Evaluation of Hemoglobin, Albumin, Lymphocyte, and Platelet Score, Neutrophil-to-Lymphocyte Ratio, and Platelet-to-Lymphocyte Ratio in Pediatric Patients with Rotavirus Enteritis

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ABSTRACT

Objective: Rotavirus enteritis (RV-e) continues to play a major role in hospitalization and morbidity in patients with acute gastroenteritis (AGE). Identifying new biomarkers that can improve risk assessment of RV-e is crucial for effective disease management. This study aimed to evaluate systemic immune/inflammatory index (SII) markers and hemoglobin, albumin, lymphocyte, and platelet score (HALP score) in children with RV-e.

Materials and Methods: This retrospective cohort study was conducted in the pediatric emergency outpatient clinic (PEOC) of a tertiary-level training and research hospital, involving 816 patients. The neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and HALP score were used to evaluate inflammation in cases of rotavirus (RV) and other types of enteritis.

Results: A total of 816 patients were included in the study, of whom 45.3% were female and 54.7% were male. The hospitalization rate due to RV-e was higher than that of non-RV-e cases, with 47.5% (n=85) of RV-e patients being hospitalized (p<0.001). Both NLR and PLR was elevated in hospitalized patients within the RV-e group (p<0.001 for both). Hospitalization was found to be 1.45 times more likely (95% confidence interval [CI]: 1.09–1.94) among patients with low HALP scores, six times more likely (95% CI: 3.52–10.26) in patients with RV-e, and 2.88 times more likely (95% CI: 1.40–5.88) in children under five years of age.

Conclusion: This study demonstrated that the frequency of hospitalization increased in patients with low HALP scores. We think that the HALP score may serve as a simple and rapid marker to aid clinicians in early treatment planning, especially for patients diagnosed with RV-e in emergency settings.

Keywords: Rotavirus, gastroenteritis, children, HALP score (hemoglobin, albumin, lymphocyte, and platelet score), platelet-to-lymphocyte ratio (PLR), neutrophil-to-lymphocyte ratio (NLR), systemic immune/inflammatory index markers.

J Clin Pract Res 2025;47(1):28–35

Demirtas et al. Evaluation of SII Markers in Rotavirus Infections

INTRODUCTION

Acute gastroenteritis (AGE), a common infectious disease in children, represents a critical public health issue and is a leading cause of morbidity and mortality, particularly in children under five years of age.[1] Although it is mostly prevalent in undeveloped and developing countries due to risk factors such as poor hygiene, inadequate sanitation, and unbalanced nutrition, it is also a significant health concern in developed countries. In these settings, it contributes to frequent emergency room visits, hospitalizations, high costs for families and communities, and can result in fatalities.[2] While numerous pathogens can cause acute gastroenteritis, rotavirus (RV) is the primary cause of diarrhea in children under five years of age.[3] Although morbidity and mortality from rotavirus enteritis (RV-e) have significantly declined due to vaccination programs, the disease remains prevalent in developing and undeveloped countries, as well as in regions where the RV vaccine is not part of routine childhood immunization programs.[4]

Recently, neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR), which are systemic immune/inflammation index (SII) markers, along with the HALP score (hemoglobin, albumin, lymphocyte, and platelet score), calculated from albumin, hemoglobin, lymphocyte, and platelet values, have been investigated as inflammatory biomarkers in pediatric populations.[5–7] Studies have demonstrated that the HALP score can be utilized by clinicians as a marker in conditions such as hypoxic-ischemic encephalopathy (HIE) and premature births.[5,6] Rotavirus leads to viral enteritis, presenting with symptoms such as fever, diarrhea, and vomiting, which can result in severe dehydration and hospitalization. Rotavirus enteritis induces inflammation of the intestinal walls, which is reflected in laboratory findings through parameters indicative of inflammation.[4,8]

To our knowledge, no study in the literature has evaluated the relationship between the HALP score, NLR, PLR biomarkers, and RV-e in children. This study aimed to evaluate inflammatory index markers in children with RV and their prognostic significance in RV-e.

