

A Nomogram Based on Immune Inflammation Indicators for Rotaviral Diarrhea in Children Under 5 years Old: A Single-Center Retrospective Cohort Study

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Objective: This study investigates the relationship between immune inflammation indicators and rotaviral-induced diarrhea in children under five years old.

Methods: This retrospective cohort study included 439 children with diarrhea between January 2022 and December 2023. Clinical and laboratory data were retrospectively collected. The least absolute shrinkage and selection operator (LASSO), univariate, and multivariate logistic regression analyses were used to identify the risk factors in the training cohort, which were used to develop a nomogram model. The accuracy of the nomogram was assessed using a calibration plot. Finally, Decision curve analysis was used to examine the clinical utility of the nomogram, and internal validation was performed in the training set.

Results: Among the 439 children, 120 developed rotaviral-induced diarrhea, with a prevalence rate of 27.33%. The systemic inflammatory response index (SIRI), lymphocyte-to-monocyte ratio (LMR), neutrophil-to-albumin ratio (NAR), and C-reactive protein-to-albumin ratio (CAR) were identified as independent predictors of rotaviral diarrhea in the training cohort. A nomogram model was established using multivariable logistic analysis, with an AUC of 0.795 (95% CI, 0.743–0.848) in the training set and 0.787 (95% CI, 0.694–0.879) in the validation set. Calibration curves indicated strong agreement between the predicted and actual probabilities. Decision curve analysis demonstrated substantial net benefits of the nomogram model for predicting the risk of rotaviral diarrhea in these children.

Conclusion: This study confirms that the immune inflammation indicators SIRI, LMR, NAR, and CAR predict the risk of rotaviral diarrhea in children under five years old. The nomogram model developed using these indicators demonstrates excellent predictive capability for the risk of rotaviral diarrhea.

Keywords: rotaviral diarrhea, children, immune inflammation indicators, nomogram

Introduction

Rotavirus (RV) is a double-stranded RNA virus that predominantly occurs in autumn and winter, and hence, RV-induced diarrhea is commonly known as autumn diarrhea.¹ Approximately 258 million cases of infectious diarrhea in children under five years old worldwide are attributed to RV infection.² Unlike gastroenteritis caused by other pathogens, the incidence of RV diarrhea is comparable between developed and developing countries.³ Rotavirus can cause viremia⁴ and infiltrate the epithelial cells of the small intestinal villi, leading to local inflammation.⁵ Furthermore, RV can cause several complications including pneumonia, disseminated intravascular coagulation, nephritis, rash, elevated transaminases, and hemophagocytic lymphohistiocytosis.^{6–10} Studies have reported that in children under five years old, RV is the third leading pathogen associated with mortality, posing a significant threat to children's health.^{11,12}

Complete blood count (CBC) is the commonest diagnostic method in pediatric emergency departments, since it is cost-effective, easy to perform, and requires minimal equipment and technical expertise. In recent years, new inflammatory markers related to CBC, namely the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), systemic immune-inflammation index (SII), and systemic inflammatory response index (SIRI), have been shown to effectively reflect inflammatory states and disease progression, playing a key role in several cancers, autoimmune diseases, and cardiovascular diseases.^{13–18} NLR is associated with systemic inflammation, cardiovascular diseases, chronic obstructive pulmonary disease, malignancies, and infectious diseases.¹⁹ NLR and PLR have diagnostic value in differentiating adult influenza A virus infection from bacterial infections.^{20,21} SII and SIRI, which are composite inflammatory markers, are key biomarkers for the occurrence and progression of cancer. Animal experiments by Ömer Aydin et al²² have shown that inflammatory markers such as the systemic inflammatory response syndrome (SIRS), SIRI, and SII are closely associated with diarrhea in newborn calves. Albumin is actively involved in acute inflammation and can be used to assess an individual's nutritional status.^{23,24} Albumin-associated inflammatory and nutritional indicators include the neutrophil-to-albumin ratio (NAR) and the C-reactive protein-to-albumin ratio (CAR), as well as the prognostic nutritional index (PNI). However, the relationship between these inflammatory markers and pediatric RV-induced diarrhea remains unclear.

Early detection of RV infection is essential for initiating timely supportive therapy, identifying complications promptly, and referring patients to appropriate hospitals. As prognostic prediction tools in medicine, nomograms integrate various prognostic variables to generate a numerical probability for clinical events. They integrate biological and clinical models, support personalized medicine, and facilitate clinical decision-making. Consequently, this study focuses on RV-induced diarrhea in children, analyzes the correlation and diagnostic value of immune inflammation indicators with the disease occurrence, and develops a nomogram model to predict the risk of RV-induced diarrhea in children under 5 years old.

Methods

The methods used in this study have been described in published manuscripts by Chen Xiao et al^{19,25} in our team.

Patient Data

Clinical data of children under 5 years old with rotaviral-induced diarrhea admitted to the Department of Pediatrics in the First People's Hospital of Neijiang, were independently collected retrospectively by the first and second authors, between January 2022 and December 2023. All discrepancies were resolved by re-evaluation to ensure accuracy. This study adhered to the principles of the 1964 Helsinki Declaration and was approved by the institutional Ethics Review Committee (approval number: 2024-lunshenpi-27). Informed consent was waived due to the retrospective study design. The study flowchart is shown in [Figure 1](#).

Inclusion criteria were: (1) children under 5 years old; (2) the diagnosis of rotaviral-induced diarrhea was based on the criteria from "Internal Medicine" (9th edition), which include symptoms like vomiting, fever, and watery diarrhea, and the detection of rotavirus in fecal samples (RT q-PCR detection technology²⁶). By combining clinical symptoms (such as vomiting, fever, and watery diarrhea) with RT q-PCR testing, the sensitivity and specificity of rotavirus infection diagnosis are improved; (3) acute onset; (4) availability of clinical and laboratory data for predictive analysis. Exclusion criteria were: (1) children with comorbidities such as primary immunodeficiency, tumors, autoimmune diseases, congenital diseases, malnutrition, and chronic gastroenteritis; (2) incomplete data.

Data Collection

The demographic and clinical data of gender, age, and weight were collated. Fasting peripheral venous blood samples were collected immediately upon admission for measurement of neutrophil count, lymphocyte count, monocyte count, platelet count, serum albumin (ALB), C-reactive protein (CRP), procalcitonin (PCT), and rotavirus antigen detection. The NLR, PLR, lymphocyte-to-monocyte ratio (LMR), SII, SIRI, aggregate index of systemic inflammation (AIS), NAR, CAR, PNI, and systemic inflammatory score (SIS) were calculated.

