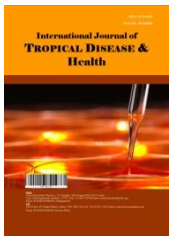

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Evaluation of Some Hepato- Renal Biochemical Parameters in Typhoid Fever Patients in Yenagoa, Bayelsa State Nigeria

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Typhoid fever infection is one of the most prevalent diseases in developing countries. It is caused by Salmonella species and can affect multiple organs in the body if left untreated. The purpose of this study was to determine the biochemical patterns of renal and liver biochemical parameters in patients admitted with typhoid fever.
Methodology: A total of 100 subjects were recruited for the study, with 50 typhoid-positive patients and 50 typhoid-negative individuals serving as controls. Blood samples collected from the subjects were analyzed for *Salmonella Typhi* titre, sodium (Na), potassium (K), chloride (Cl), urea, creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) using WHO-approved methods. The data obtained were statistically evaluated in SPSS version 22.
Results: The comparison between the positive and negative titres of *Salmonella Typhi* showed a significant increase in concentrations of creatinine and AST in the positive titres, whereas sodium decreased.

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Conclusion: This result suggests that patients with high titers of *Salmonella Typhi* are more susceptible to hepatocellular injury, muscle wasting, and hyponatremia. Therefore, liver and kidney function tests should be essential clinical tests for the management of typhoid fever.

Keywords: Typhoid fever; renal; hepatocellular; salmonella.

1. INTRODUCTION

Typhoid fever is an acute febrile infection caused by the gram-negative, facultative anaerobic bacterium *Salmonella enterica serotype Typhi.* Typhoid fever infection is transmitted by consuming water and food contaminated with urine and faeces of infected individuals [1]. The incubation period of typhoid and paratyphoid infections is 6-30 days. Salmonella represents a group of Gram-negative, facultative anaerobic pathogenic bacteria.

Typhoid fever has remained a universal public health problem and has a significant impact on low and middle-income countries. This is due to poverty, restricted access to clean water and unsanitary practices in these countries [2,3].

The World Health Organization (WHO), projected that 11–20 million people get sick from typhoid and mortality will occur in between 128 000 and 161 000 people yearly [4]. In Africa, about 4.36 million cases occur out of 427 million people [5]. It is prevalence from 0.071% in Oyo to 47.1% in Osun [6, 7].

The liver performs many important functions such as metabolism, detoxification, and formation of important compounds such as blood coagulation factors and albumin [8]. Routine liver function tests (LFT) usually include alanine and aspartate aminotransferases, total and conjugated bilirubin, alkaline phosphates, and prothrombin time. The kidneys serve as conduits for the elimination of nutrients and waste products from the body. The reabsorption of nutrients and the removal of waste products are strictly regulated by the kidneys. Assessment of renal system capacity is based on biochemical parameters such as creatinine, urea, uric acid, and electrolytes. These parameters are routinely used in the diagnosis of liver and kidney dysfunction. Similarly, these parameters are used to monitor the progression of therapeutic interventions for liver and kidney dysfunction [9,10].

Since typhoid fever is a systemic disease, it can affect any organ in the body. Studies have shown that it affects the gastrointestinal tract, liver, spleen, kidneys, lung muscles, and gallbladder [9, 11,12,13]. Reports have shown the effects of typhoid fever on renal function. These appear and are detected by various disorders of renal biochemical parameters such as electrolytes, urea and creatinine [11, 14,15].

Biochemical changes in liver enzymes that indicate liver damage have been reported in patients infected with typhoid fever [9, 16,17]. Abnormal liver biochemical tests are common in typhoid fever, and transaminase can rise to 2-3 times the normal range. There are few data on the effects of typhoid fever on hepato-renal biochemical parameters when using Bayelsa State as a case study. Therefore, this study was designed to critically examine the chemistries of the hepato-renal system concerning typhoid infection.

2. MATERIALS AND METHODS

2.1 Study Area

This research study was carried out in Yenagoa. Yenagoa is the capital city of Bayelsa State. It is a cosmopolitan city located in the Niger Delta region of Nigeria. Yenagoa city is located in latitudes 4º 51´N and 5º 22´N and Longitude 6º 12´ E and 6º 33´ E. Subjects were recruited from the Niger Delta University Teaching Hospital (NDUTH) Okolobiri, and the Federal Medical Centre, Yenagoa (FMCY) all located in Yenagoa. Both health facilities are tertiary hospitals with the highest patient traffic.

2.2 Study Design

A case-control study design was employed for this research. It involves experimental (case) and control groups that were observed for the effect of typhoid fever on the liver and renal biochemical parameters.

