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Original Article

Retrospective cross-sectional analysis of Vitamin D deficiency in pediatric patients: Clinical findings from a tertiary care center

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ABSTRACT

Objective: The 25-Hydroxyvitamin D (25(OH)D) deficiency is a prevalent global health concern, particularly among children, leading to conditions such as rickets and increasing the risk of respiratory infections and chronic diseases. Contributing factors include limited sun exposure, poor dietary intake, and growth demands. This study aimed to assess the clinical and laboratory characteristics of pediatric paients with 25-Hydroxyvitamin D (25(OH)D) deficiency at our clinic.

Material and Methods: This retrospective study was conducted at a tertiary care center in İstanbul, Türkiye, including pediatric patients diagnosed with 25-Hydroxyvitamin D (25(OH)D) deficiency between January 2020 and December 2023. Data on sociodemographic, medical history, symptoms, physical examinations, and laboratory results were extracted from electronic medical records. Patients with 25-Hydroxyvitamin D levels below 20 ng/mL were classified as deficient. Correlation analyses were employed to assess the associations between 25-Hydroxyvitamin D (25(OH)D) levels and clinical factors. The study was approved by the Istanbul Medipol University Ethical Review Board.

Results: A total of 5229 pediatric patients with 25-Hydroxyvitamin D (25(OH)D) deficiency or insufficiency were included in the study, with a slight female predominance (51%). The highest frequency of deficiency was observed among children aged 2 to 3 years. Symptom-onset complaint records were retrospectively reviewed. The most commonly documented complaints at presentation were fatigue (30.75%), followed by non-specific or asymptomatic presentations (28.95%). Given the retrospective design of the study, these symptoms may not be specific to 25-Hydroxyvitamin D (25(OH)D) deficiency and could be attributable to other concurrent conditions. Notably, in several cases, 25-Hydroxyvitamin D (25(OH)D) deficiency was detected incidentally during medical evaluations performed for unrelated reasons.

Conclusion: 25-Hydroxyvitamin D (25(OH)D) deficiency is a common condition in childhood and may present with a wide range of symptoms or remain asymptomatic. Early detection is crucial, particularly in at-risk groups such as toddlers and children with limited sun exposure. Clinicians should be aware of the non-specific nature of symptoms and consider 25-Hydroxyvitamin D (25(OH)D) status in routine pediatric evaluations. Broader awareness and preventive strategies are needed to reduce the clinical burden of this silent but prevalent deficiency.

Keywords: Asymptomatic presentation, pediatrics, primary health care, vitamin d deficiency

INTRODUCTION

The 25-Hydroxyvitamin D (25(OH)D) deficiency represents a significant global health concern, particularly among children, with notable clinical implications. In response to this growing issue, the Turkish Ministry of Health launched a "25-Hydroxyvitamin D (25(OH)D) Deficiency Prevention and Protection Program" in 2005 to prevent and control deficiency nationwide (1). Despite these efforts, 25-Hydroxyvitamin D (25(OH)D) deficiency remains a significant pediatric health problem in Türkiye, as shown in recent regional studies (2).

Clinically, 25-Hydroxyvitamin D (25(OH)D) deficiency is most notably associated with rickets, a disease marked by bone softening, skeletal deformities, delayed growth, and in severe cases, hypocalcemic seizures (3). Beyond skeletal health, emerging evidence suggests links between inadequate 25-Hydroxyvitamin D (25(OH)D) levels and mental health issues, immune-related disorders, and other chronic conditions (4). Recent findings also link deficiency to non-specific symptoms, such as fatigue and muscle weakness, which are often overlooked in clinical settings (5).

Children are particularly vulnerable due to several risk factors. Limited sun exposure (often influenced by seasonal changes,

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clothing habits, and urban indoor lifestyles) restricts natural 25-Hydroxyvitamin D (25(OH)D) synthesis, which is triggered by skin exposure to ultraviolet B (UVB) rays (3,4). In addition to frequently insufficient dietary intake, the increased physiological demand during growth further compounds the risk, as adequate 25-Hydroxyvitamin D (25(OH)D) levels are essential for bone development and overall health (6,7).

