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Original Article

Serum vitamin D levels in psoriasis and acne: Is there a relationship with disease? A comparative cross sectional study in local population

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Abstract

Background Vitamin D is an oil soluble vitamin responsible for various skeletal and non-skeletal functions, its deficiency is common in skin pathologies due to consequent abnormality in its synthesis and activation from skin cells.

Objective The study targets to study the relationship between the degrees of vitamin D in psoriasis and acne patients, the research study compares the levels in patients suffering from the mentioned diseases.

Methods The study employs a cross-sectional comparative method of analysis in Fauji Foundation Hospital Rawalpindi's Dermatology ward. 350 participants were selected by non-randomized convenient sampling, out of which 323 signed informed consent and qualified based on inclusion, and exclusion criteria were included. Out of these 323, 140 that were diagnosed with acne were included in group A based on inclusion criteria of age between 12 to 40. And, 183 participants diagnosed with psoriasis were included in group B based on inclusion criteria of age between 16 to 70. All these participants did not have a history of hypertension, diabetes mellitus, or renal and hepatic diseases, and were screened for normal RFTs and LFTs by taking blood samples. Blood samples were collected by using the technique of immune-enzyme assessment ((25(OH)-Vitamin D) with the enabling function of ELISA kit Immundiagnostik AG, Germany) that assessed the level of Vitamin D serum 25-hydroxycholecalciferol (25(OH) D). The result was analyzed on SPSS 26.

Results Values of one paired t-test depicts that there is a huge difference between the mean Vitamin D measure of acne (M=41.47, SD=19.6) and Vitamin D level of psoriasis (M=21.83, SD=8.5). Regarding the correlation between the level of serums in acne and psoriasis patients. It was assessed that there has been a direct and non-negligible negative association between the degrees of Vitamin D serum in psoriasis and acne patients (r=0.13, p=0.05). It was also instigated that there had not been vital correlation in Vitamin D serum levels in patients suffering from acne (r=1, p≥0.05).

Conclusion The research study developed that a direct and significant relationship between the level of Vitamin D serum and psoriasis whereas no vital correlations were found between levels of Vitamin D serum and acne.

Key words
Psoriasis, acne vulgaris, Serum 25(OH) D.

Introduction

Vitamin D is an important vitamin that is oil soluble and helps in delivering functions such as absorption of calcium, mineralization of bones, skeletal mineralization, bone metabolism along with homeostasis of calcium and phosphorus.[1] It is also known as sunshine vitamin as its