2.3 Study Population

The study population comprised subjects with typhoid fever attending clinics at the Federal

Medical Centre (FMC) Yenagoa and the Niger Delta University Teaching Hospital, Okolobiri. The control group consisted of subjects confirmed with non-significant Salmonella titre.

The sample size was calculated using the method of Araoye [18]. A total of 100 subjects made up the sample size. Employing simple random sampling the sample size was equally divided into typhoid and non-typhoid (control) groups.

2.4 Sample Collection

Blood samples were collected using the standard venipuncture method and consequently dispensed into plain containers. The samples were thereafter centrifuged at 3000rpm and serum was used for the Salmonella agglutination titre determination and hepatorenal biochemical analysis.

2.5 Inclusion and Exclusion Criteria

Participants who consented to the study were selected on the following criteria: (i) Patients with fever ≥ 37.5^0C and confirmed to have been having fever for at least three consecutive days (ii) Patients who had a negative blood smear preparation for malaria parasites. (iii) participants who had been off antibiotics for at least 14 days before the hospital visit and (iv) patients with signs and symptoms of typhoid fever.

Participants were excluded from the study based on the following criteria: (i) patients who had been on antibiotics for at least two weeks before the hospital visit, (ii) Patients with positive blood smear preparation for malaria parasite, (iii) patients who are HIV positive, (iv) Patients with a low titer value of 20-80, and (v) Drug addicts and drunkards.

2.6 Laboratory Analysis

The level of titre of typhoid antigen-antibody agglutination was determined using a precision test kit. Serum AST, ALT and ALP were estimated using the enzyme kinetics method (Randox kits). Serum total protein and albumin were determined by biuret and bromo-cresol green (BCG) methods respectively (Randox kits). Similarly, serum creatinine and urea were estimated using Jaffe and Berthelot methods respectively. Electrolytes were measured using an ion-selective electrode (ISE) (IFRI IONIX brand).

2.7 Statistical Analysis

Data were represented as mean ± standard deviation using SPSS version 22. Student *t*-test and One-way Anova was employed for the statistical analysis. The level of significance was pegged at 95% level of confidence.

3. RESULTS

Table 1 shows gender distribution. Total number one hundred (100) subjects were recruited for the study with a percentage of 41 to 59 for males and females respectively. Similarly, Table 2 shows a significant increase in serum AST activity in the positive titre when compared with the negative. Table 3 shows a progressive significant increase ($p \leq 0.005$) in serum protein concentrations and aspartate aminotransferase activities as the various titres increases. Table 4 shows a significant decrease ($p<0.05$) in the mean concentration of sodium concentration in the negative titre when compared with positive titres, whereas creatinine concentration increased significantly ($p<0.05$).

Table 1. Sex distribution of subjects

Sex	Number of subjects (%)
Male	50 (50%)
Female	50 (50%)
Total	**100 (100%)**

Table 2. Comparison of estimated liver biochemical parameters between studied participants

Variables	Typhoid negative Mean ±SD	Typhoid positive Mean ±SD	t-value	P-value
Protein (mmol/L)	71.18±7.42	71.35±6.02	1.164	0.288
Albumin(mmol/L)	46.56±8.58	46.70±6.37	0.670	0.418
ALT (U/L)	8.62±2.89	10.00±3.29	1.392	0.245
AST (U/L)	11.63±2.71	19.46±10.30	16.330	0.000
ALP (U/L)	106.83±57.73	140.48±83.56	0.566	0.456

Table 3. Comparison of estimated liver biochemical parameters based on typhoid titers

Variables	Control	1/20	1/40	1/80	1/160	F	P-value
Protein (mmol/L)	80.27±4.75	66.92±6.94[a]	70.18±1.48[a]	67.61±7.01[a]	69.10±3.63[a]	6.14	0.002
Albumin (mmol/L)	48.95±4.11	41.95±13.46	50.48±3.68	44.02±4.46	44.90±7.66	3.63	0.121
AST(U/L)	11.80±3.83	12.20±3.89	12.08±1.93	13.85±2.03	32.65±9.75[a,b,c,d]	15.73	0.000
ALT(U/L)	8.32±8.41	9.16±5.17	8.40±2.30	7.38±3.14	10.09±2.83	1.787	0.169
ALP(U/L)	127.92±81.59	110.92±70.68	85.85±71.10	90.79±61.22	187.03±124.17	1.221	0.332

Table 4. Comparison between the estimated renal biochemical parameters between negative and positive antibody titre of *Salmonella typhi*

