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ORIGINAL ARTICLE

# INVESTIGATING THE RELATIONSHIP BETWEEN ACUTE KIDNEY INJURY (AKI) IN PATIENTS WITH VIBRIO CHOLERAE AND ITS INFLUENCING FACTORS IN THE KIRKUK CITY

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## ABSTRACT

**Background:** Acute kidney injury (AKI) may arise as a serious complication of Vibrio cholerae infection, primarily resulting from severe dehydration and electrolyte imbalance leading to acute tubular necrosis, tubulointerstitial nephritis, and metabolic acidosis. This study aimed to assess the association between AKI and cholera among patients in Kirkuk City, with particular attention to comorbid conditions, severity of loose bowel movement (LBM), and hemodynamic status.

**Materials & Methods:** A cross-sectional study was conducted from April to October 2022 among 166 cholera patients (aged 15–80 years; 99 females, 67 males) admitted to Kirkuk Teaching Hospital. Data were collected through structured interviews and clinical assessments. Laboratory evaluations included serum creatinine, blood urea (B. Urea), electrolytes, and white blood cell (WBC) counts. Statistical analysis was performed using SPSS version 26. Categorical variables were compared using the chi-square test, and numerical variables were analyzed using unpaired t-tests or one-way ANOVA. A p-value $< 0.05$ was considered statistically significant.

**Results:** The most frequent comorbidities were hypertension (39.7%), diabetes mellitus (20.5%), urinary tract infection (17.5%), and kidney stones (6.6%). Regarding LBM severity, 11.4% of patients had mild, 44.0% moderate, and 44.6% severe episodes. Diabetic females were more prevalent (25.3%) than diabetic males (13.4%) ($p = 0.64$). Male patients exhibited significantly higher serum creatinine (6.23 vs. 3.91 mg/dL; $p = 0.005$) and B. Urea levels (129.25 vs. 94.16 mg/dL; $p < 0.001$). Severe LBM correlated with markedly elevated creatinine (6.06 mg/dL) and B. Urea (162.30 mg/dL) compared to mild or moderate cases ($p < 0.001$). Hypotensive patients showed significantly higher creatinine ($p = 0.028$), B. Urea ($p < 0.001$), and WBC counts ($p = 0.007$).

**Conclusion:** Female diabetic patients are more susceptible to cholera, while male patients with AKI have a higher risk of cholera infection. The severity of LBM is closely linked with AKI, and hypotension significantly elevates serum creatinine, B. Urea, and WBC counts in cholera patients. Elevated WBC counts were also observed in patients with AKI and severe LBM.

**KEY WORDS:** Acute Kidney Injury; Blood Urea; Cholera; Creatinine; Diarrhea.

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## INTRODUCTION

Cholera remains a major public health concern in many low- and middle-income countries, particularly in regions with limited access to safe water and sanitation. In Iraq, recurrent outbreaks of Vibrio cholerae have been documented over the past two decades, with significant epidemics reported in Baghdad[1], Kirkuk[2] and Al-Hilla (Babylon province).[3] The disease, caused primarily by serogroups O1 and O139, presents as acute, profuse watery diarrhea that can quickly progress to severe dehydration, electrolyte imbalance, and hypovolemic shock if left untreated.[4] Among its less frequently emphasized but clinically significant complications is acute kidney injury (AKI),

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which may develop as a result of prerenal azotemia due to profound volume depletion or ischemic tubular damage secondary to sustained hypoperfusion.[5]

According to the Kidney Disease Improving Global Outcomes (KDIGO) criteria, AKI is defined by an absolute rise in serum creatinine of at least 0.3 mg/dL within 48 hours[6], a threshold validated across diverse clinical and infectious disease contexts.[7] While the epidemiology of cholera in Iraq has been relatively well described, the specific relationship between V. cholerae infection and AKI, particularly in Kirkuk, a city with recurrent cholera transmission[8], remains insufficiently explored.

Evidence from other countries suggests that the occurrence of AKI in cholera patients is strongly associated with the severity of diarrhea, delayed rehydration, and pre-existing comorbidities such as diabetes mellitus and hypertension.[9] However, no published studies have systematically investigated the prevalence, biochemical features, or determinants of AKI among cholera patients in Kirkuk. This gap in knowledge limits the capacity to develop renal-protective interventions during outbreaks.

