



## **Changes in Renal Parameters Associated with Typhoid Infection**

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### **Authors' contributions**

*This work was carried out in collaboration among all authors. Author JCO designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors JCO, KCA and CAI managed the laboratory analyses of the study. Authors SCE and DKA managed the literature searches. All authors read and approved the final manuscript.*

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### **ABSTRACT**

**Background:** Typhoid is a vital health hazard globally but its incidence is greater in developing compared to developed countries owing to low sanitation, poor hygiene practices, unsafe food and drinking water.

**Objective:** This study was designed to determine the changes in renal parameters associated with male and female Typhoid patients.

**Materials and Methods:** A hundred and twenty male and hundred and twenty female Typhoid patients were divided into four groups made up of sixty Typhoid positive male, sixty Typhoid negative male, sixty Typhoid positive female and sixty Typhoid negative females. The renal parameters were evaluated using Spectrophotometer. The results were analyzed using statistical package for social science version 20 statistical software.

**Results:** The result of renal changes associated with male and female Typhoid fever patient

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showed insignificant increase ( $p < 0.05$ ) in Total serum Protein and significant increase ( $p < 0.05$ ) in Creatinine level of both male and female patient compared to their control. It showed insignificant increase ( $p < 0.05$ ) in potassium ion and sodium ion of the Typhoid positive male patient, significant decrease in sodium ion and insignificant decrease in potassium ion of the Typhoid positive female compare to their controls. Similarly, the result of the Typhoid positive male patients showed significant increase ( $p < 0.05$ ) in Chloride ion and insignificant decrease ( $p < 0.05$ ) in Chloride ion of Typhoid positive female compare to their control. Furthermore, it showed insignificant decrease ( $p < 0.05$ ) in Urea level of the Typhoid positive males and insignificant increase ( $p < 0.05$ ) in Urea level of the Typhoid positive females.

**Conclusions:** Renal parameters as a tool for examining cases of early typhoid infections may aid in detecting early complications related to typhoid fever so as to aid in patients care and avert death that may come from such complication.

**Keywords:** Typhoid; male; female; renal parameters.

## 1. INTRODUCTION

Typhoid fever is a systemic infectious disease caused by *Salmonella typhi* and is transmitted through the ingestion of food and water contaminated by the feces and urine of an infected patients [1]. The clinical scope varies from mild illness with a low-grade fever to severe clinical disease with abdominal discomfort and multiple complications, including gastrointestinal bleeding, intestinal Perforation (ileum), Rhabdomyolysis and acute renal failure [2]. Recent estimates showed that there are approximately 20.6 million cases and 223,000 typhoid-related deaths annually worldwide [3]. The outbreaks of this disease have been documented in many countries and are associated with poor sanitation, inadequate hygiene practices and unsafe food and drinking water [4].

Typhoid fever affects children and young adults, causing a global morbidity rate of over 12.6 million cases and an estimated 600000 mortality annually [5]. The attack rate as high as 1100 cases per 100000 populations have been documented in developing countries [6]. The primary source of the disease is poor sanitary hygiene especially drinking water and food contamination [7,8,9], hence, direct fecal-oral transmission is most common [10]. The transmission also occurs through eating raw fruits and vegetables fertilized by human excreta and through ingestion of contaminated milk and milk products whenever they are not well decontaminated.

In Nigeria, typhoid remains a major disease because of factors such as increased

urbanization, inadequate supplies of potable water, regional movement of large numbers of immigrant workers, inadequate facilities for processing human waste, overburdened health-care delivery systems, and over use of antibiotics that contribute to the development and spread of antibiotic-resistant *S. typhi*. Untreated typhoid fever may lead to kidney failure, or intestinal bleeding, which can be fatal [3]. If the infection spreads to the gallbladder, one could become a chronic carrier of the bacteria that causes typhoid, a carrier may be asymptomatic but is capable of spreading the infection to others. Typhoid fever leads to noteworthy biochemical alterations as well as hepatic dysfunction and the involvement of kidney is usually associated with high frequency of extra hepatic complications. Despite the high incidence and serious nature of the biochemical changes and kidney involvement, these changes are temporary and respond well to the appropriate antimicrobial therapy. Typhoid fever kills an average of 22 million patients in Africa annually [3] and in Nigeria more than 20 million people are exposed to *Salmonella typhi*, out of these 11million people get infected with Typhoid and almost 161000 deaths are being reported annually in the general population of which over 100,000 deaths are of adults [11]. There is paucity of scientific information on the effect of typhoid fever on kidney function parameters, the need to fill this knowledge gap necessitated this study and made it of great significance. If the relationship between typhoid infection and kidney function is clearly understood, it could give insight on ways to control typhoid associated kidney dysfunction and pave way for better patient care. The aim of this study is to determine changes in renal parameters associated with typhoid patients in Oyiibo Rivers State, Nigeria.

