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RESEARCH ARTICLE

The Impact of Vitamin D Status on the Clinical Outcome of Acute Rotavirus Gastroenteritis in Preschool Children

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ABSTRACT

Objective: This study aims to evaluate the impact of vitamin D on the clinical outcome of acute rotavirus gastroenteritis in children under 5 years.

Materials and Methods: This prospective study included 70 patients in a pediatric emergency department with rotavirus gastroenteritis. Patients were divided into two groups based on serum 25-hydroxy vitamin D3 (25(OH)D3) level: low vitamin D (<30 ng/mL) and normal vitamin D (≥30 ng/mL). Disease severity and clinical outcomes were compared.

Results: Out of 70 patients, 55 (78.6%) were in the low vitamin D group. The patients with normal serum 25(OH)D3 levels were younger than those with low serum 25(OH)D3 levels (p=0.01; p<0.05). The Vesikari scores, the severity of dehydration, the need for intravenous fluid, and the duration of diarrhea were similar between the groups. The low vitamin D group had higher hospitalization rates and longer hospital stays than the normal vitamin D group (p=0.015; p<0.05, and p=0.035; p<0.05, respectively). Low vitamin D was identified as a predictive risk factor increasing the risk of hospitalization (p=0.016; p<0.05) and prolonged hospital stay (p=0.003; p<0.01). Exclusive breastfeeding in the first six months was a protective predictor for reducing diarrhea duration and length of hospital stay (p = 0.024; p<0.05 and p=0.035; p<0.05, respectively).

Conclusion: This study suggests low vitamin D status is a preventable risk factor for more severe disease courses in preschool children with rotavirus gastroenteritis.

Keywords: Outcome assessment, rotavirus infections, vitamin D

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INTRODUCTION

Acute gastroenteritis continues to be a significant contributor to illness and death among children worldwide, affecting both high- and low-income regions.[1] It accounts for nearly one-fifth of all pediatric fatalities globally and stands as the second most frequent cause of death in young children, following pneumonia, particularly in under-resourced settings.[2] Among the viral agents responsible, rotavirus plays a major role, causing over 100 million mild cases managed at home, approximately 25 million outpatient visits, around two million hospital admissions, and close to 400,000 deaths annually in children under five years of age.[3] Although individuals of all ages may be affected, infants and toddlers under two years are most commonly impacted.[4] The incidence of rotavirus varies depending on the geographical characteristics, and it may even occur in different seasons across regions of the same country.[5,6] In Türkiye, the reported prevalence of rotavirus-related gastroenteritis among children ranges from 16.6% to over 50%, depending on region and season.[4,7]

Vitamin D deficiency, defined by serum 25-hydroxy vitamin D3 (25(OH)D3) levels below 20 ng/mL, and insufficiency (21–29 ng/mL) are increasingly recognized as global

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health concerns affecting both developed and developing nations. Beyond its classical role in bone health, vitamin D has emerged as a crucial modulator of immune function.[8] Low vitamin D status represents a noteworthy problem in both affluent and impoverished nations, posing a major public health concern. Extensive evidence associates low serum concentrations of vitamin 25(OH)D3 with the worsening of infectious diseases, with a focus on viral infections. Research suggests that inadequate vitamin D levels are associated with increased vulnerability to a range of infections—especially viral illnesses—and with several chronic conditions such as cardiovascular disease, autoimmune disorders, and certain cancers.[9] Vitamin D has several extraskeletal functions, particularly as an immune system modulator. Vitamin D modulates immune responses by interacting with dendritic cells, B and T lymphocytes, and natural killer cells, exerting immunosuppressive or immune-enhancing effects depending on the immunological environment. It regulates the immune system by exerting either suppressive or stimulatory effects, depending on the context.[10–12] Experimental models have indicated that vitamin D can inhibit viral replication via pathways such as the retinoic acid-inducible gene-I (RIG-I) signaling mechanism, and it has been shown to promote epithelial healing in the gut, offering potential protection against rotavirus-induced intestinal injury.[13,14] Although vitamin D's role in general infectious diseases is well studied, limited data exist regarding its association with rotavirus infections specifically in children.[15] To our knowledge, there is currently no comparative clinical study that has evaluated the influence of suboptimal vitamin D levels on the clinical course and severity of rotavirus gastroenteritis in preschool-aged populations.

