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RESEARCH ARTICLE

ASSESSMENT OF RENAL FUNCTION TESTS IN SUDANESE PATIENTS WITH RECURRENT TYPHOID FEVER IN GAZERA STATE – SUDAN

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ABSTRACT

Background: Typhoid fever is caused by Salmonella typhi bacteria. Typhoid fever is rare in industrialized countries. However, it remains a serious health threat in the developing world, especially for children. Typhoid fever spreads through contaminated food and water or through close contact with someone who's infected. Signs and symptoms usually include high fever, headache, abdominal pain, and either constipation or diarrhea. Most people with typhoid fever feel better within a few days of starting antibiotic treatment, although a small number of them may die of complications. Vaccines against typhoid fever are available, but they're only partially effective.
Objectives: The aim of this study was to assess the renal function tests in Sudanese patients with typhoid in Gazera state- Sudan.
Results: The results of the study revealed significant variation between case and control group in the plasma level of Urea, Creatinine, Sodium and potassium. (P.Value $\leq$ 0.05). There was a significant decreased in Glomerular filtration rate in case group (108 ml/minute) compared to normal subjects.
Conclusions: There were obvious effects on RFT in all biochemical parameters used to evaluate the renal function.

INTRODUCTION

Typhoid fever, also known simply as typhoid, is a bacterial infection due to Salmonella typhi that causes symptoms (Wain *et al*., 2015). Which may vary from mild to severe and usually begin six to thirty days after exposure (Anna E. Newton, 2014; Typhoid Fever, 2015). Often there is a gradual onset of a high fever over several days (Anna E. Newton, 2014). Weakness, abdominal pain, constipation, and headaches also commonly occur (Typhoid Fever, 2015; Typhoid Fever, 2015). Diarrhea is uncommon and vomiting is not usually severe (Typhoid Fever, 2015). Some people develop a skin rash with rose colored spots (Typhoid Fever, 2015). In severe cases there may be confusion (Typhoid Fever, 2015). Without treatment symptoms may last weeks or months (Typhoid Fever, 2015). Other people may carry the bacterium without being affected; however, they are still able to spread the disease to others (Typhoid vaccines, 2008). Typhoid fever is a type of enteric fever along with paratyphoid fever (Wain *et al*., 2015).

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The cause is the bacterium Salmonella typhi, also known as Salmonella enterica serotype typhi, growing in the intestines and blood (Typhoid Fever, 2015; Typhoid Fever, 2015). Typhoid is spread by eating or drinking food or water contaminated with the feces of an infected person, (Typhoid vaccines, 2008). Risk factors include poor sanitation and poor hygiene, (Wain *et al*., 2015). Those who travel to the developing world are also at risk (Typhoid Fever, 2015) and only humans can be infected, (Typhoid Fever, 2015). Diagnosis is by either culturing the bacteria or detecting the bacterium's DNA in the blood, stool, or bone marrow, (Typhoid Fever, 2015; Crump and Mintz, 2010). In 2013 there were 11 million new cases reported worldwide (Global Burden, 2013). The disease is most common in India, and children are most commonly affected (Wain, 2015). Rates of disease decreased in the developed world in the 1940s as a result of improved sanitation and use of antibiotics to treat the disease (Typhoid vaccines, 2008). About 400 cases are reported and the disease is estimated to occur in about 6,000 people per year in the United States (Typhoid Fever, 2015; Jackson *et al*., 2015). In 2013 it resulted in about 161,000 deaths – down from 181,000 in 1990 (about 0.3% of the global total), (Adu *et al*., 1975). The risk of death may be as high as 25% without treatment, while with treatment it is between 1

and 4%. (Typhoid vaccines, 2008) Many studies said that typhoid fever can cause illness and abnormality in kidney. One of them suggest typhoid fever is likely important cause of acute renal failure. Also in 1992 in India one study said this disease is the causes of 16% of patients with renal dysfunction (Khasla *et al*., 1992). *In 1998 Khan M et al* show typhoid fever complicated by both oligourea and acute renal failure, suggest that disease cause glomerulonephriti (Khan *et al*., 1998). *Hayashi M etal in 2005* reported that few cases in Japan was reported about acute nephritic syndrome associated with acute renal failure (Khan *et al*., 1998). Also *Jhawar M et al 2010* reported typhoid fever associated with number of complication in India including acute renal failure (Hayashi *et al*., 2005).

MATERIALS AND METHODS

Study design

Cross- sectional comparative study conducted at gazera state during the period April to July 2016. (100) patient with recurrent typhoid diagnosed and classified by physician as case group. (100) healthy individual as control group, age and sex of control group was matched with case group.

Sampling

Venous blood was collected from participants by clean venipuncture in lithium heparin anticoagulant tubes. Samples were centrifuged at (3000) rpm for no less than (10) minutes. Plasma removed from the tube within (60) minutes using a plastic pipette and stored in plastic tube used to measure Blood urea, Creatinine and electrolytes.