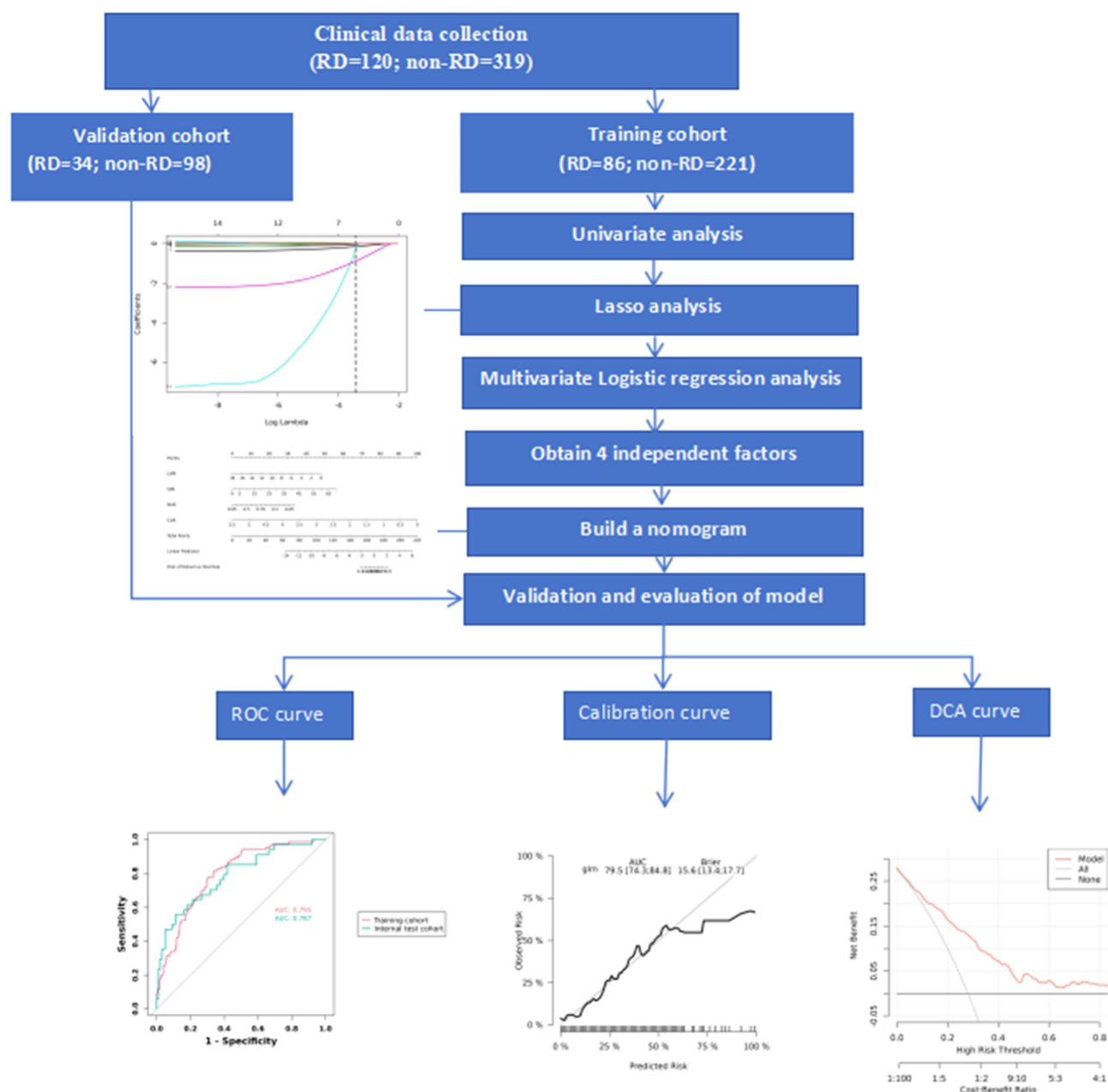


Figure 1 The enrollment flowchart.

Systemic and Albumin-Related Inflammatory Markers

Systemic and albumin-related inflammatory markers were calculated using the formulae listed in Table 1, as published by Chen Xiao et al^{19,25} in our team.

Statistical Analysis

The statistical methods used in this study have been described in published manuscripts by Chen Xiao et al^{19,25} in our team. The participants were randomized into the training and validation sets, at a ratio of 7:3. Non-normally distributed data were expressed as median and interquartile range. Categorical variables in univariate analyses were examined by the chi-square test or Fisher's exact test, while continuous variables were assessed by the Student's *t*-test or rank-sum test. Meanwhile, the least absolute shrinkage and selection operator (LASSO) was used in multivariate analysis of the training

Table 1 Systemic and Albumin-Associated Inflammatory Markers, as Well as Nutritional Markers Examined in This Study

Marker	Formula for Calculation
SII	$(\text{Neutrophil} \times \text{platelet}) \div \text{lymphocyte ratio}$
SIRI	$(\text{Neutrophil} \times \text{monocyte}) \div \text{lymphocyte ratio}$
AISI	$(\text{Neutrophil} \times \text{platelet} \times \text{monocyte}) \div \text{lymphocyte ratio}$
NLR	$\text{Neutrophil} \div \text{lymphocyte ratio}$
PLR	$\text{Platelet} \div \text{lymphocyte ratio}$
LMR	$\text{Lymphocyte} \div \text{monocyte ratio}$
NAR	$\text{Neutrophil} \div \text{albumin ratio}$
CAR	$\text{CRP} \div \text{albumin ratio}$
PNI	$\text{Albumin (g/L)} + 5 \times \text{total lymphocyte counts (10}^9\text{/L)}$
SIS=0	$\text{LMR} \geq 2.17$ and $\text{albumin} \geq 39.8 \text{ g/L}$
SIS=1	$\text{LMR} < 2.17$ or $\text{albumin} < 39.8 \text{ g/L}$
SIS=2	$\text{LMR} < 2.17$ and $\text{albumin} < 39.8 \text{ g/L}$

Abbreviations: SII, systemic immune-inflammatory index; SIRI, systemic inflammatory response index; AISI, aggregate index of systemic inflammation; CRP, C-reactive protein; PNI, prognostic nutritional index; SIS, systemic inflammation score.

set to identify independent risk factors for developing a nomogram to predict rotaviral diarrhea. The receiver operating characteristic (ROC) and calibration curves were used to examine the nomogram's performance, with areas under the ROC curve (AUCs) between 0.5 (not discriminant) and 1 (perfect discriminant). Decision curve analysis (DCA) was used to assess the net clinical benefit of the nomogram. A *p*-value <0.05 indicated statistical significance. R 4.2.2 software was used for statistical analysis.

