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Gastroenteritis Causing Derangement in Kidney Functions: A Prospective Observational Study

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A B S T R A C T

Background: Acute gastroenteritis can lead to significant kidney function derangement, but the incidence, risk factors, and outcomes remain incompletely characterized. This study investigated the relationship between gastroenteritis and kidney dysfunction in adult patients.

Methods: This prospective observational cohort study enrolled 100 consecutive adult patients with acute gastroenteritis from January to December 2024. Comprehensive clinical, laboratory, and microbiological assessments were performed. Acute kidney injury (AKI) was defined according to KDIGO criteria. Novel biomarkers, including TIMP-2 × IGFBP7, KIM-1, and NGAL, were evaluated for AKI prediction. Renal outcomes were assessed at discharge, 30 days, and 90 days.

Results: AKI occurred in 28.0% of patients, with 16.0% Stage 1, 8.0% Stage 2, and 4.0% Stage 3. Bacterial etiology was associated with higher AKI risk compared to viral (OR 3.02, 95% CI 1.24-7.37, p = 0.013), with STEC infection conferring the highest risk (OR 9.53, 95% CI 1.79-50.70, p = 0.002). Independent risk factors for AKI included age ≥65 years (aOR 2.83, p = 0.038), baseline eGFR <80 mL/min/1.73m² (aOR 3.12, p = 0.027), NSAID use (aOR 3.04, p = 0.025), severe dehydration (aOR 6.78, p < 0.001), STEC infection (aOR 7.32, p = 0.025), and symptom duration >3 days (aOR 3.18, p = 0.022). Urinary TIMP-2 × IGFBP7 demonstrated the highest predictive accuracy for AKI (AUC 0.92, 95% CI 0.86-0.98). Complete renal recovery occurred in 53.6% of AKI patients at discharge, 78.6% at 30 days, and 89.3% at 90 days, with recovery rates inversely proportional to AKI severity (p = 0.042).

Conclusion: Gastroenteritis-associated AKI is common and influenced by both pathogen-specific and host factors. Novel biomarkers outperform conventional parameters for early AKI prediction. While most patients achieve complete renal recovery, a subset develops persistent dysfunction, particularly following severe AKI.

Keywords: Gastroenteritis; Acute Kidney Injury; Biomarkers; Shiga Toxin-producing Escherichia coli; Dehydration; Risk Factors; Renal Recovery

INTRODUCTION

Gastroenteritis, characterized by inflammation of the gastrointestinal tract leading to diarrhea, vomiting, abdominal pain, and dehydration, represents a significant global health burden with approximately 1.7 billion cases of diarrheal disease occurring worldwide annually.(1) While often self-limiting, gastroenteritis can precipitate serious complications, notably renal dysfunction. The interrelationship between the gastrointestinal and renal systems exemplifies the complex physiological interdependence within the human body, where disturbance in one system can significantly impact the function of another. This pathophysiological sequence, in which gastroenteritis triggers derangements in kidney function, warrants comprehensive analysis given its clinical significance and potential for adverse outcomes if inadequately managed.

The etiological spectrum of gastroenteritis is diverse, encompassing viral, bacterial, and parasitic pathogens, each with distinct pathogenic mechanisms. Norovirus and rotavirus constitute the predominant viral agents, while Escherichia coli,

Salmonella, Shigella, and Campylobacter represent common bacterial causes. Entamoeba histolytica and Giardia lamblia feature prominently among parasitic etiologies.(2) Despite their differing pathophysiological mechanisms, these infectious agents converge in their potential to disrupt fluid and electrolyte homeostasis, thereby establishing conditions conducive to renal dysfunction.

Acute kidney injury (AKI) represents the most concerning renal complication associated with gastroenteritis. The incidence of AKI in patients hospitalized with gastroenteritis varies substantially depending on the population studied, ranging from 7% to 17%, with higher rates observed in pediatric and geriatric populations.(3) The pathophysiological mechanisms underlying gastroenteritis-induced renal dysfunction are multifaceted and include prerenal azotemia secondary to volume depletion, acute tubular necrosis from prolonged renal hypoperfusion, and direct nephrotoxicity from specific pathogens or their toxins. Additionally, inflammatory mediators released during intestinal infection may contribute to renal injury through systemic inflammatory responses.(4)

Volume depletion constitutes the predominant mechanism by which gastroenteritis precipitates renal dysfunction. Excessive fluid loss through diarrhea and vomiting leads to decreased effective circulating volume, triggering compensatory mechanisms including activation of the renin-angiotensin-aldosterone system (RAAS) and antidiuretic hormone (ADH) release. These responses initially preserve renal perfusion through vasoconstriction of the efferent arteriole and increased tubular reabsorption of sodium and water. However, persistent hypovolemia eventually overwhelms these compensatory mechanisms, resulting in diminished renal perfusion, reduced glomerular filtration rate (GFR), and prerenal azotemia.(5) If hypoperfusion persists, ischemic injury to renal tubular epithelial cells may ensue, potentially progressing to acute tubular necrosis.

Electrolyte disturbances frequently accompany gastroenteritis and can further compromise renal function. Hypokalemia, primarily resulting from gastrointestinal potassium losses and secondary hyperaldosteronism, may induce renal tubular damage and dysfunction. Similarly, metabolic acidosis, often observed in severe gastroenteritis, can impair renal tubular function, exacerbate inflammatory damage, and increase susceptibility to acute kidney injury.(6) The intricate interplay between fluid depletion, electrolyte imbalances, and acid-base disturbances establishes a complex pathophysiological milieu conducive to renal dysfunction.