Accordingly, this study was designed to assess the association between Vibrio cholerae infection and acute kidney injury among hospitalized patients in Kirkuk City, with a specific focus on key contributing factors, including comorbid conditions, severity of loose bowel movement (LBM), and hemodynamic status, particularly hypotension.

## MATERIALS AND METHODS

The current study is a cross-sectional study of 166 patients, aged (15–80) with acute kidney injury (AKI) with Cholera infection who visited Teaching Hospital in city/ from, April to October 2022, of these patients, 99 were female and 67 were male.

Basic data and medical history were collected from the patients through using of a specific questionnaire form. In regards to loose bowel motion characteristics and severity, the patients classified as; mild (Have diarrhea less than 5 times per day), moderate (Have diarrhea 5-10 times per day) and sever (Diarrhea more than 10 times per day). Blood urea (B. Urea) concentrations estimated through using of enzymatic colorimetric method (From Biomaghreb, Ref:20141, Spain). In relation to serum Creatinine levels, determined by Creatinine Jaffé Gen.2. Total white blood cells count was estimated through using of through using of fully automated Hematology autoanalyzer from GENEX Labs, USA. The levels of serum K, Cl and Na were estimated for all the patients based to manufacturer's instruction.[10]

SPSS (Statistical Package for Scientific Services) version 26 was used to conduct computerized statistical analysis. Using the unpaired T-test, one-way ANOVA (for numerical variables), Chi-square used for analyzing categorical variables and probability (P) to compare data (P value). Outcomes were considered significant when the P value was fewer than 0.05, statistically significant (S), and highly significant when the P value was fewer than 0.01. (HS). P >0.05 accounted non-significant.

## RESULTS

Among the 166 cholera patients diagnosed with acute kidney injury (AKI), baseline clinical and biochemical characteristics are summarized in Table 1.

Male patients demonstrated significantly higher mean serum creatinine levels (6.23 ± 0.38 mg/dL) compared with females (3.91 ± 0.14 mg/dL; $p = 0.005$). Similarly, blood urea (B. Urea) concentrations were markedly elevated in males (129.25 ± 6.80 mg/dL) relative to females (94.16 ± 4.34 mg/dL; $p < 0.001$). Despite this biochemical disparity, diabetes mellitus was more prevalent among female patients (25.3%) than males (13.4%), though the difference was not statistically significant ($p = 0.64$). In contrast, the proportion of severe loose bowel movement (LBM) was slightly higher among females (44.4%) than males (43.3%), with this difference reaching statistical significance ($p < 0.001$) (Table 2).

**Table 1: Baseline and demographic data of the patients**

| Variables | No. (%) | Total |
|---|---|---|
| Hypertensive patients/non-hypertensive | 66 (39.75)/100 (60.24) | 166 (100 %) |
| Diabetic patients/Non-diabetic | 34 (20.48)/132 (79.51) | 166 (100 %) |
| Patients with kidney stone/Patients without kidney stone | 11 (6.62)/ 155 (93.37) | 166 (100%) |
| Patients with urinary tract infections/Patients without urinary tract infection | 29 (17.46)/137 (82.53) | 166 (100%) |
| **LBM** | | |
| -Mild | -19 (11.44) | 166 (100%) |
| -Moderate | -73 (43.97) | |
| -Severe | -74 (44.57) | |

The severity of LBM exhibited a strong positive association with biochemical markers of renal impairment. Patients experiencing severe LBM had substantially higher mean serum creatinine (6.06 ± 0.36 mg/dL) and B. Urea (162.30 ± 3.46 mg/dL) compared with those exhibiting mild or moderate LBM severity ($p < 0.001$ for both comparisons), as shown in Table 3.

Hemodynamic instability also demonstrated a significant relationship with renal dysfunction. Hypotensive patients presented with elevated serum creatinine (5.36 ± 0.30 mg/dL vs. 4.48 ± 0.25 mg/dL; $p = 0.028$), B. Urea (120.28 ± 1.26 mg/dL vs. 97.00 ± 0.94 mg/dL; $p < 0.001$), and total white blood cell (WBC) counts (14.27 ± 0.16 × $10^9$/L vs. 13.66 ± 0.15 × $10^9$/L; $p = 0.007$) compared to normotensive or hypertensive patients (Table 4).

Although abnormal WBC counts were slightly more common among AKI cases (61.0%) than non-AKI patients (65.6%), this difference did not reach statistical significance ($p = 0.619$) (Table 5).

