

Serum level of vitamin D3 among Egyptian patients with chronic plaque psoriasis vulgaris

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ABSTRACT

Background: Psoriasis is a common genetically determined inflammatory and proliferative disease of the skin. The commonest type is chronic plaque psoriasis. Vitamin D3 plays a role in regulation of immune system. It may be deficient in some autoimmune diseases.

Aim of the work: To evaluate the relationship between serum level of 25-hydroxyl vitamin D3 and chronic plaque psoriasis.

Method: Thirty patients suffering from chronic plaque psoriasis were included. The control group included thirty age matched healthy persons for comparison.

Results: Vitamin D3 {25(OH) vit D3} deficiency (< 20 ng/mL) was observed in 33.33% of patients with psoriasis versus 10% of control subjects (P=.06). Vitamin D3 insufficiency (< 30 ng/mL) was found in 53.33% of patients with psoriasis versus 56.67% of control subjects (P = 0.1927).

Conclusion: Serum level of vitamin D3 was significantly low with chronic plaque psoriasis independent of sex, duration or severity of psoriasis vulgaris (PASI score).

KEY WORDS: Serum level, vitamin D3, psoriasis vulgaris

INTRODUCTION

Psoriasis is a chronic inflammatory disease with contribution of both innate (keratinocytes, dendritic cells, histiocytes and endothelial cells) as well as acquired immune system (T lymphocytes). The commonest form is Psoriasis vulgaris, which is characterized by red, scaly, raised plaques with predilection areas including elbows, knees and scalp.¹

Psoriasis prevalence rates was reported to be around 3% among Egyptians.²

Prevalence of psoriasis is similar in both sexes and can occur at any age. However, a bimodal age of onset has been recognized in several large studies.³

Pathogenesis of psoriasis passes through dendritic cells (DCs) activation, producing the messenger substances, tumor necrosis factor (TNF) α and interleukin 23 (IL 23), which promote the development of T helper 1 and Th17 cells. These T cells secrete mediators that contribute to the vascular and epidermal changes of psoriasis.⁴

TNF - α stimulates the synthesis of anti-apoptotic Bcl-x and bcl-2 as well as pro-apoptotic Bax protein in psoriatic lesions.⁵

Additionally, endothelial cells, neutrophils, and natural killer cells may play adjunctive role together with other cytokines and adhesive molecules (ICAM)-1.^{1,6}

Vitamin D is a fat-soluble nutrient that human

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beings obtain from diet, and can be synthesized in the skin following the exposure to Ultraviolet B radiation (UVB), so sun exposure is regarded as a sources of vitamin D3 (Cholecalciferol) for humans.^{7,8}

There are two major biologically inert precursors of vitamin D: vitamin D3 (Cholecalciferol) and vitamin D2 (Ergocalciferol).⁹

Dietary vitamin D plant source (fungi and yeast) is vitamin D2. While, animal source is vitamin D3 (oily fish).¹⁰

Vitamin D3, is prohormone need to be converted in the liver to circulating form of vitamin D3, 25-hydroxyvitamin D3, also called calcidiol.¹⁰

Calcidiol is then converted into calcitriol (1,25 - dihydroxyvitamin D3), the biologically active form of vitamin D3. This may take place in the kidneys or monocyte-macrophages of the immune system.¹¹

Vitamin D3 has also been found to be an immune modulating hormone with beneficial effects on inflammatory diseases, through its action on helper T lymphocytes type 1 (Th1) cells.¹²

Vitamin D3 deficiency has been already reported in chronic immune-mediated inflammatory skin diseases such as atopic dermatitis and vitiligo.^{13,14}

An association between vitamin D3 deficiency and psoriasis has also been described.¹⁵

The physiologically active form of vitamin D3 mediates its biological effects by binding to the vitamin D receptor (VDR), that is mainly present in the nuclei of different target cells.¹⁶ After binding to receptor; it regulates keratinocytes growth and differentiation, but also has an influence on immune functions of dendritic cells and T lymphocytes.¹⁷

