

Risk Factors and Clinical Predictors of Severe Viral Gastroenteritis in Infants: A Multicenter Study in Iraqi Pediatric Hospitals

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Abstract

Viral gastroenteritis remains one of the main causes of morbidity and hospitalization among infants in low- and middle-income countries. Although advances in vaccinations and oral rehydration therapy have been made, severe illness remains an important burden among children visiting pediatric hospitals in Iraq. Determination of clinical risk factors and predictors is vital to facilitate appropriate management of cases. Aim: The objective of the current research is the determination of risk factors and clinical predictors of severe viral gastroenteritis in infants aged 2-24 months visiting hospitals in Iraq. Methods: The multicenter cross-sectional study took place in three pediatric centers of Thi-Qar governorates in Iraq during January 2023 - December 2023. A total sample size of 420 patients diagnosed with viral gastroenteritis was examined. Severe illness was defined using the Modified Vesikari Score (MVS). Logistic regression analysis was used to determine independent predictors of severe illness. Results: Among 420 patients, 147 (35.0%) demonstrated severe gastroenteritis ($MVS \geq 11$). Rotavirus infection was found in 48.6%, norovirus – in 21.4% and adenovirus – in 12.1%. The main independent predictors of severe disease were: rotavirus infection (OR = 4.12, 95% CI: 2.54–6.68); exclusive formula feeding (OR = 3.07, 95% CI: 1.88–5.01); age <12 months (OR = 2.84, 95% CI: 1.72–4.68); insufficient rotavirus vaccination (OR = 2.65, 95% CI: 1.60–4.39); moderate and severe malnutrition (OR = 2.47, 95% CI: 1.43–4.26); vomiting ≥ 6 times/day (OR = 2.31, 95% CI: 1.39–3.84). Dehydration was observed in 62.6% of patients, and 18.4% needed intravenous hydration. Conclusion: Rotavirus infection, formula feeding, young age, incomplete immunization, and malnutrition were established as independent predictors of severe viral gastroenteritis. Increasing vaccination rate, encouraging breastfeeding, and proper nutrition should be the priorities in preventing severe disease cases.

Keywords: viral gastroenteritis, severe dehydration, infants, rotavirus, risk factors, Iraq, Modified Vesikari Score, clinical predictors

عوامل الخطر والمتنبئات السريرية لالتهاب المعدة والأمعاء الفيروسي الشديد لدى الرضع: دراسة متعددة المراكز في مستشفيات الأطفال العراقية

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الخلاصة

الخلفية: لا يزال التهاب المعدة والأمعاء الفيروسي أحد الأسباب الرئيسية للمرضة والاستشفاء بين الرضع في البلدان منخفضة ومتوسطة الدخل. يُعد تحديد عوامل الخطر السريرية والمتنبئات أمرًا حيويًا لتسهيل الإدارة المناسبة للحالات. الهدف: يهدف هذا البحث إلى تحديد عوامل الخطر والمتنبئات السريرية لالتهاب المعدة والأمعاء الفيروسي الشديد لدى الرضع الذين تتراوح أعمارهم بين 2-24 شهرًا. الطرق: أجريت دراسة مقطعية متعددة المراكز في ثلاثة مراكز أطفال في محافظة ذي قار خلال يناير 2023 - ديسمبر 2023. شملت الدراسة 420 مريضًا مصابًا بالتهاب المعدة والأمعاء الفيروسي. النتائج: من بين 420 مريضًا، أظهر 147 (35.0%) التهابًا شديدًا ($MVS \geq 11$). وُجدت عدوى فيروس الروتا في 48.6%، وفيروس النورو في 21.4%، والفيروس الغدي في 12.1%. تم تحديد عدوى فيروس الروتا، والرضاعة الصناعية، وصغر السن، وعدم اكتمال التحصين، وسوء التغذية كمتنبئات مستقلة لالتهاب المعدة والأمعاء الفيروسي الشديد. ينبغي أن تكون زيادة معدل التطعيم، وتشجيع الرضاعة الطبيعية، والتغذية السليمة من الأولويات في الوقاية من حالات المرض الشديد.

