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Original Article (Pages: 19152-19157)

Exploring the Correlation between Serum Vitamin D Levels and Cancer Stage and Grading in Pediatric Patients

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Abstract

Background: Vitamin D deficiency has been linked to an elevated risk of cancer and poor outcomes. This study was conducted to explore the potential impact of vitamin D status on cancer progression and severity in pediatric patients.

Methods: The current study adopted a case-control design to investigate the relationship between serum vitamin D levels and cancer stage and grading in pediatric patients. The case group comprised newly diagnosed cases of children and adolescents with various types of cancer admitted to Ali Asghar Hospital between 2023 - 2024. Statistical analysis was performed using SPSS software version 24, with a significance level set at less than 0.05.

Results: A total of 155 patients were included in the study, with 72 patients in the case group and 86 patients in the control group. Among the participants, 26 (36.1%) and 32 (38.6%) subjects in the case and control groups were girls, respectively. Acute lymphoblastic leukemia (ALL) accounted for 16.1% of the cases, followed by retinoblastoma (5.8%) and acute myeloid leukemia (AML) (4.5%) as the most frequent cancer types observed. Notably, the analysis of vitamin D serum levels revealed no significant difference between the case group (median: 25, range: 76-4) and the control group (median: 27, range: 69.5-12). Furthermore, the comparison of vitamin D serum levels across different cancer stages did not show any significant differences.

Conclusion: Our findings show that children with newly diagnosed cancer have 25 (OH) D3 levels identical to their healthy matches. However, the importance of our findings to cancer progression is unclear and needs further investigations.

Key Words: Cancer, Pediatrics, Vitamin D, 25-hydroxyvitamin D3.

* Please cite this article as: Aghajani Delavar M, Zargari N, Khoshnejad Ebrahimi H, Jafarnejad S, Javid SA. Exploring the Correlation between Serum Vitamin D Levels and Cancer Stage and Grading in Pediatric Patients. J Ped Perspect 2024; 12 (11):19152-19157. DOI: **10.22038/jpp.2024.80999.5463**

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1- INTRODUCTION

Vitamin D is a vital hormone that plays an essential role in a variety of physiological processes and has become a focal point in cancer research. The relationship between serum vitamin D levels and cancer stage and grading in pediatric patients is increasingly relevant because of its potential impact on cancer diagnosis and treatment outcomes (1). Numerous studies have examined how serum vitamin D levels correlate with cancer characteristics across different malignancies, revealing a complex interaction between vitamin D status and cancer progression (2-4).

Research has indicated that elevated serum levels of 25-hydroxyvitamin D3 (25-OH-D3) are linked to a significantly reduced incidence of colorectal carcinoma (5). Further investigations have shown a positive correlation between serum 25-hydroxyvitamin D levels and specific cancer features—such as tumor grade and clinical stage—particularly in pediatric patients with conditions like vasovagal syncope and gastric cancer (6). These findings highlight vitamin D's potential role in influencing cancer severity and progression.

Additionally, studies have found significant associations between low serum 25-hydroxyvitamin D levels and aggressive variants of breast cancer, as well as poor prognostic factors in patients with breast carcinoma. An inverse relationship between serum 25-hydroxyvitamin D concentrations and clinical stage, along with lymph node metastasis, has also been reported in gastric cancer patients (7). These results reinforce the importance of considering vitamin D status when evaluating cancer staging and grading, with the potential to enhance patient outcomes.

Furthermore, research indicates that serum vitamin D levels decline progressively in patients with diabetic nephropathy and chronic liver disease, suggesting a possible link between vitamin D deficiency and disease severity (8-9). Understanding the correlation between serum vitamin D levels and cancer stage and grading in pediatric patients is crucial for elucidating the hormone's role in cancer pathogenesis and identifying therapeutic opportunities.

Overall, exploring the relationship between serum vitamin D levels and cancer stage and grading in pediatric patients promises to deepen our understanding of vitamin D's intricate connection to cancer progression, potentially leading to more personalized cancer management strategies.