MATERIALS AND METHODS

Study Design

This retrospective cohort study was conducted in the Pediatric Emergency Outpatient Clinic (PEOC) of Aksaray Training and Research Hospital, a tertiary-level university hospital, between January 1 and May 31, 2022.

Study Population

The study was conducted retrospectively with 816 pediatric patients (777 Turkish and 39 refugees) who presented to the

KEY MESSAGES

- HALP score (hemoglobin, albumin, lymphocyte, and platelet score), neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR) can be used as systemic inflammatory markers in rotavirus (RV) infections.

- Since a decrease in the HALP score may be a predictor of hospitalization, we believe it could serve as a simple and rapid marker to assist clinicians in early treatment planning, especially for patients diagnosed with rotavirus enteritis (RV-e) in emergency departments.

- Given the high hospitalization rates associated with RV-e, countries should prioritize RV vaccination as part of health protection measures and include the RV vaccine in their routine vaccination schedules.

Pediatric Emergency Outpatient Clinic of Aksaray Training and Research Hospital with complaints of diarrhea and underwent stool examinations during the specified dates.

All pediatric patients with RV-e aged between 15 days and 18 years were included in the study. Among the 39 refugee patients, 32 were of Syrian origin and 7 were of Afghan origin; all hospitalized refugee patients were of Syrian origin. Children whose stool tests were requested by other outpatient clinics or departments apart from the PEOC, and those presenting to the PEOC with complaints other than diarrhea but requiring stool tests, were excluded from the study. Additionally, patients with co-infections involving viruses, bacteria, or parasites alongside RV in stool samples were not included. Blood tests were requested for a total of 376 patients with AGE exhibiting signs of dehydration, including 118 patients with RV-e and 258 patients from the non-RV-e group. Patients with sodium and creatinine values outside normal limits due to severe dehydration, as well as those with comorbidities, were excluded from the study to avoid skewing the results of inflammatory marker analysis. Additionally, patients with comorbidities, congenital diseases or syndromes, cerebral palsy, comorbid conditions such as upper or lower respiratory tract infections or urinary tract infections were excluded from the study.

Data Collection

The medical records and information of the patients were obtained retrospectively by reviewing hospital files and the hospital automation system. The collected data included age, gender, race, month and season of admission, stool test results, hemogram, biochemical parameters (Na$^+$ [135–145 mmol/L], K$^+$ [3.5–5.4 mmol/L], Cl$^-$ [100–111 mmol/L], urea [12–43 mg/

Demirtas et al. Evaluation of SII Markers in Rotavirus Infections

J Clin Pract Res 2025;47(1):28–35

Table 1. Sociodemographic features of patients

Features	All patient (n=816)		Inpatient (n=150)	
	n	%	n	%
Gender				
Female	370	45.30	62	41.30
Male	446	54.70	88	58.70
Nationality				
Turkish	777	95.20	139	92.70
Refugee	39	4.80	11	7.30
Month of application				
January	144	17.60	28	18.70
February	119	14.60	25	16.70
March	178	21.80	37	24.70
April	139	17.00	21	14.00
May	236	28.90	39	26.00
Season				
Winter	262	32.10	53	35.30
Spring	554	67.90	97	64.70
Stool test				
Rotavirus	179	21.90	85	56.70
Adenovirus	53	6.50	22	14.70
Parasite	63	7.70	3	2.00
Normal	521	63.90	40	26.60
Length of hospitalisation (day, mean±SD)	–		3.25±1.74	
Age (month, mean±SD)	50.26±50.17		30.12±30.39	

SD: Standard deviation.

dL], creatinine [0–0.6 mg/dL], albumin [35–52 g/L], C-reactive protein (CRP) [0–5 g/L]), and blood gas results. Information on inpatient treatment and the duration of hospitalization (in days) was also recorded.