1. Introduction

Gastroenteritis (AGE) in young infants and children is one of the commonest infectious illnesses worldwide. The impact of these infections is disproportionately high in LMICs. Diarrheal illnesses account for about 1.7 billion illnesses every year among children aged below five years old leading to roughly 440,000 deaths every year in which the overwhelming number of deaths occurs in Sub-Saharan Africa and South Asia [1, 2]. Virus infections are responsible for most of the AGE infections in infancy.

Rotavirus remains the leading etiological agent, historically responsible for up to 40% of hospitalizations due to diarrheal illness in children globally before the introduction of widespread vaccination [3]. Norovirus, adenovirus serotypes 40/41, astrovirus, and sapovirus collectively account for a substantial proportion of additional cases [4]. Despite the global rollout of rotavirus vaccines, substantial heterogeneity in vaccine uptake persists, particularly in resource-limited settings where the burden of disease remains highest.

Communicable diseases, particularly acute diarrhea, continue to be major causes of pediatric morbidity and mortality in Iraq. Lack of proper sanitation facilities, disruption of water supply, overcrowding, and inadequate immunization create ideal conditions for viral gastroenteritis infections [5].

Clinical spectrum of viral gastroenteritis infections ranges from a self-limiting condition to the development of severe complications such as dehydration, electrolyte imbalance, and, ultimately, death. Risk factors that influence the severity of viral gastroenteritis in infants may include virus strain, age, nutritional status, breastfeeding, and vaccination history [6, 7]. However, the role of each of these risk factors and their potential interaction in the Iraqi context has not been systematically examined yet.

Modified Vesikari Scale (MVS) is a validated tool for objective classification of the clinical severity of gastroenteritis that allows to assess its magnitude consistently and reliably and compare across various studies and clinical sites [8]. The introduction of the scoring system in underdeveloped countries could lead to more effective use of medical interventions and hospital resources allocated.

Early identification of high-risk infants will allow clinicians in both emergency and outpatient clinics to initiate appropriate treatment to prevent the development of severe complications of dehydration and hemodynamic disorders [9]. Thus, in view of the lack of systematic data in the field in Iraq, this study is designed to explore clinical and demographic predictors of viral gastroenteritis severity among infants admitted to tertiary pediatric hospitals in the Thi-Qar governorates.

The specific objectives of this study are to: (1) establish virologic characteristics of viral gastroenteritis infection in hospitalized infants; (2) estimate the incidence rate of clinically severe disease based on MVS; (3) examine independently associated clinical and virologic determinants of viral gastroenteritis severity; and (4) make evidence-based recommendations concerning viral gastroenteritis management.

2. Materials and Methods

2.1 Study Design and Setting

The research was done prospectively and multicentrically using a cross-sectional approach between January 1 and December 31, 2023. It included data obtained from three referral centers that specialize in children's health in Thi-Qar Teaching Hospital for Children.

2.2 Study Population

Children with acute gastroenteritis aged between 2 and 24 months were included in the study. Acute gastroenteritis was described as the development of at least three bouts of watery stool within 24 hours, with or without vomiting, within a period of less than 14 days.

Selection criteria: (1) children 2 to 24 months old; (2) clinically diagnosed cases of acute gastroenteritis; (3) signed consent from parents/guardians; (4) capability to provide stool samples within 48 hours of presenting.

Criteria for exclusion: (1) chronic forms of diarrhea (e.g., inflammatory bowel disease, congenital forms of diarrhea); (2) immunocompromised patients or receiving immunosuppressive drugs; (3) confirmed bacterially or parasitically induced gastroenteritis; (4) patients seen later than 14 days after the onset of illness; (5) missing information or withdrawn consents.

2.3 Sample Size

Sample size was calculated using OpenEpi version 3.0 based on an estimated prevalence of severe gastroenteritis of 30%, a confidence level of 95%, and a margin of error of 5%, yielding a minimum required sample of 323 participants. Accounting for a 20% loss to follow-up and incomplete data, a target enrolment of 420 infants was established.

