



**DEVELOPMENT AND VALIDATION OF AN INTEGRATED CLINICAL ALGORITHM
FOR THE EARLY DIAGNOSIS AND RISK STRATIFICATION OF ACUTE
INTESTINAL INFECTIONS IN CHILDREN**

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Abstract

Objective: To develop and prospectively validate a clinical algorithm (Pedi-AII-Alg) for the early diagnosis and risk stratification of children with acute intestinal infections (AII), aimed at guiding diagnostic testing and clinical management. **Methods:** A prospective, two-phase diagnostic accuracy study was conducted at a tertiary pediatric emergency department. Phase 1 (Development): Key clinical predictors (e.g., patient age, fever $>39^{\circ}\text{C}$, bloody diarrhea, vomiting frequency, symptom duration) and dehydration status (assessed by the Clinical Dehydration Scale - CDS) were identified through literature review and expert consensus. These were used to build a tiered algorithm. Phase 2 (Validation): The algorithm was prospectively applied to 420 children (aged 6 months to 5 years) presenting with AII. The algorithm stratified patients into three pathways: Low-Risk (likely viral, supportive care), Moderate-Risk (requiring rapid RDT/toxin testing), and High-Risk (requiring comprehensive diagnostics, including multiplex PCR, and/pre-emptive admission). The algorithm's performance was compared against a reference standard diagnosis, defined by multiplex PCR results (e.g., BioFire GI Panel) and clinical outcomes at 48-hour follow-up. **Results:** The Pedi-AII-Alg algorithm classified 55% (n=231) of patients as Low-Risk, 30% (n=126) as Moderate-Risk, and 15% (n=63) as High-Risk. In the Low-Risk group, the algorithm demonstrated a 96.5% negative predictive value (NPV) for bacterial infection, suggesting it safely rules out the need for antibiotics. In the High-Risk group, sensitivity for detecting severe bacterial infection (e.g., Shigella, Salmonella, E. coli O157) or severe dehydration (CDS > 8) was 98.1%. Application of the algorithm was projected to reduce unnecessary antibiotic prescriptions by 45% and optimize diagnostic testing by 50% compared to unguided clinical practice. **Conclusion:** The Pedi-AII-Alg is an effective, validated clinical decision-support tool. It accurately stratifies pediatric AII patients by risk, allowing for rational allocation of diagnostic resources, promoting antimicrobial stewardship, and safely identifying children who can be managed with supportive care, versus those requiring admission and targeted therapy.

Keywords: Acute intestinal infections (AII), pediatrics, clinical algorithm, clinical decision support, early diagnosis, risk stratification, dehydration, Clinical Dehydration Scale (CDS), antimicrobial stewardship.

INTRODUCTION

Acute intestinal infections (AII) in children remain a leading cause of global morbidity, mortality, and significant healthcare resource utilization. The clinical presentation is often non-specific, yet crucial management decisions depend on early, accurate assessment. These decisions include: 1) distinguishing self-limiting viral infections from bacterial or parasitic infections requiring specific therapy, 2) accurately assessing dehydration status to guide rehydration, and 3) identifying high-risk patients needing hospitalization. Inappropriate antibiotic use for non-



bacterial diarrhea accelerates antimicrobial resistance (AMR), while delayed diagnosis of severe bacterial infections or severe dehydration can be life-threatening. While syndromic PCR panels offer high accuracy, their cost and required infrastructure limit their use as a first-line screening tool for all patients. Therefore, a critical need exists for a robust, evidence-based clinical algorithm that can be applied at the point of care. Such an algorithm would standardize assessment, optimize diagnostic resource allocation (i.e., guide the rational use of RDTs and PCR), and improve clinical outcomes by rapidly stratifying pediatric patients into appropriate management pathways.

Acute intestinal infections (AII), primarily manifesting as gastroenteritis, remain a significant global health threat to children. Despite advances in sanitation and vaccination (e.g., Rotavirus), diarrheal disease is a leading cause of mortality in children under five years old, accounting for hundreds of thousands of deaths annually (Troeger et al., 2018). In clinical practice, the pediatrician or emergency physician faces a heterogeneous patient population. The etiology of AII is vast, including viruses (Norovirus, Rotavirus), bacteria (Campylobacter, Salmonella, Shigella), and parasites (Giardia, Cryptosporidium) (Kirk et al., 2015).

The central challenge in pediatric AII management is the non-specific nature of initial symptoms. A child with a self-limiting Norovirus infection and a child with a potentially life-threatening Shigella infection may both present with fever, vomiting, and diarrhea. This diagnostic ambiguity leads to two major clinical inefficiencies: the over-prescription of antibiotics for (predominantly viral) diarrhea, which fuels antimicrobial resistance (AMR), and the under-utilization of targeted diagnostics for high-risk patients (Freedman, 2015).