Inflammatory Biomarkers

The NLR and PLR, which are systemic SII markers, were calculated using hemogram parameters and served as indicators of the severity of inflammation in diseases. These markers are important for the early detection of disease and the timely initiation of supportive treatment.[9] The HALP score, another critical marker, serves as an indicator of both the severity of inflammation and nutritional status. It is a scoring system that has recently been investigated for its potential in diagnosis and prognosis.[10] The inflammatory biomarkers were calculated using the following formulas:

NLR = (Neutrophil count/Lymphocyte count)

PLR = (Platelet count/Lymphocyte count)

HALP Score = ([Hemoglobin (g/dL) × Albumin (g/dL) × Lymphocyte count (n/L)] / [Platelet count (n/L)])

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics version 22.0 (SPSS, Inc., Chicago, IL, USA). The data were presented as median (minimum–maximum), mean (standard deviation), and number (percentage). Compliance with normal distribution was assessed using the Shapiro-Wilk test. The Pearson chi-square test was used for statistical analysis of two or more qualitative variables. The Student's t-test was applied to compare two independent quantitative continuous variables that were normally distributed according to the Shapiro-Wilk test. Independent factors influencing hospitalization were evaluated using binary logistic regression analysis. A p value of <0.05 was considered statistically significant.

J Clin Pract Res 2025;47(1):28–35

Demirtas et al. Evaluation of SII Markers in Rotavirus Infections

Table 2. Evaluation of laboratory results of patients with rotavirus enteritis (RV-e) and non-RV-e

Parameter	All patients (n=376) Mean±SD	Rotavirus (n=118) Mean±SD	Others¥ (n=258) Mean±SD	p
WBC (×10³/µL)	10.80±4.60	9.20±3.13	11.56±4.96	**<0.001**
Neutrophil (×10³/µL)	6.22±4.01	5.80±3.21	6.40±4.32	0.180
Lymphocyte (×10³/µL)	3.63±2.59	2.64±2.05	4.08±2.69	**<0.001**
Hemoglobin (g/dL)	12.59±1.50	12.54±1.19	12.61±1.62	0.678
Platelets (×10³/µL)	357±107	333±88	368±113	**0.003**
Albuminᵃ (g/dL)	43.22±3.38	43.39±2.89	43.14±3.59	0.727
CRP (mg/L)	15.95±30.02	12.64±20.12	17.50±33.61	0.147
pH	7.35±0.06	7.34±0.05	7.36±0.06	**<0.001**
Lactate	1.82±0.98	1.73±0.64	1.86±1.11	0.200
pCO₂	34.24±6.62	32.13±5.23	35.30±6.99	**<0.001**
Base Excess	-5.33±4.27	-7.18±3.64	-4.40±4.27	**<0.001**
Bicarbonate (mmol/L)	19.49±4.29	17.80±3.84	20.33±4.26	**<0.001**

SD: Standart deviation; WBC: White blood cell count; CRP: C-reactive protein; pCO_2: Partial pressure of carbon dioxide; ¥: Adenovirus and other gastroenteritis pathogens combined; *: Student's t-test was used to compare RV-e and non-RV-e groups; α: Albumin values based on a total of 111 patients (35 with RV-e, 76 with non-RV-e).

Ethics

Approval for the study was obtained from Aksaray University Clinical Research Ethics Committee on December 22, 2022, with protocol number 151-SBKAEK.

RESULTS

Among the included patients, 45.3% were female, and 54.7% were male. A majority of the patients (67.9%) presented in the spring, with 28.9% presenting in May. Rotavirus was detected in 21.9% (n=179) of stool analyses. The demographic characteristics of the patients are summarized in Table 1.