Certain enteropathogens exhibit specific mechanisms by which they induce renal injury. Shiga toxin-producing Escherichia coli (STEC), particularly serotype O157:H7, represents the archetypal example, serving as the primary etiological agent of hemolytic uremic syndrome (HUS). This syndrome, characterized by the triad of microangiopathic hemolytic anemia, thrombocytopenia, and acute kidney injury, develops in approximately 5-15% of individuals infected with STEC.(7) The pathogenesis involves translocation of Shiga toxins from the intestinal lumen to the systemic circulation, with subsequent binding to globotriaosylceramide (Gb3) receptors on renal endothelial cells, leading to endothelial damage, microvascular thrombosis, and ultimately, renal dysfunction. Similarly, non-typhoidal Salmonella species have been implicated in the development of rhabdomyolysis-associated acute kidney injury through mechanisms involving direct invasion of skeletal muscle and systemic inflammatory responses.(8)

The clinical presentation of gastroenteritis-induced kidney dysfunction spans a spectrum from subtle alterations in renal biomarkers to overt renal failure necessitating renal replacement therapy. Early manifestations typically include oliguria and elevated serum creatinine, often accompanied by electrolyte abnormalities such as hyponatremia, hypokalemia, or hyperkalemia depending on the specific pathophysiological processes involved. Clinical assessment is complicated by the fact that conventional markers of renal function, particularly serum creatinine, may be influenced by numerous factors including muscle mass, hydration status, and medications, potentially obscuring the true extent of renal impairment. This diagnostic challenge has stimulated research into novel biomarkers such as neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule-1 (KIM-1), and cystatin C, which may offer improved sensitivity and specificity in detecting early renal injury in the context of gastroenteritis.(9)

Management of gastroenteritis-induced kidney dysfunction necessitates a multifaceted approach addressing both the primary gastrointestinal infection and the secondary renal complications. Fluid resuscitation constitutes the cornerstone of therapy, with the aim of restoring intravascular volume, improving renal perfusion, and enhancing toxin clearance. The composition, volume, and rate of fluid administration require careful consideration, taking into account the patient's age, comorbidities, and the severity of volume depletion. In cases of severe volume depletion or significant electrolyte disturbances, intravenous rehydration may be necessary, whereas oral rehydration therapy suffices for milder cases. Antimicrobial therapy may be indicated for specific bacterial pathogens, though judicious use is warranted given concerns regarding antimicrobial resistance and, in the case of STEC infections, the potential for increased Shiga toxin production with certain antibiotics.(10)

Prevention strategies for gastroenteritis-induced kidney dysfunction encompass both primary prevention of gastroenteritis and early intervention to prevent progression to renal complications once gastroenteritis has developed. Improved sanitation, access to clean water, food safety practices, and vaccination against specific pathogens such as rotavirus constitute essential elements of primary prevention. Early recognition of gastroenteritis, particularly in high-risk

populations such as young children and the elderly, coupled with prompt initiation of appropriate rehydration therapy, represents a critical strategy for preventing progression to renal dysfunction.
In conclusion, the relationship between gastroenteritis and kidney dysfunction epitomizes the complex interrelationships within human physiology, where disturbance in one system can precipitate dysfunction in another. Understanding the pathophysiological mechanisms, clinical manifestations, and management principles of gastroenteritis-induced kidney dysfunction is essential for optimizing outcomes in affected patients.

AIMS AND OBJECTIVES

Primary Aim

The primary aim of this study was to investigate the association between gastroenteritis and subsequent renal function derangement in adult patients. The study sought to characterize the incidence, severity, and duration of kidney dysfunction following episodes of acute gastroenteritis and to identify potential risk factors that predisposed patients to renal complications.

Secondary Objectives

The secondary objectives of this study included the determination of specific pathophysiological mechanisms by which different etiological agents of gastroenteritis affected renal function. We aimed to evaluate the relationship between the severity of gastroenteritis (as measured by frequency of diarrhea, degree of dehydration, and duration of illness) and the extent of kidney function impairment. Furthermore, we aimed to assess the utility of novel biomarkers in predicting the development of acute kidney injury (AKI) in the setting of gastroenteritis. We also sought to establish the efficacy of early fluid resuscitation protocols in preventing renal complications and to evaluate the long-term renal outcomes in patients who experienced kidney dysfunction during acute gastroenteritis.

MATERIALS AND METHODS

Study Design and Setting

This prospective observational cohort study was conducted at the Department of Gastroenterology and Nephrology at University Medical Center from January 2024 to December 2024. The study protocol was approved by the Institutional Ethics Committee (approval number: UMCEC-2023-1245), and the research was performed in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants or their legal representatives prior to enrollment in the study.

Study Population

The study enrolled 100 consecutive adult patients (aged 18 years and above) who presented to the emergency department or outpatient clinic with clinical features of acute gastroenteritis, defined as the acute onset of diarrhea (≥3 loose stools in a 24-hour period) with or without associated symptoms of nausea, vomiting, abdominal pain, or fever, with symptom duration of less than 14 days. We included patients regardless of the suspected etiology of gastroenteritis (viral, bacterial, or parasitic). The recruitment process involved systematic screening of all patients presenting with gastrointestinal symptoms during the study period. The diagnosis of gastroenteritis was confirmed by clinical evaluation performed by a gastroenterologist, supported by laboratory investigations including stool microscopy, culture, and polymerase chain reaction (PCR) testing for common enteropathogens.

Inclusion and Exclusion Criteria

Patients were included in the study if they met the clinical criteria for acute gastroenteritis as defined above, were aged 18 years or older, and provided informed consent. We excluded patients with pre-existing chronic kidney disease (estimated glomerular filtration rate [eGFR] <60 mL/min/1.73m² for ≥3 months), history of kidney transplantation, known structural renal abnormalities, active urinary tract infection, pregnancy, congestive heart failure (New York Heart Association class III or IV), hepatic cirrhosis, active malignancy, or patients who were receiving nephrotoxic medications within the previous 7 days. Additionally, patients with evidence of other causes of acute kidney injury unrelated to gastroenteritis, such as obstructive uropathy, glomerulonephritis, or vasculitis, were excluded. We also excluded patients who were unable to provide informed consent and those who were expected to be transferred to another facility within 48 hours of presentation, which would compromise follow-up assessment.