This study was designed to investigate the potential link between serum vitamin D status and the clinical severity and outcomes of rotavirus gastroenteritis in children under the age of five, with a focus on hospitalization rates, symptom duration, and complications.

MATERIALS and METHODS

Study Design and Setting

This prospective observational study was carried out in the pediatric emergency department (PED) of a tertiary care hospital located in Istanbul, Türkiye. The department receives approximately 120,000 pediatric patient visits annually. The study population included children under the age of five who presented with clinical features consistent with rotavirus gastroenteritis between September 1, 2018, and March 1, 2019. Ethical approval was obtained from the Health Sciences Istanbul Medeniyet University Goztepe Training and Research Hospital's institutional review board (approval number: 2018/0302), and written informed consent was secured from parents or legal guardians in accordance with the Declaration of Helsinki.

Diagnostic Criteria and Severity Assessment

Acute gastroenteritis was defined as the passage of three or more loose or watery stools within a 24-hour period, persisting for no longer than 14 days.[16] Stool consistency was evaluated using the Bristol Stool Form Scale, with types 6 and 7 indicating diarrhea, and types 3 to 5 considered normal.[17] The severity of gastroenteritis was assessed by applying the Vesikari clinical scoring system, categorizing the illness as mild (<7), moderate (7–10), or severe (≥11) (Table 1).[18]

Table 1. Vesikari scoring system

	Score		
Parameters	**1**	**2**	**3**
Maximum number of stools per day	1–3	4–5	≥6
Duration of diarrhea (days)	1–4	5	≥6
Maximum number of vomiting per day	1	2–4	≥5
Duration of vomiting (days)	1	2	≥3
Maximum body temperature (°C)	37.1–38. 4	38.5–38. 9	≥39.0
Degree of dehydration	N/A	%1–5	≥%6
Treatment	Rehydration	Hospitalization	N/A

Severity rating scales: <7 mild; 7–10 (moderate); ≥11 (severe); N/A-Not Available

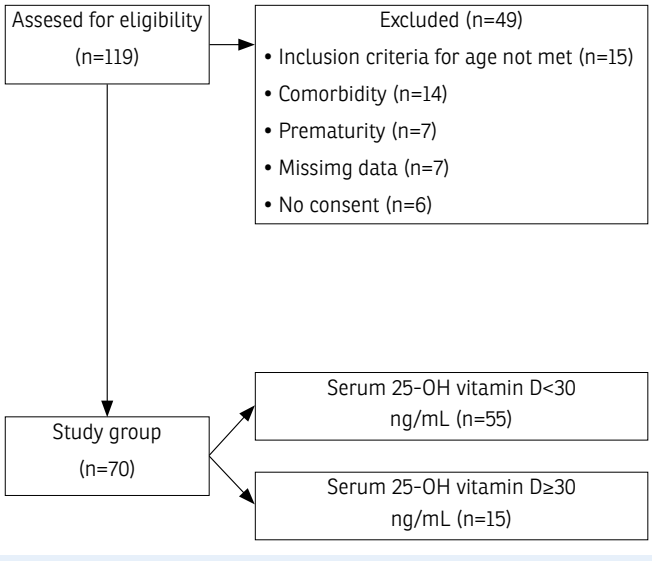

Figure 1. Flowchart for the selection of the study population

Participant Selection and Grouping

Children aged between six months and five years diagnosed with rotavirus gastroenteritis in the PED were considered eligible. Exclusion criteria included prematurity, underlying chronic gastrointestinal disorders, immunosuppression, malnutrition, and absence of informed parental consent. A total of 70 patients met the inclusion criteria. Participants were stratified into two groups based on serum 25-hydroxy vitamin D3 (25(OH)D3) levels: those with low vitamin D (<30 ng/mL) and those with normal levels (≥30 ng/mL).[8,15] The study flow is illustrated in Figure 1.