The mean white blood cell (WBC) count (×10³/µL) across all patients was 10.8±4.6. The mean WBC was 9.20±3.13 in the RV-e group and 11.56±4.96 in the non-RV-e group (p<0.001). The mean lymphocyte count (×10³/µL) was 2.64±2.05 in the RV-e group and 4.08±2.69 in the non-RV-e group (p<0.001). Although the platelet count was within the normal range in the RV-e group, it was significantly lower compared to the non-RV-e group (p=0.003) (Table 2). In blood gas parameters, significant decreases in pH, bicarbonate (HCO₃), and base deficit values were observed, indicating metabolic acidosis in the RV-e group compared to the non-RV-e group (p<0.001 for all). No differences were found between the groups in terms of hemoglobin, serum albumin, and serum CRP levels (p=0.678, p=0.727, p=147, respectively) (Table 2).

Overall, 18.4% of the patients were hospitalized. Among the hospitalized cases, no significant differences were observed with respect to gender, nationality, season of presentation, or month of presentation (p>0.05). When hospitalization rates were compared based on pathogens detected in stool examinations, 47.5% (n=85) of the patients with RV-e were hospitalized, and the rate of hospitalization due to RV-e was higher than that in the non-RV-e group (p<0.001) (Table 3). Among hospitalized patients, 90% were under five years of age. When patients were grouped by age (<5 years vs. ≥5 years), no differences were observed between the groups regarding gender, nationality, season of admission, month of admission, or stool examination results (p>0.05) (Table 3).

The NLR, PLR, and HALP score of hospitalized patients were compared based on viral agent, gender, and season of admission. In the RV-e group, NLR and PLR were significantly higher (p<0.001 for both), while the HALP score was significantly lower (p=0.001) compared to the non-RV-e group. It was observed that NLR, PLR, and HALP scores did not show variations based on gender or season of admission (p>0.05) (Table 4). No significant differences in NLR, PLR, or HALP scores were observed in relation to season or gender (p>0.05) (Table 4).

When the effects of independent variables such as stool examination, age, nationality, gender, season of admission, NLR, PLR, and HALP score on hospitalization were evaluated, it was found that hospitalization was 1.45 times (95% confidence interval [CI]: 1.09–1.94) higher among patients with low HALP scores, 6 times (95% CI: 3.52–10.26) higher in patients with RV-e, and 2.88 times (95% CI: 1.40–5.88) higher in children under five years of age (Table 5).

Demirtas et al. Evaluation of SII Markers in Rotavirus Infections

J Clin Pract Res 2025;47(1):28–35

Table 3. Analysis of inpatient demographics and age groups according to variables

Features	Inpatient				Inpatient-age				p1*	p2**
	Yes		No		<5 year		≥5 year			
	n	%	n	%	n	%	n	%		
Gender										
Female	16.80	62	83.20	308	87.10	54	12.90	8	0.275	0.320
Male	19.70	88	80.30	358	92.00	81	8.00	7		
Nationality										
Turkish	17.90	139	82.10	638	89.20	124	10.80	15	0.105	0.251
Refugee	28.20	11	71.80	28	100.00	11	0.00	0		
Season										
Winter	20.20	53	79.80	209	94.30	50	5.70	3	0.349	0.190
Spring	17.50	97	82.50	457	87.60	85	12.40	12		
Month of application										
January	19.40	28	80.60	116	78.00	12	25.00	4	0.579	0.172
February	21.00	25	79.00	94	88.80	32	11.20	4		
March	20.80	37	79.20	141	94.10	48	5.90	3		
April	15.10	21	84.90	118	90.00	18	10.00	2		
May	16.50	39	83.50	197	96.10	25	3.90	1		
Stool test										
Rotavirus	47.50	85	52.50	94	90.50	77	9.50	8	**<0.001**	0.784
Others¥	10.20	65	89.80	568	89.20	58	10.80	7		

*p1: Inpatient vs features; **p2: Inpatient-age; ¥: Adenovirus and other gastroenteritis pathogens combined.

DISCUSSION

In our study, we found that 47.5% of patients with RV-e were hospitalized. with RV-related hospitalizations being most frequent in children under five years of age. The most notable findings were that hospitalization was 1.45 times higher among patients with low HALP scores, 6 times higher in those with RV-e, and 2.88 times higher in children under five years of age. Additionally, the higher NLR and PLR levels in the RV-e group compared to the non-RV-e group was important results of this study.