Data Collection and Patient Evaluation

Upon enrollment, comprehensive demographic information was collected from each participant, including age, sex, race, comorbidities, and current medications. A detailed medical history was obtained, focusing on the onset, duration, and severity of gastrointestinal symptoms, fluid intake, urine output, and symptoms of volume depletion. Physical examination was performed by trained physicians, with particular attention to vital signs, hydration status, and signs of

systemic inflammation. The degree of dehydration was assessed using clinical parameters including skin turgor, mucous membrane dryness, capillary refill time, and orthostatic changes in blood pressure and heart rate. The severity of gastroenteritis was classified as mild, moderate, or severe based on a composite assessment of symptom intensity, frequency of diarrhea, volume of fluid loss, and objective measures of dehydration.

Laboratory Investigations

Blood samples were collected from all participants at presentation for hematological, biochemical, and microbiological analyses. Complete blood count, serum electrolytes (sodium, potassium, chloride, bicarbonate), blood urea nitrogen, serum creatinine, and liver function tests were performed using standard laboratory techniques. Baseline renal function was established using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation to calculate eGFR. Additional biomarkers of kidney injury, including serum neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule-1 (KIM-1), and urinary albumin-to-creatinine ratio, were measured using enzyme-linked immunosorbent assay (ELISA) techniques. Arterial blood gas analysis was performed in patients with moderate to severe dehydration to assess acid-base status.

Stool samples were collected from all participants and subjected to microscopic examination, bacterial culture, enzyme immunoassay for rotavirus and norovirus antigens, and multiplex PCR for the detection of common bacterial, viral, and parasitic enteropathogens. Blood cultures were obtained from patients with fever or signs of systemic inflammatory response syndrome. Urine samples were collected for urinalysis, microscopy, culture, and biomarker analysis. All laboratory tests were performed in an accredited clinical laboratory following standardized protocols and quality control procedures.

Renal Function Assessment and Monitoring

Renal function was assessed at presentation and monitored daily during hospitalization, with subsequent follow-up evaluations at 7, 14, 30, and 90 days after the initial episode of gastroenteritis. Acute kidney injury was defined and staged according to the Kidney Disease: Improving Global Outcomes (KDIGO) criteria, based on changes in serum creatinine and urine output. In patients who developed AKI, additional investigations including renal ultrasonography were performed to exclude other causes of kidney injury. Urinary electrolyte excretion, fractional excretion of sodium, and urine osmolality were measured to differentiate between prerenal azotemia and intrinsic renal injury.

Treatment Protocol

All patients received treatment according to a standardized protocol for the management of acute gastroenteritis, which was not modified for the purpose of the study. Fluid resuscitation was administered based on the degree of dehydration, with oral rehydration solution preferred for mild to moderate cases and intravenous fluid therapy for severe dehydration or patients unable to tolerate oral intake. The composition and volume of intravenous fluids were determined by the treating physician based on the patient's clinical and biochemical parameters. Antimicrobial therapy was initiated when indicated by clinical features or laboratory evidence of bacterial infection. Symptomatic treatment with antiemetics and antidiarrheal agents was prescribed according to standard clinical practice. Patients who developed severe AKI requiring renal replacement therapy were managed in collaboration with nephrologists.

Outcome Measures

The primary outcome measure was the incidence of acute kidney injury, defined as an increase in serum creatinine by ≥0.3 mg/dL within 48 hours or ≥1.5 times baseline within 7 days, in accordance with KDIGO criteria. Secondary outcomes included the severity of AKI as per KDIGO staging, need for renal replacement therapy, time to resolution of kidney dysfunction, length of hospital stay, and renal function status at 90 days follow-up. We also analyzed the correlation between the type of enteropathogen, severity of gastroenteritis, degree of dehydration, and the development of kidney dysfunction.

Statistical Analysis

Sample size calculation was performed based on previously published data on the incidence of AKI in patients with acute gastroenteritis, with an expected incidence of 15%. A sample size of 100 patients provided a precision of ±7% with a 95% confidence interval for the primary outcome. Descriptive statistics were used to summarize demographic and clinical characteristics, with continuous variables reported as means ± standard deviations or medians with interquartile ranges depending on the distribution of data, and categorical variables presented as frequencies and percentages.

The association between potential risk factors and the development of AKI was analyzed using univariate and multivariate logistic regression models. Variables with $p < 0.1$ in the univariate analysis were included in the multivariate model. The predictive value of various biomarkers for AKI was assessed using receiver operating characteristic (ROC) curve analysis. Time-to-event outcomes were analyzed using Kaplan-Meier curves and Cox proportional hazards models.

A p-value < 0.05 was considered statistically significant for all analyses. Statistical analyses were performed using SPSS version 28.0 (IBM Corp., Armonk, NY, USA) and R version 4.2.0 (R Foundation for Statistical Computing, Vienna, Austria).

Ethical Considerations

The study protocol was designed to minimize potential risks to participants. No additional blood sampling beyond what was clinically indicated was performed, and the volume of blood drawn for research purposes did not exceed 30 mL per participant. Patient confidentiality was maintained through the use of coded identification numbers, and all data were stored in a secure, password-protected database with access limited to authorized research personnel. An independent Data and Safety Monitoring Board reviewed the study progress and adverse events at predetermined intervals. Participants were informed of their right to withdraw from the study at any time without affecting their standard clinical care.

RESULTS

Demographics and Baseline Characteristics

A total of 100 patients with acute gastroenteritis were enrolled in the study from January 2024 to December 2024. The mean age of the participants was 47.3 ± 18.6 years, with 53 (53.0%) males and 47 (47.0%) females. The most common comorbidities were hypertension (34.0%), history of NSAID use within 30 days (28.0%), and diabetes mellitus (22.0%). Based on clinical assessment, 43 (43.0%) patients presented with mild gastroenteritis, 38 (38.0%) with moderate gastroenteritis, and 19 (19.0%) with severe gastroenteritis. The median duration of symptoms before presentation was 2.4 days (IQR: 1.2-3.8).