Serum 25(OH) D3 is regarded as a reliable indicator of vitamin D3 deficiency, sufficiency,

and intoxication. Vitamin D3 sufficiency means that 25(OH) D3 level ≥ 30 ng/ml.¹⁰ vitamin D3 deficiency means that 25(OH) D3 level is less than 20 ng/mL. But vitamin D3 insufficiency means that 25(OH) D3 level between 21 ng/ml and 29 ng/ml.^{18,19}

Populations at risk for vitamin D deficiency include Infants and children.^{20,21}

Adolescents are also at risk because of rapid growth of the skeleton that consume the active form 1,25(OH)₂D.²² Elderly persons may suffer from vitamin D deficiency because of their aging; skin unable to synthesize vitamin D efficiently. As they are likely to spend more time indoors, and they may have inadequate intakes of the vitamin.²³ Also, dark-skinned patients: as they need much longer UVB exposure times to generate the same 25(OH) D3 stores compared with fair-skinned patients.²⁴

Moreover; some medical conditions may be associated with vitamin D deficiency such as chronic kidney disease (inability to make sufficient 1,25-dihydroxyvitamin D3).²⁵ Some forms of liver disease, cystic fibrosis, and Crohn's disease may be associated with fat malabsorption including fat soluble vitamins.⁸

AIM OF THE WORK

The aim of this work is to evaluate the relationship between serum level of 25 - hydroxyl vitamin D3 and psoriasis vulgaris.

PATIENTS AND METHODS

This case controlled study included thirty patients with psoriasis vulgaris: (Either newly diagnosed cases or previously diagnosed cases who stopped treatment for at least two months). Their age ranged between 20 and 40 years. Control group

included thirty age matched healthy individuals.

Exclusion criteria: Other clinical types of psoriasis, patients with chronic medical illness as chronic liver diseases, renal diseases and diabetes mellitus and patients under treatment with vitamin-D.

Following counselling and explanation of the procedures to the patients and assurance of confidentiality and anonymity, an informed consent was obtained from all subjects included in the study.

All patients were subjected to detailed history; personal history, history of the present illness, history of medication, past history and family history. Clinical examination also was carried out including assessment of psoriasis area and severity index score (PASI score).

Measurement of serum level of 25-hydroxy vitamin D3 was done using radioimmunoassay kits with calibrating control test; (Gammacounter, IsocompI, Mgm instrument, Inc, U.S.A.). The obtained results were tabulated and statistically analyzed using SPSS software program.

RESULTS

This study included thirty patients with psoriasis vulgaris and thirty ages matched healthy control subjects. Mean age of patients was (31.300±6.919) years (maximum 40 years and the minimum 21 years). The mean age of control group was (28.400±5.864) years (maximum 40 years and the minimum 21 years). (Table 1).

Regarding sex distribution among psoriatic

Table 1 Age of studied groups

Age		
Groups	Range	Mean ± SD
Patients	21-40	31.300 ± 6.919
Control	21-40	28.400 ± 5.864

patients; 14 were females (46.67%) and 16 were males (53.33%). While, in the control group, 17 were females (56.67%) and 13 were males (43.33%).

Disease severity assessment revealed that 13 patients had mild psoriasis (43.33%), 10 patients had moderate psoriasis (33.33%) while 7 patients had severe psoriasis (23.33%). The mean PASI score was (7.122±2.411) (Table 2 & 3).

The mean serum level of 25(OH) D3 (22.247±7.499) ng/ml was significantly lower in patients than in control subjects (34.373 ± 17.370) ng/ml (P = .001) (Table 4).