Results

Baseline Characteristics of the Patients

Between January 2022 and December 2023, this study enrolled 439 children under 5 years old with diarrhea at the Department of Pediatrics, the First People's Hospital of Neijiang, who met the predefined inclusion and exclusion criteria. The prevalence of rotaviral diarrhea was 27.33% (120 of 439 patients). Patients were randomly assigned to the training cohort (70%) and the internal validation cohort (30%). Baseline demographic and clinical characteristics were compared between the training group (N = 307) and the validation group (N = 132), with no significant differences in gender (*p* = 0.563), age (*p* = 0.466), and weight (*p* = 0.753). Laboratory indicators including PCT, NLR, PLR, LMR, SII, SIRI, AISI, NAR, CAR, PNI, and SIS also showed no significant variations between the two cohorts (*p* > 0.05), thereby ensuring the comparability of baseline characteristics across cohorts (Table 2) for the predictive model analysis.

Development of a Nomogram with Logistic Regression

In the initial model, potential predictors, namely gender, age, weight, NLR, PLR, LMR, SII, SIRI, AISI, NAR, CAR, PNI, and SIS were included (Table 3), which was subsequently refined to a subset of six variables through LASSO regression within the training cohort. The coefficients are listed in Table 4, and a coefficient profile is shown in Figure 2A. A cross-validated error plot of the most regularized and parsimonious LASSO regression model is shown in Figure 2B, with a cross-validated error within one standard error of the minimum, which included six variables.

Except for age (AUC = 0.413), the AUCs of all other aforementioned variables exceeded 0.5, with PLR at 0.650, LMR at 0.652, SIRI at 0.585, NAR at 0.510, and CAR at 0.637 (Figure 3). Multivariate logistic analysis (Table 5) was

Table 2 Demographic and Baseline Attributes of the Patients

Characteristic	Cohort		p-value
	Training Cohort (N = 307)	Internal Validation Cohort (N = 132)	
Gender, n (%)			0.563
Male	172 (56.0%)	70 (53.0%)	
Female	135 (44.0%)	62 (47.0%)	
Age (years)			0.466
Mean \pm SD	1.91 \pm 2.01	2.07 \pm 2.24	
Weight			0.753
Mean \pm SD	12.1 \pm 6.7	12.4 \pm 7.3	
PCT			0.788
Mean \pm SD	0.63 \pm 1.45	0.60 \pm 0.96	
NLR			0.977
Mean \pm SD	4.3 \pm 6.6	4.3 \pm 5.5	
PLR			0.676
Mean \pm SD	172 \pm 156	179 \pm 159	
LMR			0.540
Mean \pm SD	4.23 \pm 2.69	4.06 \pm 2.70	
SII			0.742
Mean \pm SD	1385 \pm 2431	1317 \pm 1768	
SIRI			0.436
Mean \pm SD	3.2 \pm 7.0	2.8 \pm 3.6	
AISI			0.407
Mean \pm SD	1102 \pm 2699	937 \pm 1451	
NAR			0.857
Mean \pm SD	0.15 \pm 0.10	0.14 \pm 0.10	
CAR			0.050
Mean \pm SD	0.43 \pm 0.69	0.61 \pm 0.90	
PNI			0.377
Mean \pm SD	58 \pm 10	57 \pm 10	
SIS			0.121
Mean \pm SD	0.35 \pm 0.52	0.43 \pm 0.54	

Abbreviations: PCT, procalcitonin; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammatory index; SIRI, systemic inflammatory response index; AISI, aggregate index of systemic inflammation; NAR, neutrophil-to-albumin ratio; LMR, lymphocyte-to-monocyte ratio; CAR, CRP-to-albumin ratio; PNI, prognostic nutritional index; SIS, systemic inflammation score.

Table 3 Demographic and Baseline Characteristics of the Patients

Characteristic	Training Cohort			Internal Validation Cohort		
	No-RD (n=221)	RD (n=86)	p-value	No-RD (n=98)	RD (n=34)	p-value
Gender, n (%)			0.762			0.236
Male	125 (57%)	47 (55%)		49 (50%)	21 (62%)	
Female	96 (43%)	39 (45%)		49 (50%)	13 (38%)	
Age (years)			0.571			0.334
Mean \pm SD	1.94 \pm 2.24	1.82 \pm 1.28		1.97 \pm 2.30	2.38 \pm 2.04	
Weight			0.438			0.779
Mean \pm SD	12.3 \pm 7.6	11.8 \pm 3.5		12.3 \pm 8.1	12.6 \pm 4.6	
PCT			0.112			0.315
Mean \pm SD	0.68 \pm 1.69	0.49 \pm 0.38		0.64 \pm 1.06	0.49 \pm 0.57	

(Continued)

Table 3 (Continued).

Characteristic	Training Cohort			Internal Validation Cohort		
	No-RD (n=221)	RD (n=86)	p-value	No-RD (n=98)	RD (n=34)	p-value
NLR			0.006			0.029
Mean ± SD	3.4 ± 4.9	6.4 ± 9.4		3.5 ± 4.6	6.4 ± 7.1	
PLR			<0.001			0.006
Mean ± SD	144 ± 114	244 ± 217		149 ± 116	265 ± 224	
LMR			<0.001			<0.001
Mean ± SD	4.64 ± 2.83	3.20 ± 1.97		4.59 ± 2.82	2.54 ± 1.51	
SII			0.007			0.052
Mean ± SD	1090 ± 1872	2145 ± 3376		1089 ± 1417	1974 ± 2431	
SIRI			0.013			0.030
Mean ± SD	2.4 ± 4.2	5.5 ± 11.2		2.3 ± 2.8	4.4 ± 5.1	
AISI			0.015			0.072
Mean ± SD	768 ± 1565	1962 ± 4342		748 ± 1009	1480 ± 2226	
NAR			0.693			0.681
Mean ± SD	0.15 ± 0.11	0.14 ± 0.10		0.14 ± 0.10	0.15 ± 0.11	
CAR			<0.001			0.013
Mean ± SD	0.53 ± 0.77	0.17 ± 0.26		0.70 ± 0.98	0.35 ± 0.54	
PNI			0.003			<0.001
Mean ± SD	59 ± 10	55 ± 9		59 ± 10	51 ± 5	
SIS			0.055			0.035
Mean ± SD	0.31 ± 0.49	0.44 ± 0.57		0.37 ± 0.51	0.62 ± 0.60	

Abbreviations: PCT, procalcitonin; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammatory index; SIRI, systemic inflammatory response index; AISI, aggregate index of systemic inflammation; NAR, neutrophil-to-albumin ratio; LMR, lymphocyte-to-monocyte ratio; CAR, CRP-to-albumin ratio; PNI, prognostic nutritional index; SIS, systemic inflammation score.

