

**ACUTE RENAL FAILURE INDUCED BY CHOLERA: OUTBREAK OF HODEIDAH,  
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**ABSTRACT**

Patients with acute renal failure (ARF) induced by cholera, aged from 5 to 92 years (250 cases) were investigated. The male/female ratio (%) was 59/41. The age was  $49.77 \pm 18.98$  years (mean  $\pm$  standard deviation). Ranged of serum creatinine levels was 4 mg/dl to 14 mg/dl and serum potassium level was 1.5 mg/dl to 2.5 mg/dl. The patients were categorized as under 5 years, from 6 to 18 years, and more than 18 years old. The minimum age was 5 years and the maximum age was 92 years. Statistically significant factor was the age ( $p < 0.05$ ) and non - statistically significant factor was the sex ( $p > 0.05$ ). The maximum cases were recorded in Biat AL-Faqih namely 25 cases. and the minimum cases were recorded in AL- Dihi, AL-Doriahmi, AL - Munera, AL Salif, and AL - Hojiala namely 1 cases for each district. On the other hand, 151 cases of Hodeidah Governorate and 99 cases of other Governorates. Finally, 46 cases were dead and the case fatality rate (CFR) was 18.4% (46 /250).

**KEYWORDS:** Renal Failure, Cholera, Yemen.**INTRODUCTION**

Cholera is a gastroenteric disease caused by epidemic or pandemic *Vibrio cholerae* which still is responsible for over 100,000 annual deaths worldwide.<sup>[1]</sup> The hallmark of the disease is profuse secretory diarrhea, the disease may be asymptomatic or mild, severe cholera can cause dehydration and death within hours of onset. Before the development of effective regimens for replacing fluids and electrolyte losses, the mortality in severe cholera was more than 50%. Mortality rates are lowest where intravenous therapy is available. Recent estimates indicate that the global burden of cholera is high with approximately 2.9 million cases and 95,000 deaths annually.<sup>[2]</sup> Since 2010, cholera continued to hit vulnerable communities affected by war, earthquakes, conflicts and famines.<sup>[3]</sup> For example, in 2015, such tragedies triggered reemergence of cholera in the Middle East, where some countries are already cholera endemic. Yemen, currently faces the world's largest cholera outbreak, with over 600,000 suspected cases and more than 2,000 deaths reported since April 2017.<sup>[4]</sup> The recent data from Yemen indicate that the cumulative total from 27 April 2017 to 11 Mar 2018 is 1,077,945 suspected

cholera cases and 2,265 associated deaths that the Case Fatality Rate (CFR) was recorded 0.21%.<sup>[5]</sup>

Clinically; Diarrhea can be progressively watery with classic rice water, fishy odor diarrhea. Other symptoms such as vomiting, muscle cramps or ileus are common, however, severity of illness is usually related to the degree of dehydration.<sup>[6]</sup> In severe cases, dehydration resulting in death can occur within 6-12 hours after the onset of symptoms especially with absence of or delayed rehydration therapy. Severe dehydration might manifest as lethargy, a rapid radial pulse, loss of skin turgor, diminished urine output, low blood pressure, rapid breathing, sunken eyes and eventually hypovolemic shock.<sup>[7,8]</sup> Complications are notable consequences of organ hypoperfusion (such as acute tubular necrosis and stroke) and electrolyte imbalances especially hypokalemia and hypernatremia as well as hypoglycemia from insufficient liver gluconeogenesis.<sup>[7]</sup> Renal complication can be present in the course of cholera and other gastrointestinal infections.<sup>[1]</sup> Oligoanuric acute kidney injury, tubulointerstitial nephritis and persistent

metabolic acidosis, could be a potential complication of the infection itself or secondary to volume depletion.<sup>[9]</sup>

There are non/or limited studies addressed renal failure in cholera patients<sup>[1,10,11]</sup> especially in Yemen. The aim of this study is to describe the acute renal failure in cholera patients during outbreak in 2017 in Hodeidah governorate at western Yemen.

## MATERIAL AND METHODS

### Study area

Hodeidah city is localized in the fourth largest governorate in Yemen "Hodeidah governorate". It is located on a flat and narrow coastal plain, between the foothills of the highlands and the Red Sea known as Tehama, the area is 181 km<sup>2</sup>, involve three districts (AL-Hawa, AL Hali and AL Mina) as major districts, with a number of population which are 415,283 according to the last population enumeration on 2004.<sup>[12]</sup> The main diarrhea treatment center in Hodeidah were chosen as sample collection sites.