Laboratory Analysis

Serum 25(OH)D3 levels were determined using a chemiluminescence immunoassay method (ARCHITECT i2000SR, Abbott Laboratories, USA). Rotavirus antigen in stool samples was detected through a rapid immunochromatographic test (One Step Rapid Test, True Line Diagnostic Center, Bangalore). Blood samples were obtained as part of routine clinical evaluation, and the residual serum was used for 25(OH) D3 measurement.

Data Collection

Collected data included demographic characteristics (age, sex), infant feeding practices during the first six months, vitamin D prophylaxis during the first year (defined as regular intake of ≥400 IU/day for at least six months), current vitamin D use (within the last month), rotavirus vaccination status, and antibiotic usage in the preceding month. Clinical data recorded at admission included timing of presentation, number and duration of diarrhea and vomiting episodes, and prior intravenous (IV) fluid therapy. For hospitalized patients, detailed information such as daily frequency of vomiting and diarrhea, peak body temperature, administered treatments, Vesikari score, and length of hospital stay was documented on standardized inpatient forms. After discharge, families were contacted daily to monitor symptom resolution, defined as being symptom-free for at least four consecutive days.

Statistical Analysis

All statistical analyses were conducted using SPSS software version 22.0 (IBM Corp., Armonk, NY). The normality of continuous variables was tested with the Shapiro–Wilk test. Descriptive data included means, standard deviations, medians, interquartile ranges, and frequencies. For group comparisons, we applied Student's t-tests for normally distributed continuous data and Mann–Whitney U tests for non-normally distributed data. Categorical comparisons utilized chi-square tests. We employed Spearman correlation to investigate relationships between numerical variables. To identify independent predictors of hospitalization, length of stay, and symptom duration, multivariate logistic and linear regression models were used. A p-value below 0.05 was considered statistically significant.

RESULTS

A total of 70 children diagnosed with acute rotavirus gastroenteritis were enrolled in the study. Of these, 28 (40%) were male and 42 (60%) were female. The overall median age of the participants was 20.5 months (interquartile range [IQR]: 18 months), with 54.3% (n=38) being younger than two years. The median serum 25(OH)D3 level was 21.6 ng/mL (IQR:12.6), with values ranging from 6.5 to 94.5 ng/mL.

Based on vitamin D levels, 55 patients (78.6%) were assigned to the low vitamin D group (<30 ng/mL), while 15 children (21.4%) had levels considered within the normal range (≥30 ng/mL). Children with normal vitamin D levels were significantly younger and more likely to be using vitamin D supplements at the time of presentation compared to those in the low vitamin D group (p=0.01 and p=0.004, respectively). No statistically significant differences were observed between the two groups regarding early feeding practices, vitamin D supplementation during infancy, rotavirus vaccination status, or antibiotic use within the preceding month (Table 2).

Clinical indicators such as Vesikari score, degree of dehydration, need for intravenous hydration, and duration of diarrhea showed no meaningful differences between the two

Table 2. Demographic characteristics of the patients

	Serum 25-(OH) Vitamin D Level (ng/ml)						
	Total (n=70)		Low (<30) (n=55)		Normal (≥30) (n=15)		p
	n	%	n	%	n	%	
Sex, male[a]	28	40	21	38.2	7	46.7	0.552
Age, months[b]	20.5	18	23	16	11.5	17	0.010*
Age groups, months[a]							
<24	38	54.3	27	49.1	11	73.3	0.095
≥24	32	45.7	28	49.1	4	26.7	
Breastfeeding only in the first 6 months[a]	43	61.4	35	63.6	8	53.3	0.467
Vitamin D prophylaxis in the first 6 months[a]	54	77.1	43	78.2	11	73.3	0.692
Current vitamin D usage[a]	24	34.3	14	25.5	10	66.7	0.004**
Rotavirus vaccination[a]	7	10	6	10.9	1	6.7	0.627
Antibiotic usage in the last month[a]	27	38.6	23	41.8	4	26.7	0.285

