Typhoid Fever and Liver Enzyme Activity

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ABSTRACT:

Typhoid fever is a systemic infection caused by the Gram-negative bacillus Salmonella typhi and occasionally by Salmonella paratyphi. This study was carried out to assess the biochemical parameters AST, ALT and ALP in patients with Typhoid Fever. The study was designed to evaluate the serum liver enzymes’ activities during the incidence of typhoid fever. The aminotransferases (AST and ALT) and alkaline phosphatase (ALP) activities were demonstrated using Reitman and Frankel method and King and Armstrong method respectively. A total of 200 subjects were studied, which was divided into 100 healthy individuals (controls) and 100 diagnosed typhoid fever patients. The results revealed a highly elevated levels of AST (25.6±17.6), ALT (22.5±8.8) and ALP (32.0±16.1) (p<0.05) observed in typhoid patients as compared to controls (1.0±1.7) (6.5±2.8) and (24.0±6.4) respectively. It could be noted from the findings of this study that there is a derangement of the liver enzyme values in typhoid patients. This study appears to have ample evidence based on the physiological and biochemical parameters in typhoid patients to help explain the influence of typhoid morbidity.

Keywords: Salmonella typhi; Typhoid fever; Liver enzymes

INTRODUCTION:

Typhoid fever is a systemic infection caused by the Gram-negative bacillus Salmonella typhi and occasionally by Salmonella paratyphi (Gienella, 1991). Salmonella are fermentative, facultative anaerobic, oxidase-negative Gram-negative rods. They are generally motile, aergenic, non-lactose fermenting, urease negative, citrate utilizing and acetyl methyl carbinol negative organisms. They cause localized infection of the gastrointestinal tract but can also multiply in the reticulo-endothelial system resulting in systemic infection and death. Salmonella typhi invade host cells by subverting host-cell signal transduction pathways and promoting cytoskeletal rearrangements. This results in the uptake of the microorganism via large vesicles or macropinosomes. To avoid the intracellular environment of the host, Salmonella invade macrophages, where they proliferate within a membrane-bound vacuole. The incubation period for typhoid is longer than that for salmonellosis, usually one week. Historical accounts of typhoid written before the development of antimicrobial chemotherapy emphasized four main stages, lasting roughly one week each. The first week was characterized by rising fever, the second by rose spots, abdominal pain and splenomegaly and the third by the abdominal complications of haemorrhage or perforation followed by recovery in the fourth week (Stuart and Pullen, 1946).

The World Health Organization estimates there are 17 million typhoid cases annually and that these infections are associated with about 600 000 deaths (Pang et al., 1998). Typhoid is predominantly a disease of the developing world: the incidence in the Far East is approximately 1000/100 000 (Sinha et al., 1999, Lin et al., 2000). In some developing countries the majority of cases are reported to be in the 5–14 year age
group, whereas other reports show a more even distribution but confirm that typhoid is an uncommon but serious infection in patients over 20 (Butler et al., 1991, Lin et al., 2000). In industrialized countries the majority of S. typhi infections are acquired abroad. Infection is acquired by ingestion of contaminated food and water or contact with a patient or carrier of the disease. It is restricted in host range to human beings, and there is no known animal reservoir. The incidence of typhoid is falling worldwide due to improvements in public health, such as provision of clean water and good sewage systems, but it still remains a major threat to human health.

Liver enzymes are proteins that help to speed up the rate of chemical reaction in the liver. Liver enzymes which are found in normal plasma or serum, can be divided into different groups. They are: aspartate amino transferase (AST), alanine amino transferase (ALT) together they are known as transaminases. Alkaline phosphatase (ALP) and gamma-glutamyl transferase (GGT) are known as cholestatic enzymes. Elevations of these enzymes can indicate liver disease (Perry, 1998).

Hepatitis due to typhoid fever is not only associated with other potentially life threatening extra-hepatic complications but relapse rate also is observed higher in patients with hepatic complications than those without hepatic involvement (WHO, 1997). This study is designed to determine the activities of liver enzymes in patients with typhoid fever. This can be achieved by comparing the results of liver enzyme levels obtained from typhoid fever patients with those of control individuals.

MATERIALS AND METHOD

STUDY AREA
The study was conducted at the University of Maiduguri Teaching Hospital, a tertiary care hospital. It is situated in Maiduguri town, the capital of Borno State, Nigeria. It lies on latitude 11°N and longitude 12°E in the sudano-sahelian savanna zone with a dense population that are mostly crop farmers, fishermen, herders and traders (Udo 1978).

STUDY SUBJECTS
A total of 200 subjects were recruited for the study. This consisted of 100 known typhoid fever patients attending University of Maiduguri Teaching Hospital and 100 apparently healthy individuals (controls).

INCLUSION CRITERIA
- Informed consent of the subjects was sought for before sample collection.
- Sample collection was strictly based on clinically diagnosed typhoid patients.
- Clinically diagnosed typhoid fever patients of all age-groups were recruited for the study.
- Apparently healthy individuals without typhoid fever were selected as the control for the study.

EXCLUSION CRITERIA
- Subjects who declined the consent will be excluded.
- All patients with confirmed or diagnosed with liver disease or salmonella hepatitis are excluded because their liver enzyme levels are already distorted.

ETHICAL CONSIDERATION
Ethical approval for the study was obtained from the ethical committee of the University of Maiduguri Teaching Hospital (UMTH).