Considering the critical importance of 25-Hydroxyvitamin D (25(OH)D) in children, the associated health risks, and the ongoing national efforts, our study aimed to evaluate the clinical and laboratory characteristics of children diagnosed with 25-Hydroxyvitamin D (25(OH)D) deficiency at our clinic.

MATERIALS and METHODS

Study Design

This retrospective cross-sectional study was conducted at İstanbul Medipol University Mega Hospital in İstanbul, Türkiye. Patients who were diagnosed with 25-Hydroxyvitamin D (25(OH)D) deficiency in the pediatric clinic between January 1, 2020, and December 31, 2023, were included in the study. The epicrisis forms and laboratory records of the patients were retrospectively reviewed through electronic records. The data collected included sociodemographic information, patients' medical history, presenting symptoms, physical examination findings, and laboratory test results. These data were recorded in an Excel data form.

Data Collection and Patient Selection

Patients were included in the study if they had a confirmed diagnosis of 25-Hydroxyvitamin D (25(OH)D) deficiency or insufficiency, as defined by serum 25-Hydroxyvitamin D (25(OH)D) levels below 20 ng/mL for deficiency and between 21–30 ng/mL for insufficiency. In order to be included in the study, participants were required to have complete medical records, which should encompass demographic, clinical, and laboratory data.

Data were extracted from the electronic medical records at İstanbul Medipol University Mega Hospital by trained research staff. Collected data included demographic information such as age and gender, relevant medical history (including dietary intake and sun exposure), and comprehensive laboratory results. Although data on relevant medical history were collected from the medical records, these variables were inconsistently recorded across the patient population. Due to the limited availability and incomplete nature of these entries, a comprehensive correlation analysis could not be performed. Therefore, these factors were not included in the final statistical analysis, as their incorporation could have introduced bias or misinterpretation.

The laboratory results encompassed serum 25-Hydroxyvitamin D levels and various hematological parameters. Specifically, the hematological parameters included hemoglobin (Hb), hematocrit (Hct), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width – standard deviation (RDW-SD), red cell distribution width – coefficient of variation (RDW-CV), white blood cell count (WBC), platelet count (PLT), differential counts (lymphocytes, neutrophils, monocytes, eosinophils, and basophils), plateletcrit (PCT), platelet distribution width (PDW), immature granulocytes (IG#), immature granulocytes percentage (IG%), platelet large cell ratio (P-LCR), nucleated red blood cell count (NRBC#), nucleated red blood cell percentage (NRBC%), and mean platelet volume (MPV). Records with missing key data, such as serum 25-Hydroxyvitamin D (25(OH)D) levels or critical hematological parameters, were excluded from the analysis to maintain data integrity and avoid bias. No data imputation was performed.

Clinical symptoms were recorded systematically during the initial clinical visits, prior to the confirmation of 25-Hydroxy25-Hydroxyvitamin D (25(OH)D) status. However, due to the retrospective design, these presenting complaints cannot be considered specific to 25-Hydroxyvitamin D (25(OH)D) deficiency and may also be attributable to other concurrent conditions. Therefore, the documentation of symptoms in this study should be interpreted as presenting complaints rather than definitive clinical manifestations of 25-Hydroxyvitamin D (25(OH)D) deficiency.

Statistical Analysis

Descriptive statistics were employed to summarize the demographic and clinical characteristics of the study population. Continuous variables, such as age and laboratory values, were reported as either means with standard deviations (SD) or medians with interquartile ranges (IQR), depending on the distribution of the data. Categorical variables, including gender, comorbidities, and treatment outcomes, were expressed as frequencies and percentages.

Correlation analyses were conducted to investigate the potential relationships between 25-Hydroxyvitamin D (25(OH)D) levels and other hematologic parameters. Pearson's correlation coefficients were calculated based on the distribution of the data.

The significance level was set at $p<0.050$ for all tests. All statistical analyses were performed using the software package SPSS version 25.0.