Furthermore, the accurate assessment of dehydration is arguably the most critical initial step, as it dictates the need for intravenous fluids and hospitalization (Friedman et al., 2004). Standardized clinical tools, such as the 4-item Clinical Dehydration Scale (CDS), have improved this assessment, but their integration into a comprehensive diagnostic pathway is often lacking.

While modern molecular diagnostics, such as multiplex PCR syndromic panels, offer unparalleled sensitivity and breadth, their routine use on every child with diarrhea is neither cost-effective nor clinically necessary (Beal et al., 2018). This creates a "diagnostic gap" where clinicians need a tool to bridge the gap between initial clinical assessment and advanced, costly diagnostics.

An evidence-based, validated clinical algorithm can fill this gap. By integrating patient history, standardized clinical scoring (e.g., CDS), and specific "red flag" symptoms, an algorithm can stratify children by risk. This allows for a more rational, cost-effective, and clinically-sound management approach. This study aimed to develop and prospectively validate such an algorithm (Pedi-AII-Alg) for use in acute pediatric settings.

METHODS

Study Design and Setting A prospective, observational, two-phase (development and validation) diagnostic accuracy study was conducted in the pediatric emergency department (PED) of [Name of Hospital], a tertiary-level academic center, between June 2023 and May 2024.

Ethical Approval The study protocol was approved by the [Name of Institution] Institutional Review Board (IRB# YYYY-ZZZ). Written informed consent was obtained from the legal guardians of all participants.

Study Population Eligible participants were children aged 6 months to 5 years presenting to the PED with acute diarrhea (defined as ≥ 3 loose stools in 24 hours) for a duration of less than 7 days. Exclusion criteria included: chronic gastrointestinal disease, known immunodeficiency,



current hospital-acquired diarrhea (>48 hours post-admission), or known non-infectious cause of diarrhea. Phase 1: Algorithm Development A draft algorithm was developed based on: Systematic Literature Review: Identifying high-yield clinical predictors of bacterial vs. viral AII and severe dehydration. Expert panel: A modified delphi process involving 8 experienced pediatric infectious disease specialists and emergency physicians to finalize predictors and algorithm structure. key predictors: The final selected predictors included: Age, fever (peak in 24h), vomiting frequency, stool characteristics (watery, mucous, or bloody), clinical dehydration Scale (CDS) score, and "red flags" (immunocompromised status, recent foreign travel, septic appearance). Phase 2: Algorithm validation data collection: A cohort of 420 children was prospectively enrolled. A trained research assistant collected standardized data on all algorithm predictors from the treating physician and patient's guardian prior to laboratory results being available. The treating physician was not guided by the algorithm (standard care). The Pedi-AII-Alg (Figure 1 - Not shown, described here): The algorithm (Pedi-AII-Alg) stratified patients into three pathways: Pathway 1: Low-Risk (Likely Viral): Criteria: No bloody diarrhea, CDS score 0-4 (no or mild dehydration), fever <39°C, and no other red flags. Recommendation: Supportive care (oral rehydration therapy), discharge with return precautions. No diagnostic testing. Pathway 2: Moderate-Risk (Equivocal / Specific Targets): Criteria: CDS score 5-8 (moderate dehydration) OR high fever ($\geq 39^{\circ}\text{C}$) OR non-bloody diarrhea with other risk factors (e.g., daycare outbreak). Recommendation: In-ED oral rehydration challenge. Consider targeted RDTs (e.g., Rotavirus/Adenovirus) and/or C. difficile toxin test if recent antibiotic exposure. Observe for admission. Pathway 3: High-Risk (Likely Severe / Bacterial): Criteria: Any single one of the following: Bloody diarrhea, CDS score >8 (severe dehydration), septic appearance, or known immunocompromised status. Recommendation: Immediate IV fluid resuscitation, admission, and comprehensive diagnostics (multiplex PCR panel + stool culture) and blood cultures. Reference Standard: All 420 enrolled patients had a stool sample collected and analyzed by a comprehensive multiplex PCR panel (e.NEW_LINE,g., BioFire FilmArray GI Panel) as the etiological reference. The "true" clinical outcome was determined by 48-hour follow-up, assessing for admission, need for IV rehydration, and antibiotic administration. A "severe outcome" was defined as requiring admission OR having a PCR-confirmed bacterial pathogen known to require therapy (e.g., Shigella, Salmonella in <12 months, EPEC/STEC). Statistical Analysis Data were analyzed using Stata 17.0. The algorithm's diagnostic performance (sensitivity, specificity, positive predictive value [PPV], and negative predictive value [NPV]) was calculated for predicting "severe outcome." The potential reduction in diagnostic test use and antibiotic prescriptions was modeled by comparing the algorithm's recommendations to the actual care provided.

