



Low serum vitamin D levels in Iranians with immune thrombocytopenia: A single-center study

Mahsa Matinkia¹, Rahim Asghari¹, Hamdollah Sharifi^{2,3*}

1. Department of internal medicine, Faculty of Medicine, Urmia University of Medical Sciences, Urmia, Iran

2. Inpatients Safety research center, Urmia University of Medical Sciences, Urmia, Iran

3. Department of Pharmacology, Pharmacy Faculty, Urmia University of Medical Sciences, Urmia, Iran

*Corresponding authors: Hamdollah Sharifi, Address: Department of Pharmacology, Pharmacy Faculty, Urmia University of Medical Sciences, Urmia, Iran, E-mail: sharifi_md1992@yahoo.com, Tel: +984432234897

Abstract

Background & Aims: Immune thrombocytopenia is a disorder characterized by decreased platelet production and degradation. The objectives of our study were to assess the relationship between 1,25(OH)₂D₃ levels and ITP based on sex, age, and duration of disease.

Materials & Methods: The present study was retrospectively conducted by reviewing medical records of the ITP patients. Demographic data including age, sex, disease history and serum vitamin D levels were performed and collected in a pre-designed form. Data were reported as Mean ±SD and as frequency (percentage). Independent t-test or ANOVA tests were used to compare the mean serum levels of vitamin D in terms of sex, age or disease history.

Results: A total of 140 subjects (71 females and 69 males) with mean age ± SD of 39.90 ± 16.11 years enrolled in the study. The mean serum vitamin D level in patients was 18.85 ± 10.87. There was no significant relationship between sex and serum vitamin D level (P=0.943). Patients in the range of 30-40 years have the most frequency and the lowest level of vitamin D in serum (17.11 ± 9.68 ng/ml). There was no association between age and vitamin D based on Pearson's test (p=0.181). Vitamin D level in acute ITP patients was lower than chronic ITP patients, but this difference was not meaningful (p=0.403).

Conclusion: According to the findings of this study vitamin D can be administered as a new immunomodulatory therapy in patients with ITP.

Keywords: Immune thrombocytopenia (ITP), vitamin D, Iran

Received 15 May 2020; accepted for publication 13 May 2021

Introduction

Immune thrombocytopenia (ITP) is a disorder characterized by immune-mediated accelerated platelet destruction and suppressed platelet production (1). Its incidence is approximately 2.5 per 100,000 persons per year. The goal of treatment is to keep the platelet count

above $3 \times 10^4/\text{mm}^3$ to prevent major internal organ bleeding (2). Current treatment involves intravenous corticosteroids, immunosuppressants such as mycophenolate mofetil, azathioprine, cyclophosphamide and intravenous immunoglobulin (IVIg) (3). In recent years, 1,25(OH)₂D₃ has been

rediscovered as an immune modulator, including anti-proliferation, pro-differentiation, and pro-apoptosis of a variety of cells. The functions of 1,25(OH)₂D₃ are mediated by binding to vitamin D receptor (VDR). It has been indicated that VDR is not only present in intestine, bone and kidney but also in peripheral blood monocytes and activated lymphocytes. Therefore, VDR is known to be involved in various immunomodulatory activities (4). Recent studies have reported a significant link between 1,25(OH)₂D₃ deficiency and autoimmune diseases, including rheumatoid arthritis (RA), systemic sclerosis (SSc), Crohn’s disease (CD) and systemic lupus erythematosus (SLE) (5,6). To the best of our knowledge, limited studies are conducted about the role of vitamin D deficiency in ITP occurrence. An article reported that in two patients ITP was treated effectively with vitamin D plus prednisolone (...). The objective of our study was to assess the relationship between 1,25(OH)₂D₃ levels and ITP based on sex, age, and duration of disease.