Table 4 The Coefficients of the LASSO Regression Analysis

Coefficient	Variable
-0.260115472	(Intercept)
-0.022963240	Age_level_
0.000000000	Weight_level_
0.000000000	Gender_level_1
0.000000000	PCT_level_
0.000000000	NLR_level_
0.001679438	PLR_level_
-0.147765079	LMR_level_
0.000000000	SII_level_
0.002694530	SIRI_level_
0.000000000	AISI_level_
-0.351079511	NAR_level_
-0.887526088	CAR_level_
0.000000000	PNI_level_
0.000000000	SIS_level_

Abbreviations: PCT, procalcitonin; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammatory index; SIRI, systemic inflammatory response index; AISI, aggregate index of systemic inflammation; NAR, neutrophil-to-albumin ratio; LMR, lymphocyte-to-monocyte ratio; CAR, CRP-to-albumin ratio; PNI, prognostic nutritional index; SIS, systemic inflammation score.

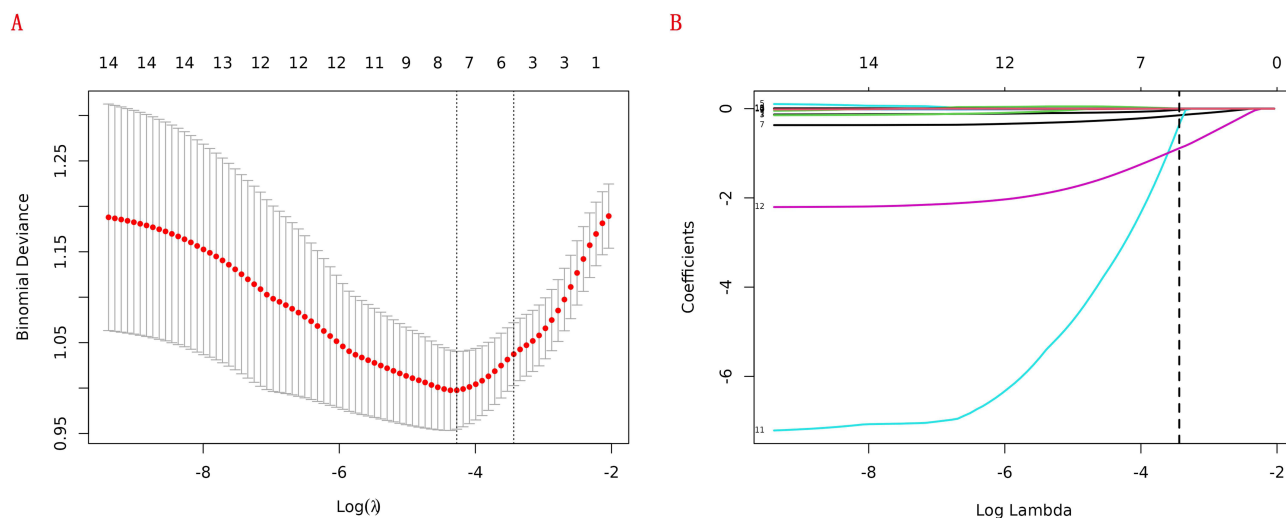


Figure 2 LASSO regression cross-validation plot (A) and LASSO regression coefficient path plot (B).

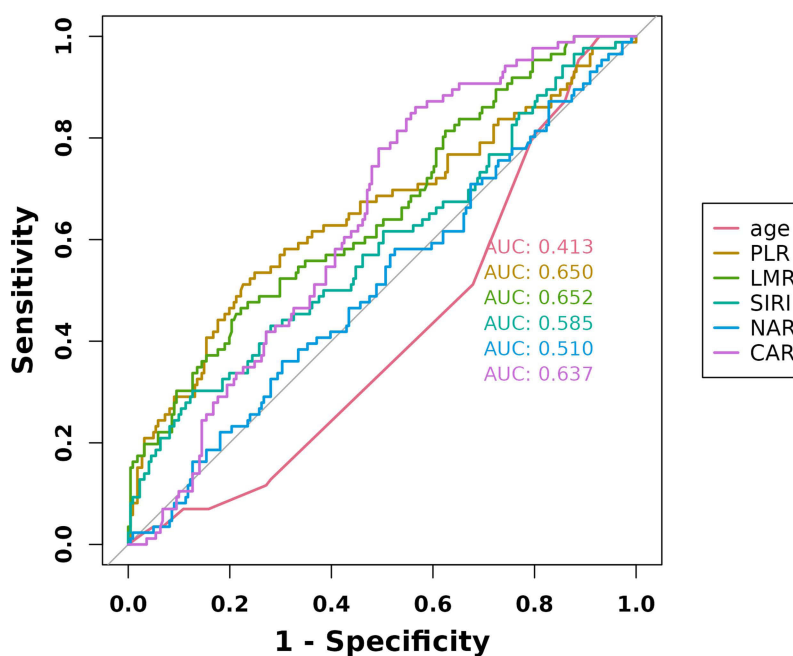


Figure 3 ROC curve analysis 6 candidate diagnostic indicators.

conducted on the training cohort. The final nomogram model was developed by incorporating four independent predictive factors LMR, SIRI, NAR and CAR (Figure 4). The model's performance is shown in Figure 5, with an AUC of 0.795 (95% CI, 0.743–0.848) for the training set and 0.787 (95% CI, 0.694–0.879) for the internal validation set. Both AUCs are superior to those of single indices, indicating excellent predictive capability. Sensitivity and specificity are shown in Table 6. Calibration plots in Figures 6A-B demonstrate a strong correlation between observed and predicted rotaviral-induced diarrhea. The original nomogram could be accurately used in the validation sets, with a calibration curve similar to the ideal curve, indicating consistency between prediction and observation. The DCA curves associated with the nomogram are shown in Figures 7A-B, indicating substantial net benefits of the nomogram for clinical application. The high-risk threshold probability shows that the model retains predictive accuracy without significant bias, even during diagnostic and decision-making challenges.

Table 5 Multivariate Logistic Regression Analysis on the Training Cohort

Characteristic	N	Event N	OR	95% CI	p-value
Age	307	86	0.84	0.71, 1.00	0.056
PLR	307	86	1.00	1.00, 1.00	0.321
LMR	307	86	0.71	0.59, 0.84	<0.001
SIRI	307	86	1.10	1.01, 1.20	0.031
NAR	307	86	0.00	0.00, 0.16	0.006
CAR	307	86	0.11	0.03, 0.34	<0.001

Abbreviations: OR, odds ratio; CI, confidence interval; PLR, platelet-to-lymphocyte ratio; SIRI, systemic inflammatory response index; NAR, neutrophil-to-albumin ratio; LMR, lymphocyte-to-monocyte ratio; CAR, CRP-to-albumin ratio.