Acute kidney injury (AKI) was diagnosed in 28 (28.0%) patients. Significant differences were observed in the demographic and clinical characteristics between patients who developed AKI and those who did not. Patients with AKI were significantly older (58.7 ± 16.4 vs. 42.9 ± 17.5 years, $p = 0.001$) and had a higher prevalence of hypertension (53.6% vs. 26.4%, $p = 0.010$), diabetes mellitus (39.3% vs. 15.3%, $p = 0.008$), and cardiovascular disease (32.1% vs. 12.5%, $p = 0.019$). Moreover, patients who developed AKI had significantly lower baseline estimated glomerular filtration rate (eGFR) (85.2 ± 18.3 vs. 96.8 ± 14.9 mL/min/1.73m², $p = 0.002$) and were more likely to have used NSAIDs within 30 days before presentation (46.4% vs. 20.8%, $p = 0.009$) compared to those without AKI.

The severity of gastroenteritis was significantly associated with the development of AKI ($p < 0.001$). Half of the patients (50.0%) who developed AKI had severe gastroenteritis, compared to only 6.9% of patients without AKI. Conversely, mild gastroenteritis was present in only 14.3% of patients with AKI compared to 54.2% of patients without AKI. Furthermore, patients with AKI had a significantly longer duration of symptoms before presentation (median: 3.6 vs. 1.9 days, $p = 0.001$).

Etiological Agents and Association with Acute Kidney Injury

Comprehensive microbiological investigations identified the etiological agent in 92 (92.0%) of the 100 patients. Viral pathogens were the most common cause of gastroenteritis, identified in 48 (48.0%) patients, followed by bacterial pathogens in 38 (38.0%) patients and parasitic infections in 6 (6.0%) patients. The etiology remained undetermined in 8 (8.0%) cases despite extensive testing.

Among viral pathogens, norovirus was the most frequently isolated agent (26.0%), followed by rotavirus (15.0%). Among bacterial causes, Salmonella species were most common (12.0%), followed by Campylobacter species (11.0%) and Shiga toxin-producing Escherichia coli (STEC) (8.0%).

The etiology of gastroenteritis significantly influenced the risk of developing AKI. Patients with bacterial gastroenteritis had a significantly higher incidence of AKI compared to those with viral gastroenteritis (57.1% vs. 32.1%, $p = 0.013$; OR 3.02, 95% CI 1.24-7.37). Particularly notable was the strong association between STEC infection and AKI development; 6 of 8 (75.0%) patients with STEC infection developed AKI, resulting in a significantly increased odds ratio of 9.53 (95% CI 1.79-50.70, $p = 0.002$). Conversely, viral gastroenteritis was associated with a reduced risk of AKI (OR 0.40, 95% CI 0.16-0.99, $p = 0.045$).

Incidence and Severity of Acute Kidney Injury

Of the 28 patients who developed AKI, 16 (57.1%) had Stage 1 AKI, 8 (28.6%) had Stage 2 AKI, and 4 (14.3%) had Stage 3 AKI according to the KDIGO criteria. Renal replacement therapy was required in 2 (7.1%) patients, both of whom had Stage 3 AKI.

The median time to AKI onset from presentation was 35.4 hours (IQR: 18.7-58.2). A notable trend was observed in the timing of AKI onset in relation to its severity; more severe AKI tended to develop earlier after presentation. The median time to AKI onset was 42.3 hours (IQR: 23.5-61.8) for Stage 1, 28.6 hours (IQR: 16.9-44.3) for Stage 2, and 18.2 hours

(IQR: 12.4-29.7) for Stage 3 AKI. Patients requiring renal replacement therapy developed AKI particularly early, with a median time to onset of 16.5 hours (IQR: 14.2-18.8).

Risk Factors for Acute Kidney Injury

Univariate logistic regression analysis identified several factors associated with an increased risk of AKI in patients with gastroenteritis. These included age ≥65 years (OR 3.47, 95% CI 1.46-8.22, p = 0.005), diabetes mellitus (OR 3.58, 95% CI 1.34-9.56, p = 0.011), hypertension (OR 3.21, 95% CI 1.33-7.79, p = 0.010), baseline eGFR <80 mL/min/1.73m² (OR 3.76, 95% CI 1.49-9.48, p = 0.005), NSAID use within 30 days (OR 3.29, 95% CI 1.33-8.14, p = 0.010), severe dehydration (OR 8.42, 95% CI 3.19-22.21, p < 0.001), bacterial etiology (OR 3.02, 95% CI 1.24-7.37, p = 0.015), STEC infection (OR 9.53, 95% CI 1.79-50.70, p = 0.008), fever >38.5°C (OR 2.75, 95% CI 1.14-6.64, p = 0.024), and duration of symptoms >3 days before presentation (OR 4.32, 95% CI 1.74-10.68, p = 0.002).

In the multivariate analysis, after adjusting for potential confounders, five factors remained independently associated with AKI development: age ≥65 years (adjusted OR [aOR] 2.83, 95% CI 1.06-7.58, p = 0.038), baseline eGFR <80 mL/min/1.73m² (aOR 3.12, 95% CI 1.14-8.54, p = 0.027), NSAID use within 30 days (aOR 3.04, 95% CI 1.15-8.02, p = 0.025), severe dehydration (aOR 6.78, 95% CI 2.39-19.25, p < 0.001), STEC infection (aOR 7.32, 95% CI 1.28-41.95, p = 0.025), and duration of symptoms >3 days before presentation (aOR 3.18, 95% CI 1.18-8.57, p = 0.022).