Ethical consideration

Ethical consideration was taken verbally. This study posed no physical risk to participants though an interview of (10) min, might have been convenient to some participants. It is a convenient study, thus neither the participants name nor his institution in use in any of the study materials and each participant was assigned a unique identification number. Collected data will be secured in a computer protected by password.

Measurement of Blood urea, Creatinine & Electrolytes

The (200) plasma samples obtained from the subject was analyzed for Renal Function tests (RFT), Blood urea, Creatinine and Electrolyte, in Academic Hospital Central laboratory using full automated Biochemistry analyzer (Cobas C-111, Roche for determination of Blood urea & Creatinine) and (Roche 9180 Ion Selective Electrode Analyzer for determination of sodium and potassium level). Blood urea level was determined by using Berthelot Reagent kit utilizes the Urease enzymetic method. Serum Creatinine level was determined by using Jaffe kinetic Reaction which utilize picric acid & sodium hydroxide, while the level of electrolytes were measured using indirect potenciometry method.

Statistical analysis

All data was analyzed using statistical analysis soft ware *(SPSS)* version *(16)*. Statistical analysis included description statistic of mean and standard deviation.

RESULTS AND DISCUSSION

When Salmonella penetrates the intestinal wall and enters the bloodstream, it can trigger a potentially life-threatening disease. While many strains of Salmonella can cause invasive disease, typhoid fever due to Salmonella typhi is a classic example. About 2 to 3 percent of patients with typhoid fever develop kidney complications, according to a 2005 case report in Internal Medicine. Renal damage can occur in many ways: The toxins can cause direct injury to the kidneys' delicate filtering units; antibodies and other immune molecules can accumulate within the organs; or proteins from damaged skeletal muscles can plug the kidney tubules and damage them. Blood urea, Creatinine and electrolytes are useful bio-markers used in assessing specific function and integrity of the glomeruli. An increase level in these biochemical parameters in the plasma are linked to Glomerular damage. This study was done to evaluate Renal Function Tests among Sudanese patients with enteric fever, (100 subjects were tested for *RFTs*, to assess their renal status during the onset of illness, as Blood urea, plasma Creatinine, plasma Sodium and potassium mean$\pm$ SD obtained as (27.7 $\pm$ 5.1), (1.0$\pm$ 0.62), (141.5$\pm$ 2.9), , and (4.1 $\pm$ 0.61) respectively.

Table 1. Shows Plasma Biochemical values in case versus Control group

No	parameter	Case group (Mean ±SD)	Control group (Mean ±SD)	P. value	Remark
1	Blood Urea (mg/dl)	27.7 $\pm$ 5.1	24.6 $\pm$ 4.5	0.000	a
2	Creatinine (mg/dl)	1.0$\pm$ 0.62	0.64$\pm$ 0.2	0.002	a
3	Sodium (mmol/L)	141.5$\pm$ 2.9	137.8$\pm$ 2.9	0.000	a
4	Potassium (mmol/L)	4.1 $\pm$ 0.61	5.0 $\pm$ 0.48	0.000	a

- Key: a = Significant, b = not significant
- Result expressed as mean ± SD
- Significant different consider as p.value ≤ 0.05

Table 2. Glomerular Filtration Rate among cases & Control Group

No	test	Case group (Mean ±SD)	Control group (Mean ±SD)	P. value	Remark
1	Glomerular Filtration Rate (ml/minute)	108 $\pm$ 61	130 $\pm$ 28	0.000	a

- Key: a = Significant, b = not significant
- Result expressed as mean ± SD
- Significant different consider as p.value ≤ 0.05

And for other (100 subjects who were control group as (24.6 + 4.5), (0.64+ 0.2), (137.8+ 2.9), and (5.0 + 0.48) respectively. Statistical analysis conducted using independent T- test comparing the two groups gave significant difference in all studied parameters, (P.Value less than 0.05). While renal involvement is a rare complication of Typhoid fever, the clinical presentations of Glomerular involvement and possibly Acute Tubular Necrosis should make physicians consider this diagnosis and make changes to the treatment plan accordingly. Decreased Glomerular filtration Rate (108 ml/minute) as in table 2, may result from sever vomiting & diarrhea which spontaneously lead to dehydration and decreased renal blood flow. Salmonellae pass through lymphatic system of the intestine to the blood of patient (typhoid form) and carried to various organs including kidneys. To form secondary foci (septic form) endotoxins first act on vascular and nervous apparatus resulting in increased permeability and decrease tone of the vessels. In severe form of disease liquid and electrolytes are lost upset the water salt metabolism, decrease circulating blood volume and arterial pressure and cause hypovolemic shock and septic shock, also cause oliguria and azotemia. This study in agreement with study conducted by *Michael Koster et al* [12] in Haiti 2014 they identified 6 cases of late-stage typhoid fever in which the patients demonstrated signs of kidney failure. Our study is also agree with other study done by *Khan M1, Coovadia Y, Sturm AW* they reported Four cases of typhoid fever complicated by acute oligourea and renal failure.

Conclusion

There were obvious effects on RFT in all studied parameters, but RFT should be assessed with the frequency of the infection to correlate between the infection frequency and deterioration of renal function.

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