Discussion

Improvements in economic and sanitary conditions have led to a sharp decline in bacterial diarrhea worldwide. However, viral diarrhea has become the primary cause of acute gastroenteritis in infants and young children.²⁷ The main viruses causing acute gastroenteritis include rotavirus, norovirus, astrovirus, hepatitis virus, and adenovirus.^{28,29} Rotaviral-induced severe gastroenteritis occurs worldwide, particularly in developing countries, with high morbidity and mortality rates,³⁰ and it is the commonest cause of viral gastroenteritis in children under five years old, with a higher prevalence in males.^{31,32} This may be because children under five years old are more likely to put their hands in their mouths after touching toys or other objects contaminated by rotavirus, thereby increasing the risk of infection. Rotaviral infection is

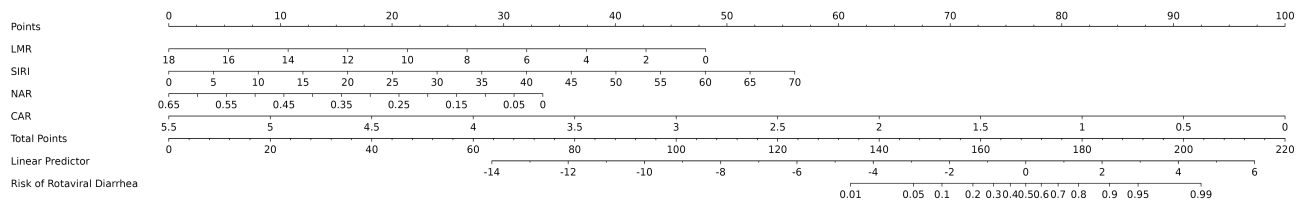


Figure 4 Nomogram of probability to develop rotavirus infection-induced diarrhea in children using immune inflammation-related indicators. To use the nomogram, draw an upward vertical line from each covariate to the points bar to calculate the number of points. Based on the sum of the covariate points, draw a downward vertical line from the total points line to calculate the probability of developing rotavirus infection-induced diarrhea.

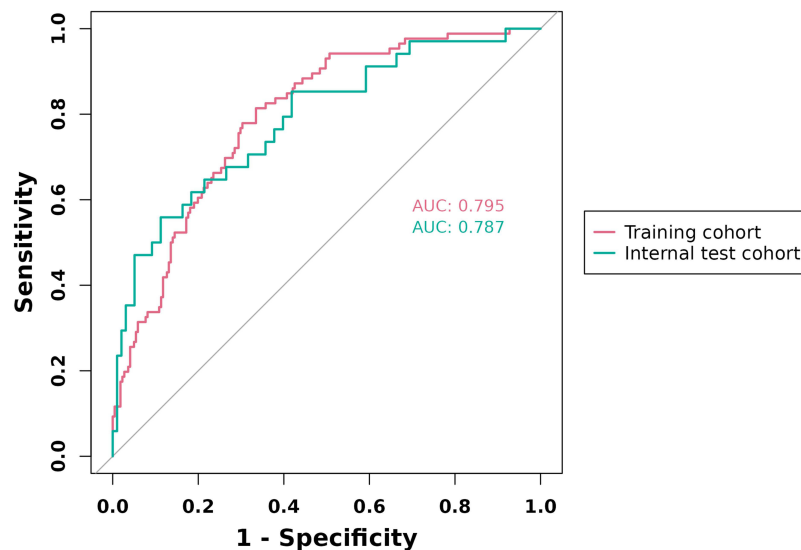


Figure 5 ROC curve for the nomogram based on the training cohort (The AUC is 0.795) and internal validation cohort (The AUC is 0.787).

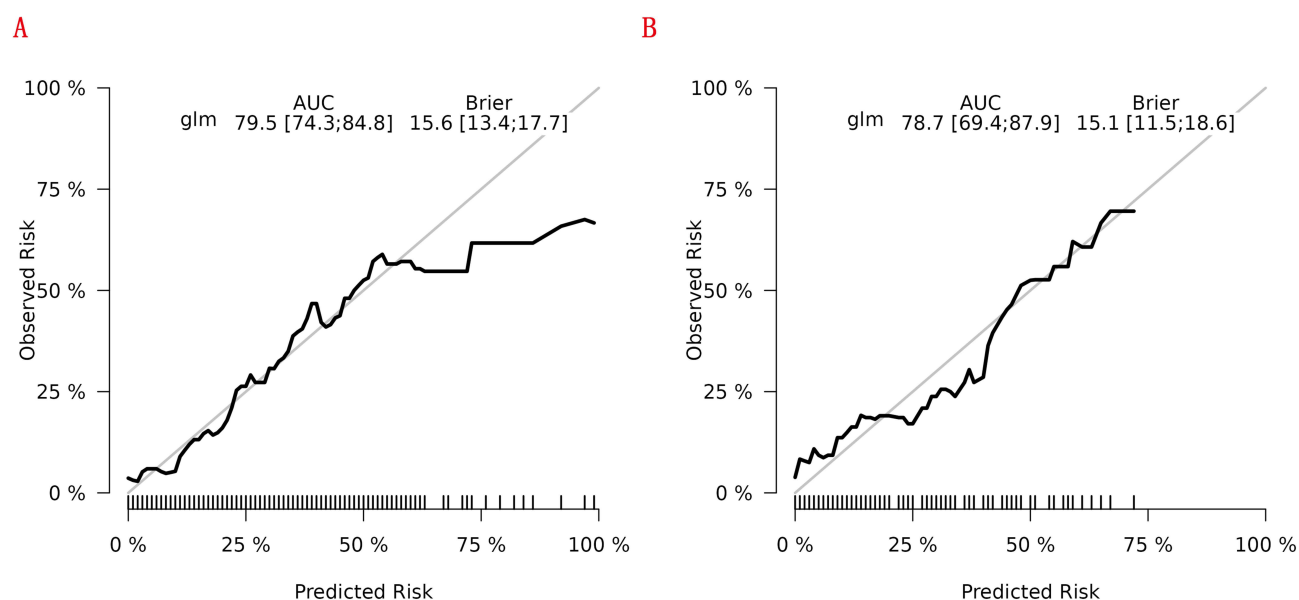
Table 6 Results of Optimum Sensibility, Specificity, and AUC of Training Cohort and Internal Test Cohort