SAMPLE COLLECTION AND PROCESSING
Blood sample (2mls) was collected from the superficial vein of antecubital region. A tourniquet was applied to the upper arm to pause blood flow and the region was disinfected with 70% alcohol and allowed to dry. The blood was
drawn using sterile syringe and needle into a labeled plain vacutainer bottle. The blood was allowed to clot at room temperature and centrifuged at 4000 revolution per minute for 5 minutes. The serum was separated and transferred to a labeled plain sample container and stored in a refrigerator for further analysis (Cheesebrough 2006).

**ANALYTICAL METHODS**

**Determination of Serum Aspartate Transaminase (AST) Activity**

Serum AST activity was measured using colorimetric method as described by Reitman and Frankel, (1957).

**Principle.**

AST catalyses the transfer of amino group from aspartate to oxoglutarate forming glutamate and oxaloacetate when incubated at 27°C of pH 7.4 buffered substrate containing aspartate and alpha-oxoglutarate. The oxaloacetate reacts with 2,4 dinitrophenylhydrazine to form oxaloacetate hydrazone which in alkaline medium gives a red brown colour. The absorbance was read at 546nm. α-Oxoglutarate +L-Aspartate L-glutamate+ Oxaloacetate Glutamate-Oxaloacetate (Schmidt, 1962).

**Determination of Serum Alanine Transaminase Activity (ALT):**

The ALT activity was measured using the method described by Reitman and Frankel, (1957).

**Principle**

ALT catalyses the transfer of amino group from alanine to oxoglutarate forming glutamate and pyruvate when incubated at 27°C for 20mins at PH 7.4 buffered substrate containing alanine and alpha oxoglutarate. The pyruvate reacts with 2,4 dinitrophenylhydrazine to form pyruvate hydrazine which in alkaline medium gives red brown colour. This was measured spectrophotometrically at 546nm wavelength. α-Oxoglutarate +L-alanine L-glutamate+ pyruvate (Schmidt, 1962).

**Determination of Alkaline Phosphatase Activity (ALP)**

Serum ALP activity will be estimated using King and Amstrong method as described by Balistreri and Shaw, (1987).

**Principle**

Serum ALP hydrolys a colourless substrate of phenolphthalein monophosphate giving rise to phosphoric acid and phenolphthalein which at alkaline PH turns into a pink colour that can be determined photometrically (Klein, 1960).

**STATISTICAL ANALYSIS**

Data generated will be analysed using SPSS software. The results of serum aspartate transferase, alanine transferase and alkaline phosphatase obtained from patients with typhoid fever will be compared with those from controls using student’s t-test statistical method.

**RESULTS**

The results obtained were expressed as mean ± SD (standard deviation). A total of one hundred (100) diagnosed typhoid subjects participated in this study, fifty five (55) females and forty five (45) males. One hundred (100) apparently healthy individuals were recruited as control subjects. Probability values were determined at p≤0.05.

Table 1 shows the mean ± SD values of serum liver enzyme activities among typhoid patients. AST (25.6 ±17.6), ALT (22.5±8.8) and ALP (32.0±16.1).

Table 2 shows the comparison between the mean ± SD values of serum liver enzyme activities of typhoid patient and that of the controls. The levels of AST, ALT and ALP were 25.6±17.6, 22.5±8.8 and 32.0±16.1 respectively, and are significantly elevated when compared to the controls; 8.1±1.7, 6.5±2.8 and 24.0±6.4 respectively at p<0.05.
Table 1: Mean ± SD of liver enzyme activities in patient with Typhoid Fever

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>AST (iu/l)</td>
<td>25.6 ± 17.6</td>
</tr>
<tr>
<td>ALT (iu/l)</td>
<td>22.5 ± 8.8</td>
</tr>
<tr>
<td>ALP (iu/l)</td>
<td>32.0 ± 16.1</td>
</tr>
</tbody>
</table>

p<0.05=significant  p>0.05=not significant

Table 2 Comparison of mean±SD of liver enzyme activities between typhoid patients and controls

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Typhoid patients</th>
<th>Controls</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AST (iu/l)</td>
<td>25.6±17.6</td>
<td>8.1±1.7</td>
<td>0.00</td>
</tr>
<tr>
<td>ALT (iu/l)</td>
<td>22.5±8.8</td>
<td>6.5±2.8</td>
<td>0.00</td>
</tr>
<tr>
<td>ALP (iu/l)</td>
<td>32.0± 16.1</td>
<td>24.0±6.4</td>
<td>0.00</td>
</tr>
</tbody>
</table>

p<0.05=significant  p>0.05=not significant

DISCUSSION AND RECOMMENDATION:

In this study, the biochemical parameters, AST, ALT and ALP in the typhoid patients were found to be significantly elevated when compared with the control groups. This study tallies with the one reported by Al-shamamam et al, 2011 and Shamim et al, 2012. This severe hepatic involvement in Salmonella infection may be multifactorial, involving end toxin, local inflammatory and or host of immune reactions. SA salmonella endotoxin induced consumptive coagulopathy, damage to hepatocytes, arteritis, direct invasion of the hepatocytes by the organisms, immune complexes and consumption of complement are believed to contribute to hepatic insult. The clinical presentation and extent of hepatic dysfunction in typhoid fever would, therefore, depend upon these contributory factors and may or may not be associated with hepatomegaly typhoid.

This study has provided ample evidence on the activity of liver enzymes in typhoid patients, which reflects the influence of typhoid morbidity. It further shows that typhoid fever increases the rate of liver enzyme activity and as a result, could be useful in the diagnosis of typhoid fever. As such, it is advisable that routine evaluation of liver function test be considered as part of the management of typhoid patients to ensure proper control of hepatic function in the affected individuals.

REFERENCES


[34] Perry II, Shaper AG (1998). Prospective study of serum gamma-glutamyltransferase and risk of NIDDM.