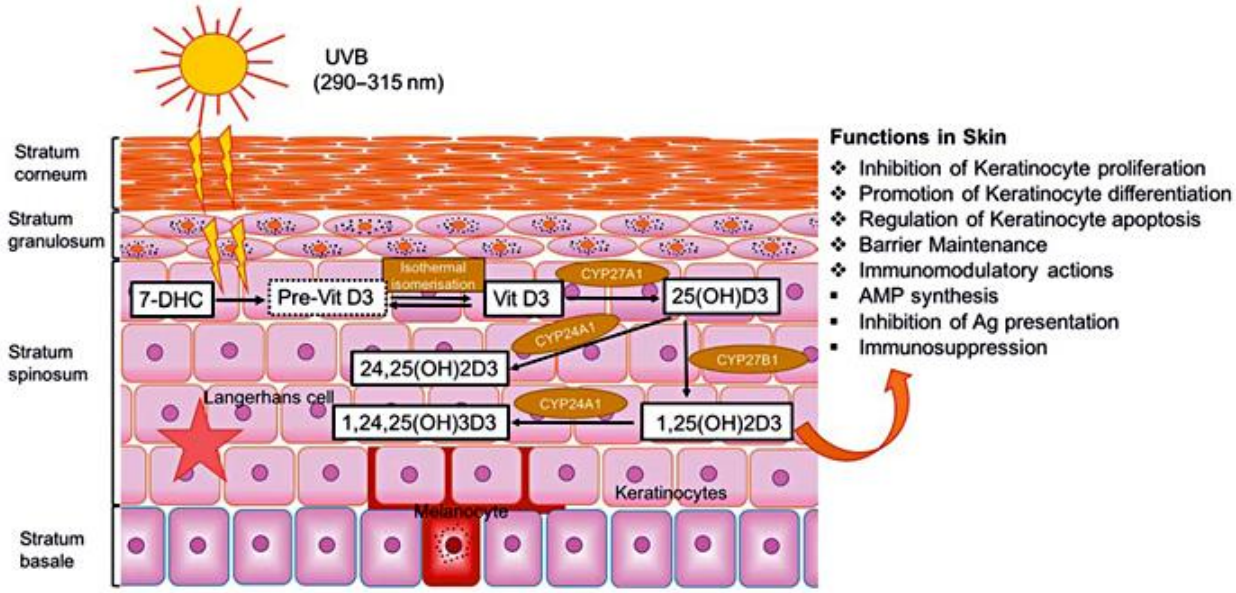

Figure 1 The process of synthesis and activation related to Vitamin D in skin.[4]

synthesis in keratinocytes from its precursor 7-DHC, as cholecalciferol and later its conversion to active metabolite 1.25 dihydroxy cholecalciferol under the effect of CYP27A1 and CYP27B1 enzyme is directly influenced by UVB of wavelength 290-315 to thermally isomerize pre-Vitamin D to stable Vitamin D i.e., cholecalciferol even if Vitamin D is consumed through diet or skin, it has to go through 2 hydroxylation reaction reactions.[2] **Figure 1** shows multiple stages of Vitamin D passing through to form 1,25-dihydroxyvitamin D, 1,25(OH)2D i.e. the first stage converts Vitamin D 25-hydroxylase (CYP2R1) enzyme in the sections of the liver to manufacture 25-hydroxyvitamin D. The next step helps in the manufacturing of 1,25-dihydroxyvitamin D, 1,25(OH)2D with the help of 1α-hydroxylase (CYP27B1) which is found in the kidney. However, the by-products formed in the kidney and liver can be easily deactivated through hydroxylation carried out by the 24-hydroxylase (CYP24A1) enzyme.[3]

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Formerly, the role of Vitamin D was described to be restricted to the skeletal functions of the body. However, recent literature enlightened its role in various non-skeletal functions as in the immunoregulatory process however it has a significant role in the skin for keratinocyte proliferation, barrier maintenance, epidermal cell differentiation, and apoptosis.[4] The capacity of Vitamin D is facilitated by calcium to carry out important functions of differentiation and proliferation. Various studies show that 1.25 (OH) 2D3 enhances keratinocyte proliferation at low serum levels i.e., <10-9 M, while inhibits proliferation and promoting differentiation at higher levels i.e., >10 M.[5] Keratinocyte apoptosis on the skin is facilitated by the dosage of Vitamin D because it seems to prevent apoptosis at physiological concentrations and induce it at higher concentrations, it also regulates AMP synthesis. The anti-apoptotic and cytoprotective effect is mediated by sphingosine-1-phosphate.[6]

There are various factors affecting the bioavailability of Vitamin D. out of these some

have a stronger impact than others. According to various studies, basal (OH)2D concentration is one of the important factors. Other less important factors include; BMI, body fat, season, dietary calcium and fat intake, and genetics.[8] The assessment of Vitamin D level is done through the vital method of measurement of the serum25 (OH) D level. If the level of serum 25(OH) D below 20 ng/mL (50 nmol/L) then the US Endocrine Society guidelines define it as a deficiency, similarly, if the level of serum is serum 25(OH) D level between 21 and 29 ng/mL (52.5–72.5 nmol/L) then it is defined as insufficient.[7] Studies show that the insufficient production and retention of Vitamin D is ordinary all around the world, and is estimated to be 68% among adults in south Asia.[9] The cause of this deficiency is multifactorial; however, it seems to increase inflammatory and immunological skin pathology like psoriasis and acne. Psoriasis is an inflammatory condition caused by a disruption in the immune system due to the interference of innate and adaptive immunity. It is noticed that after the proliferation of skin, several factors such as innate immune system effectors are increased, these effectors are named neutrophils, plasmacytoid dendritic cells (pDCs), NK cells, and myeloid dendritic cells (CD11c+ mDCs).