**Table 2: Relation of risk factors and AKI with male and female Cholera infected**

| Variables | Male No. (%) Mean ± SE | Female No. (%) Mean±SE | P. Value |
|---|---|---|---|
| Diabetic/Non-Diabetic | 9 (13.4 )/58 (86.6) | 25 (25.3) /74(74.7 ) | 0.64 |
| S. Creatinine | 6.23±0.38 | 3.91±0.14 | 0.005** |
| B. Urea | 129.25±6.80 | 94.16±4.34 | 0.000** |
| Kidney stone | 8 (66.7) | 3 (60) | 0.09 |
| LBM Characteristics<br>-Mild<br>-Moderate<br>-Sever | 9 (13.4)<br>29 (43.3)<br>29 (43.3) | 10 (10.1)<br>45 (45.5)<br>44 (44.4) | 0.000** |
| Chi-square used for categorical variables, while unpaired t-test used for numerical variables. *P value less than 0.05 considered significant, higher than 0.05 non-significant, and highly significant if the **P value less than 0.01. | | | |

**Table 3: Relation of LBM characteristics, and AKI in Cholera infected patients**

| Variables | LBM Characteristics Mean±SE, No. (%) | | | P. Value |
|---|---|---|---|---|
| | Mild | Moderate | severe | |
| S. Creatinine | 3.65±0.38 | 4.02±0.17 | 6.06±0.36 | 0.000 |
| B. Urea | 86.80±0.73 | 113.96±1.19 | 162.30±3.46 | 0.000 |
| For categorical variables, the chi-square test is employed, whereas the one-way ANOVA test is used for numerical variables. P values less than 0.05 are regarded as significant, those greater than 0.05 as non-significant, and those less than 0.01 as highly significant. | | | | |

**Table 4: Correlation of Hemodynamic status (Blood Pressure), WBCs count and AKI in patients infected with Cholera**

| Variables | Hemodynamic status (Blood Pressure) Mean ±SE | | P. Value |
|---|---|---|---|
| | Normal or High blood pressure | Hypotension | |
| S. Creatinine | 4.48±0.25 | 5.36±0.30 | 0.028 |
| B. Urea | 97.00±0.94 | 120.28±1.26 | 0.000 |
| WBCs | 13.66±0.15 | 14.27±0.16 | 0.007 |

**Table 5: Association between AKI and non-AKI in regards to WBCs counts among Cholera infected patients**

| WBCs counts | AKI No. (%) | Non-AKI No. (%) | *P. Value |
|---|---|---|---|
| Normal WBCs/ Abnormal WBCs | 41 (39)/64 (61) | 21 (34.4)/ 40 (65.6) | 0.619 |

**By Fisher's exact test*

**Table 6: Relationship of LBM characteristics with WBCs counts in Cholera infected patients**

| WBCs counts | LBM characteristics | | | *P. Value |
|---|---|---|---|---|
| | Mild | Moderate | Severe | |
| Normal WBCs/ Abnormal WBCs | 8 (44.4)/ 10 (56.6) | 36 (49.3)/ 37 (50.7) | 19 (25.3)/ 56 (74.7) | 0.000 |

*By Chi-square test

However, WBC elevation correlated strongly with LBM severity: abnormal counts were observed in 74.7% of patients with severe LBM, compared to 56.6% and 50.7% in mild and moderate cases, respectively ($p < 0.001$) (Table 6).

## DISCUSSION

This study investigated the association between Vibrio cholerae infection and acute kidney injury (AKI) among hospitalized patients in Kirkuk City, with emphasis on demographic, clinical, and hemodynamic determinants. The findings demonstrate that AKI in cholera is not a random occurrence but a predictable outcome associated with identifiable clinical factors, particularly the severity of loose bowel movement (LBM), hypotension, and sex-specific comorbidity patterns, thus directly addressing the study's primary objective.