According to data from the World Health Organization (WHO), AGE, particularly in children under five years of age, is a significant health concern in both developed and developing countries.[11] In a study conducted in Qatar in 2021, RV-e was found to occur most frequently in children aged 1–3 years, with hospitalization rates being highest in children aged 14–22 months.[12] In our study, 90% of hospitalized patients were under five years of age, and the likelihood of hospitalization was 2.88 times higher in this age group.

Although the causative agents of gastroenteritis vary by city, country, and region based on factors such as access to clean water, sanitation, vaccination coverage, socioeconomic development levels, and national health policies, RV is responsible for approximately 70% of AGE cases in the childhood age group.[13] A study investigating the etiology of AGE outbreaks in Nigeria identified rotavirus as the most common agent, accounting for 69.7% of cases.[14] Similarly, a study conducted in Nepal in 2019 found that RV was the main cause of AGE in children under five years of age, with a prevalence of 28%, surpassing other etiological agents.[15] In Tanzania, a study involving 300 pediatric patients reported a rotavirus positivity rate of 20.7%.[16] In Western Europe, rotavirus was detected in 45–75% of stool samples from children with AGE,[17] while a study in China found RV in stool examinations of 22% of 3,147 children hospitalized due to AGE.[18] Rotavirus diarrhoea is one of the leading causes of hospitalization among pediatric patients in Türkiye and globally. In our study, RV was the most frequently detected pathogen (21.9%), and 47.5% of patients with RV-e were hospitalized. Our finding

J Clin Pract Res 2025;47(1):28–35

Demirtas et al. Evaluation of SII Markers in Rotavirus Infections

Table 4. Comparison of NLR, PLR, and HALP score by rotavirus status, season, and gender among inpatients

	Subgroups	n¥	Mean±SD	t	df	95% CI	p
NLR	Rotavirus	81	4.79±6.25	3.64	142	1.36/4.57	**<0.001**
	Others	63	1.83±1.75				
PLR	Rotavirus	81	220.10±207.30	3.88	142	52.06/160.0	**<0.001**
	Others	63	114.10±70.70				
HALP score	Rotavirus	35	3.90±2.36	-3.52	109	-3.20/-0.90	**0.001**
	Others	76	5.95±3.03				
NLR	Winter	51	2.90±2.57	-1.06	142	-2.66/0.80	0.290
	Spring	93	3.83±5.96				
PLR	Winter	51	164.60±129.40	-0.47	142	-72.91/44.73	0.637
	Spring	93	178.70±189.50				
HALP score	Winter	35	5.18±2.61	-0.29	109	-1.39/1.03	0.770
	Spring	76	5.36±3.16				
NLR	Female	60	3.46±4.45	-0.07	142	-1.75/1.62	0.938
	Male	84	3.52±5.44				
PLR	Female	60	161.70±148.30	-0.71	142	-77.62/36.40	0.476
	Male	84	182.30±184.80				
HALP score	Female	43	5.29±2.95	-0.05	109	-1.18/1.13	0.961
	Male	68	5.32±3.03				

NLR: Neutrophil-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; HALP: Hemoglobin, albumin, lymphocyte, and platelet; CI: Confidence interval; SD: Standard deviation; df: Degrees of freedom; ¥: Of the 150 inpatients, hemogram tests were not performed for 6 patients and albumin tests were not performed for 39 patients, excluding them from the analysis.