[a]: Number (%); [b]: Median (interquartile range). *: p<0.05; **: p<0.01

Table 3. Comparison of vitamin D level with disease severity and course

	Serum 25-(OH) Vitamin D Level (ng/ml)						
	Total (n=70)		Low (<30) (n=55)		Normal (≥30) (n=15)		p
	n	%	n	%	n	%	
Severity of dehydration[a]							
Mild	18	25.7	13	23.6	5	33.3	0.408
Moderate	47	67.2	37	67.3	10	66.7	
Severe	5	7.1	5	9.1	0	0	
Vesikari score[a]							
<11	10	14.3	8	14.5	2	13.3	0.905
≥11	60	85.7	47	85.5	13	86.7	
IV fluid therapy[a]	40	57.1	32	58.2	8	53.3	0.737
Hospitalization[a]	38	54.3	34	61.8	4	26.7	0.015*
Duration of hospitalization, days[b] (n=38)	4.37±1.72		4.62±1.67		2.75±0.96		0.004*
Duration of diarrhea, days[b]	5	3.3	5	3	5	4	0.578

[a]: Number (%); [b]: Median (interquartile range). *: p<0.05. IV: Intravenous.

groups. However, hospitalization was significantly more frequent among patients with low vitamin D levels (p=0.015). In the subgroup of hospitalized patients, the average length of hospital stay was notably longer in the low vitamin D group compared to those with normal levels (4.62±1.67 days vs. 2.75±0.96 days, p=0.004) (Table 3).

According to multivariate logistic regression analysis, serum 25(OH)D3 levels below 30 ng/mL independently increased the likelihood of hospitalization by nearly sixfold in children with rotavirus gastroenteritis (p=0.016) (Table 4). Additionally, multivariate linear regression revealed that low vitamin D was a significant predictor of extended hospital stay

Table 4. Logistic regression analysis of the risk factors for hospitalization

	Univariate logistic regression			Multivariate logistic regression		
Parameter	**OR**	**95% CI**	**p**	**OR**	**95% CI**	**p**
Age	0.78	0.78–1.22	0.887	1.0	0.96–1.04	0.942
Sex	1.33	0.51–3.48	0.557	1.51	0.52–4.44	0.450
Breastfeeding only in the first 6 months	0.56	0.21–1.50	0.248	0.44	1.36–1.43	0.172
Vitamin D level <30 ng/ml	4.45	1.25–15.80	0.015*	5.69	1.39–23.31	0.016*
Antibiotic usage in the last month	1.78	0.67–4.76	0.248	1.04	0.33–3.30	0.944
Rotavirus vaccination	3.33	0.60–18.50	0.150	3.44	0.53–22.50	0.197

*: p<0.05. OR: Odds ratio; CI: Confidence interval

Table 5. Multivariate linear regression analysis of the factors affecting hospitalization length

Parameter	**Non-standardized coefficients B**	**Standardized coefficients SE**	**Beta (β)**	**t**	**p**
Age	0.003	0.021	0.02	0.161	0.873
Sex	0.476	0.582	0.093	0.817	0.417
Breastfeeding only in the first 6 months	-1.332	0.617	-0.259	-2.159	0.035*
Vitamin D level <30 ng/ml	2.226	0.722	0.364	3.083	0.003**
Antibiotic usage in the last month	0.941	0.63	0.097	0.797	0.429
Rotavirus vaccination	-0.905	0.932	-0.108	-0.922	0.36

Constant=0.494, F=3.097, R=4.477, R^2=0.228. *: p<0.05; **: p<0.01. SE: Standart error

Table 6. Multivariate linear regression analysis of the factors affecting diarrhea duration

Parameter	**Non-standardized coefficients B**	**Standardized coefficients SE**	**Beta (β)**	**t**	**p**
Age	-0.039	0.024	-0.208	-1.621	0.110
Sex	0.017	0.661	0.003	0.026	0.980
Breastfeeding only in the first 6 months	-1.615	0.700	-0.286	-2.306	0.024*
Vitamin D level <30 ng/ml	0.614	0.819	0.092	0.749	0.457
Antibiotic usage in the last month	-0.527	0.715	-0.094	-0.737	0.464
Rotavirus vaccination	-1.216	1.115	-0.133	-1.091	0.279

Constant=7.079, F=2.141, R=0.412, R^2=0.169. *: p<0.05. SE: Standart error

(p=0.003), while exclusive breastfeeding during the first six months of life was associated with a reduced length of stay (p=0.035) (Table 5). Exclusive breastfeeding was also significantly correlated with shorter diarrhea duration (p=0.024), whereas no direct relationship was identified between serum 25(OH)D3 levels and diarrhea duration (Table 6).