RESULTS

A total of 5229 cases diagnosed with 25-Hydroxyvitamin D (25(OH)D) deficiency or insufficiency were included in the study. Of the total number of cases, 2561 (49.0%) were male and 2668 (51.0%) were female, indicating a slight predominance of 25-Hydroxyvitamin D (25(OH)D)-related issues in femaleswithin

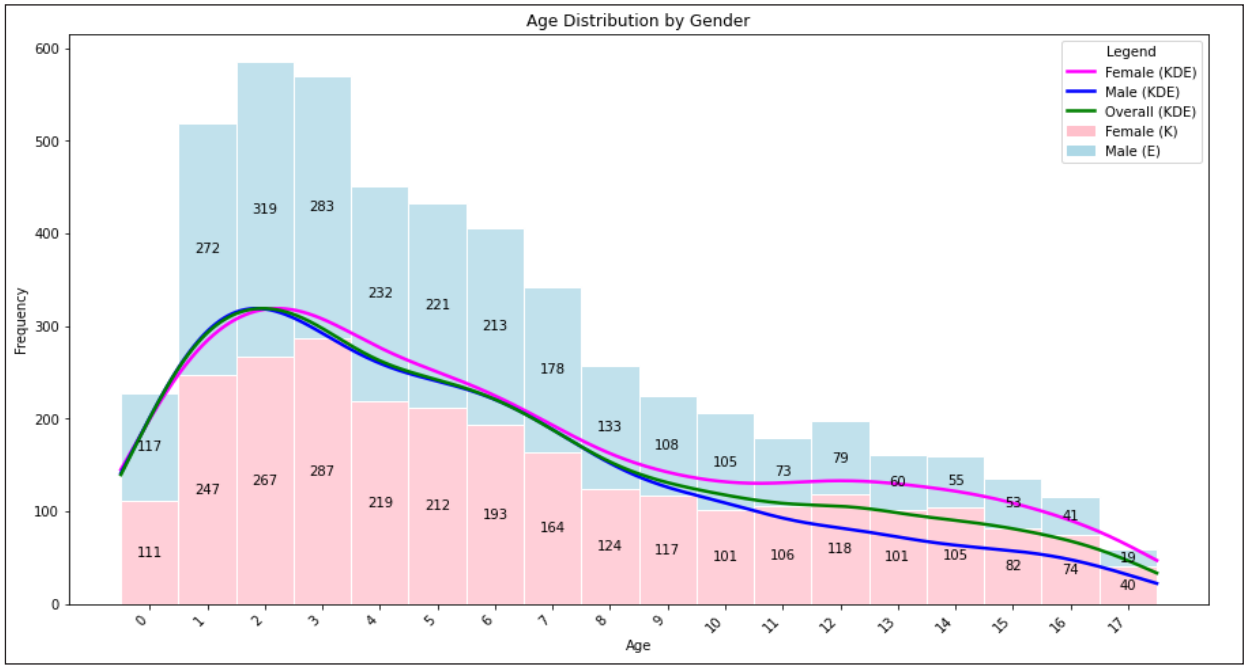

Figure 1: 25-Hydroxyvitamin D (25(OH)D) Level Gender Distribution Across Different Age Group

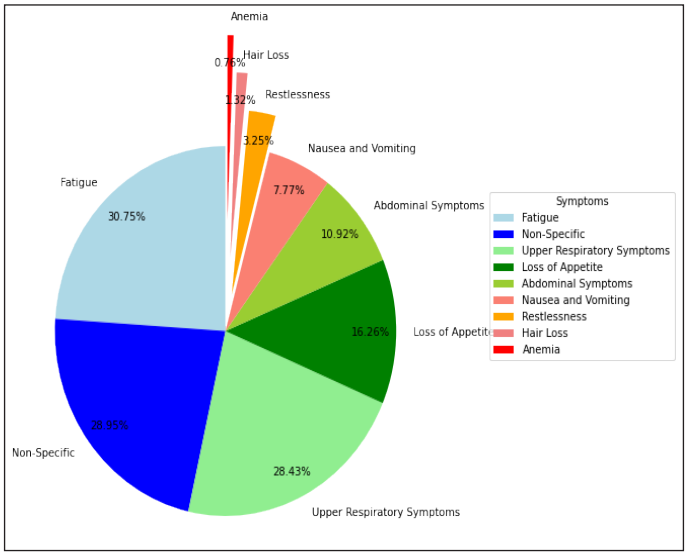

Figure 2: Symptom Distribution in Pediatric Patients with 25-Hydroxyvitamin D (25(OH)D) Deficiency or Insufficiency