Characteristic	Cut-Off Value	Sensitivity	Specificity	AUC (95% CI)
Training cohort				
LMR	2.64	46.51%	77.83%	0.652 (0.583–0.721)
SIRI	4.11	30.23%	87.33%	0.585 (0.511–0.659)
NAR	0.09	36.05%	69.68%	0.510 (0.438–0.583)
CAR	0.29	86.05%	43.44%	0.637 (0.574–0.700)
Combined	/	100%	100%	0.795 (0.743–0.848)
Internal test cohort				
LMR	3.18	73.53%	62.24%	0.745 (0.650–0.839)
SIRI	1.24	76.47%	48.98%	0.655 (0.552–0.757)
NAR	0.13	61.76%	43.88%	0.467 (0.357–0.576)
CAR	0.85	94.12%	31.63%	0.564 (0.463–0.665)
Combined	/	100%	100%	0.787 (0.694–0.879)

Abbreviations: OR, odds ratio; CI, confidence interval; SIRI, systemic inflammatory response index; NAR, neutrophil-to-albumin ratio; LMR, lymphocyte-to-monocyte ratio; CAR, CRP-to-albumin ratio.

mainly localized in the intestinal mucosa, with rare instances of viral replication in distant sites such as the lamina propria and local lymphatics, especially in immunocompromised patients.¹¹ In immunocompetent individuals, viral replication and systemic dissemination is rare in these extraintestinal sites. Rotaviral diarrhea is induced by multiple viral activities, with complex pathogenesis that remains unclear.³³ In children under five years old, rotaviral infection can cause several severe complications, with a high mortality rate. Therefore, identifying independent predictors of rotaviral-induced diarrhea in this age group is crucial for clinicians to implement timely preventive and therapeutic measures.

Neutrophils, lymphocytes, and monocytes are essential for the immune response. Rotaviral infection can activate genes encoding chemokines, with inflammatory mediators linked to neutrophil chemotaxis. The increased neutrophil count may be associated with delayed neutrophil apoptosis. The decreased lymphocyte count is linked to increased cortisol levels and apoptosis due to physiological stress, such as infection.³⁴ Wang et al³⁵ demonstrated that rotaviral infections can inhibit the expression of molecules essential for T lymphocyte survival, leading to a reduced lymphocyte count. Viral infections can also release neutrophils from the storage pool to the peripheral circulation, resulting in an

**Figure 6** Calibration curves of the nomogram for predicting rotavirus diarrhea from the training cohort (A) and the internal validation cohort (B).

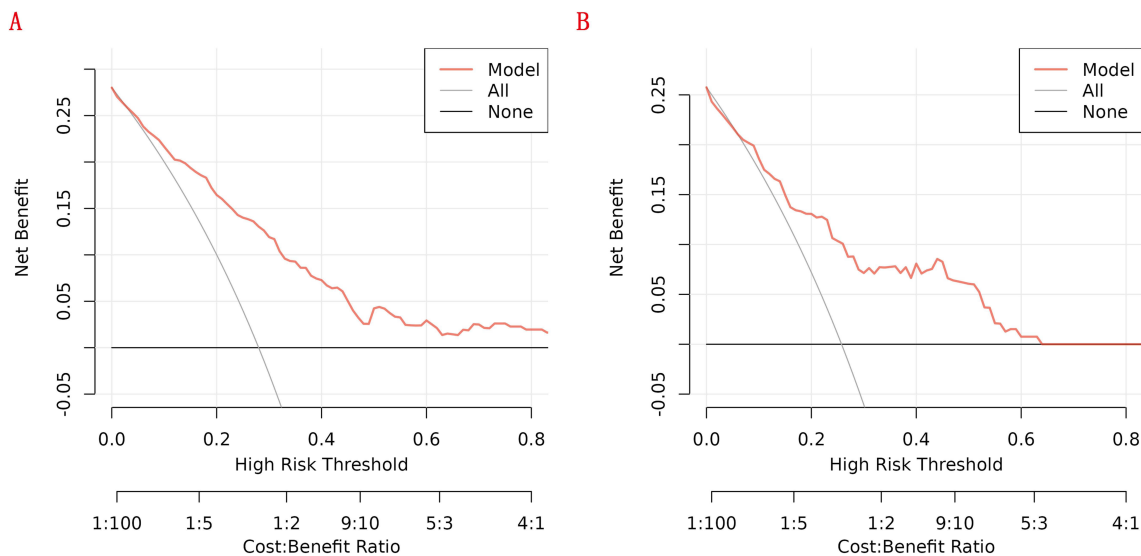


Figure 7 Decision curve analysis (DCA) of the nomogram: **(A)** the training cohort; **(B)** the internal validation cohort.

increased neutrophil count.³⁶ Stress responses due to inflammation, trauma, surgery, and anesthesia can activate the peripheral immune system, thereby increasing neutrophils and monocytes while reducing lymphocytes.³⁷ Anaerobic free radicals, chemokines and inflammatory cytokines are secreted by activated neutrophils and monocytes, indicating a possible mechanism of rotaviral infection.³⁸ SIRI and LMR integrate these three cell types, providing a comprehensive assessment of the immune-inflammatory state and disease progression.^{39,40} This study shows that SIRI and LMR are independent predictors of rotaviral-induced diarrhea in children under five years old. CRP is produced by the liver post-infection, inflammation, and tissue damage, and is a specific inflammatory marker of the stress state and recovery in infected children.^{41,42} Serum albumin level is an important clinical biomarker for evaluating a patient's nutritional status. Changes in albumin levels due to acute infection, stress, bleeding, immobilization, and poor nutrition can seriously affect the prognosis of pediatric patients.⁴³ This study integrated the CRP-to-albumin ratio (CAR) and the neutrophil-to-albumin ratio (NAR) to provide a comprehensive infection assessment.

Using multivariable logistic and LASSO regression analyses on a cohort of 439 cases, a nomogram was developed and validated for predicting rotaviral-induced diarrhea in children under five years old. The nomogram included four statistically significant immune-inflammatory predictors SIRI, LMR, NAR, and CAR. The model showed excellent predictive capability, with an AUC of 0.795 (95% CI, 0.743–0.848) in the training set. The Hosmer-Lemeshow test confirmed the model's calibration, indicating its strong predictive accuracy. DCA demonstrated the model's value in risk prediction for rotaviral-induced diarrhea in children under five. Internal validation further confirmed the model's predictive accuracy. Based on DCA and internal validation, this study provides a refined approach for risk prediction in this age group.

