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Prevalence of vitamin D deficiency in children with hemato-oncological diseases at a tertiary hospital in Buenos Aires

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ABSTRACT

Hypovitaminosis D (HD) is a relevant deficit. This vitamin has implications in bone health, as well as immunological and metabolic functions, and in the pathophysiology of cancer. Pediatric oncology patients are at increased risk for this deficiency.

A cross-sectional, retrospective study was conducted to determine the prevalence of HD in pediatric oncology patients in a high-complexity hospital between January 2019 and August 2023. Eighty-nine patients were included. The overall median vitamin D levels were 18.3 ng/mL (IQR: 11.1-26.7). The prevalence of HD was 52.8% (95%CI: 41.9-63.5). These results indicate that, in this sample, more than half of pediatric oncology patients present HD.

We emphasize the importance of determining the levels of this vitamin at diagnosis and during treatment of the disease in this highly vulnerable group.

Keywords: *vitamin D; vitamin D deficiency; pediatrics; oncology; neoplasms.*

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INTRODUCTION

Vitamin D is primarily related to bone metabolism.[1,2] Its receptor is present in multiple tissues; thus, it has both immunological and metabolic functions and plays a role in the pathophysiology of cancer.[3-5]

The primary biochemical forms are cholecalciferol and ergocalciferol, which are produced through cutaneous synthesis via solar exposure and dietary intake.[1] In the liver, both forms are hydroxylated to originate 25-hydroxyvitamin D -also known as 25-hydroxycholecalciferol or 25(OH)D-, the primary circulating metabolite. Subsequently, at the renal level, this form undergoes a second hydroxylation, resulting in 1,25-dihydroxyvitamin D (calcitriol), the active form of vitamin D.[6] In clinical practice, the serum concentration of 25-hydroxyvitamin (25[OH]D) is used to assess sufficiency status.[1]

Hypovitaminosis D (HD) is a common deficit worldwide.[2] It is estimated that one in seven people (14%) presents with HD.[1,7,8] The United States reported a prevalence of HD in the general pediatric population of 15%[7,8] and in pediatric oncology patients between 65%[3] and 72%.[4] In India, a prevalence of 80% was found.[9] In Argentina, the prevalence of HD in the general population is 43%.[7]

A known risk factor is living in latitudes located between the 40° parallels (e.g., the province of Rio Negro in Argentina) and the corresponsing Poles, which implies poor exposure to solar radiation.[4]

HD has been associated with cardiovascular disease, risk of fractures, rickets, dyslipidemia, infections, and cognitive dysfunction, among others.[1,2]

Oncology patients are at increased risk for HD due to poor nutrition, low sun exposure, baseline disease, neoplastic infiltration, and adverse effects of treatment.[1,4,5,9] The prevalence of HD in pediatric oncology patients in our region is unknown.

Our primary objective was to determine the prevalence of vitamin D deficiency and insufficiency in pediatric oncology patients, and the secondary objective was to explore variables associated with these conditions.

POPULATION AND METHODS

A cross-sectional, descriptive study was conducted in a high-complexity hospital.

Data was collected retrospectively from the electronic medical record.

Patients under 18 years of age with a diagnosis of oncohematologic disease who had undergone part of their chemotherapy in the inpatient ward between January 1, 2019, and August 31, 2023, and had a vitamin D determination were included. Patients supplemented with vitamin D and/or renal, hepatic, or intestinal insufficiency were excluded.

Sex, age, tumor type (leukemias/lymphomas vs. solid tumors, including central nervous system tumors), date of disease diagnosis, date of first 25(OH)D determination (indicated according to medical criteria), season of year of measurement (winter/spring vs. summer/fall), place of origin (above or below the 40° parallel), determination of 25(OH)D, alkaline phosphatase and/or parathormone, vitamin D supplementation, and hospitalizations due to infectious causes. The recommendations of the Global Consensus on the Prevention and Management of Rickets,[10] were used to classify the determination of 25(OH) D: sufficiency (25[OH]D >20 ng/mL), insufficiency (between 12 and 20 ng/mL), and deficiency (<12 ng/mL).

Quantitative data were expressed as mean and standard deviation or median and interquartile range (IQR) 25-75. Qualitative data were expressed as absolute and relative frequencies (proportions). To compare continuous variables, we used the Wilcoxon test. For correlations between two continuous variables, the Spearman test was employed. The Cuzick trend test was used for associations between categorical variables with more than two categories.

Univariate analysis was performed to explore factors associated with HD. A *p*-value <0.05 was considered statistically significant. The study was performed with Stata 14.0™.

The study was approved by the Hospital Research Ethics Committee (protocol number #6655).

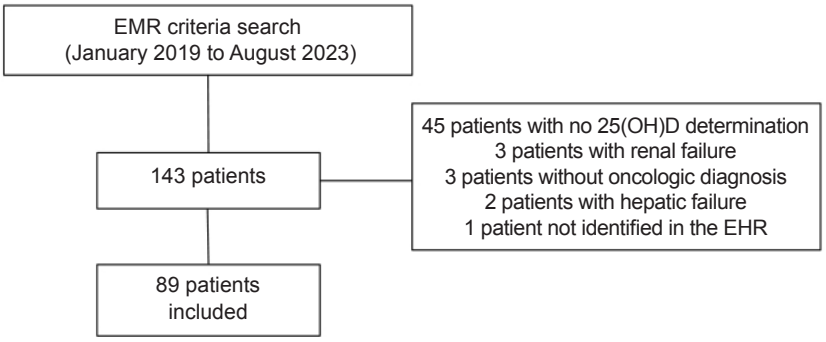
RESULTS

Eighty-nine pediatric oncology patients were included. *Figure 1* illustrates the study's flow chart, and *Table 1* presents the patient characteristics.