### Study design

A cross-sectional observational study was conducted by recruiting case-series of children, young, and elderly who have diarrhea within the age group from 5 to 92 years. The study was done in Hodeidah from May to July 2017.

### Data Collection

Data were collected using a special designed questionnaire including demographic data, symptoms, and biochemical parameters namely creatinine and potassium.

### Sample collection

#### Laboratory Analysis

##### Detection of *Vibrio cholerae* by Rapid Test

*Cholera* status was ascertained by rapid test because different area in Hodeidah with limited to no laboratory testing, rapid test can provide an early warning to public health officials that an outbreak of cholera is occurring. that fecal specimens that test positive for *Vibrio cholerae* O1 and/or O139 by rapid test be confirmed using traditional culture-based methods suitable for the isolation and identification of *Vibrio cholerae* Isolation and Identification by Standard Methods.

Isolation and identification of *Vibrio cholerae* serogroup O1 or O139 by culture of a stool specimen remains the gold standard for the laboratory diagnosis of cholera. Cary Blair media is ideal for transport, and the selective thiosulfate–citrate–bile salts agar (TCBS) is ideal for isolation and identification. Reagents for serotyping *Vibrio cholerae* isolates was used in this outbreak the U.S.<sup>[13]</sup>

## Diagnosis of Acute Renal Failure

The renal function tests were monitored with severe acute diarrhea namely cholera to avoid the acute renal impairment. Serum creatinine level was assayed based on spectrophotometric method and serum potassium level were assayed based on ion sensory method.<sup>[14]</sup>

## Hemodialysis Therapy

The dialysis for cholera patients was done by hemodialysis (HD) machine and the procedure was as the following : HD time: 3 h/wk. HD bath: calcium 2.5 mEq/L, bicarbonate 35 mEq/L, potassium 2.0 mEq/L, magnesium 1.0 mEq/L, sodium 138 mEq/L and chloride 109.5 mEq/L. Adjust based on weekly measurements of electrolytes, calcium, and phosphorus.<sup>[15]</sup> Hemodialysis therapy was carried out in Center of Renal Diseases and Dialysis, Hodedah city, Yemen.

## Statistical Analysis

The data were entered and analyzed using suitable statistical tools. Chi square were performed at a 95% confidence interval and a significance level of 0.05 were used.

## RESULTS

### Epidemiological characteristics

Patients with acute renal failure (ARF) induced by cholera, aged from 5 to 92 years (250 cases) were investigated. The male/female ratio (%) was 59/41. The age was  $49.77 \pm 18.98$  years (mean  $\pm$  standard deviation). Patients were categorized as under 5 years, from 6 to 18 years, from 18 to 50 years old, more than 50 year old. The minimum age was 5 years and the maximum age was 92 years. Statistically significant factor was the age ( $p < 0.05$ ) and non - statistically significant factor was the sex ( $p > 0.05$ ). The maximum cases were recorded in Biat AL-Faqih namely 25 cases, and the minimum cases were recorded in AL- Dihi, AL-Doriahmi, AL - Munera, AL Salif, and AL - Hojiala namely 1 cases for each district. On the other hand, 151 cases of Hodeidah Governorate and 99 cases of other Governorates. Finally, 46 cases were dead and the case fatality rate (CFR) was 18.4% (46 /250).