Table 5. Evaluation of independent factors affecting hospitalisation by logistic regression analysis

Features	Regression factor	Standard error	p	Odds ratio	95% CI
Stool (Rotavirus)	1.79	0.27	**<0.001**	6.01	3.52–10.26
Age (<5 year)	1.06	0.37	**0.004**	2.87	1.40–5.88
HALP score	0.37	0.15	**0.004**	1.45	1.09–1.94
NLR	0.03	0.01	0.598	1.03	0.92–1.16
PLR	-0.01	0.01	0.435	0.99	0.99–1.00
Nationality	-0.83	0.47	0.079	0.44	0.17–1.10
Season	-0.22	0.25	0.384	0.80	0.49–1.32
Gender	-0.08	0.24	0.733	0.92	0.57–3.49

NLR: Neutrophil-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; HALP: Hemoglobin, albumin, lymphocyte, and platelet; CI: Confidence interval.

that hospitalization was six times more likely in patients with RV-e underscores the need for taking necessary precautions against RV. Additionally, the RV vaccine should be included in the routine childhood vaccination programs in countries such as Türkiye, where it is not currently part of the standard immunization schedule.

Since hemogram parameters are rapid and easily accessible, they can serve as an effective method for early disease recognition, timely initiation of supportive treatment, determination of inflammation severity, and assessment of prognosis.[19,20] The negative impact of NLR and PLR levels, calculated from hemogram parameters, on disease

Demirtas et al. Evaluation of SII Markers in Rotavirus Infections

J Clin Pract Res 2025;47(1):28–35

prognosis has been well-documented.[21] Studies evaluating the prognosis and complications of acute appendicitis using inflammatory markers have demonstrated that NLR and PLR exhibit high sensitivity and specificity, comparable to CRP and procalcitonin (PCT).[22,23] Other studies comparing inflammatory markers in patients with sepsis have shown that NLR and PLR are comparable to PCT and CRP in terms of high specificity for evaluating prognosis in sepsis patients, supporting their use as inflammatory markers.[24,25] One study concluded that elevated NLR and PLR levels negatively affect the prognosis of RV-e.[9] Similarly, in our study, NLR and PLR levels were found to be higher in patients hospitalized with RV diarrhea compared to those hospitalized for other reasons. We believe that RV gastroenteritis is a condition that substantially increases inflammation and may lead to hospitalization.

The HALP score is a novel marker of systemic inflammation calculated using hemoglobin, albumin, platelet, and lymphocyte values. Its application in pediatric diseases is steadily increasing.[5,6] Research has indicated that low HALP scores are associated with systemic inflammation and poor nutritional status.[5,6,26] In patients with acute appendicitis, HALP scores have been shown to aid in determining prognosis and the degree of complications.[10] In our study, hospitalization was found to be 1.45 times more likely in patients with low HALP scores. This finding suggests that HALP scores, especially when evaluated during emergency admissions, could serve as an important marker for hospitalization and disease severity. They may also assist clinicians in making decisions regarding hospitalization and early treatment planning.

Strengths and Limitations

The strengths of our study include being the first to evaluate NLR, PLR, and HALP score in RV-e in children, the inclusion of other viral agents, and the broad age distribution of the study population. However, the inability to determine the RV vaccination status of patients, as it was not recorded in the system, and the single-center design of our study were limitations. Nevertheless, we believe that our study serves as a pioneering effort for multicenter cohort studies investigating inflammatory markers in RV-e and other AGE cases.

CONCLUSION

Despite the success and extensive coverage of vaccination programs, RV-e remains one of the most common causes of AGE, particularly in children under five years of age in underdeveloped and developing countries. Our findings show that NLR and PLR levels increased in RV-e, while HALP scores decreased. This suggests that HALP scores, NLR, and PLR can serve as systemic inflammatory markers in RV-e. Since a decrease in HALP score may be a predictor of hospitalization,

we propose that HALP scores could be a simple and rapid marker to aid clinicians in early treatment planning, especially for patients diagnosed with RV-e in emergency departments. Additionally, our results indicate that the hospitalization rate for RV-e is high, highlighting the need to include RV vaccination in routine childhood vaccination programs to prevent and reduce this burden.

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J Clin Pract Res 2025;47(1):28–35

Demirtas et al. Evaluation of SII Markers in Rotavirus Infections

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