To our knowledge, this is the first study to use immune inflammatory indicators to predict the risk of rotaviral-induced diarrhea in children under five. A nomogram model was developed to visually depict complex regression equations, offering a simple and effective approach. This model can assist pediatricians in identifying high-risk patients and support early intervention strategies to reduce the incidence of rotaviral-induced diarrhea in this age group. Clinicians can use this model for personalized risk assessment and intervention, potentially improving prevention and treatment outcomes, and reducing the burden on healthcare systems and society. Furthermore, the indicators included in the model are readily available and cost-effective, minimizing the economic burden on patients and facilitating widespread clinical adoption.

However, this study has a few limitations. First, the small sample size may limit the robustness of the results. Second, as a single-center retrospective cohort study, it may not represent a broader demographic, and its design may introduce selection bias. Last, the nomogram model has not undergone external validation in different populations, which is necessary to establish the generalizability of the findings. These limitations highlight the need for validation in future large-scale, multi-center, prospective studies.

Conclusions

This study confirms that the immune inflammatory indicators SIRI, LMR, NAR, and CAR predict the risk of rotaviral-induced diarrhea in children under five years old. A nomogram model integrating these markers demonstrates strong predictive capability for the risk of rotaviral-induced diarrhea in this age group.

Data Sharing Statement

Data used and/or analyzed in this study can be requested from the corresponding author.

Ethical Approval and Consent to Participate

Given the retrospective study design, informed consent was waived. The study was approved by the institutional ethics committee (approval number: 2024-lunshenpi-27). Strict confidentiality was maintained with all patient data.

Author Contributions

All authors significantly contributed to the conception, study design, execution, data acquisition, analysis and interpretation; drafted, revised or critically reviewed the article; approved the version to be published; agreed on the journal for submission of the article; and are accountable for all aspects of the work.

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Disclosure

All authors declare no conflict of interest.

References

- Lestari FB, Vongpunsawad S, Wanlapakorn N, Poovorawan Y. Rotavirus infection in children in Southeast Asia 2008-2018: disease burden, genotype distribution, seasonality, and vaccination. *J Biomed Sci.* 2020;27(1):66. doi:10.1186/s12929-020-00649-8
- Troeger C, Khalil IA, Rao PC, et al. Rotavirus vaccination and the global burden of rotavirus diarrhea among children younger than 5 years. *JAMA Pediatrics.* 2018;172(10):958–965. doi:10.1001/jamapediatrics.2018.1960
- Tate JE, Burton AH, Boschi-Pinto C, Parashar UD. Global, regional, and national estimates of rotavirus mortality in children <5 years of age, 2000–2013. *Clin Infectious Dis.* 2016;62 Suppl 2:S96–s105. doi:10.1093/cid/civ1013
- Blutt SE, Matson DO, Crawford SE, et al. Rotavirus antigenemia in children is associated with viremia. *PLoS Med.* 2007;4(4):e121. doi:10.1371/journal.pmed.0040121
- Baradaran B, Hazrati A, Kazemi-Sefat NA, Soleimanzahi H, Soudi S. Umbilical cord-derived mesenchymal stem cell condition medium effect on rotavirus-infected Caco-2 cells survival and inflammatory responses. *Tissue Cell.* 2025;93:102699. doi:10.1016/j.tice.2024.102699
- Zhaori GT, Fu LT, Xu YH, Guo YR, Peng ZJ, Shan WS. Detection of rotavirus antigen in tracheal aspirates of infants and children with pneumonia. *Chinese Med J.* 1991;104(10):830–833.
- Limbos MA, Lieberman JM. Disseminated intravascular coagulation associated with rotavirus gastroenteritis: report of two cases. *Clin Infectious Dis.* 1996;22(5):834–836. doi:10.1093/clinids/22.5.834
- Teitelbaum JE, Daghistani R. Rotavirus causes hepatic transaminase elevation. *Dig Dis Sci.* 2007;52(12):3396–3398. doi:10.1007/s10620-007-9743-2
- Park M, Yun YJ, Woo SI, Lee JW, Chung NG, Cho B. Rotavirus-associated hemophagocytic lymphohistiocytosis (HLH) after hematopoietic stem cell transplantation for familial HLH. *Pediatrics Int.* 2015;57(2):e77–80. doi:10.1111/ped.12567
- Ishige M, Fuchigami T, Furukawa M, et al. Primary carnitine deficiency with severe acute hepatitis following rotavirus gastroenteritis. *J Infection Chemother.* 2019;25(11):913–916. doi:10.1016/j.jiac.2019.04.020
- Omatola CA, Olaniran AO. Rotaviruses: from pathogenesis to disease control-A critical review. *Viruses.* 2022;14(5):875. doi:10.3390/v14050875
- Parashar UD, Hummelman EG, Bresee JS, Miller MA, Glass RI. Global illness and deaths caused by rotavirus disease in children. *Emerging Infectious Dis.* 2003;9(5):565–572. doi:10.3201/eid0905.020562
- Chao B, Ju X, Zhang L, Xu X, Zhao Y. A novel prognostic marker systemic inflammation response index (SIRI) for operable cervical cancer patients. *Front Oncol.* 2020;10:766. doi:10.3389/fonc.2020.00766
- Cho JH, Cho HJ, Lee HY, et al. Neutrophil-lymphocyte ratio in patients with acute heart failure predicts in-hospital and long-term mortality. *J Clin Med.* 2020;9(2):557. doi:10.3390/jcm9020557
- Pacheco-Barcia V, Mondéjar Solís R, France T, et al. A systemic inflammation response index (SIRI) correlates with survival and predicts oncological outcome for mFOLFIRINOX therapy in metastatic pancreatic cancer. *Pancreatol.* 2020;20(2):254–264. doi:10.1016/j.pan.2019.12.010
- Zhao G, Liu N, Wang S, et al. Prognostic significance of the neutrophil-to-lymphocyte and platelet-to-lymphocyte ratio in patients with metastatic gastric cancer. *Medicine.* 2020;99(10):e19405. doi:10.1097/md.00000000000019405