the study population. The analysis of age-related data revealed a notable concentration of 25-Hydroxyvitamin D (25(OH)D) deficiency and insufficiencies in early childhood. The highest prevalence was observed in children aged 2 and 3 years, comprising 11.21% and 10.90% of the cohort, respectively. The gender distribution across different age groups demonstrated that both genders were similarly affected by 25-Hydroxyvitamin D (25(OH)D) challenges. The detailed age and gender breakdown is provided in Figure 1, which elucidates the distribution patterns across the cohort.

The records related to patients' presenting complaints documented at the time of the initial visit were examined. These complaints represent symptoms recorded during presentation and cannot be considered specific clinical findings of 25-Hydroxyvitamin D (25(OH)D) deficiency. The most frequently reported complaint was fatigue, observed in 30.75% of cases, while non-specific or asymptomatic presentations were noted in 28.95%. The distribution of presenting complaints is illustrated in Figure 2. Upper respiratory tract–related complaints, including cough, sore throat, and rhinorrhea, were reported by 1,487 children (28.43%). Loss of appetite was documented in 850 children (16.26%). Abdominal complaints, encompassing abdominal pain, diarrhea, and constipation, were reported by 571 children (10.92%). Nausea and vomiting were noted in 406 children (7.77%). Restlessness, including irritability, severe crying, and sleeplessness, was documented in 170 children (3.25%). Hair loss was recorded in 69 children (1.32%). Anemia was the least frequently noted complaint, affecting 40 children (0.76%). A total of 1.514 children (28.95%) did not present with any of the listed complaints.

In this study, we conducted a Pearson correlation analysis to investigate the relationships between 25-Hydroxyvitamin D levels and various hematological parameters. Our analysis revealed several statistically significant correlations; however, the strength of these associations was generally weak.

The correlation analysis showed a weak positive correlation between 25-Hydroxyvitamin D and both lymphocyte count ($r=0.229$, $p<0.001$) and lymphocyte percentage ($r=0.211$, $p<0.001$). Also, there is weak negative correlation between neutrophil percentage and 25-Hydroxyvitamin D ($r=-0.203$, $p<0.001$). Weak negative correlations between 25-Hydroxyvitamin D and both hematocrit ($r=-0.169$, $p<0.001$) and hemoglobin ($r=-0.140$, $p<0.001$).