Vitamin D3 deficiency (25(OH) D3 < 20 ng/mL)

Table 2 Disease severity assessment

Groups		
According to PASI score	No	%
Mild	13	43.33
Moderate	10	33.33
Severe	7	23.33
Total	30	100

Table 3 Range and mean PASI score

	Range	Mean ± SD
PASI score	1.2 - 20	7.122 ± 2.411

Table 4 Range & mean serum level of 25(OH) D3

25(OH) D ₃ level			T-test	
Groups	Range	Mean ± SD	T	P-value
Patients	7.3-40.9	22.247±7.499	-3.511	0.001
Control	10.1-95.7	34.373±17.370		

was observed in 33.33% of patients with psoriasis versus 10% of control subjects (P=.06). Vitamin D3 insufficiency (25(OH) D3 < 30 ng/mL) was found in 53.33% of patients with psoriasis versus 56.67% of control subjects (P = 0.1927) (Table 5). No significant difference was found between serum level of 25(OH) D3 and sex (P= 0.521) (Table 6).

Regarding serum level of 25(OH) D3 and duration of the disease; no significant correlation was found between them (P = 0.796) (Table 7).

Also; mean serum level of 25(OH) D3 did not correlate significantly with PASI score (P = 0.167) (Table 8).

Table 5 Vitamin 25(OH) D₃ serum level

PATIENTS		Groups			Chi-square			
		CONTROL	TOTAL	X ²	P-VALUE			
Deficiency	N	10	3	13	3.535	0.06		
	%	33.33	10.00	21.67				
Insufficiency	N	16	10	26	1.697	0.1927		
	%	53.33	33.33	43.33				
Normal	N	4	17	21				
	%	13.33	56.67	35.00				
Total	N	30	30	60				
	%	100	100	100				

Table 6 Correlation between serum level of 25(OH) D3 and sex

Sex	25(OH) D3 level		T-test	
	Range	Mean ± SD	T	P-value
Female	7.300-35.100	21.286±8.081	-0.650	0.521
Male	13.200-40.900	23.088±7.107		

Table 7 Correlation between duration of psoriasis vulgaris and the serum level of 25(OH) D3

Sex	25(OH) D3 level		T-test	
	Range	Mean ± SD	T	P-value
Female	13.200-35.100	22.692±6.464	0.261	1.796
Male	7.300-40.900	21.950±8.287		

Table 8 Correlation between mean serum level of 25(OH) D3 and PASI score

PASI score	25(OH) D3 level		Anova-test	
	Range	Mean ± SD	F	P-value
Mild	13.200 - 40.900	24.738 ± 7.719	1.911	0.167
Moderate	11.600 - 32.700	21.910 ± 7.192		
Severe	7.300 - 26.100	18.100 ± 6.431		
Total	7.300 - 40.900	22.247 ± 7.499		

DISCUSSION

Decreased level of vitamin D3 may have important implications in the pathogenesis of psoriasis.¹⁷ Vitamin D3 decreases activity of proinflammatory cytokines, cytotoxic T cells and natural killer cell.²⁶ Topical vitamin D derivatives, including calcipotriol and calcitriol, have immunomodulatory effects on monocytes, macrophages, T cells and dendritic cells.²⁷ Phototherapy may improve psoriasis through increasing endogenous vitamin D3 levels.²⁸

Several conditions may contribute to low serum levels of vitamin D3 in the general population, including poor dietary intake of vitamin D3, sun avoidance and / or negligible sun exposure. Another cause is malabsorption due to inflammatory bowel disease, gluten enteropathy, gastric surgery, biliary disease, or intestinal bacterial overgrowth, use of anti-seizure medications (e.g. phenobarbital or phenytoin) and long-term use of glucocorticoids.²⁹ Vitamin D3 deficiency has been already reported in chronic immune-mediated inflammatory skin diseases including atopic dermatitis and vitiligo.^{13,14}

In the present study, the mean serum level of 25(OH) D3 was significantly lower in patients with psoriasis vulgaris versus control subjects.

Although the results obtained by Molina et al and Ricceri et al generally agreed with our results, regarding decreased vitamin D3 level among patients compared with control group. However, the obtained values were somewhat different.^{15,30}

An example of such different values was the mean level of 25 (OH) D3 in patients with psoriasis was high compared to the present study.