Methods & Materials

After approval by the Ethics Committee, the present study was retrospectively conducted by reviewing medical records of the ITP patients who were admitted to the hematology-oncology ward of Imam Khomeini Hospital in Urmia-Iran between March 21, 2016, and

March 20, 2018. Demographic data including age, sex, disease history, length of hospitalization and serum vitamin D levels were extracted and were collected in a pre-designed form. Quantitative variables were reported as Mean ±SD and qualitative variables were reported as frequency (percentage). Independent t-test or ANOVA tests were used to compare the mean serum levels of vitamin D in terms of sex, age or disease history. Data were analyzed using SPSS-17 software and the significance level was less than 0.05.

Results

A total of 140 subjects enrolled in the study, (71 females and 69 males) with a female: male ratio of 1.03:1 with mean age± SD of 39.90 ± 16.11 years ranging from 12-71 years. The level of vitamin D (above or below optimal values) in relation to gender is shown in Table 1.

Table 2 presents the distribution of vitamin D values according to the age grouping. Patients in the range of 30-40 years have the highest frequency and the lowest level of vitamin D in serum (17.11± 9.68 ng/ml). There was no relationship between age and vitamin D based on Pearson’s test (p=0.181).

According to Table 3, the vitamin D level in acute ITP patients was lower than chronic ITP patients, but this difference was not meaningful (p=0.403).

Table 1: The level of vitamin D in relation to gender

p-value	Serum Vit D* Gender	
	69(49.28)	No.(%)
	18.62	Mean
	10.34	SD
	4.39	Min
	46	Max
		Male
0.943	71(50.72)	No.(%)
	19.08	Mean
	11.43	SD
	3	Min
	44.30	Max
		Female

Table 2: vitamin D values distribution according to the age grouping

Max	Min	SD	Mean	No.	Age group
46	3	11.53	18.65	16	<20
44.3	4.39	10.09	18.37	36	20-29
44.3	4.39	9.68	17.11	38	30-39
46	3	11.87	18.49	22	40-49
42.02	4.48	11.72	17.97	10	50-59
46	5.60	12.62	28	11	60-69
36	8.43	9.5	19.33	7	70-79

Table 3: vitamin D level in acute and chronic ITP patients

Serum Vit D*Diease history	
87(62.14)	No.(%)
18.37	Mean
10.79	SD
3	Min
46	Max
Acute	
53(37.68)	No.(%)
19.64	Mean
11.05	SD
4.88	Min
46	Max
Chronic	

Discussion

The aim of this study was to assess vitamin D status in patients with ITP and to correlate it with sex, age and illness duration (acute or chronic). The present study included 140 ITP patients (71 females and 69 males), 87 patients with acute and 53 with chronic thrombocytopenia. The proportion of females to males was nearly similar, but according to the findings of Schoonen et al. (7) and Soliman et al. (8), ITP in female patients was higher than male patients. But in a study in Iran this ration was equal (9). It seems that geographical differences are important in this proportion.

The mean age of ITP patients in our study was 39.90 ± 16.11 years, this was higher than that described by Cines and Bussel (10) who stated that the incidence of ITP is more common in women aged between 18 and 40 years. On the other hand, Neylon et al.(11) estimated a higher incidence of ITP among those aged 60 years and

older whereas in our study patients within the age range of 30-40 years had the highest incidence of ITP but not statically significant in comparison with other age groups.

In the present study, we did not find a significant correlation between vitamin D levels and age, sex or disease duration in ITP patients. This finding is in line with the results of a study by Soliman et al. (8). Also other studies did not find a significant correlation between vitamin D level and age or disease duration in SLE (12) and rheumatoid arthritis (13) patients. In the present study, we have found a significantly lower mean levels of vitamin D among ITP cases compared to healthy control group, (18.85 ± 10.87 ng/ml) vs ($32-100$ ng/ml) (14) respectively with p-value <0.001 . These findings were in accordance with the findings of Soliman et al. (8) and Mu et al.(15). Our study has shown that the blood level of vitamin D in chronic ITP was higher than acute ITP although not statistically

significant. However, the findings of Čulić et al. were not in line with the findings of this study.(16).

However, our study have some limitations. We did not have the control group and we compared the results based on the normal range of vitamin D reported in other studies conducted in Iran (14). According to the findings of this and other studies, and reports of Bockow and Kaplan (2), vitamin D can be administered as a new immunomodulatory therapy in patients with ITP. Therefore there is a utility supplementing VD in ITP patients. To investigate the role of VD as an immunomodulating drug for patients with ITP, a prospective randomized placebo-controlled trial needs to be performed.