Biomarkers and Their Predictive Value for Acute Kidney Injury

All measured biomarkers showed significant differences between patients who developed AKI and those who did not (p < 0.001 for all comparisons). Urinary tissue inhibitor of metalloproteinases-2 multiplied by insulin-like growth factor-binding protein 7 (TIMP-2 × IGFBP7) demonstrated the highest diagnostic performance for early prediction of AKI, with an area under the receiver operating characteristic curve (AUC) of 0.92 (95% CI 0.86-0.98), sensitivity of 89.3%, and specificity of 87.5% at the optimal cut-off value of 0.75.

Urinary kidney injury molecule-1 (KIM-1) also showed excellent predictive ability with an AUC of 0.89 (95% CI 0.82-0.96), followed by serum neutrophil gelatinase-associated lipocalin (NGAL) with an AUC of 0.86 (95% CI 0.78-0.94), urinary liver-type fatty acid-binding protein (L-FABP) with an AUC of 0.84 (95% CI 0.76-0.92), and urinary albumin/creatinine ratio with an AUC of 0.79 (95% CI 0.70-0.88).

Conventional markers of kidney function showed relatively lower diagnostic performance compared to novel biomarkers. The blood urea nitrogen (BUN)/creatinine ratio had an AUC of 0.76 (95% CI 0.66-0.86), while serum creatinine at presentation had an AUC of 0.71 (95% CI 0.60-0.82).

Renal Outcomes and Recovery Patterns

The median time to peak serum creatinine was 2.3 days (IQR: 1.6-3.4) for all AKI patients, with significant differences across AKI severity stages (p = 0.008): 1.9 days (IQR: 1.4-2.7) for Stage 1, 2.8 days (IQR: 1.9-3.6) for Stage 2, and 3.7 days (IQR: 2.5-4.8) for Stage 3.

The median time to AKI resolution was 5.8 days (IQR: 3.2-9.6) overall and varied significantly by AKI severity (p < 0.001): 3.6 days (IQR: 2.4-5.7) for Stage 1, 7.9 days (IQR: 5.3-11.4) for Stage 2, and 13.2 days (IQR: 8.6-18.7) for Stage 3. Mean hospital stay was also significantly longer with increasing AKI severity (p < 0.001): 4.8 ± 2.3 days for Stage 1, 7.4 ± 3.2 days for Stage 2, and 11.5 ± 4.7 days for Stage 3.

At hospital discharge, complete renal recovery was observed in 15 (53.6%) patients with AKI, partial recovery in 11 (39.3%), and no recovery in 2 (7.1%). Recovery status at discharge varied significantly with AKI severity (p < 0.001), with complete recovery in 81.3% of Stage 1 patients, 25.0% of Stage 2 patients, and none of the Stage 3 patients.

Follow-up assessment at 30 days showed substantial improvement, with complete renal recovery in 22 (78.6%) patients, partial recovery in 5 (17.9%), and persistent chronic kidney disease (CKD) in 1 (3.6%) patient. Again, significant differences by AKI severity were observed (p = 0.002): all Stage 1 patients (100.0%) achieved complete recovery, compared to 62.5% of Stage 2 and 25.0% of Stage 3 patients.

By the 90-day follow-up, further improvement was noted, with complete recovery in 25 (89.3%) patients, partial recovery in 2 (7.1%), and persistent CKD in 1 (3.6%) patient. Although the recovery rates improved across all severity categories, significant differences persisted (p = 0.042), with complete recovery in 100.0% of Stage 1, 87.5% of Stage 2, and 50.0% of Stage 3 patients.

Table 1: Demographics and Baseline Characteristics of Study Participants

Characteristic	All Patients (n=100)	Patients with AKI (n=28)	Patients without AKI (n=72)	p-value
Age (years), mean ± SD	47.3 ± 18.6	58.7 ± 16.4	42.9 ± 17.5	0.001
Sex, n (%)				0.346
Male	53 (53.0)	17 (60.7)	36 (50.0)	
Female	47 (47.0)	11 (39.3)	36 (50.0)	
BMI (kg/m²), mean ± SD	26.4 ± 5.2	27.9 ± 5.8	25.8 ± 4.9	0.068
Comorbidities, n (%)				
Hypertension	34 (34.0)	15 (53.6)	19 (26.4)	0.010
Diabetes mellitus	22 (22.0)	11 (39.3)	11 (15.3)	0.008
Cardiovascular disease	18 (18.0)	9 (32.1)	9 (12.5)	0.019
NSAID use within 30 days	28 (28.0)	13 (46.4)	15 (20.8)	0.009
Baseline eGFR (mL/min/1.73m²), mean ± SD	93.6 ± 16.7	85.2 ± 18.3	96.8 ± 14.9	0.002
Severity of gastroenteritis, n (%)				<0.001
Mild	43 (43.0)	4 (14.3)	39 (54.2)	
Moderate	38 (38.0)	10 (35.7)	28 (38.9)	
Severe	19 (19.0)	14 (50.0)	5 (6.9)	
Duration of symptoms before presentation (days), median (IQR)	2.4 (1.2-3.8)	3.6 (2.1-5.2)	1.9 (1.0-3.1)	0.001

AKI: Acute Kidney Injury; BMI: Body Mass Index; eGFR: estimated Glomerular Filtration Rate; IQR: Interquartile Range; NSAID: Non-Steroidal Anti-Inflammatory Drug; SD: Standard Deviation

Table 2: Etiological Agents of Gastroenteritis and Association with Acute Kidney Injury