2.4 Data Collection

A structured data collection form was administered by trained research nurses and physicians at enrolment. The following variables were recorded: gestational age, birth weight, current age and weight, sex, feeding practices (exclusive breastfeeding, mixed feeding, formula feeding), nutritional status assessed by weight-for-age z-score (WAZ) using WHO growth standards, vaccination history (rotavirus vaccine doses received), duration of illness prior to presentation, stool frequency and consistency (Bristol Stool Scale), vomiting frequency, presence and degree of fever, clinical signs of dehydration assessed by the WHO dehydration scale, and relevant comorbidities.

2.5 Severity Assessment

Disease severity was assessed using the Modified Vesikari Score (MVS), a validated 20-point scoring tool incorporating diarrhea frequency and duration, vomiting frequency and duration, maximum temperature, dehydration status, and treatment requirements. Scores were categorized as: mild (1–5), moderate (6–10), and severe (≥ 11). For this analysis, the primary outcome was severe gastroenteritis (MVS ≥ 11).

2.6 Virological Testing

Stool specimens were collected from each enrolled infant within 48 hours of presentation. Specimens were stored at -20°C and processed in batches. Rotavirus antigen detection was performed using the RIDASCREEN® Rotavirus enzyme-linked immunosorbent assay (ELISA; R-Biopharm, Germany). Norovirus (genogroup I and II), adenovirus, and astrovirus were detected by reverse transcription-polymerase chain reaction (RT-PCR) using standardized protocols.

2.7 Nutritional Assessment

Nutritional status was classified using WHO weight-for-age z-scores as: normal (WAZ ≥ -2 SD), mild undernutrition (WAZ -2 to -2.99 SD), and moderate-to-severe undernutrition (WAZ < -3 SD). Measurements were taken on admission using calibrated digital scales.

2.8 Statistical Analysis

Data analysis was carried out using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA). For continuous data, values are expressed as mean \pm standard deviation (SD) or median [interquartile range (IQR)], while for categorical data, values are presented as numbers with percentage values. Variables with a univariate analysis p-value < 0.20 were included in a binary logistic regression analysis model. Statistical significance was set at p-value < 0.05 .

2.9 Ethical Approval

Ethical approval was obtained from the Institutional Review Board of the University of Thi-Qar College of Medicine. Written informed consent was obtained from parents or legal guardians of all enrolled infants. All procedures complied with the principles of the Declaration of Helsinki.

3. Results

3.1 Study Population and General Characteristics

A total of 448 infants were assessed for eligibility, of whom 420 met the inclusion criteria and were enrolled. Of these, 147 (35.0%) had severe gastroenteritis (MVS ≥ 11), 183 (43.6%) had moderate disease (MVS 6–10), and 90 (21.4%) had mild disease (MVS 1–5). The mean age of enrolled infants was 11.3 ± 4.8 months. Male infants constituted 56.4% of the sample. The mean MVS for the severe group was 14.2 ± 1.9 compared to 7.4 ± 1.8 in the non-severe group ($p < 0.001$). Baseline demographic and clinical characteristics are detailed in Table 1.

Table- 1 . Demographic and Clinical Characteristics of Study Population by Disease Severity

Variable	Severe (n=147) n (%)	Non-Severe (n=273) n (%)	p-value
Age < 12 months	112 (76.2%)	131 (48.0%)	< 0.001
Male sex	85 (57.8%)	152 (55.7%)	0.682
Exclusive formula feeding	89 (60.5%)	78 (28.6%)	< 0.001
Incomplete rotavirus vaccination	97 (66.0%)	104 (38.1%)	< 0.001
Moderate-to-severe malnutrition (WAZ < -3)	62 (42.2%)	54 (19.8%)	< 0.001
Mean age (months) \pm SD	9.1 ± 3.9	12.5 ± 5.1	< 0.001
Mean MVS \pm SD	14.2 ± 1.9	7.4 ± 1.8	< 0.001
Fever $\geq 38.5^\circ\text{C}$	103 (70.1%)	141 (51.6%)	< 0.001
Vomiting ≥ 6 episodes/day	94 (63.9%)	74 (27.1%)	< 0.001
Diarrhea ≥ 8 episodes/day	88 (59.9%)	64 (23.4%)	< 0.001

MVS = Modified Vesikari Score; WAZ = weight-for-age z-score; SD = standard deviation.