DISCUSSION

Rotavirus is a major cause of acute gastroenteritis in preschool children, leading to about 200,000 deaths annually worldwide.[19] Vitamin D insufficiency is a significant public health issue, affecting 30–80% of the global population.[20,21] A study conducted in Ankara, Turkey, found that 40% of 440

healthy children under 17 years had vitamin D deficiency or insufficiency.[22] Similar findings have been reported in various provinces across Türkiye.[23,24] In this study, we found that approximately two-thirds of the patients with rotavirus gastroenteritis had low vitamin D. None of these patients exhibited clinical signs or symptoms of rickets. We observed that the rate of vitamin D deficiency was significantly lower in patients who were currently using vitamin D. This underscores the importance of regular vitamin D supplementation in childhood to prevent vitamin D deficiency, a common public health problem.

Recent studies have shown that low vitamin D levels are associated with a higher risk of both the frequency and severity of infectious diseases, including upper and lower respiratory tract infections, tuberculosis, and viral illnesses. These deficiencies may contribute to a more severe disease course and increased mortality rates.[25–28] In a study by Abed et al.,[29] serum vitamin D levels were compared between 60 children aged 4–12 years with recurrent acute diarrhea and 20 healthy controls. The results showed that 78% of the children with diarrhea had either vitamin D deficiency or insufficiency, a rate significantly higher than that of the healthy controls. Children with vitamin D deficiency were also more likely to have recurrent episodes of diarrhea and Giardia lamblia infections. In a similar study, Thornton et al.[30] observed that vitamin D deficiency was associated with higher rates of vomiting and diarrhea among 475 pediatric patients diagnosed with gastroenteritis and otitis. Moreover, deficient patients were found to have a twofold increased risk of hospitalization for these symptoms within one year. Bener et al.[31] also found that vitamin D deficiency raised the incidence of gastroenteritis in 458 Qatari children under 16 years. In a study conducted by Bucak et al.[32] from Türkiye, serum 25(OH)D3 was compared between hospitalized patients with rotavirus gastroenteritis and healthy controls. They found serum 25(OH)D3 in the rotaviral diarrhea patients was significantly lower than in healthy controls. The authors argued that low vitamin D could be a potential risk factor for rotaviral diarrhea in children under five years. In another study conducted in 2022, Başaran and colleagues determined that serum 25(OH)D3, ferritin, and vitamin B12 levels were lower in individuals with rotavirus infection.[33]

Our study findings revealed that low vitamin D levels serve as an independent risk factor, increasing the likelihood of hospitalization by approximately six times in preschool children with acute rotavirus gastroenteritis. Furthermore, low vitamin D was identified as a prognostic factor associated with an average increase of 1.9 days in the duration of hospital stay. However, no significant differences in Vesikari scores, intravenous fluid needs, or diarrhea duration were observed between those with normal and low vitamin D levels. All patients with normal vitamin D experienced mild to moderate dehydration, while all with severe dehydration had low vitamin D, though this was not statistically significant—most probably due to the small sample size. Although low vitamin D levels did not directly affect disease severity, it might contribute to increased hospital admission rates and prolonged hospitalization through its effects on regulating the gastrointestinal system. It was thought that low vitamin D may lead to secondary impacts, such as loss of appetite and decreased tolerance to oral intake, which could influence the clinical outcomes. Based on this, appropriate vitamin D levels may potentially increase the success of oral rehydration therapy and oral intake in children with rotavirus-associated diarrhea. Consequently, we argued that the potential anti-rotavirus and anti-inflammatory activity of vitamin D on the intestinal system may have a protective effect on the course of the disease by reducing hospitalization rates and shortening the recovery time.