Etiological Agent	All Patients (n=100)	Patients with AKI (n=28)	Patients without AKI (n=72)	p-value	Odds Ratio (95% CI)
Viral, n (%)	48 (48.0)	9 (32.1)	39 (54.2)	0.045	0.40 (0.16-0.99)
Norovirus	26 (26.0)	4 (14.3)	22 (30.6)	0.097	0.38 (0.12-1.21)
Rotavirus	15 (15.0)	3 (10.7)	12 (16.7)	0.459	0.60 (0.16-2.29)
Other viral agents	7 (7.0)	2 (7.1)	5 (6.9)	0.974	1.03 (0.19-5.61)
Bacterial, n (%)	38 (38.0)	16 (57.1)	22 (30.6)	0.013	3.02 (1.24-7.37)
STEC	8 (8.0)	6 (21.4)	2 (2.8)	0.002	9.53 (1.79-50.70)
Salmonella spp.	12 (12.0)	5 (17.9)	7 (9.7)	0.255	2.02 (0.59-6.95)
Campylobacter spp.	11 (11.0)	3 (10.7)	8 (11.1)	0.955	0.96 (0.24-3.89)
Other bacterial agents	7 (7.0)	2 (7.1)	5 (6.9)	0.974	1.03 (0.19-5.61)
Parasitic, n (%)	6 (6.0)	1 (3.6)	5 (6.9)	0.523	0.50 (0.06-4.45)
Unknown etiology, n (%)	8 (8.0)	2 (7.1)	6 (8.3)	0.843	0.85 (0.16-4.45)

AKI: Acute Kidney Injury; CI: Confidence Interval; STEC: Shiga Toxin-producing Escherichia coli

Table 3: Incidence and Severity of Acute Kidney Injury According to KDIGO Criteria

AKI Classification	Number of Patients (n=100)	Percentage (%)	Time to AKI Onset (hours), median (IQR)
No AKI	72	72.0	-
AKI (All Stages)	28	28.0	35.4 (18.7-58.2)
Stage 1	16	16.0	42.3 (23.5-61.8)

AKI Classification	Number of Patients (n=100)	Percentage (%)	Time to AKI Onset (hours), median (IQR)
Stage 2	8	8.0	28.6 (16.9-44.3)
Stage 3	4	4.0	18.2 (12.4-29.7)
Requiring RRT	2	2.0	16.5 (14.2-18.8)

AKI: Acute Kidney Injury; IQR: Interquartile Range; KDIGO: Kidney Disease: Improving Global Outcomes; RRT: Renal Replacement Therapy

Table 4: Risk Factors for Development of Acute Kidney Injury in Patients with Gastroenteritis

Risk Factor	Univariate Analysis		Multivariate Analysis	
	OR (95% CI)	p-value	aOR (95% CI)	p-value
Age ≥65 years	3.47 (1.46-8.22)	0.005	2.83 (1.06-7.58)	0.038
Diabetes mellitus	3.58 (1.34-9.56)	0.011	2.75 (0.92-8.26)	0.071
Hypertension	3.21 (1.33-7.79)	0.010	2.31 (0.87-6.19)	0.095
Baseline eGFR <80 mL/min/1.73m²	3.76 (1.49-9.48)	0.005	3.12 (1.14-8.54)	0.027
NSAID use within 30 days	3.29 (1.33-8.14)	0.010	3.04 (1.15-8.02)	0.025
Severe dehydration	8.42 (3.19-22.21)	<0.001	6.78 (2.39-19.25)	<0.001
Bacterial etiology	3.02 (1.24-7.37)	0.015	2.54 (0.97-6.69)	0.059
STEC infection	9.53 (1.79-50.70)	0.008	7.32 (1.28-41.95)	0.025
Fever >38.5°C	2.75 (1.14-6.64)	0.024	1.86 (0.69-4.98)	0.219
Duration of symptoms >3 days before presentation	4.32 (1.74-10.68)	0.002	3.18 (1.18-8.57)	0.022

aOR: adjusted Odds Ratio; CI: Confidence Interval; eGFR: estimated Glomerular Filtration Rate; NSAID: Non-Steroidal Anti-Inflammatory Drug; OR: Odds Ratio; STEC: Shiga Toxin-producing Escherichia coli

Table 5: Biomarkers and Their Predictive Value for Acute Kidney Injury

Biomarker	Patients with AKI (n=28)	Patients without AKI (n=72)	p-value	AUC (95% CI)	Sensitivity (%)	Specificity (%)	Optimal Cut-off Value
Serum NGAL (ng/mL), median (IQR)	236.8 (178.5-325.3)	97.4 (65.2-142.6)	<0.001	0.86 (0.78-0.94)	82.1	81.9	165.7
Urinary KIM-1 (pg/mL), median (IQR)	2.84 (1.92-4.37)	0.86 (0.54-1.38)	<0.001	0.89 (0.82-0.96)	85.7	84.7	1.65
Urinary L-FABP (ng/mL), median (IQR)	68.3 (42.6-96.5)	18.9 (12.3-28.7)	<0.001	0.84 (0.76-0.92)	78.6	79.2	35.8
Urinary TIMP-2 × IGFBP7, median (IQR)	1.82 (0.98-2.64)	0.34 (0.19-0.56)	<0.001	0.92 (0.86-0.98)	89.3	87.5	0.75
Urinary albumin/creatinine ratio (mg/g), median (IQR)	186.3 (98.7-285.4)	24.6 (12.8-48.3)	<0.001	0.79 (0.70-0.88)	75.0	76.4	78.5
Serum creatinine at presentation (mg/dL), mean ± SD	1.28 ± 0.43	0.89 ± 0.24	<0.001	0.71 (0.60-0.82)	67.9	69.4	1.05
BUN/creatinine ratio, mean ± SD	23.8 ± 6.7	16.5 ± 5.2	<0.001	0.76 (0.66-0.86)	71.4	72.2	19.5

AKI: Acute Kidney Injury; AUC: Area Under the Curve; BUN: Blood Urea Nitrogen; CI: Confidence Interval; IGFBP7: Insulin-like Growth Factor-Binding Protein 7; IQR: Interquartile Range; KIM-1: Kidney Injury Molecule-1; L-FABP: Liver-type Fatty Acid-Binding Protein; NGAL: Neutrophil Gelatinase-Associated Lipocalin; SD: Standard Deviation; TIMP-2: Tissue Inhibitor of Metalloproteinases-2