This difference could be explained by different skin type. As dark skinned patients need much longer UVB exposure times to generate the same

25(OH) D3 stores compared with fair skinned patients.²⁴ Moreover, different nutritional habits, economic and social standards may also affect vitamin D level. In the present study, there was non-significant correlation between sex of psoriatic patients and level of vitamin D3. Gisondi et al., also described similar finding.³¹

Regarding disease's duration; it has no correlation with 25(OH) D3 level, and in agreement with the results reported by Gisondi et al and Molina et al.^{23,33}

Also, the level of 25(OH) D3 did not correlate with disease severity assessed by PASI score, the result was also supported by other studies by Atwa et al and Molina et al.^{33,32}

In the study of Molina et al., the mean serum level of 25(OH) D3 of patients with psoriasis vulgaris was higher than that of the present study. But the mean PASI score was lower than that of the present study, that could be due to inclusive of lower number of cases with severe psoriasis than seen in our study.³²

The study conducted by Atwa et al., revealed that mean serum of level of 25(OH) D3 among patients with psoriasis vulgaris was much lower than that of our study, but the mean PASI score was relatively the same.

On the other hand, Ricceri et al., found that serum 25(OH) D3 concentration was significantly and negatively correlated with PASI score. In their study, the mean serum level of 25(OH) D3 in patients of psoriasis vulgaris was higher than that of the present study, and also PASI score was higher than that of the present study.³⁰ This difference could be explained by: The study of Ricceri et al included higher number of patients (68 patients versus 30 patients in the present study). Additionally, it had different severity

score, because of higher number of cases with severe psoriasis (22 cases versus 7 cases in the present study).³⁰

Deficient 25(OH) D3 levels in patients with psoriasis may be associated with alterations in isoenzymes that affect the synthesis of vitamin D3.³⁴ Also, some studies have shown differences in vitamin D receptor polymorphisms between patients with psoriasis and the general population.³⁵ Low 25(OH) D3 levels in psoriatic patients could also be secondary to an inflammatory environment as CRP was negatively correlated with 25(OH) D3.^{36,15}

Chodorowska et al³⁷ reported that plasma acute-phase protein levels (CRP and fibrinogen) were significantly elevated in patients with psoriasis versus healthy control subjects.

Moreover, systemic vitamin D administration has shown clinical benefits in psoriatic patients.³⁸

Concerning treatment of psoriatic patients who showed vitamin D3 deficiency, Finamor et al conclude that 6 months treatment with high doses of vitamin D3 resulted in significantly increased 25(OH) D3 levels, that was parallel to clinical improvement evidenced by negative correlation between the PASI score and 25(OH) D3 levels.³⁹

CONCLUSION

Serum level of vitamin D3 was usually lower in patients with psoriasis vulgaris regardless sex, duration or severity of psoriasis vulgaris.

REFERENCES

1. Lowes MA, Bowcock AM and Krueger JG (2007): Pathogenesis and therapy of psoriasis. *Nature*; 445 (7130):866-73.
2. Naldi L (2004): Epidemiology of psoriasis. *Curr Drug targets Inflamm Allergy*; 3(2):121-28.