## 2. METHODOLOGY

### 2.1 Specimen Collection

Ethical approval was granted by the ethical committee of Cliniscan Diagnostics Center, informed consent was obtained from patients aged between 20 - 65 years old and the study was carried out in Cliniscan Diagnostic Center between 1<sup>st</sup> May and 14<sup>th</sup> June, 2019. Specimens were only obtained from consenting patients attending the clinic.

### 2.2 Study Design

Two hundred and forty participants were selected through simple random sampling and put into four experimental groups that is made up of sixty typhoid positive male (TPM), sixty typhoid negative male (TNM), sixty typhoid positive female (TPF) and sixty typhoid negative female (TNF).

### 2.3 Inclusion and Exclusion Criteria

Participants who consented to the study were selected on the following criteria: Patients with fever of up to 37.5°C and confirmed to have been having fever for at least three consecutive days, patients who had a negative blood smear preparation for malaria parasites, participants who had been off antibiotics for at least 14 days prior to hospital visit and patients with signs and symptoms of typhoid fever.

Participants were excluded from the study based on the following criteria: patients who had been on antibiotics for at least two weeks prior to the hospital visit, Patients with positive blood smear preparation for malaria parasite, patients who are HIV positive, Patients with low titer value 20-80, Drug addicts and drinkers.

### 2.4 Evaluation of Renal Parameters

Renal parameters such as urea, sodium ion, potassium ion, chloride ion, total serum protein and creatinine were measured using a Spectrophotometer and RandoxKit.

### 2.5 Data Analysis

The data collected were pooled and analyzed for their central tendencies using descriptive statistics, values were given as mean ± standard deviation of sixty (60) observations. ANOVA and

LSD were employed to test the significant differences ( $p < 0.5$ ) among treatment means. All analysis was performed using SPSS for windows statistical software package version 20. The resulting output was presented in tables.

## 3. RESULTS

### 3.1 Renal Changes Associated with Typhoid Male Patients

The renal changes associated with Typhoid male patients showed that Potassium ion ( $K^+$ ) and Total Serum Protein (TSP) were increased from ( $3.74 \pm 0.96$ ) to ( $3.99 \pm 1.57$ ) and ( $6.24 \pm 0.89$ ) to ( $6.41 \pm 1.24$ ) respectively and both differences were statistically insignificant at ( $p < 0.05$ ) compared to their control (Table 1). Also, Chloride ion ( $Cl^-$ ) and Creatinine (CRT) were increased from ( $84.90 \pm 24.52$ ) to ( $93.80 \pm 9.55$ ) and ( $1.29 \pm 0.45$ ) to ( $2.0 \pm 1.82$ ) and both differences were statistically significant at ( $p < 0.05$ ) compared to their controls (Table 1). On the other hand, Sodium ion ( $Na^+$ ) was increased from ( $128.20 \pm 15.19$ ) to ( $137.33 \pm 13.66$ ) and the differences were statistically insignificant at ( $p < 0.05$ ) compared to the control. Finally, Urea (UR) was decreased from ( $5.10 \pm 3.98$ ) to ( $4.82 \pm 3.029$ ) and the difference was statistically insignificant at ( $p < 0.05$ ) compared to the control (Table 1).