Parameter	Non-significant Titre n=50	Significant Titre n=50	t-value	P – value	Not significant (NS) vs. Significant Titre (S)
Sodium (mmol/l)	134.12±12.34	125.85±11.32	2.84	0.006	S
Potassium (mmol/l)	4.46±0.35	4.35±0.53	0.10	0.322	NS
Chloride (mmol/l)	110.95±8.48	114.92±8.63	-1.88	0.064	NS
Urea (µmol/l)	4.14±0.51	4.10±0.75	0.21	0.834	NS
Creatinine (µmol/l)	102.90±28.96	115.56±9.28	-2.39	0.022	S

4. DISCUSSION

Typhoid fever is a systemic disease that affects multiple organs in the body. The body's liver and kidney systems are essential for the proper functioning of the body. Therefore, damage to these organs affects the health of infected individuals. The purpose of this study was to critically investigate the effects of typhoid fever on various hepato-renal biochemical parameters routinely used to assess the physiological and pathological conditions of the liver and kidney, respectively.

The study subjects were selected from both genders to eliminate gender prejudice (Table 1). Statistical analysis revealed a significant increase in serum creatinine and AST levels in the Salmonella-positive titres compared to the negative tires. Similarly, serum sodium was significantly decreased (Tables 2, 3, and 4).

Aspartate aminotransferase (AST) is widely used as a biomarker for liver damage but is also expressed in other tissues such as the brain, cardiomyocytes, and skeletal muscle cells [19]. Injury to hepatocytes causes leakage of AST into the extracellular compartment, followed by increased serum AST activity [20,21, 22]. In this study, AST serum activities were elevated due to salmonella infection-induced hepatocyte damage. Similar results were reported by Ozougwu et al. [11] in Nigeria, Srikanth and Kumar [23] in India and Al-Dahhan [24] in Iraq.

Creatinine is a by-product of muscle metabolism. Creatinine serum concentrations are regulated and maintained by continued production and urinary excretion [25]. Hypercreatininemia occurs in skeletal muscle necrosis or atrophy, hyperthyroidism, infections, burns, or fractures Myopathy was reported as a complication of typhoid fever and it can cause severe myoglobinuria and elevated creatinine concentrations [27]. Significant increases in creatinine concentrations in the typhoid-positive titres in this study may be due to renal dysfunction and/or myopathy. A simultaneous increase in concentrations of serum creatinine and urea indicates renal failure, and an increase in serum creatinine concentration alone may indicate a muscle cause [28]. Based on this, it can be concluded that the single increase in creatinine is a product of muscle damage and not due to renal dysfunction. This is consistent with the reports of other authors [16,17,29].

There was no significant increase in concentration of serum urea in Salmonella-positive titres compared to the negative group. This means that typhoid fever did not affect the renal system in this study. This is consistent with the position of Ozougwu et al. [11]. The authors reported that urea was unaffected in patients with typhoid fever. The views of this study on urea concentrations are in contrast to the results of studies by Ndukaku [16] and Natheu et al. [9]. These researchers reported that urea concentrations were significantly elevated.

Sodium (Na^+) is the primary cation found in extracellular or intravascular fluid and is the major regulator of extracellular fluid volume [30]. Sodium shifts into cells as potassium is shifted out. This is necessary to maintain water balance [31]. The decrease in sodium concentration observed in this study may have been caused by typhoid fever. Some signs and symptoms of typhoid such as fever, diarrhoea and vomiting can lead to dehydration and sodium deficiency. This is confirmed by the stance of Kabiru et al. [14]. Significant reductions in sodium concentrations when potassium and chloride levels are stable may be due to the ability of typhoid fever to cause fever, diarrhoea, vomiting and ultimately hyponatremia due to sodium loss. On the contrary, this study was inconsistent with the findings by Ozougwu, et al. [11] and Ndukaku. [16]. These authors reported that sodium was unaffected by typhoid fever. George et al. [32], reported that the cause of infection-induced hyponatremia was multifactorial. This may be due to an appropriate or inappropriate increase in antidiuretic hormone secretion. In addition, above 38 °C, the insensible loss of water from the body increases by 10% per degree Celsius.

5. CONCLUSION

The study opined that typhoid fever causes hyponatremia, muscle wastage and hepatocellular derangement. These presentations call for prompt arrest of typhoid fever proliferation via early diagnosis and prompt treatment. Inclusion of liver and renal function tests should be integral laboratory investigations in the management of patients with typhoid fever.

ETHICAL APPROVAL

The study was performed after ethical approval was obtained from the Ethics Committee of the

Federal Medical Centre Yenagoa and that of the Niger Delta University Teaching Hospital, Okolobiri Bayelsa State. The samples were taken randomly.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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