2- METHOD

2-1. Design and Population

The research conducted in this study followed a case-control design. The case group comprised newly diagnosed cases of children and adolescents with various types of cancer who were admitted to Ali Asghar Teaching Hospital during the period of 1401-1402. The control group consisted of healthy children selected from siblings of the case group or individuals presenting with general complaints.

2-2. Sampling

Random sampling was employed in this study. Sample size calculation was based on an estimated vitamin D deficiency prevalence of 0.8 in the case group and 0.6 in the control group, with adjustments made according to the studies by Iran Sharif and Forough Shakiba. A total of 71 individuals were included in each group.

2-3. Inclusion and Exclusion Criteria

The participants included in the study were required to have consent from parents; and children over 13 years of age, be within the age range of 1-18 years, were to have newly diagnosed malignant cases confirmed by the oncologist, and not have

received regular vitamin D supplements for at least one year. Exclusion criteria involved individuals with cholestatic liver disease, bile acid metabolism defects, cystic fibrosis, pancreatic exocrine dysfunction, celiac disease, Crohn's disease, and those taking specific medications such as phenobarbital, phenytoin, isoniazid, and rifampin.

2-4. Procedure

The study was conducted at Ali Asghar Children's Hospital and Rasool Akram Hospital. After obtaining voluntary consent from all participants, blood samples were collected at the time of cancer diagnosis and prior to the initiation of treatment for vitamin D measurement. No interventions were carried out on the subjects. Data collection was facilitated through a checklist developed by the researcher, which encompassed demographic details, clinical information, and laboratory findings of the patients.

2-5. Data Analysis

Data analysis was conducted using SPSS version 24 software. Quantitative variables are presented as means and standard deviations, while categorical variables are expressed as frequencies and percentages. The normality of data distribution was assessed with the Kolmogorov-Smirnov test. To compare average vitamin D levels between the case and control groups, Mann-Whitney U test was applied. Multivariate linear regression was utilized to examine the effects of age and body mass index on vitamin D levels. Furthermore, the Kruskal-Wallis test was employed to evaluate vitamin D levels across different cancer stages. A significance level of less than 0.05 was established for all statistical tests.

3- RESULTS

A total of 155 patients were included in the study, with 72 patients in the case group and 86 patients in the control group. Among these, 26 (36.1%) of the case group and 32 (38.6%) of the control group were female, showing no significant difference in gender distribution between the two groups (P value=0.754).

The most prevalent type of cancer observed was ALL with a relative frequency of 16.1%, followed by retinoblastoma at 5.8% and AML at 4.5%.

Assessment of normal distribution using the Kolmogorov-Smirnov test revealed that neither age nor BMI followed a normal distribution in either group (P <0.001).

Regarding the disease stages, 21 cases (55.3%) were classified as stage 1, while 14 cases (36.8%) were categorized as stage 2.

Comparison of age and body mass index between the case and control groups using the Mann-Whitney test indicated no significant difference in age. However, the BMI of the case group (mean: 15.8, range: 11.31-28.31) was significantly lower than that of the control group (mean: 20.7, range: 12.4-27.97) (P <0.001).

Analysis of family cancer history in the case group revealed that 64 patients had no family history of cancer in first and second-degree relatives, while 8 patients (11.11%) had a family history of cancer, including breast cancer, stomach cancer, leukemia, brain cancer, kidney cancer, and sarcoma.

Regarding previous medical records, 54 patients (72%) had no documented medical history.

Laboratory variable comparisons between the case and control groups showed significant differences in serum levels of urea, creatinine, calcium, and phosphorus, while no significant variations were observed in alkaline phosphatase and white blood cell levels (Table 1).