3.2 Virological Profile

Viral pathogens were identified in 374 (89.0%) of stool specimens. Rotavirus was the most prevalent pathogen, identified in 204 (48.6%) specimens. Norovirus was detected in 90 (21.4%) cases, adenovirus in 51 (12.1%), astrovirus in 18 (4.3%), and sapovirus in 11 (2.6%). Co-infections were present in 22 (5.2%) samples. No pathogen was identified in 46 (11.0%) specimens. The distribution of viral pathogens by disease severity is presented in Table 2.

Table -2 Distribution of Viral Pathogens by Disease Severity

Pathogen	Total n (%)	Severe n (%)	Non-Severe n (%)	p-value
Rotavirus	204 (48.6%)	96 (65.3%)	108 (39.6%)	< 0.001
Norovirus	90 (21.4%)	28 (19.0%)	62 (22.7%)	0.396
Adenovirus	51 (12.1%)	12 (8.2%)	39 (14.3%)	0.071
Astrovirus	18 (4.3%)	4 (2.7%)	14 (5.1%)	0.241
Sapovirus	11 (2.6%)	3 (2.0%)	8 (2.9%)	0.571
Co-infections	22 (5.2%)	4 (2.7%)	18 (6.6%)	0.076
No pathogen identified	46 (11.0%)	4 (2.7%)	42 (15.4%)	< 0.001

3.3 Complications and Clinical Outcomes

Dehydration was the most prevalent complication, occurring in 263 (62.6%) infants overall, with significantly higher rates in the severe group (n=138, 93.9%) compared to non-severe infants (n=125, 45.8%; $p < 0.001$). Among severely ill infants, 27 (18.4%) required intravenous fluid resuscitation, 14 (9.5%) required electrolyte correction, and 4 (2.7%) experienced seizure activity attributed to febrile convulsions or hyponatremia. Mean hospital length of stay was significantly longer in the severe group (4.8 ± 2.1 days) compared to the non-severe group (1.9 ± 1.1 days; $p < 0.001$). No deaths were recorded during the study period.

3.4 Multivariate Analysis: Independent Predictors of Severe Disease

Variables significant at $p < 0.2$ on univariate analysis were entered into the multivariate logistic regression model. After adjustment for confounders, six variables remained independently associated with severe gastroenteritis. Results of the final multivariate model are presented in Table 3.

Table 3- Multivariate Logistic Regression: Independent Predictors of Severe Viral Gastroenteritis

Variable	Adj. OR	95% CI	p-value	Interpretation
Rotavirus infection	4.12	2.54 – 6.68	< 0.001	Strongest predictor
Exclusive formula feeding	3.07	1.88 – 5.01	< 0.001	Protective effect of breastfeeding
Age < 12 months	2.84	1.72 – 4.68	< 0.001	Higher vulnerability
Incomplete rotavirus vaccination	2.65	1.60 – 4.39	< 0.001	Vaccine efficacy confirmed
Moderate-to-severe malnutrition (WAZ < -3)	2.47	1.43 – 4.26	0.001	Nutritional risk
Vomiting ≥ 6 episodes/day	2.31	1.39 – 3.84	0.001	Clinical severity marker

OR = odds ratio; CI = confidence interval; WAZ = weight-for-age z-score. Model Nagelkerke $R^2 = 0.48$; Hosmer-Lemeshow $p = 0.61$.

4. Discussion

This multicenter prospective study provides the first comprehensive analysis of risk factors and clinical predictors of severe viral gastroenteritis in infants from multiple Iraqi pediatric hospitals. Our findings demonstrate that 35.0% of enrolled infants had severe gastroenteritis as defined by the Modified Vesikari Score, a prevalence consistent with estimates reported in comparable LMIC settings [10].