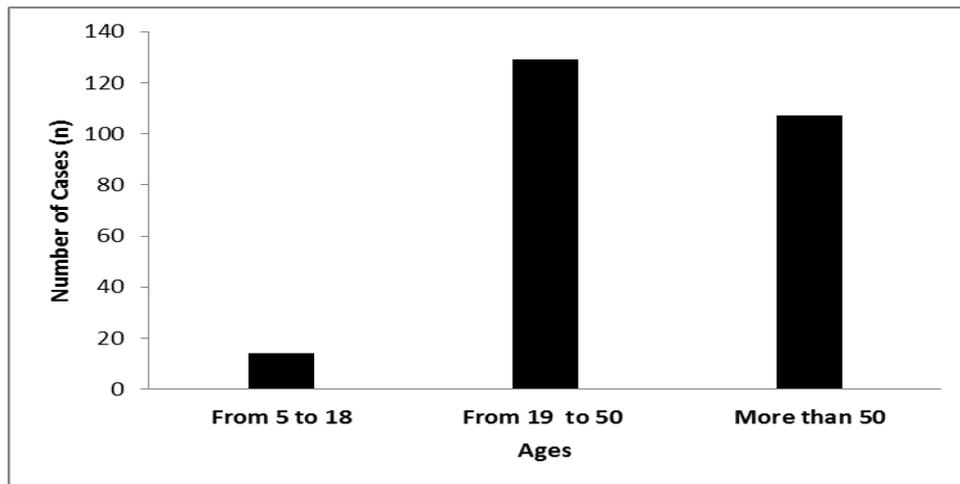


Figure 1: Relationship between cholera patients with acute renal failure in and age.

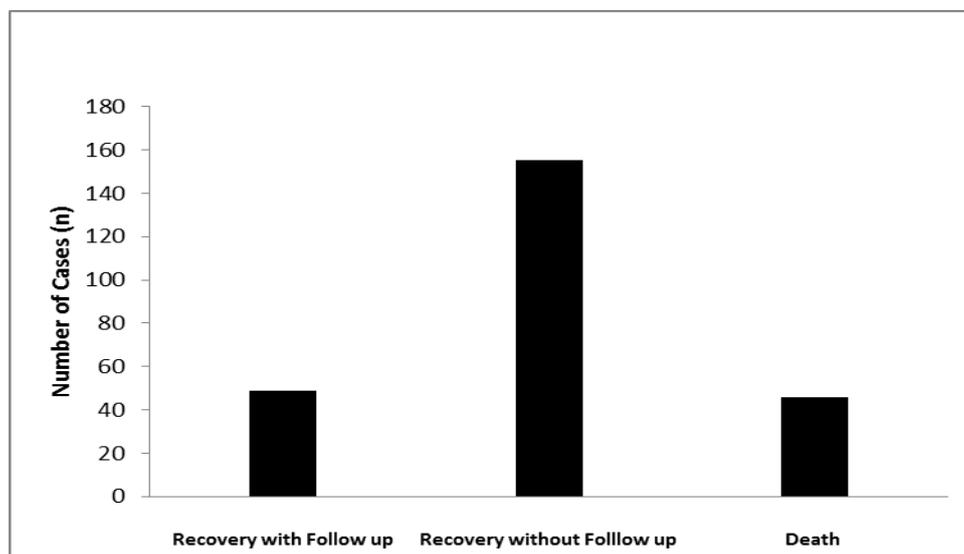


Figure 2: Number of cases (n) death and recovery of cholera patients with acute renal failure.

