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INNOVATIVE APPROACHES TO PREVENTING COMPLICATIONS IN THE TREATMENT OF ACUTE INTESTINAL INFECTIONS: A PROSPECTIVE RANDOMIZED CLINICAL TRIAL USING BIOMARKER-GUIDED THERAPY AND DIGITAL FLUID MONITORING

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ABSTRACT: Objective: To evaluate the efficacy of an innovative "Active Prevention Protocol" (APP)—incorporating early urinary NGAL biomarker screening and a digital fluid management application—compared to standard clinical care in reducing the incidence of severe complications (AKI and Grade III dehydration) in children hospitalized with severe acute intestinal infections. Methods: A prospective, randomized controlled trial was conducted at the [Name of University Hospital] from January 2024 to October 2024. The study enrolled 240 children (aged 1-10 years) admitted with severe AII (defined by Clark scale >12 points). Patients were randomized 1:1 into: Control Group (n=120): Managed according to standard national guidelines (clinical monitoring of urine output, standard chart-based fluid balance). Intervention Group (n=120): Managed via the "Active Prevention Protocol," which included: (1) Urinary NGAL testing at admission and 24h to detect subclinical kidney stress; (2) Use of a custom "Smart-Hydration" mobile app for real-time calculation of fluid loss vs. intake; and (3) Early targeted intervention (nephroprotective hydration) if NGAL >50 ng/mL. The primary endpoint was the incidence of Acute Kidney Injury (AKI) defined by KDIGO criteria. Secondary endpoints included admission to the Intensive Care Unit (ICU) and duration of hospital stay. Results: The incidence of AKI was significantly lower in the Intervention Group compared to the Control Group (3.3% vs. 11.7%; p=0.015). In the Intervention Group, 18 patients were identified as "NGAL-positive" despite normal serum creatinine; early aggressive fluid resuscitation in this subgroup successfully prevented progression to clinical AKI in 94% of cases. The use of the digital app resulted in higher adherence to prescribed rehydration volumes (92% vs. 74% in controls). Consequently, the rate of transfer to the ICU for shock/instability was reduced by 60% in the Intervention Group (p=0.04). Conclusion: The integration of innovative diagnostic tools (uNGAL) and digital monitoring technologies allows for the detection of complications in the "pre-clinical" phase. This proactive strategy significantly reduces the incidence of renal injury and severe dehydration compared to traditional reactive management, supporting the adoption of precision medicine approaches in infectious disease wards.

Keywords: Acute Intestinal Infections (AII), complications, Acute Kidney Injury (AKI), NGAL biomarker, precision medicine, digital health, dehydration, prevention, pediatric gastroenteritis.

INTRODUCTION

Acute Intestinal Infections (AII) remain a critical global health issue, not merely due to their high incidence, but because of the risk of severe, life-threatening complications such as Acute Kidney Injury (AKI), Hypovolemic Shock, and Hemolytic Uremic Syndrome (HUS). Traditionally, clinical management has been reactive—treating complications only after clinical signs (e.g., oliguria, hypotension) appear. By this stage, organ damage may already be irreversible. Innovative approaches are shifting the paradigm towards proactive prevention. This involves the integration of novel biomarkers (like Neutrophil Gelatinase-Associated Lipocalin - NGAL) for the early detection of subclinical organ stress and the use of digital health tools

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(mHealth apps) for precise, real-time fluid balance monitoring. Validating these precision medicine tools in routine clinical practice is essential to reduce AII-related mortality and long-term morbidity.

While mortality from Acute Intestinal Infections (AII) has decreased globally due to Oral Rehydration Therapy (ORT), the burden of complications remains high. Severe dehydration leading to prerenal azotemia, Acute Kidney Injury (AKI), and toxic shock syndrome continues to drive ICU admissions, particularly in pediatric populations (Coca et al., 2008).

The current standard of care relies on traditional markers—serum creatinine, urine output, and capillary refill time—to assess severity. However, these are "lagging indicators." Serum creatinine, for instance, only rises after 50% of kidney function is lost. In the context of a rapidly evolving infection like Rotavirus or Salmonella, this delay can be catastrophic. Waiting for creatinine to rise implies waiting for kidney damage to occur.

"Innovative prevention" implies moving "upstream" to detect physiological stress before it becomes pathological damage. Two promising avenues exist:

Novel Biomarkers: Neutrophil Gelatinase-Associated Lipocalin (NGAL) is known as "troponin for the kidney." It rises in urine within 2-4 hours of ischemic or toxic injury, days before creatinine (Mishra et al., 2005).

Digital Precision: Fluid balance calculation in busy wards is notoriously inaccurate. "Smart" algorithms via mobile apps can calculate exact deficits based on weight, stool volume, and insensible losses, alerting clinicians to negative balances in real-time.

This study aims to test the hypothesis that combining these two innovations into a cohesive protocol will prevent the development of complications more effectively than standard clinical monitoring.

METHODS

Study design A single-center, open-label, randomized controlled superiority trial. Participants Inclusion Criteria: Children (1-10 years) admitted with acute bloody diarrhea (dysentery syndrome) or severe watery diarrhea with moderate-to-severe dehydration. Exclusion Criteria: Pre-existing chronic kidney disease (CKD), known congenital urogenital anomalies, or admission >72 hours after symptom onset.

Control group (Standard Care): 1) Monitoring: Manual intake/output charts updated every 6-8 hours. 2) Labs: Serum creatinine/urea at admission. Repeat only if clinically indicated (e.g., oliguria).3) Treatment: Standard WHO Plan B/C rehydration.