**Table 1. Renal changes associated with male typhoid patients**

Renal parameters	Typhoid negative males	Typhoid positive males
$K^+$ (mEq/l)	$3.70 \pm 0.96^a$	$3.99 \pm 1.57^a$
$Cl^-$ (mEq/l)	$84.90 \pm 24.52^a$	$93.80 \pm 9.55^b$
TSP (g/l)	$6.24 \pm 0.89^a$	$6.41 \pm 1.24^a$
CRT (Mg/dl)	$1.29 \pm 0.45^a$	$2.00 \pm 1.82^b$
UR (Mmol/l)	$5.10 \pm 3.98^a$	$4.82 \pm 3.029^a$
Na (mEq/l)	$128.20 \pm 15.19^a$	$137.33 \pm 13.66^c$

Values are given as Mean ± Standard Deviation (N= 60). Mean values in the same row with different superscripts differ significantly ( $p < 0.05$ ).

KEY:  $K^+$  = Potassium ion,  $Cl^-$  = Chloride ion, CRT= Creatinine, UR= Urea, TSP= Total Serum protein, Na = Sodium ion

### 3.2 Renal Changes Associated with Female Typhoid Patients

The renal changes associated with Typhoid female patients showed that Potassium ion ( $K^+$ )

and Chloride ion (Cl<sup>-</sup>) were decreased from (4.27 ± 0.72) to (4.24 ± 0.94) and (98.73 ± 10.55) to (88.73 ± 10.91) respectively and both differences were statistically insignificant at (p < 0.05) compared to their control (Table 2). Also, Total Serum Protein (TSP) and Urea (UR) were increased from (5.43 ± 1.88) to (6.41 ± 1.63) and (4.29 ± 1.63) to (5.67 ± 6.40), both differences were statistically insignificant at (p < 0.05) compared to their controls. Also, Creatinine (CRT) was increased from (0.77 ± 0.15) to (1.63 ± 1.80) and the difference was statistically significant compared to its control (p < 0.05). Finally, Sodium ion (Na<sup>+</sup>) was decreased from (140.53 ± 4.87) to (127.87 ± 2163) and the differences was statistically significant compared to the control (p < 0.05) (Table 2).

**Table 2. Renal changes associated with female typhoid patients**

Renal parameters	Typhoid negative females	Typhoid positive females
K <sup>+</sup> (mEq/l)	4.27 ± 0.72 <sup>a</sup>	4.24 ± 0.94 <sup>a</sup>
Cl <sup>-</sup> (mEq/l)	98.73 ± 10.55 <sup>a</sup>	88.73 ± 10.91 <sup>a</sup>
TSP (g/d)	5.43 ± 1.88 <sup>a</sup>	6.41 ± 1.63 <sup>a</sup>
CRT (Mg/dl)	0.77 ± 0.15 <sup>a</sup>	1.63 ± 1.80 <sup>b</sup>
UR (Mmol/l)	4.29 ± 1.63 <sup>a</sup>	5.67 ± 6.40 <sup>a</sup>
Na (mEq/l)	140.53 ± 4.87 <sup>a</sup>	127.87 ± 21.63 <sup>b</sup>

Values are given as Mean ± Standard Deviation (N= 60). Mean values in the same row with different superscripts differ significantly (p < 0.05).

KEY: K<sup>+</sup> = Potassium ion, Cl<sup>-</sup> = Chloride ion, CRT= Creatinine, UR= Urea, TSP= Total Serum protein, Na = Sodium ion

### 3.3 Comparative Effects of Renal Changes Associated with Male and Female Typhoid Patients

The comparative effects of renal changes associated with male and female typhoid patients showed that three renal parameters that is Potassium ion (K<sup>+</sup>), Chloride ion (Cl<sup>-</sup>) and Sodium ion (Na<sup>+</sup>) were more affected in males than females. The percentage (%) changes were (+ 7.84 & -0.70), (+ 10.48 & -10.12) and (+ 7.12 & -9.01) respectively (Table 3). On the other hand, three renal parameters that is Total Serum Protein (TSP), Creatinine (CRT) and Urea (UR) were more affected in females than males. The percentage (%) differences were (+ 2.72 & +18.05), (+ 55.04 & + 111.69) and (- 5.49 & + 7.50) respectively (Table 3). Finally, the females were more affected than the males overall as they recorded very high percentage changes

compared to the males (+ 55.04 & + 11.69) and (+ 2.72 & + 18.05) (Table 3).