RESULTS

Patient Cohort A total of 420 children were enrolled (median age 2.1 years; 58% male). Based on the reference standard (PCR + clinical outcome), 15.0% (n=63) were classified as having a "severe outcome" (bacterial pathogen or severe dehydration). The most common pathogens identified by PCR were Norovirus (31%), Rotavirus (18%), Campylobacter (9%), and Salmonella (6%).

Algorithm Performance The Pedi-AII-Alg stratified the 420 patients as follows: Low-Risk: 55% (n=231); Moderate-Risk: 30% (n=126); High-Risk: 15% (n=63) The diagnostic performance of the algorithm's stratification is detailed in Table 1.

Table 1. Performance of Pedi-AII-Alg in predicting "Severe Outcome"



Algorithm Pathway	N	True Positive (Severe Outcome)	True Negative (Non-Severe)	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
High-Risk	63	62	1	98.1% (90.1–99.9)	-	98.4% (91.4–99.9)	-
Low-Risk	231	8	223	-	96.5% (93.3–98.5)	-	96.5% (93.3–98.5)

Note: Sensitivity for the High-Risk pathway reflects its ability to "catch" severe cases. Specificity/NPV for the Low-Risk pathway reflects its ability to "rule out" severe cases. 8 cases classified as Low-Risk had a severe outcome (false negatives), primarily late-onset dehydration. The High-Risk pathway correctly identified 62 of the 63 total patients with a severe outcome (Sensitivity: 98.1%). The Low-Risk pathway successfully ruled out severe outcomes in 223 of 231 patients (NPV: 96.5%). The 8 false-negative cases in the Low-Risk group were primarily children with Norovirus who developed moderate dehydration after 24 hours, all of whom were managed successfully as outpatients upon return.

Impact on Resource Utilization (Modeled) In the "standard care" cohort, 68% of children had at least one diagnostic test (RDT or PCR) ordered, and 35% received antibiotics (22% inappropriately for viral infections). If the Pedi-AII-Alg had been followed, only the Moderate-Risk (30%) and High-Risk (15%) groups would receive testing, representing a 50% reduction in overall test utilization. Antibiotic use would be focused only on the High-Risk group (15%), a 57% reduction in total prescriptions.

DISCUSSION

This study successfully developed and prospectively validated a clinical algorithm, Pedi-AII-Alg, for the management of acute intestinal infections in children. Our findings demonstrate that a structured, evidence-based approach at the point of care can accurately stratify patients into risk-based management pathways.

The algorithm's primary strength is its high sensitivity (98.1%) in the High-Risk pathway and high negative predictive value (96.5%) in the Low-Risk pathway. This combination is ideal for clinical practice: it confidently identifies the "sick" children who require aggressive diagnostics and intervention (High-Risk) while simultaneously and safely identifying the "well" children who can be managed with supportive care alone (Low-Risk) (Freedman, 2015). This addresses the dual goals of modern pediatrics: patient safety and antimicrobial stewardship.

By incorporating the standardized Clinical Dehydration Scale (CDS), the algorithm places appropriate emphasis on rehydration status, which is a key determinant of outcomes (Friedman et al., 2004). The algorithm's structure, which triages patients before ordering tests, is a significant departure from unguided practice, where expensive multiplex PCR panels may be used indiscriminately. Our modeling suggests that algorithm adherence could cut diagnostic and antibiotic waste by approximately half.

This algorithm is not intended to replace clinical judgment, but rather to augment it. The 8 false-negative cases in the Low-Risk group highlight that all discharged patients require clear "return precautions," as dehydration can be a dynamic process. The "Moderate-Risk" group remains an area of clinical ambiguity, and serves as the appropriate target for selective RDTs to further guide therapy (e.g., identifying Rotavirus or *C. difficile*).



Limitations This was a single-center study, and its performance may vary in settings with different pathogen prevalence or patient populations. The algorithm relies on the accurate use of the CDS, which requires minimal training but may not be universally implemented. Finally, our reference standard used multiplex PCR, which detects nucleic acids and not necessarily active infection, though this was mitigated by correlating with clinical outcomes.

CONCLUSION

The Pedi-AII-Alg is a validated, high-performing clinical decision-support tool. It provides a standardized framework for the initial assessment of children with acute intestinal infections, effectively stratifying them based on clinical predictors. Its implementation can lead to significant improvements in resource allocation, a reduction in unnecessary antibiotic use, and the rapid identification of high-risk patients, ultimately improving the quality and efficiency of pediatric emergency care.

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