual and infrequently reported in children, it declares the occurrence of complication. The aim was to evaluate the efficacy of some anti-typhoid drugs in typhoid hepatitis in children through measuring liver transaminase enzymes levels.

**Patients and Methods:** 123 typhoid pediatric patients with high liver transaminase enzymes levels were participated and randomly allocated into 3 groups receiving cefixime (20 mg/kg/day), chloramphenicol (50 mg/kg/day) and amoxicillin (100mg/kg/ day) for two weeks. The obtained data were analyzed using SPSS (version 12) and were expressed as mean  $\pm$  SEM and the difference among means has been analyzed by student's t test.

**Results:** 64.8% had higher levels of Alanine transaminase than Aspartate transaminase while only 12.5% showed the opposite. At the end of the treatment; 68.3% had normally-returned alanine transaminase level before aspartate transaminase level, while 31.7% had the opposite.

**Conclusion:** Estimation of alanine transaminase level in typhoid hepatitis during and after treatment gives a clue for the efficacy of the used drugs.

**Keywords:** Aspartate transaminase, Cefixime, Chloramphenicol, Fever abatement.

## 1. INTRODUCTION

Many organs other than gastrointestinal tract may be involved with typhoid fever including liver. Hepatic manifestations of typhoid can occur with or without jaundice, but, when the levels of liver transaminases [Aspartate transaminase (AST); enzyme of high metabolic activity tissues like liver, brain and skeletal muscles and Alanine transaminase (ALT); enzyme presents in high concentrations in liver and low concentrations in heart and muscles] become twice the reference range<sup>[1]</sup>, it is indicative of hepatocellular disorder<sup>[2]</sup> which may be due to viral hepatitis, liver damage by ingestion of certain drugs such as Zileuton, or infection by some high virulent S.Typhi strains.<sup>[3]</sup> Although many literatures reported the complications of drug-resistant S.typhi infection<sup>[4]</sup> and its effects on liver functions<sup>[5]</sup>, no study was made to explore the efficacy of anti-typhoid drugs in typhoid hepatitis in

children through measuring liver transaminase enzymes levels as the present study tried.

## 2. PATIENTS AND METHODS

One hundred and thirty one pediatric patients were participated in this prospective and single-blind study which was approved by the ethical committee in Baghdad College of Medicine (Approval No.HEC/17/2008/CMBU). The patients were recruited from outpatient clinics of department of pediatrics in two Baghdad teaching hospitals from March 2008 to June 2011. After initial diagnosis, they were proven as typhoid cases by polymerase chain reaction (PCR)<sup>[6]</sup> and their blood samples were estimated for AST and ALT enzymes levels using colorimetric method<sup>[7]</sup> and spectrophotometer. During the treatment, eight PCR-proven typhoid patients were excluded due to different reasons.

Therefore, only one hundred and twenty three pediatric patients (78 males and 45 females) ranging in age from 6 to 15 years (mean 11.7±0.1 SD) and their weights ranged from 16.7 to 34.2 Kilograms (mean 24.9±0.3 kg SD) were participated after written consents from their parents were taken.

They were randomly allocated into 3 groups and were given a daily dose of the following drugs as oral suspension for two weeks;

Group I (41 patients) -received cefixime (surtax; Anvaxx laboratory/ Burkshire/ MA/ USA) as 20 mg/kg in two divided doses.

Group II (41 patients) -received chloramphenicol (chloramycitin; Dalta pharmacoceuticals /Almahalla/ Egypt) as 50 mg/kg in four divided doses.

### 3. RESULTS

At the time of consultation; 97.7% (128 out of 131 typhoid pediatric patients with hepatic manifestation) had elevated liver enzyme levels, so 3 patients were excluded because they had normal enzyme levels. 64.8% (83 out of 128) had higher levels of ALT than AST, 22.7% (29 out of 128) had

Group III (41 patients) -received amoxicillin (amoxil; cidomox/Shanghai pharmaceuticals co. limited / Shanghai / China) as 100mg/kg in three divided doses.