The release of certain chemicals like cytokines is facilitated through the receptors of DCs and T-cells. The secretions from these receptors activate keratinocyte that aids in the production of AMPs in the psoriatic lesions due to AMPs (like β-defensins, S100 proteins, or LL-37) in huge amounts. The secretions from the mentioned receptors aid in the secretion of cytokines which helps in activating proinflammatory cytokines (IL-1, IL-6, and TNF-α), chemokines (CXCL8 through CXCL11 and CXCL20), and S100 proteins, these secretions are known to be chemo attractants for immune cells and neutrophils. Consequently, a positive feedback system is established relating to keratinocytes and infiltrating immune cells that maintain a process of the constant decontrolled inflammatory process (S100A7–9).[10] Psoriasis is clinically diagnosed based on the size and distribution of lesion along with systemic manifestations. It is commonly classified as plaque, guttate, pustular, and erythrodermic psoriasis.[11]

Although this disease can occur in any age, literature shows two peak age ranges 16-22 and 57-60.[12] The assessment of psoriasis severity is established by using the tool of psoriatic area and severity index (PASI).[14] There are many studies conducted that show Vitamin D deficiency is psoriasis.[18] Kinase *et al*. laid an analysis to interrogate the capacity of Vitamin D and the levels of the mineral density of bones in patients suffering from psoriasis and arthritis caused by psoriasis. The study established that there is a contrasting relationship between psoriasis severity and Vitamin D levels. The patients that had inadequate capacities of Vitamin D were found to have higher PA activity.[13] However, some studies showed that no correlation has been found between the degrees of Vitamin D and psoriasis.[15] Low serum 25 (OH)D levels increase the risk of developing Th1-mediated autoimmune disease. The expression of two keratin altered in psoriasis i.e. K1 and K10 are also modulated by vitamin D.[16] It also normalizes the distribution of integrins CD26 and ICAM-1 in the dermal-epidermal junction that is altered in psoriatic skin.[17] A study suggested that the cause of vitamin deficiency among psoriasis patients could be multifactorial; lack of sun exposure, use of medications such as glucocorticoids, and immunosuppressants that may interfere with 25(OH)D metabolism. Or low intake of 25(OH) D.[19] Various studies show the association of acne with vitamin D deficiency.

Research conducted through Mustafa Turgut Yildizgören *et al.,* aimed at finding the correlation between the occurrence of acne and Vitamin D serum levels. The study compared the serum levels of acne patients diagnosed with nodulocystic acne and people that had low to no acne i.e., the healthy population. The analysis suggested that the capacity of Vitamin D was majorly below average in acne patients ($p<0.05$) as compared to the healthy population.[20] Pilosebaceous units cause an inflammatory disorder of Acne vulgaris. It appears as inflammation of open or closed comedones. Which eventually form papules, pustules, or nodules in areas of skin densely populated with pilosebaceous ducts such as the skin of the face, upper trunk, neck back, and shoulder.[21] Acne is formed by colonization of Propionibacterium acnes (P. acnes) due to inflammation caused by increased sebum secretion in response to follicular plugs and hyperkeratinization of the pilosebaceous unit.[23] The severity of acne is determined by physical examination of the lesion; a mild case of acne may present as open and closed comedones accompanying a few inflammatory signs on the face and trunk. Moderate acne is clinically presented as papules and pustules on the face along with marked inflammation. Whereas nodules and cysts are a hallmark of severe acne along with widespread lesions on the face and trunk.[22]