Rotavirus was the dominant viral pathogen, identified in 48.6% of cases, and emerged as the strongest independent predictor of disease severity (OR = 4.12). This aligns with extensive literature documenting the disproportionate severity of rotavirus-associated gastroenteritis compared to other viral etiologies [3, 11]. Rotavirus strains characteristically cause more profound villous damage, greater secretory diarrhea, and more significant fluid losses than other enteric viruses, contributing to higher rates of severe dehydration [12]. The predominance of rotavirus in this cohort, despite the availability of oral rotavirus vaccines, likely reflects the incomplete vaccination coverage documented in our sample (66.0% of severe cases were incompletely vaccinated), a well-recognized challenge in Iraq [13].

The protective effect of breastfeeding against severe gastroenteritis, reflected in our finding that exclusive formula feeding was an independent predictor of severity (OR = 3.07), is consistent with a large body of published evidence. Human breast milk confers passive immunity through secretory immunoglobulin A (sIgA), lactoferrin, lysozyme, and a variety of bioactive factors that modulate intestinal immunity and reduce both the susceptibility to and severity of enteric infections [14, 15]. Promotion of exclusive breastfeeding for the first six months of life, as recommended by the WHO, thus represents a critical preventive intervention in the Iraqi context, where breastfeeding rates remain below optimal levels [5].

Infants younger than 12 months had significantly higher odds of severe disease (OR = 2.84), a finding reflecting the developmental immaturity of mucosal immunity, smaller fluid reserves relative to body weight, and greater physiological vulnerability to dehydration-related complications in this age group [6]. These results confirm the existing international recommendations, which promote rapid and vigorous oral rehydration treatment, while intravenous fluid therapy is used in selected cases for children under 12 months with gastroenteritis [16].

Incompleteness of rotavirus immunization was found to increase by almost three times the risk of developing severe gastroenteritis (OR = 2.65). This finding supports the evidence on the efficacy of rotavirus vaccinations in preventing severe rotavirus gastroenteritis [17]. Numerous randomized controlled trials and post-market surveillance have shown an 85% to 98% efficacy rate of Rotarix and RotaTeq against severe rotavirus disease in wealthy countries and a slightly lower but still significant rate in low and middle-income countries [18]. Low vaccination coverage in the studied group emphasizes the importance of improving the vaccination program in Iraq.

Moderate/severe malnutrition was significantly associated with increased severity (OR = 2.47), pointing to the bidirectional link between malnutrition and infectious diarrhea [19]. Malnutrition compromises mucosal barrier integrity, impairs lymphocyte-mediated immune responses, and reduces the capacity for rapid intestinal recovery following epithelial damage [20]. Conversely, repeated episodes of severe gastroenteritis contribute to persistent enteropathy, nutrient malabsorption, and worsening of nutritional status, creating a vicious cycle that perpetuates both infection severity and growth faltering.

High vomiting frequency (≥ 6 episodes/day) was an independent clinical predictor of severity (OR = 2.31), likely reflecting underlying disease burden and potentially limiting oral rehydration therapy effectiveness. Frequent vomiting is a recognized barrier to successful oral rehydration and a common reason for intravenous fluid therapy initiation [21].

The substantial sample size and multiple governorates make this study more representative compared to single-center studies.

The study had some limitations, including: (1) being confined to tertiary hospitals, hence limiting generalizability to other settings; (2) detecting the virus at one time, thus missing possible coinfections arising in the subsequent stages of infection; (3) the presence of confounding variables that were not considered such as household socio-economic status, poor source of water, and use of antibiotics; and (4) lack of strain typing of the rotavirus.

5. Conclusion

The multi-center study suggests that rotavirus infection, formula feeding only, age of less than 12 months, non-complete vaccination against rotavirus, malnutrition at moderate or severe levels, and high incidences of vomiting are independent risk factors for developing severe viral gastroenteritis in infants of Iraq. The results identify specific high-risk groups that need immediate attention. On a public health scale, more urgent measures are needed to increase the rate of immunization against rotavirus infection, promote exclusive breastfeeding, prevent malnutrition in children, and improve sanitary facilities.

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