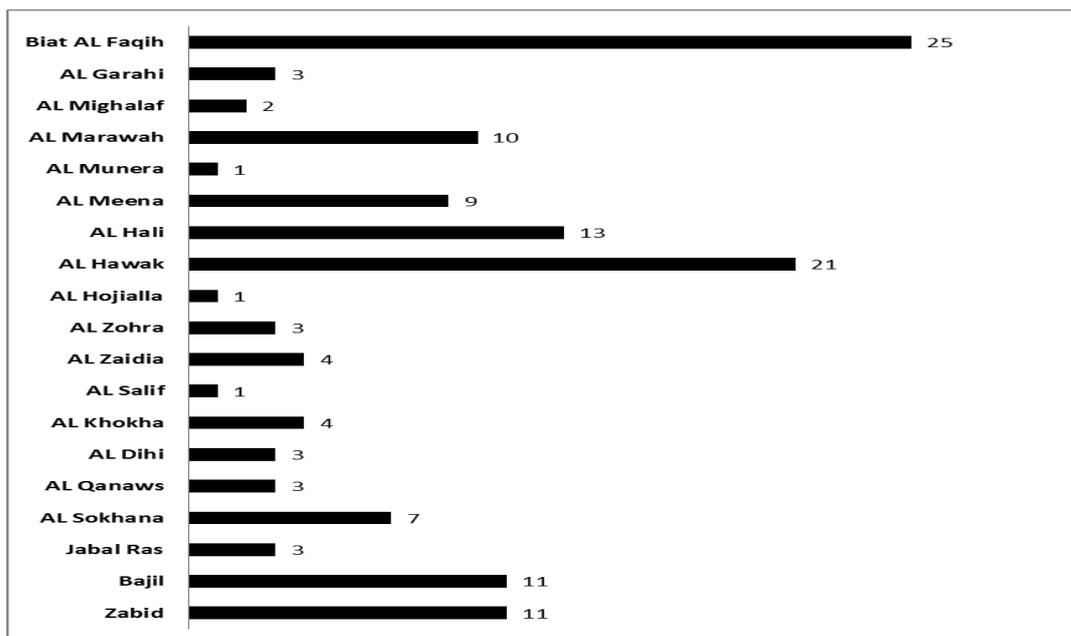


Figure 3: Number of cases (n) of cholera patients with acute renal failure from May 2017 - July 2017 based on geographic distribution of districts in Hodeidah, Yemen.

### Biochemical characteristics

Serum samples were collected from 250 patients attending several diarrhea treatment center of Authority of General Al-Thawra hospital, Al-Salakana hospital, Al-Alufi hospital, Biat AL Faqih hospital, AL Monsoria health center, and AL Garahi hospital. Ranged of serum creatinine levels was 4 mg/dl to 14 mg/dl with median 7 mg/dl serum potassium level was 1.5 mg/dl to 2.5 mg/dl with median 2 mg/dl. The patient with one session hemodialysis that the creatinine level decreases within normal rang.

### DISCUSSION

Progressive renal impairment has long been recognized as a late and often fatal complication of Asiatic cholera. In 1921, anuria in cholera was attributed by Rogers to a fall in blood pressure leading to impaired circulation through the kidneys.<sup>[16]</sup> Two decades later, Tomb stated that the renal pathologic changes in cholera resembled those seen in renal anoxia<sup>[17,18]</sup>, a concept supported by Wilkinson<sup>4</sup> and by Maegraith *et al.*<sup>5.</sup><sup>[19,20]</sup> In 1911, Rogers Wrote that the most late complication of cholera was continued suppression of urine which would lead to uremia and toxemia unless it was of strictly limited duration.<sup>[21]</sup> In nonfatal cases, prolonged oliguria was followed by the diuretic phase typical of recovery from acute tubular necrosis. Oliver *et al.*<sup>[22]</sup> have demonstrated that renal ischemia is the common denominator in the pathogenesis of acute tubular necrosis. Special staining procedures have demonstrated marked renal ischemia<sup>[23]</sup> in cholera patients dying acutely in shock. The occurrence of renal ischemia is further supported by reports of lowered glomerular filtration rates,<sup>[21]</sup> 18 renal plasma flows 18 and urea clearances<sup>[24]</sup> in cholera.

Either severe hemoconcentration or prolonged shock in our patients could have led to renal ischemia. These findings imply that prompt and adequate fluid therapy, designed to eliminate shock and to correct dehydration, is necessary in acute cholera to restore renal blood flow and to prevent or lessen the severity of acute tubular necrosis. Losses averaging 131 mEq. of potassium per day during the diarrhea of acute cholera (with a fall in serum potassium during convalescence) were documented by Watten *et al.*<sup>[25]</sup> Stool losses, coupled with a poor nutritional state in several of our cases (opium addicts), accounted for an apparent severe depletion of total body potassium.

The etiologic relation of potassium depletion in humans to these hydropic or vacuolar tubular changes has been recognized,<sup>[26,27]</sup> and is supported by previous studies which showed that potassium-deficient diets lead to vacuolar degeneration in tubular cells.<sup>[28,31]</sup>

### CONCLUSION

Acute renal failure during severe attacks of diarrhea caused by *Vibrio cholerae*. Patterns of acute tubular necrosis and tubulointerstitial nephritis developed following hypotension and decrease in renal blood flow,

causing secondary renal ischemia. There was severe dehydration with profound hypovolemia and infection. The clinical picture included fever, weakness, arthralgia, pedal edema, mild bilateral, and pleural effusions with a maximum of 14 mg/dl of creatinine. A short oliguric phase was followed by a polyuric phase lasting about 10 days, and glomerular and tubular function became normal after about 3 weeks.

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