Table 6: Renal Outcomes and Recovery Patterns

Outcome	All AKI Patients (n=28)	Stage 1 AKI (n=16)	Stage 2 AKI (n=8)	Stage 3 AKI (n=4)	p-value
Time to peak creatinine (days), median (IQR)	2.3 (1.6-3.4)	1.9 (1.4-2.7)	2.8 (1.9-3.6)	3.7 (2.5-4.8)	0.008
Time to AKI resolution (days), median (IQR)	5.8 (3.2-9.6)	3.6 (2.4-5.7)	7.9 (5.3-11.4)	13.2 (8.6-18.7)	<0.001
Length of hospital stay (days), mean ± SD	6.3 ± 3.8	4.8 ± 2.3	7.4 ± 3.2	11.5 ± 4.7	<0.001
eGFR at discharge (mL/min/1.73m²), mean ± SD	74.8 ± 19.5	82.3 ± 16.7	70.2 ± 18.3	54.6 ± 14.8	0.005
Renal recovery at discharge, n (%)					<0.001
Complete recovery	15 (53.6)	13 (81.3)	2 (25.0)	0 (0.0)	
Partial recovery	11 (39.3)	3 (18.8)	6 (75.0)	2 (50.0)	
No recovery	2 (7.1)	0 (0.0)	0 (0.0)	2 (50.0)	
Renal function at 30 days, n (%)					0.002
Complete recovery	22 (78.6)	16 (100.0)	5 (62.5)	1 (25.0)	
Partial recovery	5 (17.9)	0 (0.0)	3 (37.5)	2 (50.0)	
Persistent CKD	1 (3.6)	0 (0.0)	0 (0.0)	1 (25.0)	
Renal function at 90 days, n (%)					0.042
Complete recovery	25 (89.3)	16 (100.0)	7 (87.5)	2 (50.0)	
Partial recovery	2 (7.1)	0 (0.0)	1 (12.5)	1 (25.0)	
Persistent CKD	1 (3.6)	0 (0.0)	0 (0.0)	1 (25.0)	

AKI: Acute Kidney Injury; CKD: Chronic Kidney Disease; eGFR: estimated Glomerular Filtration Rate; IQR: Interquartile Range; SD: Standard Deviation

DISCUSSION

The present study investigated the intricate relationship between gastroenteritis and kidney function derangement, finding an overall AKI incidence of 28.0% among 100 patients with acute gastroenteritis. This incidence falls within the range reported by previous studies, though with considerable variation depending on the population studied and diagnostic criteria employed. Chiurchiu et al. reported a comparable AKI incidence of 25.3% among 273 hospitalized adults with acute gastroenteritis, while a retrospective study by Watanabe et al. found a somewhat lower rate of 17.1% among patients presenting with viral gastroenteritis.(11,12) Conversely, Basu et al. documented a higher incidence of 36.4% in a pediatric population with severe gastroenteritis requiring hospitalization, highlighting the increased vulnerability of children to renal complications.(13)

Our findings regarding the influence of etiological agents on AKI risk align with previous research but also provide new insights. The significant association between bacterial gastroenteritis and increased AKI risk (OR 3.02, 95% CI 1.24-7.37, p = 0.013) corroborates the findings of Proulx et al., who reported bacterial pathogens as causative agents in 68.7% of gastroenteritis-associated AKI cases compared to 32.4% of those without AKI (p < 0.001).(14) The particularly strong association between STEC infection and AKI development observed in our study (OR 9.53, 95% CI 1.79-50.70, p = 0.002) is consistent with the well-documented nephrotoxic potential of Shiga toxin. Gould et al., in their multi-center study of 394 patients with confirmed STEC infection, reported AKI development in 47.2% of cases, with progression to hemolytic uremic syndrome in 15.7%.(15) However, our observed rate of 75.0% AKI in STEC-infected patients exceeds these previous estimates, possibly reflecting differences in strain virulence or diagnostic vigilance.

The identification of independent risk factors for AKI development in the context of gastroenteritis constitutes a valuable contribution to the literature. Our multivariable analysis identified age ≥65 years (aOR 2.83, 95% CI 1.06-7.58, p =

0.038), baseline eGFR <80 mL/min/1.73m² (aOR 3.12, 95% CI 1.14-8.54, p = 0.027), NSAID use within 30 days (aOR 3.04, 95% CI 1.15-8.02, p = 0.025), severe dehydration (aOR 6.78, 95% CI 2.39-19.25, p < 0.001), STEC infection (aOR 7.32, 95% CI 1.28-41.95, p = 0.025), and prolonged symptom duration before presentation (aOR 3.18, 95% CI 1.18-8.57, p = 0.022) as independent predictors. These findings expand upon those of Raines et al., who identified advanced age (OR 1.71 per decade, 95% CI 1.28-2.27, p < 0.001) and pre-existing CKD (OR 3.62, 95% CI 1.84-7.12, p < 0.001) as risk factors but did not assess NSAID use or symptom duration.(16)

The association between NSAID use and increased AKI risk merits particular attention. Our finding of a threefold increased risk (aOR 3.04, 95% CI 1.15-8.02, p = 0.025) with recent NSAID exposure is consistent with the results of a case-control study by Ungprasert et al., who reported an adjusted OR of 2.7 (95% CI 1.8-4.1) for AKI development with NSAID use in the setting of volume depletion.(17) This synergistic nephrotoxicity likely stems from NSAID-induced inhibition of prostaglandin synthesis, which compromises renal autoregulation, particularly in states of reduced effective circulating volume such as gastroenteritis-associated dehydration.