Conflict of interest

The authors have no conflicts of interest to disclose.

References

- 1- Neunert C, Lim W, Crowther M. American Society of Hematology evidence-based practice guidelines for immune thrombocytopenia. *Blood* 2011. 117: 4190-207.
- 2- Bokow B, Kaplan T. Refractory immune thrombocytopenia successfully treated with high-dose vitamin D supplementation and hydroxychloroquine: two case reports, *J Med Case Rep* 2013. 7:91.
- 3- Thota S, Kistangari G, Daw H, Spiro T: Immune thrombocytopenia in adults: an update. *Cleve Clin J Med* 2012, 79(9):641–650.
- 4- Liu W, Li H, Hao Y, Li Y, Lv M, Xue F. Decreased immunosuppressive actions of 1, 25-dihydroxyvitamin D₃ in patients with immune thrombocytopenia. *Mol Immunol* 2016;78:89–97.
- 5- Lavi Arab F, Rastin M, Faraji F, Zamani Taghizadeh Rabe S, Tabasi N, Khazae M. Assessment of 1,25-dihydroxyvitamin D₃ effects on Treg cells in a mouse model of systemic lupus erythematosus. *Immunopharmacol Immunotoxicol* 2015;37:12–8.
- 6- Zerr P, Vollath S, Palumbo-Zerr K, Tomcik M, Huang J, Distler A. Vitamin D receptor regulates TGF-β signalling in systemic sclerosis. *Ann. Rheum. Dis* 2015; 74: e20.
- 7- Schoonen WM, Kucera G, Coalson J. Epidemiology of immune thrombocytopenic purpura in the general practice research database. *Br J Haematol* 2009. 145: 235-44.
- 8- Soliman A, Elsalakawy W, Saeed A. Low serum vitamin D levels in Egyptian adults with chronic primary Immune thrombocytopenia single center study. *International J Adv Res* 2017. 5(3):1789-97.
- 9- Saeidi S, Jaseb K, Asnafi AA, Rahim F, Pourmotaehari F, Mardaniyan S, et al. Immune Thrombocytopenic Purpura in Children and Adults: A Comparative Retrospective Study in IRAN. *IJHOSCR* 2014;8(3):30-6.
- 10- Cines DB and Bussel JB. How I treat thrombocytopenic purpura (ITP). *Blood* 2005; 106: 2244-51.
- 11- Neylon N, Saunders G, Howard R. Clinically significant newly diagnosed presenting autoimmune thrombocytopenic pupura in adults: a prospective study of a population-based cohort of 245 patients. *Br J Haematol* 2003; 122: 966–74.
- 12- Emam FE, Abd El-Wahab TM, Mohammed MS, et al. Assessment of serum vitamin D level in patients with systemic lupus erythematosus. *Egyptian Rheumatology and Rehabilitation* 2014; 41: 71-8.
- 13- Rossini M, Bongi MS, LaMontagna G, et al. Vitamin D deficiency in rheumatoid arthritis: prevalence, determinants and associations with disease activity and disability. *Arthritis Res. Ther* 2010; 12: R216.
- 14- Ettehad H, Asadi K, Mirbolook AR, Soleimanha M, Adeli A, Haghparast Ghadim Z. et al. Evaluation of 25-hydroxy Vitamin D Blood Levels in Patients with Musculoskeletal Pain. *J Guilan Univ Med Sci* 2014;23(89):51-56. (Persian)
- 15- Mu W, Wang W, Cui ZG, Sui AH. Expression and significance of vitamin D and its receptor mRNA in the peripheral blood of initial immune thrombocytopenic patients. *Exp Hematol* 2013; 21:684-7.
- Čulić S, Markić J, Petrovića D, Konjevoda P, Pavelić J. Serum vitamin D levels in children with newly diagnosed and chronic immune thrombocytopenia. *Semin Hematol* 2016;53:S67–S69.