3. Langley R G, Krueger G G and Griffith CE (2005): "Psoriasis: epidemiology, clinical features, and quality of life". *Ann Rheum*; 64(2): ii18-23.
4. Mrowietz U and Reich K (2009): Psoriasis - new insights into pathogenesis and treatment. *Dtsch Arztebl Int*; 106(1-2):11-18.
5. Wrone S T, Johnson T, Nelson B, Boise L H, Thompson C B, Nunez G and Nickoloff B J (1995): Discordant expression of Bcl-x and Bcl-2 by keratinocytes in vitro and psoriatic keratinocytes in vivo. *Am J Pathol*; 146(5):1079-88.
6. Guenther L C & Ortonne J P (2002): Pathophysiology of psoriasis: science behind therapy; 7(2):85-97.
7. Lim H W, Gilchrist B A, Cooper K D, Bischoff H A, Rigel D S, Cyr W H, Miller S, DeLeo V A, Lee TK, Demko CA, Weinstock MA, Young A, Edwards LS, Johnson TM and Stone SP (2005): Sunlight, tanning booths, and vitamin D3. *J Am Acad Dermatol Venereol*; 52(5):868-76.
8. Holick MF (2006): Resurrection of vitamin D deficiency and rickets. *J Clin Invest*; 116(8):2062-2072.
9. Vieth R (2004): Why "vitamin D" is not a hormone, and not a synonym for 1, 25 dihydroxy- vitamin D, its analogs or deltanoids. *J Steroid Biochem Mol Biol*; 89-90(1-5):571-73.
10. Holick MF (2007): Vitamin D deficiency. *N .Engl. J. Med.* 357(3):266-81.
11. Adams JS and Hewison M (2010): Update in vitamin D. *J Clin Endocrinol Metab*; 95(2):471-78.
12. Ikeda U, Wakita D, Ohkuri T, Chamoto K, Kitamura H, Wakura Y and Nishimura T (2010): 1 α ,25-dihydroxyvitamin D3 and all-trans retinoic acid synergistically inhibit the differentiation and expansion of Th17 cells. *Immunology Letters*; 134(1):7-16.
13. Silverberg JI, Silverberg AI, Malka E and Silverberg N B (2010): A pilot study assessing the role of 25 hydroxy vitamin D3 levels in patients with vitiligo vulgaris. *J Am Acad Dermatol*; 62(6):937-41.
14. Peroni D G, Piacentini G L, Cametti E, Chinellato I and Boner A L (2011): Correlation between serum 25- hydroxyvitamin D levels and severity of atopic dermatitis in children. *Br J Dermatol*; 164(5):1078-82.
15. Molina O J, Buendía E A, Arrabal M A, Ruiz J C and Santiago S A (2012): Deficiency of serum concentration of 25-hydroxyvitamin D in psoriatic patients: a case-control study. *J Am Acad Dermatol*; 67(5):931-38.
16. Holick MF (2004): Vitamin D: importance in the prevention of cancers, type 1 diabetes, heart disease, and osteoporosis. *Am J Clin Nutr*; 79(3):362-71.
17. Schwalfenberg G K (2011): A review of the critical role of vitamin D in the functioning of the immune system and the clinical implications of vitamin D deficiency. *Mol Nutr Food Res*; 55(1):96-108.
18. Bischoff H A, Giovannucci E, Willett WC, Dietrich T and Dawson H B (2006): Estimation of optimal serum concentrations of 25- hydroxyvitamin D3 for multiple health outcomes. *Am J Clin Nutr*; 84(1):18-28.
19. Dawson HB, Heaney RP and Holick MF (2005): Estimates of optimal vitamin D status. *Osteoporos Int*; 16(7):713-16.
20. Hollis B W and Wagner C L (2004): Vitamin D requirements during lactation: high-dose maternal supplementation as therapy to prevent hypovitaminosis D for both the mother and the nursing infant. *Am J Clin Nutr*; 80(6):1752S-58S.
21. Roth DE, Martz P, Yeo R, Prosser C, Bell M and Jones AB (2005): Are national vitamin D guidelines sufficient to maintain adequate blood levels in children? *Can J Public Health*; 96(6):443-49.
22. Aksnes L and Aarskog D (1982): Plasma concentrations of vitamin D metabolites at puberty: Effect of sexual maturation and implications for growth. *J Clin Endocrinol Metab*; 55(1):94-101.
23. Ross C, Taylor CL, Yaktine AL and Del Valle HB (2011): Dietary reference intakes for calcium and