The knowledge regarding the effect of vitamin D on the severity and prognosis of various infectious diseases is limited and conflicting. Two studies found an association between low vitamin D levels and longer stays in pediatric intensive care in critically ill children.[34,35] Erol et al.[36] reported that vitamin D deficiency (<20 ng/mL) increased the severity of bronchiolitis and the risk of hospitalization but did not affect the length of stay. A recent meta-analysis found that high-dose vitamin D supplementation in preschool-aged children did not significantly reduce the incidence of bronchiolitis, croup, bronchitis, otitis media, or diarrhea/gastroenteritis when compared to standard doses. Additionally, it showed no significant impact on hospital admission rates, the number of primary care visits, antibiotic use frequency, or all-cause and cause-specific mortality.[37] A prospective study by Rahmati et al.[38] found that a single dose of 100,000 IU vitamin D significantly reduced the length of hospital stay in children aged 3 to 14 years hospitalized with acute gastroenteritis compared to those given a placebo. However, they reported no association between baseline vitamin D levels and hospital stay duration. Similarly, a meta-analysis showed that children under 18 with vitamin D deficiency experienced more frequent and prolonged episodes of diarrhea caused by various pathogens.[33] To the best of our knowledge, this

is the first study to focus exclusively on preschool-aged children with rotavirus gastroenteritis, identifying low vitamin D levels as a modifiable factor associated with worse clinical outcomes. These findings support the need for larger, well-controlled clinical trials to further investigate the role of vitamin D in pediatric gastroenteritis.

An additional strength of our study is the identification of exclusive breastfeeding in the first six months of life as a protective factor. We found that breastfeeding was associated with shorter durations of both diarrhea and hospital stay. This aligns with prior research demonstrating the protective effects of breastfeeding against infectious diseases. For example, a multicenter study indicated that breastfeeding reduced the risk of diarrhea and improved survival in children under two years,[39] while Wayse et al.[27] found that exclusive breastfeeding lowered the incidence of lower respiratory infections. Our data support these findings and emphasize the importance of promoting exclusive breastfeeding during early infancy to improve outcomes in children with rotavirus infection.

The findings of this study indicate that suboptimal vitamin D levels—specifically serum 25(OH)D3 concentrations below 30 ng/mL—are associated with a significantly increased risk of hospitalization and extended hospital stays in preschool-aged children affected by rotavirus gastroenteritis. Although no significant differences were observed in disease severity scores or the duration of diarrhea, low vitamin D status emerged as a predictive factor for adverse clinical outcomes, potentially due to its immunological and mucosal effects on the gastrointestinal system.

In addition, exclusive breastfeeding during the first six months of life was shown to have a protective role, contributing to shorter durations of both diarrhea and hospitalization. These findings highlight the importance of two key preventive strategies: maintaining adequate vitamin D levels through regular supplementation and promoting exclusive breastfeeding in early infancy.

Limitations

Our study is limited by its single-center design and relatively small sample size, which may restrict the generalizability of the findings and reduce statistical power for detecting certain associations, as well as the lack of evaluation of seasonal variations in sun exposure, nutritional and socioeconomic factors that may influence vitamin D status and could have provided further insights into the underlying mechanisms of vitamin D deficiency in our patient population.

CONCLUSION

These findings have significant clinical implications, as vitamin D deficiency represents a modifiable risk factor that can be addressed through targeted supplementation programs in pediatric populations. Since low vitamin D levels were associated with increased hospitalization rates and prolonged hospital stays, routine vitamin D screening and supplementation, combined with promoting exclusive breastfeeding in early infancy, may serve as cost-effective interventions to reduce healthcare burden and improve patient outcomes in rotavirus gastroenteritis.

We recommend that public health policies should prioritize vitamin D supplementation programs for preschool children, particularly during seasons with limited sun exposure. In clinical practice, pediatricians should consider routine vitamin D status assessment in children presenting with gastroenteritis and implement early supplementation strategies as part of comprehensive care.

Further large-scale, multicenter studies are warranted to confirm these associations and inform evidence-based public health policies for pediatric infectious disease management.

Disclosures

Ethics Committee Approval: The study was approved by the Medeniyet University Goztepe Training and Research Hospital Clinical Research Ethics Committee (No: 2018/0302, Date: 15/08/2018).

Informed Consent: Informed consent was obtained from all participants.

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