The evaluation of biomarkers for early AKI prediction represents a particularly novel aspect of our study. The superior performance of urinary TIMP-2 × IGFBP7 (AUC 0.92, 95% CI 0.86-0.98) aligns with findings from Pajenda et al., who reported an AUC of 0.85 (95% CI 0.78-0.93) for this marker in a mixed critical care population.(18) However, their study did not specifically examine gastroenteritis-associated AKI. Similarly, the excellent performance of urinary KIM-1 in our study (AUC 0.89, 95% CI 0.82-0.96) exceeds that reported by Huang et al. (AUC 0.71, 95% CI 0.62-0.80) in a heterogeneous AKI population, suggesting potential disease-specific variations in biomarker utility.(19)

The relatively modest performance of serum creatinine at presentation (AUC 0.71, 95% CI 0.60-0.82) underscores the limitations of conventional renal function markers for early AKI detection, as previously highlighted by Ostermann et al. in their comprehensive review of AKI biomarkers.(20) This finding emphasizes the potential clinical utility of novel biomarkers for early risk stratification and intervention in gastroenteritis patients at risk for renal complications.

Our study provides valuable insights into the temporal dynamics and recovery patterns of gastroenteritis-associated AKI. The observed relationship between AKI severity and time to onset, with more severe AKI developing earlier (median 18.2 hours for Stage 3 vs. 42.3 hours for Stage 1, p < 0.001), has not been extensively documented in previous literature. This finding may reflect the rapid progression of severe renal injury in the context of significant pathophysiological insults, such as profound dehydration or direct nephrotoxicity.

The recovery patterns observed in our cohort, with 89.3% of patients achieving complete renal recovery by 90 days, are somewhat more favorable than those reported by Coca et al. in their meta-analysis of AKI outcomes, which documented complete recovery in approximately 70% of general AKI cases.(21) This disparity may reflect the predominantly prerenal and potentially reversible nature of gastroenteritis-associated kidney injury, in contrast to the heterogeneous etiologies included in the meta-analysis. Nevertheless, the incomplete recovery observed in 10.7% of our patients, including persistent CKD in 3.6%, aligns with growing recognition of the potential for AKI to initiate or accelerate chronic kidney disease, as documented by Heung et al.(22)

The strong association between AKI severity and recovery trajectories in our cohort (100% complete recovery in Stage 1 vs. 50% in Stage 3 by 90 days, p = 0.042) corroborates the findings of Pannu et al., who reported a stepwise decrease in recovery probability with increasing AKI severity in a large population-based study (91.7% in Stage 1 vs. 78.5% in Stage 3, p < 0.001).(23) However, their study examined all-cause AKI rather than specifically gastroenteritis-associated cases.

Our findings have important clinical implications. The identified risk factors and biomarkers could inform risk stratification strategies to guide monitoring intensity and preventive interventions. The relationship between delayed presentation and increased AKI risk (aOR 3.18, 95% CI 1.18-8.57, p = 0.022) highlights the potential benefits of early medical attention and fluid resuscitation, supporting public health messaging regarding the importance of prompt care-seeking for severe or persistent gastroenteritis, particularly in vulnerable populations.

Several limitations warrant acknowledgment. The single-center design may limit generalizability to other settings with different patient demographics or pathogen profiles. The moderate sample size, while adequate for primary analyses, resulted in relatively small numbers in certain subgroups, particularly for rare outcomes such as requirement for renal replacement therapy. Additionally, the 90-day follow-up period, while longer than many acute care studies, may not capture very late renal function changes. Finally, while our multivariate analyses adjusted for major confounders, residual confounding from unmeasured variables remains possible.

Future research directions include larger, multicenter studies to validate our findings across diverse populations and healthcare settings. Longer follow-up periods would enhance understanding of the potential long-term renal sequelae of gastroenteritis-associated AKI. Intervention studies targeting the modifiable risk factors identified in our analysis could evaluate strategies to mitigate AKI risk, such as NSAID avoidance protocols or early, aggressive fluid resuscitation algorithms. Further investigation of the predictive biomarkers, particularly TIMP-2 × IGFBP7 and KIM-1, could establish clinically useful cut-off values and implementation strategies.

CONCLUSION

This prospective observational study has demonstrated that acute kidney injury represents a common and potentially serious complication of gastroenteritis, affecting 28.0% of the studied cohort. The pathophysiology of this association is multifactorial, with both pathogen-specific factors and host characteristics contributing to renal risk. Bacterial etiology, particularly STEC infection, conferred substantially higher risk compared to viral gastroenteritis, highlighting the importance of etiological diagnosis in risk stratification.

Several independent risk factors for AKI development were identified, including advanced age, reduced baseline renal function, NSAID use, severe dehydration, STEC infection, and delayed presentation. These factors provide valuable insights for clinical risk assessment and identify potentially modifiable targets for preventive interventions. The superior performance of novel biomarkers, particularly urinary TIMP-2 × IGFBP7 and KIM-1, over conventional renal function parameters for early AKI prediction suggests their potential utility in clinical practice, pending further validation.

The temporal dynamics of gastroenteritis-associated AKI revealed in this study, including the earlier onset of more severe disease and the relationship between AKI severity and recovery trajectories, enhance our understanding of the natural history of this condition. While the majority of patients (89.3%) achieved complete renal recovery by 90 days, the incomplete recovery observed in 10.7% of cases underscores the potential for long-term renal sequelae, particularly in those with severe AKI.

These findings have substantial implications for clinical practice and public health. They support the importance of early recognition and intervention in gastroenteritis, particularly in high-risk populations, and suggest potential strategies to mitigate renal risk, such as NSAID avoidance and aggressive fluid resuscitation. The biomarker data provide a foundation for the development of risk-stratified monitoring and management protocols. From a public health perspective, these results highlight the importance of preventive measures for both gastroenteritis and its renal complications, including improved sanitation, food safety practices, and public education regarding appropriate care-seeking behaviors.

In conclusion, the relationship between gastroenteritis and kidney function derangement represents a significant clinical entity with implications for both acute management and long-term outcomes. A multifaceted approach to prevention, early detection, and appropriate management is essential to mitigate the renal impact of this common infectious condition.

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