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Vitamin D and Primary Immunodeficiencies

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Authors' contributions

This work was carried out in collaboration between all authors. Authors ROSS, FISS and BTCC designed the study, wrote the protocol, and wrote the first draft of the manuscript. Authors TLP, MNR, RS and ECSV managed the literature searches and collect data. Author FISS did the statistical analysis. All authors read and approved the final manuscript.

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Short Communication

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ABSTRACT

Some of the recognized actions of vitamin D include immunological effects such as keeping tolerance and to promote protective immunity. These functions are related to the blocking of B cell differentiation and immunoglobulin secretion as well as decreased production of inflammatory cytokines. The aim of this study was to describe the frequency of vitamin D deficiency in patients with primary immunodeficiencies. We studied 31 patients: 14 with Ataxia-telangiectasia (11 male, mean age 13.1±4.9 years) and 17 with Common variable immunodeficiency (8 males, mean age 28.5±11.3 years). Classification of nutritional status and percentage of fat mass were evaluated. 25-hydroxyvitamin D was analyzed by high performance liquid chromatography and deficiency was

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considered when 25-hydroxyvitamin D< 20 ng/mL. Malnutrition was the most common nutritional disorder: 7/14 (50%) and 4/17 (23.5%) in Ataxia-telangiectasia and Common variable immunodeficiency groups, respectively. We found a high percentage of 25-hydroxyvitamin D deficiency in the Ataxia-telangiectasia group 6/14 (42.8%) and Common variable immunodeficiency group 3/17 (17.6%). There was no association between vitamin D deficiency and high-sensitivity C-reactive protein, lymphocyte count (CD3, CD4 and CD8) and body fat percentage. Considering the frequency of autoimmune diseases and infections in patients with primary immunodeficiencies, strict monitoring of the vitamin levels are recommended with the aim to reduce morbidity.

Keywords: Primary immunodeficiency; vitamin D; human; common variable immunodeficiency; ataxiatelangiectasia.

1. INTRODUCTION

Caring about nutrition in primary immunodeficiency (PID) patients is mandatory as increased morbidity and mortality are associated with nutritional status [1]. We recently reported elevated high-sensitivity C-reactive protein (hsCRP) levels in patients with common variable immunodeficiency (CVID) reflecting a chronic inflammatory process and also lower levels of retinol and zinc compared to controls [2]. On the other hand, the levels of these micronutrients with were normal in patients Ataxiatelangiectasia (AT), a disease that courses under a constant state of oxidative stress with high levels of reactive oxygen species (ROS) [3].

Some of the recognized actions of vitamin D (VITD) include immunologic effects such as keeping tolerance and promoting protective immunity. These functions are related to the blocking of B cell differentiation and immunoglobulin secretion as well as decreased production of inflammatory cytokines [4].

The aim of this study was to describe the frequency of VITD deficiency in patients with AT and CVID and to determine the association between VITD deficiency and body fat percentage, hsCRP and number of CD3, CD4 and CD8 counts.

2. MATERIALS AND METHODS

We studied 31 patients with PIDs, 14 AT (11 male, mean age 13.1±4.9 years) and 17 CVID (8 males, mean age 28.5±11.3 years) diagnosed according to European Society for

Immunodeficiencies criteria (www.esid.org). None of the patients had acute infections at the time of sample collection. We evaluated weight, height, arm circumference and skinfold thickness (triceps, subscapular, biceps and supra-iliac) and used them for classification of nutritional status (malnutrition was defined as z score body mass index < -2 for children and body mass index <18.5 kg/m² for adults) [5] and for calculating the percentage of fat mass [6]. 25-hydroxyvitamin D (25OH-D) was collected during spring season and analyzed by high performance liquid chromatography. The coefficient of variation (CV) of the intra and inter-assay precision was <3.0%. CD3. CD4 and CD8 lymphocytes was determined by flow citometry. Deficiency was considered when 25OH-D <20 ng/mL [7]. Statistical analysis: Shapiro-Wilk (normality test), Chi-square or Fisher's exact test, Student's t test and Mann-Whitney test (5% of significance level was adopted). The study was approved by the Ethics Committee of the Federal University of São Paulo.

3. RESULTS

Malnutrition was the most common nutritional disorder: 7/14 (50%) and 4/17 (23.5%) in AT and CVID groups, respectively. We found a high percentage of 25OH-D deficiency in the AT group 6/14 (42.8%) and CVID group 3/17 (17.6%) (p=0.233). Some patients presented low number of CD4+ and CD8+ T cells but there was no association between VITD deficiency and these values. Absence of association was also seen when we analyzed hsCRP and body fat percentage (Table 1).

| Table 1. Variables studied according to vitamin D deficiency (< 20 ng/mL) in patients with | | | | |
|--|--|--|--|--|
| primary immunodeficiencies | | | | |

| Variables | < 20 ng/mL (n=9) | ≥ 20 ng/mL (n=22) | P value |
|--------------------------------------|------------------|-------------------|--------------------|
| Fat mass (%) | 17.9±6.4 | 21.3±8.7 | 0.312 ² |
| Neutrophils (cells/mm ³) | 3205±1533 | 3917±2059 | 0.386² |
| Leukocytes (cells/mm ³) | 6398±1969 | 6656.0±2244 | 0.779 ² |
| CD3 (cells/mm ³) | 1146 (741;2074) | 1252.0 (317;3703) | 0.581³ |
| CD4 (cells/mm ³) | 588±284 | 605±314 | 0.897² |
| CD8 (cells/mm ³) | 430 (93;819) | 525 (89;2442) | 0.383³ |
| hsCRP (mg/dL) | 1.50 (0.24;54.9) | 3.15 (0.15;36.2) | 0.901³ |

Mean±standard deviation; median (minimum; maximum), ¹level of significance of Fisher's exact test ²Level of significance of Student's t test, ³level of significance of Mann-Whitney test, AT ataxia telangiectasia; CVID - common variable immunodeficiency; CD3, CD4, CD8 lymphocyte counts

4. DISCUSSION AND CONCLUSION

Vitamin D has a role in antibacterial response and its deficiency may predispose to some infectious diseases [8].

CVID and AT patients present a high frequency of lung dysfunction it being an important cause of mortality in these diseases. VITD deficiency is frequent in patients with chronic obstructive pulmonary disease (COPD) and this deficiency is dependent on the severity of the disease [9].

We previously showed that some CVID and AT patients present zinc and retinol deficiencies [2,10] and these same groups also showed a high frequency of vitamin D deficiency that may aggravate their immune conditions. VITD deficiency has been reported in autoimmune disorders with encouraging results in the improvement of the disease after treatment [11].

Considering the frequency of VITD deficiency in patients with CVID and AT, we recommend strict monitoring of vitamin levels with the aim to reduce morbidity.

CONSENT

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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