17. Zheng L, Wang Z, Li Y, et al. Prognostic significance of systemic immune inflammation index in patients with urothelial carcinoma: a systematic review and meta-analysis. *Front Oncol.* 2024;14:1469444. doi:10.3389/fonc.2024.1469444
18. Hamakawa Y, Hirahara A, Hayashi A, et al. Prognostic value of systemic immune-inflammation index in patients with small-cell lung cancer treated with immune checkpoint inhibitors. *BMC Cancer.* 2025;25(1):17. doi:10.1186/s12885-025-13440-5
19. Chen X, Fan Y, Tu H, Chen J. A novel nomogram developed based on preoperative immune inflammation-related indicators for the prediction of postoperative delirium risk in elderly hip fracture cases: a single-center retrospective cohort study. *J Inflamm Res.* 2024;17:7155–7169. doi:10.2147/jir.s485181
20. Ng WW, Lam SM, Yan -W-W, Shum H-P. NLR, MLR, PLR and RDW to predict outcome and differentiate between viral and bacterial pneumonia in the intensive care unit. *Sci Rep.* 2022;12(1):15974. doi:10.1038/s41598-022-20385-3
21. Liao Y, Liu C, He W, Wang D. Study on the value of blood biomarkers NLR and PLR in the clinical diagnosis of influenza a virus infection in children. *Clin Lab.* 2021;67(11). doi:10.7754/Clin.Lab.2021.210319
22. Aydın Ö, Apaydın Yıldırım B. Determination of systemic inflammation response index (SIRI), systemic inflammatory index (SII), HMGB1, Mx1 and TNF levels in neonatal calf diarrhea with systemic inflammatory response syndrome. *Vet Immunol Immunopathol.* 2024;275:110815. doi:10.1016/j.vetimm.2024.110815
23. Midik MM, Gunenc D, Acar PF, Karaca BS. Prognostic value of blood-based inflammatory markers in cancer patients receiving immune checkpoint inhibitors. *Cancers.* 2024;17(1):37. doi:10.3390/cancers17010037
24. Yang SB, Zhao HW. Associations between albumin/neutrophil-to-lymphocyte ratio score and new-onset atrial fibrillation in patients with acute myocardial infarction undergoing PCI. *J Inflamm Res.* 2025;18:61–71. doi:10.2147/jir.s500743
25. Chen X, Fan Y, Tu H, Chen J, Li R. A nomogram model based on the systemic immune-inflammation index to predict the risk of venous thromboembolism in elderly patients after hip fracture: a retrospective cohort study. *Heliyon.* 2024;10(6):e28389. doi:10.1016/j.heliyon.2024.e28389
26. Wang Y, Li Y, Zheng Y, et al. Development of a rapid homogeneous immunoassay for detection of rotavirus in stool samples. *Front Public Health.* 2022;10:975720. doi:10.3389/fpubh.2022.975720
27. Jiang H, Zhang Y, Xu X, et al. Clinical, epidemiological, and genotypic characteristics of rotavirus infection in hospitalized infants and young children in Yunnan Province. *Arch Virol.* 2023;168(9):229. doi:10.1007/s00705-023-05849-9
28. Ghonaim AH, Yi G, Lei M, et al. Isolation, characterization and whole-genome analysis of G9 group a rotaviruses in China: evidence for possible Porcine-Human interspecies transmission. *Virology.* 2024;597:110129. doi:10.1016/j.virol.2024.110129
29. Ghonaim AH, Rouby SR, Nageeb WM, et al. Insights into recent advancements in human and animal rotavirus vaccines: exploring new frontiers. *Virologica Sin.* 2025;40(1):1–14. doi:10.1016/j.virs.2024.12.001
30. Mousavi-Nasab SD, Sabahi F, Kaghazian H, et al. A real-time RT-PCR assay for genotyping of rotavirus. *Iran Biomed J.* 2020;24(6):399–404. doi:10.29252/ibj.24.6.394
31. Kim A, Chang JY, Shin S. Epidemiology and factors related to clinical severity of acute gastroenteritis in hospitalized children after the introduction of rotavirus vaccination. *J Korean Med Sci.* 2017;32(3):465–474. doi:10.3346/jkms.2017.32.3.465
32. Ojobor CD, Olovo CV, Onah LO, Ike AC. Prevalence and associated factors to rotavirus infection in children less than 5 years in Enugu State, Nigeria. *Virus Disease.* 2020;31(3):316–322. doi:10.1007/s13337-020-00614-x
33. Cárcamo-Calvo R, Muñoz C, Buesa J, Rodríguez-Díaz J, Gozalbo-Rovira R. The rotavirus vaccine landscape, an update. *Pathogens.* 2021;10(5):520. doi:10.3390/pathogens10050520
34. Tzur T, Sheiner E. Is there an association between platelet count during the first trimester and preeclampsia or other obstetric complications later in pregnancy? *Hypertension Pregn.* 2013;32(1):74–82. doi:10.3109/10641955.2012.704109
35. Wang Y, Dennehy PH, Keyserling HL, et al. Rotavirus infection alters peripheral T-cell homeostasis in children with acute diarrhea. *J Virol.* 2007;81(8):3904–3912. doi:10.1128/jvi.01887-06
36. Kılıçaslan O, Sav NM, Karaca S, Şahin IE, Öksüz S, Kocabay K. Role of routine laboratory markers in the diagnosis of rotavirus and adenovirus gastroenteritis. *J Med Sci Res.* 2022;10(2):76–81. doi:10.17727/JMSR.2022/10-15
37. Margraf A, Perretti M. Immune cell plasticity in inflammation: insights into description and regulation of immune cell phenotypes. *Cells.* 2022;11(11):1824. doi:10.3390/cells11111824
38. Bongers SH, Chen N, van Grinsven E, et al. Kinetics of neutrophil subsets in acute, subacute, and chronic inflammation. *Front Immunol.* 2021;12:674079. doi:10.3389/fimmu.2021.674079
39. Li X, Lin H, Ouyang R, Yang Y, Peng J. Prognostic significance of the systemic immune-inflammation index in pancreatic carcinoma patients: a meta-analysis. *Biosci Rep.* 2021;41(8). doi:10.1042/bsr20204401
40. Meng L, Yang Y, Hu X, Zhang R, Li X. Prognostic value of the pretreatment systemic immune-inflammation index in patients with prostate cancer: a systematic review and meta-analysis. *J Transl Med.* 2023;21(1):79. doi:10.1186/s12967-023-03924-y
41. Liu Z, Shi H, Chen L. Prognostic role of pre-treatment C-reactive protein/albumin ratio in esophageal cancer: a meta-analysis. *BMC Cancer.* 2019;19(1):1161. doi:10.1186/s12885-019-6373-y
42. Althaus T, Thaipadungpanit J, Greer RC, et al. Causes of fever in primary care in Southeast Asia and the performance of C-reactive protein in discriminating bacterial from viral pathogens. *Int J Infectious Dis.* 2020;96:334–342. doi:10.1016/j.ijid.2020.05.016
43. Zhang Y, Lin S, Yang X, Wang R, Luo L. Prognostic value of pretreatment systemic immune-inflammation index in patients with gastrointestinal cancers. *J Cell Physiol.* 2019;234(5):5555–5563. doi:10.1002/jcp.27373

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