Table-1: Laboratory variable comparisons between the case and control groups

Test	Mean	Median	SD	P-Value
Urea (mg/dL)	11.49	10.50	6.75	0.043
Creatinine (mg/dL)	0.68	0.60	0.23	0.005
Sodium (mmol/L)	137.36	3.97	122.00	0.512
Potassium (mmol/L)	4.21	0.56	3.10	-
Calcium (mg/dL)	9.63	1.02	7.40	0.051
Phosphorus (mg/dL)	4.80	1.20	1.90	0.017
Alkaline Phosphatase (U/L)	474.00	235.41	127.00	0.314
Albumin (g/dL)	4.10	0.62	2.90	0.332
White Blood Cell Count (10^3/µL)	16.69	32.33	0.90	0.198
Parathyroid Hormone (pg/mL)	59.21	70.59	7.50	0.234

Evaluation of vitamin D serum levels between the case and control groups indicated no significant difference, with median levels of 25 and 27, respectively. After adjusting for age and BMI using linear regression due to variations in basic variables, no significant differences were found in vitamin D levels between the two groups. The regression coefficients for the study group, age, and BMI were not significant post-adjustment (Table 2).

Table-2: Evaluation of vitamin D serum levels between the case and control groups adjusting for group, age and BMI through linear regression

Coefficients	B	Std. Error	Beta	t	Sig.
(Constant)	39.71	6.194		6.411	.000
Group	-1.29	2.766	-.045	-.467	.642
Age	-.279	.317	-.085	-.881	.380
BMI	-.456	.327	-.146	-1.394	.165

Further analysis of vitamin D serum levels across different disease stages did not reveal any significant differences (P =0.208).

Classification based on the adequacy of vitamin D serum levels showed that 67 cases (80.7%) in the control group and 49 cases (68%) in the patient group had sufficient vitamin D levels, approaching significance (P =0.07).

The odds ratio and its 95% confidence interval for the adequacy of serum vitamin D levels between healthy and sick groups were calculated as 1.96 (0.944-0.9) (Table 3).

Table-3: Adequacy of serum vitamin D levels between the case and control groups

Parameter	Sufficiency		Total	P value
	Yes	No		
Control	67(80.7)	16(19.3)	83(100)	0.07
case	49(68.1)	23(31.9)	72(100)	0.07
	116(74.8)	39(25.2)	155(100)	0.07

4- CONCLUSION

The study yielded several notable results. Firstly, the gender distribution was similar between the case and control groups. The most common cancers observed were Acute Lymphoblastic Leukemia (ALL), retinoblastoma, and Acute Myeloid Leukemia (AML). Both age and BMI deviated from a normal distribution in both groups, with the case group having a significantly lower BMI than the control group. Additionally, family cancer history, medical records, and laboratory variables differed significantly between the two groups. After adjusting for age and BMI, no significant difference in vitamin D levels was found between the case and control groups. Furthermore, vitamin D levels did not vary significantly across different disease stages. However, the classification of vitamin D serum levels by adequacy showed a trend towards significance, with more control group participants having sufficient levels. The odds ratio for adequate serum vitamin D levels between healthy and sick groups was calculated to further understand this relationship.

These findings must be considered within the context of existing research on vitamin D and cancer. Previous studies have investigated the relationship between vitamin D levels and cancer outcomes, suggesting that vitamin D deficiency may influence prognosis in various cancers, including breast cancer (10), liver cancer (11), and prostate cancer (12). The potential benefits of vitamin D supplementation in cancer prevention and treatment have also been explored (13), though results have been mixed. Some studies indicate a potential benefit in reducing cancer mortality (14), while others have found no significant effect on primary outcomes such as cancer incidence and mortality (15).

This study contributes to the growing body of literature on vitamin D and cancer by highlighting the importance of considering laboratory variables and trends in vitamin D levels in cancer research. Although no significant differences in vitamin D levels were found between groups after adjusting for age and BMI, the classification based on vitamin D adequacy suggests a potential association that warrants further investigation.

Overall, this study provides valuable insights into the relationship between vitamin D levels and cancer, considering the need for further research to clarify the role of vitamin D in cancer outcomes. Elucidating the impact of vitamin D on different types of cancer and disease stages could have profound implications for the development in cancer prevention and treatment strategies. Future studies should aim to explore these relationships in more depth, considering the complexities of vitamin D's role in cancer biology.

5- ETHICAL CONSIDERATIONS

The study received approval from the Ethics Committee of Iran University of Medical Sciences under the ethics code of IR.IUMS.FMD.REC.1401.483. All procedures adhered to the principles outlined in the Declarations of Helsinki, ensuring confidentiality of patient information and the security of data throughout the study.

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