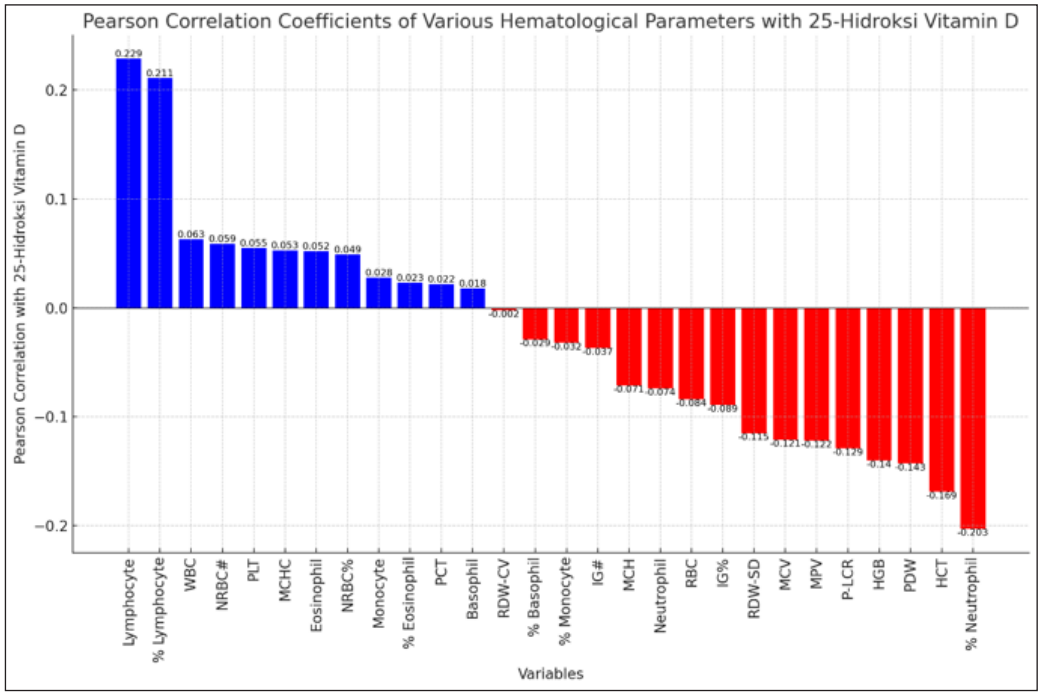

Figure 3: Pearson Correlation Coefficients of Various Hematological Parameters with 25- Hydroxyvitamin D

DISCUSSION

25-Hydroxyvitamin D (25(OH)D) deficiency in children remains a significant global and national public health concern. Our study, which includes one of the largest recent pediatric cohorts from Turkey, provides valuable insights into the prevalence of deficiency, the distribution of presenting complaints, and hematological correlations.

In this study, the prevalence of 25(OH)D deficiency was highest among children aged 2–3 years. This age range represents a critical developmental period characterized by rapid skeletal growth and immune maturation. The relatively lower prevalence observed in infants under one year of age may reflect the effectiveness of the Turkish Ministry of Health's free 25(OH)D supplementation program, which aims to prevent rickets and related complications during early infancy (1).

With respect to clinical presentation, fatigue was the most frequently documented complaint. Fatigue and muscle weakness have often been described in the literature as possible manifestations of 25(OH)D deficiency, given its role in muscle metabolism and energy regulation (5,7). Research has also linked 25(OH)D deficiency with chronic fatigue syndrome, suggesting that adequate levels are important for maintaining energy balance and overall vitality (8,9). Nevertheless, due to the retrospective design of our study, these findings should be interpreted with caution, as non-specific symptoms such as fatigue may also arise from a variety of infectious or non-infectious causes. Therefore, the observed complaints should be considered as presenting symptoms rather than definitive clinical manifestations of 25(OH)D deficiency.

Upper respiratory complaints, including cough, rhinorrhea, and sore throat, were the second most frequently recorded. Previous studies have suggested that 25(OH)D contributes to immune regulation and may play a protective role against respiratory infections (10). Research has shown that supplementation can reduce the incidence of respiratory infections (11,12) and enhance the expression of antimicrobial peptides in the respiratory epithelium, thereby strengthening the first line of defense against pathogens (13,14). However, in our cohort it was not possible to determine whether 25(OH)D testing was requested as part of the evaluation for acute respiratory illness or as a routine laboratory investigation. Given the retrospective nature of the study, these findings should be interpreted with caution and not considered direct evidence of causality. Nevertheless, previous research supports a potential link between low 25(OH)D status and impaired immune defense mechanisms, which may increase susceptibility to respiratory tract infections.

Loss of appetite was another significant complaint. The association between 25(OH)D deficiency and reduced appetite has been documented in previous studies, with suggested mechanisms including effects on leptin and other appetite-regulating hormones (15), as well as disruption of the hypothalamic-pituitary-adrenal (HPA) axis that may influence appetite and food intake (16).

Gastrointestinal complaints such as abdominal pain, diarrhea, and constipation were also commonly reported, representing the third most frequent group of complaints in our study. Previous research has suggested a possible association between

25(OH)D deficiency and gastrointestinal health, particularly through its effects on calcium absorption and maintenance of gut homeostasis (17,18). Studies have further indicated that deficiency may exacerbate gastrointestinal disorders such as irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD), leading to symptoms like abdominal pain and altered bowel habits (19,20). Moreover, 25(OH)D contributes to gut mucosal integrity and regulation of the gut microbiome, underscoring its potential role in gastrointestinal function (21). However, due to the retrospective design of this study, it is not possible to determine whether these complaints were primarily related to 25(OH)D deficiency or whether 25(OH)D levels were measured as part of an additional work-up in children presenting with other complaints. Therefore, the observed association between gastrointestinal complaints and 25(OH)D deficiency should be interpreted cautiously, considering the methodological limitations.