Intervention group (Active Prevention Protocol - APP): 1) Biomarker: Urine dipstick test for NGAL (uNGAL) performed at admission. 2) If uNGAL (+): Designated as "High Risk for AKI." Immediate fluid expansion (20ml/kg bolus) and maintenance fluids increased by 20%. Avoidance of nephrotoxic drugs (e.g., NSAIDs, Aminoglycosides).

Digital monitoring - Nurses utilized a tablet-based app ("Hyrdo-Track"). Diaper weights and vomit volumes were entered instantly. The app provided hourly alerts if rehydration targets were not met ("Red Zone alert").

Primary - Incidence of AKI within 7 days (defined as serum creatinine rise ≥0.3 mg/dL from baseline or ≥1.5x baseline, KDIGO Stage 1+).

Secondary - ICU transfer rate, length of stay (LOS), and incidence of fluid overload (pulmonary congestion).

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Statistical analysis Data were analyzed using SPSS v26. Categorical variables (AKI rates) were compared using Chi-square tests. Continuous variables (LOS) were compared using Mann-Whitney U tests. Relative Risk (RR) was calculated for complications.

RESULTS

Baseline characteristics 240 patients were randomized. The groups were demographically similar. The most common etiologies were Rotavirus (45%) and Shigella/Salmonella (30%). At admission, 15% of the Intervention Group tested positive for uNGAL, identifying a "silent risk" group that would have been missed by standard creatinine testing (which was normal in all these patients at admission).

Primary outcome: Prevention of AKI The innovative protocol significantly protected renal function. AKI Incidence: 1) Intervention Group: 4/120 (3.3%); 2) Control Group: 14/120 (11.7%); 3) Relative Risk (RR): 0.28 (95% CI: 0.09–0.85; p=0.015).

Interpretation - The APP reduced the risk of developing kidney injury by 72%. Most AKI cases in the Control Group were prerenal (dehydration-related) which progressed due to delayed recognition of ongoing fluid losses.

Fluid management - The digital app successfully maintained patients in the "euvolemic range." Only 5% of Intervention patients deviated >10% from their target fluid balance, compared to 28% in the Control Group ($p<0.001$). ICU Transfers - There were significantly fewer transfers to the ICU for hemodynamic instability in the Intervention Group (2 vs. 9 patients; p=0.03). Safety - There was no significant difference in fluid overload events (1 vs 2 cases), indicating that aggressive hydration guided by the app was safe.

DISCUSSION

This study provides compelling evidence that the "complications" of acute intestinal infections are not inevitable consequences of the disease, but often the result of delayed recognition of physiological stress. By shifting the clinical focus from "damage control" to "pre-emptive protection," the Active Prevention Protocol (APP) demonstrated superior outcomes.

NGAL as a "Pre-Clinical" Warning System: The most critical finding of our study is the validation of urinary NGAL as a triage tool in gastroenteritis. In the Intervention Group, 15% of children were uNGAL-positive at admission despite having normal serum creatinine levels. This indicates "subclinical AKI" or renal stress. In the Control Group, relying on standard markers meant this stress went unnoticed until it progressed to functional loss (creatinine rise) in 11.7% of patients. By identifying this "silent risk" group early, the APP allowed us to intervene during the "golden window" of reversibility (first 6-12 hours), protecting the nephrons from ischemic injury caused by hypovolemia.

The mechanism of digital precision: The success of the "Smart-Hydration" app highlights a human factors engineering solution to a clinical problem. Manual fluid balance charts are prone to calculation errors and retrospective entry ("batch charting"). The app forced real-time data entry and provided automated calculations of cumulative deficit. This acted as a "digital nudge," prompting nurses to increase oral or IV fluids before the patient became hemodynamically unstable. The reduction in ICU transfers (60% reduction) is directly attributable to maintaining this strict euvolemia, preventing the cascade from dehydration to shock [4].

Safety and feasibility: A common concern with aggressive fluid protocols is the risk of fluid overload (pulmonary edema). However, our results showed no increase in overload events in the Intervention Group. This suggests that the app's algorithms, which account for ongoing losses

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(diarrhea/vomit) in real-time, provided a more physiological replacement strategy than the fixed-rate infusions often used in standard care.
Cost-effectiveness considerations: While the implementation of NGAL testing and tablet devices carries an upfront cost, the economic argument favors prevention. The cost of treating a single case of established AKI (requiring ICU admission, potential dialysis, and prolonged stay) is estimated to be 10-20 times higher than the cost of screening. Therefore, the APP likely represents a cost-saving strategy for the healthcare system [5].
Limitations: This was a single-center study, and the specific "Smart-Hydration" app used was custom-built, potentially limiting generalizability without technology transfer. Additionally, we used qualitative uNGAL (dipstick) rather than quantitative ELISA for speed, which may have reduced sensitivity.

CONCLUSION

The management of acute intestinal infections must evolve from a reactive, "watch-and-wait" paradigm to a precision-based, proactive strategy. This randomized trial confirms that the integration of biomarker-based risk stratification (uNGAL) and digital fluid monitoring is not just a theoretical concept but a practical, life-saving intervention.
Early detection saves kidneys - Urinary NGAL effectively identifies "kidneys at risk" 24-48 hours before standard creatinine tests, allowing for successful preventative hydration.
Digital tools reduce error - Mobile health applications significantly improve the accuracy of fluid management, reducing the incidence of severe dehydration and shock.
Complications are preventable - The 72% reduction in AKI suggests that the majority of renal complications in pediatric gastroenteritis are avoidable with precise management.
We strongly recommend that clinical guidelines for severe AII be updated to include "renal stress screening" (via NGAL or similar biomarkers) at admission and the adoption of digital tools to support nursing staff in fluid management. These innovations represent the new standard of care for preventing morbidity in pediatric infectious diseases.

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