The overall median serum 25(OH)D level was 18.3 ng/mL (IQR: 11.1-26.7 ng/mL). The prevalence of HD (serum value less than 20 ng/mL) was 52.8% (95%CI: 41.9-63.5). *Table 2* summarizes the characteristics of patients based on their vitamin D levels.

The median time between the diagnosis of oncologic disease and the first 25(OH)D

Figure 1. Flowchart of patient selection for the study



EMR: electronic medical record; 25(OH)D: 25-hydroxyvitamin D.

Table 1. Characteristics of pediatric oncologic patients with vitamin D determination (n = 89)

Age, years (SD)	9.7 (4.68)
Male sex, n (%)	58 (65)
Tumor type	
-Leukemias/lymphomas, n (%)	56 (63)
-Solid and CNS tumors, n (%)	33 (37)
City of origin located above the 40° parallel, n (%)	83 (93)
Time elapsed between the cancer diagnosis and the first vitamin D determination, days (IQR)	189 (56-416)

SD: standard deviation; CNS: central nervous system; IQR: interquartile range.

Table 2. Epidemiological characteristics of pediatric oncology patients according to serum vitamin D determination

	25(OH)D value (n = 89)			
	<12 ng/mL (n = 24)	12-20 ng/mL (n = 23)	>20 ng/mL (n = 42)	*P*-value
Age, years (SD)	10.2 (4.5)	10.2 (4.7)	9.32 (4.7)	0.27[a]
Sex male, n (%)	17 (70.8)	16 (69.5)	25 (59.5)	0.311[b]
Tumor type				
- Leukemias/lymphomas, n (%	14 (58.3))	18 (78.3)	24 (57.1)	
- Solid and CNS tumors, n (%)	10 (41.7)	5 (21.7)	18 (42.9)	0.56[c]
ALP, UI/L (IQR)	104 (85-145)	80 (69-126)	132 (105-163)	0.0834[a]
PTH, pg/mL (IQR)	46.4 (35-90.7)	54.4 (37.8-77.3)	35.2 (22.7-50)	0.0078[a]

SD: standard deviation; CNS: central nervous system; IQR: interquartile range; PTH: parathormone; 25(OH)D: 25-hydroxyvitamin D; ALP: alkaline phosphatase.
[a]Spearman correlation test. [b]Nonparametric trend test (Kuzcik). [c]Wilcoxon test.

determination was 189 days (IQR: 56-416). A low inverse correlation (Spearman correlation coefficient of -0.22; $p = 0.0329$) was evident between the time elapsed from disease diagnosis to the first 25(OH)D determination, and their serum levels.

The results of 25(OH)D determination obtained during winter-spring (15.75 ng/mL, IQR: 9.5-24.3) were lower than those of summer-autumn (23.6 ng/mL, IQR: 16.1-29.4), with a statistically significant difference ($p = 0.006$).

No correlation was observed between 25(OH)D value and age (Spearman correlation coefficient of -0.11, $p = 0.27$) or with tumor type ($p = 0.56$).

In patients with vitamin deficiency, we observed a very low (Spearman correlation coefficient of -0.10; $p = 0.32$) and statistically nonsignificant inverse correlation between the number of febrile hospitalizations and 25(OH)D levels.

Regarding treatment, 46 (52%) patients did not receive supplementation, 31 patients (35%) received daily supplementation, and 12 patients (13%) received weekly supplementation.

DISCUSSION

We documented the prevalence of HD of 52.8% in pediatric oncology patients, with a median 25(OH)D of 18.3 ng/mL.

As with all retrospective research, it has limitations. Not all patients undergoing oncologic treatment had their vitamin D levels determined. The decision to measure it is unlikely to have been a random phenomenon, since it is likely that the subgroup with determined vitamin D is composed of a subpopulation with greater severity, vulnerability, etc. Because of the retrospective nature of the investigation, we were unable to obtain reliable data on dietary patterns, physical activity, and hours of sun exposure. Furthermore, given the homogeneity of the geographical origin, we could not explore the possible influence of latitude on the measurements.

Data on the prevalence of HD in the pediatric oncology population are inconclusive. A study in India[11] that included children with a history or recent oncologic diagnosis of less than two years of age showed a prevalence of HD of 80%, higher than the one we found (52.8%). Others recorded variable prevalences: 13% in Finland[12] (a country where it has been supplemented since 1940), 21% in England,[13] 33% in the USA (California),[3] and 63% in Turkey.[14] However, there is no standardized value for the childhood oncology population to define deficiency and insufficiency, making comparison difficult.

Sun exposure is involved in the metabolism of this vitamin, and both latitude and season could influence its levels. We documented a statistically significant association between 25(OH)D levels and the season of the year in which they were determined. These findings are consistent with those of Bahar Genc et al.

It could also affect the levels of 25(OH)D, as well as the time elapsed from diagnosis of an oncohematologic disease to the first determination. Although reports have documented HD in patients with a recent diagnosis of untreated oncologic disease, such as the 72% reported in Richmond (USA),[4] we inferred that the longer the time elapsed from diagnosis to the first determination, the higher the prevalence of HD could be. Our results were consistent with this hypothesis. We emphasize that the time from diagnosis of the disease to the first measurement in our study was shorter (189 days; IQR: 56-416) than that reported in England (693 days).[13]

Our study is the first to document the prevalence of HD in the pediatric oncology population at a South American facility, which was high in our institution.

CONCLUSION

Our results show that vitamin D deficiency and insufficiency affected 52.8% of the pediatric oncology patients included in this study. Measurement during sunny months was associated with higher levels of vitamin D. We emphasize the importance of determining levels at diagnosis and during follow-up treatment in this highly vulnerable group. ■

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