**Table 3. Comparative effects of renal changes associated with male and female typhoid patients**

Renal parameters	% Change in typhoid male patients	% Change in typhoid female patients
K <sup>+</sup> (mEq/l)	+ 7.84 <sup>*</sup>	-0.70
Cl <sup>-</sup> (mEq/l)	+ 10.48 <sup>*</sup>	-10.12
TSP (g/d)	+ 2.72	+ 18.05 <sup>*</sup>
CRT (Mg/dl)	+ 55.04	+111.69 <sup>*</sup>
UR (Mmol/l)	- 5.49	+ 7.50 <sup>*</sup>
Na <sup>+</sup> (mEq/l)	+ 7.12 <sup>*</sup>	-9.01

Key = \* indicated as superscript shows which sex was more affected in the parameters under consideration. -ve denotes negative percentage change (decreased). +ve denotes positive percentage change (increased). Changes were compared to the controls (negative male and female patients)

## 4. DISCUSSION

This study showed an insignificant increase (p < 0.05) in Potassium ion, Total Serum Protein, Sodium ion and insignificant decrease (p < 0.05) in Urea level of Typhoid positive male compare to the control. This result also showed significant increase (p < 0.05) in creatinine level and Chloride ion level of Typhoid positive male compare to the control. The insignificant increase has no effect on the typhoid positive male compare to the control and may not lead to Hypernatremia which is characterized by high levels of sodium ion in the blood. The insignificant decrease in Urea level showed typhoid fever has no effect on Urea level. The insignificant increase in Potassium ion level showed it has no effect on Typhoid positive male and may not lead to Hyperkalemia which is characterized by abnormally high potassium ion levels in the blood. Furthermore, the insignificant increase in Total Serum Protein level shows typhoid has no effect on Total Serum Protein level and may not lead to Hyperproteinemia which is characterized by abnormally elevated plasma protein concentration [12]. The significant increase in creatinine level may lead to Azotemia which is characterized by abnormally high levels of nitrogen-containing compounds in the blood [13], it could also lead to Rhabdomyolysis, a condition in which damaged skeletal muscle breaks down rapidly [14]. Finally, the significant increase in Chloride level may lead to Hyperchloremia which is characterized by an

elevated level of metabolic Alkalosis in the blood.

This present study showed insignificant decrease ( $p < 0.05$ ) in Potassium ion and Chloride ion level and also significant decrease ( $p < 0.05$ ) in Sodium ion level of the Typhoid positive females compare to their control. It also showed insignificant increase ( $p < 0.05$ ) in Total Serum Protein and Urea level and significant increase in Creatinine level of Typhoid fever positive female compared to their control. The significant increase in Creatinine level may lead to Azotemia which is increased levels of Nitrogenous compound in the blood [13]. The significance decrease in sodium ion may result to Hyponatremia which is low levels of sodium concentration in the blood. The insignificant increase in Total Serum Protein may not lead to Hyperproteinemia which is characterized by high level of protein in the blood [12]. The insignificant increase in urea level may not lead to Uremia which is characterized by high levels of Urea in the blood or Azotemia which is characterized by abnormally high levels of nitrogen-containing compounds in the blood [13]. Also, the insignificant decrease in Potassium ion and Chloride ion level has no effect in Typhoid positive females compare to their control and may not lead to Hypochloremia and Hypokalemia.

## 5. CONCLUSION

From the findings of this study, it can be safely concluded that Typhoid may lead to Azotemia in both male and female. It may also lead to Hyperchloremia in male and Hyponatremia in female. Another implication of this result is that Typhoid has no effect on Potassium level of both male and female Typhoid patients and may not lead to Hyperkalemia or Hypokalemia. Typhoid affected potassium ion, chloride ion and sodium ion level of male patient more than female. On the other hand, it affected urea, creatinine and total serum protein level in female more than male patients. Renal parameters as a tool for examining cases of early typhoid infections may aid in detecting early complications related to typhoid fever so as to aid in patients care and avert death that may come from such complication.

## CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the author(s).

## ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the author(s).

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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