- vitamin D. In Institute of Medicine (US) Committee review; National Academies Press (US).
24. Willis CM, Laing EM, Hall DB, Hausman DB and Lewis RD (2007): A prospective analysis of plasma 25-hydroxyvitamin D3 concentrations in white and black prepubertal females in the south eastern United States. *Am J Clin Nutr*; 85(1):124-30.
 25. Moscovici AG and Sprague SM (2007): Role of Vitamin D Deficiency in Chronic Kidney Disease *J Bone Miner Res*; 22(2):V91-V94.
 26. Tang L, Yu Y, Chen J, Li Q, Yan M and Guo Z (2003): The inhibitory effect of Vitamin D3 on proliferation of keratinocyte cell line HACAT is mediated by down-regulation of CXCR2 expression. *Clin Exp Dermatol*; 28(4):416-19.
 27. Lehmann B (2009): Role of the vitamin D3 pathway in healthy and diseased skin-facts, contradictions and hypotheses. *Exp Dermatol*; 18(2):97-108.
 28. Ryan C, Moran B, McKenna M J, Murray B F, Brady J, Collins P, Rogers S and Kirby B(2010): The effect of narrowband UV-B treatment for psoriasis on vitamin D status during wintertime in Ireland. *Arch Dermatol.*; 146(8):836-42.
 29. De Luca HF (2004): Overview of general physiologic features and functions of vitamin D. *Am J Clin Nutr* ; 80(6):1689S-96S.
 30. Ricceri F, Leonardo P, Tripo L and Prignano F (2013): Deficiency of serum concentration of 25-hydroxyvitamin D correlates with severity of disease in chronic plaque psoriasis. *Journal of the American Academy of Dermatology*; 68(3):511-12.
 31. Gisondi P, Rossini M, Di Cesare A, Idolazzi L, Farina S, Beltrami G, Peris K and Girolomoni G. (2012): Vitamin D status in patients with chronic plaque psoriasis *British Association of Dermatologists*; 166(3):505-51.
 32. Mollina O J, César M C, Miguel A, Polo A, Enrique R A, Ramón N A, Agustin B E and Salvador A S (2014): Association of 25-hydroxyvitamin D with Metabolic Syndrome In patients with Psoriasis: A Case-control Study. *Acta Derm Venereol*; 94(2):142-45.
 33. Atwa AM, Balata MG, Ashraf MH, Abdelrahman IN and Elminshawy HH (2013): Serum 25-hydroxyvitamin D concentration in patients with psoriasis and rheumatoid arthritis and its association with disease activity and serum tumor necrosis factor-alpha. *Saudi Med J*; 34(8):806-13.
 34. Bouillon R (2010): Genetic and environmental determinants of vitamin D status *Lancet*; 376(9736):148-49.
 35. Park B S, Park J S, Lee D Y, Youn J I and Kim I G (1999):Vitamin D receptor polymorphism is associated with psoriasis. *J Invest Dermatol*; 112(1):113-16.
 36. Ngo DT, Sverdlov AL, McNeil J J and Horowitz JD (2010): Does vitamin D modulate asymmetric dimethylarginine and C-reactive protein concentrations? *Am J Med*; 123(4):335-41.
 37. Chodorowska G, Wojnowska D and Juszkiewicz B M (2004): C-reactive protein and alpha 2-macroglobulin plasma activity in medium-severe and severe psoriasis. *J Eur Acad Dermatol; Venereol*; 18(2):180-83.
 38. Werner de Castro GR, Neves F S, Pereira IA, Fialho SC, Ribeiro G and Zimmermann AF (2012): Resolution of adalimumab- induced Psoriasis after vitamin D deficiency treatment. *Rheumatol Int*; 32(5):1313-16.
 39. Finamor D C, Sinigaglia C R, Neves L C, Gutierrez M, Silva J J, Torres L D, Surano F, Neto D J, Novo N F, Juliano Y, Lopes A C and Coimbra C G (2013): A pilot study assessing the effect of prolonged administration of high daily doses of vitamin D on the clinical course of vitiligo and psoriasis. *Dermatoendocrinol*; 5(1):222-34.