Daily temperature checking was done to follow up the fever abatement and observing any drug side effects to stop it and excluding the participants. At the end of the treatment, PCR and liver enzymes estimations were done again.<sup>[8]</sup>

### Statistical Analysis

The data were analyzed using SPSS version (version 12) and were expressed as mean ± SEM. The difference among means has been analyzed by student's t test. A probability value of  $P < 0.05$  was considered to be statistically significant

somewhat equal elevated transaminase enzymes levels, while only 12.5% (16 out of 128) showed higher levels of AST than ALT [table 1].

**Table 1: Frequency distribution of typhoid pediatric patients at the time of consultation according to elevated liver enzymes levels**

Participated patients No. (%)	patients with high enzymes levels		
	ALT > AST	ALT = AST	AST > ALT
128 (100)	83 (64.8)	29 (22.7)	16 (12.5)

ALT; alanine aminotransferase, AST; aspartate aminotransferase

During the treatment, 5 patients were again excluded out of 41) for GII and 12.2% (5 out of 41) for GIII, while on because of diarrhea (a drug side effect). On 5<sup>th</sup> post- 7<sup>th</sup> post-treatment day, they represented 92.7% (38 out of treatment day, only children from GI had normal ALT levels 41) for GI, 34.1% (14 out of 41) for GII and 17% (7 out of 41) and represented 36.6% (15 out of 41). On 6<sup>th</sup> post-treatment for GIII [table 2]. day, they represented 75.6% (31 out of 41) for GI, 19.5% (8

**Table 2: Frequency distribution of typhoid pediatric patients with normally- returned ALT level before normally- returned AST level according to post-treatment day**

Group	dose/day	(No.)	patients have normal ALT before AST levels according to treatment day				total (%)
			5 <sup>th</sup>	6 <sup>th</sup>	7 <sup>th</sup>	8 <sup>th</sup>	
I (cefixime)	20 mg/kg	41	15	16	7	-	38 (92.7)
II (chloramphenicol 50 mg/kg		41	-	8	6	2	16 (39.0)
III (amoxicillin 100mg/kg		41	-	5	2	6	13 (31.7)

ALT; alanine aminotransferase, AST; aspartate aminotransferase

At the end of the treatment, the patients were cured; 68.3% (84 out of 123) had normally-returned ALT levels before AST levels returned to normal, while 31.7% (39 out of 123) had normally-returned AST levels before ALT levels returned to normal [table 3].

**Table 3: Frequency distribution of cured patients according to what liver enzymes firstly returned normal**

Cured patients	cured patients with normal enzymes levels	
	ALT before AST	AST before ALT
No. (%)		
123 (100)	84 (68.3)	39 (31.7)

ALT; alanine aminotransferase, AST; aspartate aminotransferase

#### 4. DISCUSSION

Our study focuses on the efficacy of certain anti-typhoid drugs (cefexime, amoxicillin and chloramphenicol) in the treatment of typhoid hepatitis in children by estimation the titers of AST and ALT which consider the reliable markers of hepatocellular injury, but ALT enzyme is thought to be more specific because it is mainly present inside the liver cells. However, elevated ALT level does not always mean that medical problems exist as its elevation is normal over the day course, and in strenuous physical exercise.<sup>[9]</sup> Salmonella typhi is postulated to produce hepatic dysfunction either via a) invasion of intestinal lymphatic tissue by host macrophages which attracted by Vi capsular antigen of *S typhi*<sup>[10]</sup> or b) interaction between *S. typhi* endotoxin and hepatic macrophages (Kupffer cells).<sup>[11]</sup> Our study showed that at the time of consultation; 97.7% had elevated AST and ALT titers which revealed hepatic cell injury and this agreed with the results of Kumar et al.<sup>[12]</sup> 64.8% had higher levels of ALT than AST and it was agreed with Balasubramanian et al.<sup>[13]</sup> After using anti-typhoid drugs, ALT levels returned rapidly to

normal value as two times as AST levels (84/39). This largely comes from using cefexime (38/41) and to less extent chloramphenicol (14/41) in comparison to amoxicillin (7/41). The rapid fall-down level of ALT enzyme to normal values, revealed hepatocellular recovery, besides, it explained the safety use of cefexime in typhoid hepatitis because most cephalosporins are excreted via the kidney, largely by tubular secretion.

#### 5. CONCLUSION

Estimation of ALT enzyme level in children with typhoid hepatitis gives a clue for the efficacy of the used anti-typhoid drugs.

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