A prominent observation was the strong dose–response relationship between LBM severity and renal dysfunction. Patients experiencing severe LBM showed markedly elevated serum creatinine (6.06 mg/dL) and blood urea (162.30 mg/dL) levels compared with those presenting with mild or moderate LBM ($p < 0.001$). This trend parallels the findings of Vakrani and Nambakam[11], who reported a similar relationship during a cholera outbreak in Bengaluru, and supports the established pathophysiological mechanism wherein profound dehydration precipitates prerenal azotemia, which can progress to acute tubular necrosis if left uncorrected. The clinical importance of this relationship is underscored by data from Yemen, where cholera-associated AKI accounted for a substantial share of inpatient complications during the 2017 epidemic.[12]

Sex-related differences revealed a complex pattern. Although female patients exhibited a higher prevalence of diabetes (25.3% vs. 13.4%), consistent with the case report by Qasem and Rabbani[13] involving a female cholera patient with diabetic nephropathy, male patients demonstrated significantly worse renal biochemical parameters, including higher serum creatinine ($p = 0.005$) and urea ($p < 0.001$) concentrations. This divergence may be attributable to differences in health-seeking behavior, baseline cardiovascular comorbidities, or delayed access to medical care among men. Supporting this observation, Lu et al.[14] identified a higher overall incidence of AKI among males across multiple etiologies, implying that biological and behavioral factors may jointly contribute to sex-specific susceptibility, an area that warrants further investigation in Middle Eastern cohorts.

Hemodynamic instability emerged as a key determinant of renal impairment. Hypotensive patients had significantly elevated creatinine ($p = 0.028$), blood urea ($p < 0.001$), and white blood cell (WBC) counts ($p = 0.007$) compared to normotensive individuals, echoing the findings of Runge et al.[15], who identified hypotension as an independent predictor of AKI. Within the pathophysiological cascade of cholera, this likely reflects progressive fluid depletion leading to hypovolemia, renal hypoperfusion, and ischemic tubular damage. Comparable results from Karachi[16] have demonstrated that early and aggressive rehydration can significantly reduce the incidence of AKI during cholera outbreaks, underscoring the importance of timely volume resuscitation.

Although AKI was not independently associated with abnormal WBC counts ($p = 0.619$), a significant correlation was observed between leukocytosis and LBM severity: 74.7% of patients with severe LBM exhibited elevated WBC counts, compared with 56.6% and 50.7% in mild and moderate cases, respectively ($p < 0.001$). This pattern aligns with the findings of Pielok et al.[17] and may suggest that systemic inflammation contributes to renal stress through endothelial or microvascular dysfunction, as proposed by Gameiro and Lopes.[18]

The higher prevalence of kidney stones among males (66.7% vs. 60%), although statistically nonsignificant, is consistent with prior Iraqi data. Yaser Saadoon .[19] reported that approximately 80% of urinary stone cases in Iraq occur in men, a pattern influenced by dietary, hormonal, and occupational factors. This preexisting risk may predispose male cholera patients to more pronounced renal dysfunction during episodes of acute dehydration.

This study is limited by its single-center, cross-sectional design, which precludes causal inference between cholera, LBM severity, and AKI. Biomarkers of tubular injury (e.g., neutrophil gelatinase-associated lipocalin [NGAL], kidney injury molecule-1 [KIM-1]) were not assessed, and hydration status upon admission was not quantified. Additionally, as the study population consisted

exclusively of hospitalized cases, the results may overrepresent severe disease and may not fully reflect outcomes in mild or outpatient cholera cases.

## CONCLUSION

This study demonstrates that in Kirkuk City, acute kidney injury (AKI) associated with Vibrio cholerae infection is significantly influenced by several interrelated clinical determinants. Female patients with diabetes appeared more susceptible to cholera infection, whereas male patients exhibited greater biochemical severity of AKI, as reflected by markedly higher serum creatinine and blood urea levels. The severity of loose bowel movement (LBM) showed a strong positive association with renal dysfunction, with severe LBM corresponding to the highest levels of creatinine and urea. Hypotension further amplified renal and inflammatory disturbances, leading to significant elevations in serum creatinine, blood urea, and white blood cell (WBC) counts. Although WBC elevation was not independently predictive of AKI, its pronounced increase among patients with severe LBM suggests its potential as an adjunct marker of disease severity. These findings underscore the need for early hemodynamic assessment, prompt rehydration, and proactive management of comorbidities to prevent or mitigate cholera-related AKI in high-risk populations.

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CONFLICT OF INTEREST
Authors declare no conflict of interest.
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## AUTHORS' CONTRIBUTION

The following authors have made substantial contributions to the manuscript as under:

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| Conception or Design: | AAR, FFM |
| Acquisition, Analysis or Interpretation of Data: | AAR, FFM, AAG |
| Manuscript Writing & Approval: | AAR, FFM, AAG |

All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.