Interestingly, nearly one-fourth of the children in our study did not present with any of the listed complaints, underscoring that 25(OH)D deficiency can be asymptomatic or manifest only through subtle, non-specific findings. In such cases, serum 25(OH)D levels were often measured during routine check-ups, upon parental request, or as part of broader diagnostic evaluations. Although routine 25(OH)D testing is not generally recommended in healthy children, it can be justified in specific clinical contexts. According to the Turkish Ministry of Health's Vitamin D Deficiency Prevention and Protection Program, measurement of serum 25(OH)D is advised only for children at risk—such as those showing signs of rickets, with chronic conditions affecting absorption (e.g., celiac disease, cystic fibrosis), long-term use of corticosteroids or antiepileptic drugs, or limited sun exposure due to neurological or cultural reasons (1). However, given the retrospective nature of our study, detailed clinical justifications were not consistently documented, making it difficult to determine the exact indication for testing in asymptomatic cases.

In terms of hematological findings, we observed several statistically significant but weak correlations between serum 25(OH)D levels and hematological parameters, most notably a positive correlation with lymphocyte counts and percentages and a negative correlation with neutrophil percentages. These findings are consistent with previous reports, including the study by Konuksever et al. (22), which demonstrated a significant negative correlation between 25(OH)D levels and the neutrophil-to-lymphocyte ratio (NLR). While our study supports the presence of certain associations, the strength of these correlations was modest, and several expected associations were not observed.

Overall, our findings indicate that 25(OH)D deficiency in childhood is not limited to a specific clinical presentation but may manifest through a wide spectrum of complaints—or remain entirely asymptomatic, being detected only through incidental or routine evaluations. Given these findings, targeted testing of at-risk pediatric populations is essential for timely detection and prevention. Furthermore, healthcare professionals should play an active role in educating families about the importance of adequate sun exposure, appropriate supplementation, and balanced nutrition. To clarify the causal pathways between 25(OH)D status, symptomatology, and hematological outcomes, further prospective, multicenter studies with larger sample sizes and standardized clinical documentation are warranted.

CONCLUSION

This study demonstrates that 25-Hydroxyvitamin D (25(OH)D) deficiency is a frequently encountered condition in childhood and may often be identified incidentally during medical evaluations for unrelated complaints. It may present with non-specific symptoms or remain entirely asymptomatic. Due to the retrospective design of the study, establishing a direct causal relationship between 25(OH)D deficiency and accompanying symptoms was not possible. Nevertheless, the findings are noteworthy in highlighting the overall frequency and potential clinical relevance of the condition. Regular assessment of 25(OH)D levels in at-risk children is important for preventive healthcare. Healthcare providers should also play an active role in educating families about the importance of adequate sun exposure, appropriate 25(OH)D supplementation, and a balanced diet. Further large-scale, multicenter studies are warranted to better clarify the underlying causes and broader impact of 25(OH)D deficiency in pediatric populations.

Limitations

This study has several limitations, primarily related to its retrospective design. Clinical records frequently lacked detailed documentation regarding the onset, duration, and clinical context of symptoms, which limited the ability to establish direct causal relationships between 25-Hydroxyvitamin D (25(OH)D) deficiency and the reported complaints. In some cases, 25(OH)D levels may have been measured as part of broader diagnostic workups unrelated to the presenting symptoms. Furthermore, the absence of standardized symptom classification and potential variability in physician documentation may have influenced the accuracy of symptom frequency data. Despite these limitations, the study provides valuable insights into the prevalence, clinical presentations, and hematological correlations of 25(OH)D deficiency in pediatric patients.

Ethics committee approval

This study was conducted in accordance with the Helsinki Declaration Principles. The Istanbul Medipol University Non-Interventional Clinical Research Review Board granted ethical approval for this study (date: 12/07/2023; number: 1009).

Contribution of the authors

Study conception and design: **GM, SN**; data collection: GM; analysis and interpretation of results: **GM,ÖN,SN**; draft

manuscript preparation: **GM,ÖN,SN**. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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