Acne usually occurs during adolescence and early adulthood. Multiple factors influence the pathogenesis of acne which hormonal factors and an insulinotropic diet being the most important.[20] Serum Vitamin D levels may influence the pathogenesis of acne, due to its antioxidant and anti-comedogenic properties. Its deficiency may exacerbate pathogenesis as a Low level of serum Vitamin D may result in cosmogenesis due to its impact on the proliferation and differentiation of sebocytes and keratinocytes. Increased sebum production facilitates the growth of propionibacterium acnes and exacerbates inflammation by stimulation of toll-like receptors resulting in exacerbation of inflammation and comedogenic.[20] Diseases like Psoriasis and acne have been related with Vitamin D capacities and degrees in various studies. There can be differences in the opinions promulgated by different scholars and their findings. Hence, the study at-hand aims to investigate the significance of Vitamin D levels in patients with psoriasis and acne.

Objective

The study targets to assess and contrast the connection and association between Vitamin D levels in acne and psoriasis patients by investigating the degree of Vitamin D serum release in psoriasis and acne.

Method

The methodology of the study is laid on the foundations of comparative and cross-sectional functions. The study was performed in dermatology OPD of Fauji Foundation Hospital Rawalpindi. 350 participants were selected by non-randomized convenient sampling, out of which 323 signed informed consent and qualified based on inclusion, and exclusion criteria were included. Out of these 323, 140 that were diagnosed with acne were included in group A based on inclusion criteria of age between 12 to 40, and normal renal function test and liver function tests values. And, 183 participants diagnosed with psoriasis were included in group B based on inclusion criteria of age between 16 to 70 and normal renal function and liver function test values. All these participants did not have a history of hypertension, diabetes mellitus, or renal and hepatic diseases, and were screened for normal RFTs and LFTs by taking blood samples. Fauji Foundation Hospital was asked for permission

and approval, through means Institutional Ethical Research Board (IERB).

History of patient records included information regarding age, gender, socio-demographic characters and diagnosis. Serum RFTs and LFTs were done to rule out any underlying pathology.

The use of the immuno-enzyme technique (25(OH)-Vitamin D Xpress ELISA kit Immundiagnostik AG, Germany) facilitated the assessment of 25-hydroxycholecalciferol (25(OH) D) serum levels. The method's sensitivity was pegged at 6.2 nmol/l, in-series error 6%, and inter-series error 7.4%. The assessment of the found information was preceded in the Institute of Basic Medical Sciences and Research Center situated in Islamabad's Fauji Foundation Hospital. SPSS 26 was utilized to process the information in a computerized fashion. The normality of data was assessed using the Shapiro-Wilk test. Tables are used to express demographic characteristics and vitamin D levels. Paired t-test was used to determine the difference in serum vitamin D levels in both groups. After the application of the test of significance, the calculated P-value was calculated as <0.05 which was taken as significant, and the Pearson correlation test shows the relation of disease with mean serum vitamin D level.

Results

The total human subjects for the study were 323 and were divided into 2 groups A and B. Group A contained 140 participants who were clinically diagnosed with acne and the remaining 184 participants were placed in group B that were clinically diagnosed with psoriasis.

Table 1 shows the demographic characteristics of participants. 144 participants included in group A were between age of 16 to 40 with mean age of 25.63. While 184 participants that were included in group B were in the age group of 12-75 with mean age of 39.9. It was further seen that among the participants in group A, 12 (8.5%) were males and 128 (91.5%) were females. And in group B, 37 (20.2%) were males and 146 (79.7%) were females.

Table 1 Demographics of population.

Variable	*Group 1 Acne*	*Group 2 Psoriasis*
Age (year)		
Range	16-40	12-75
Mean	25.6357	39.9016
Sex %		
Male	12(8.5%)	37(20.2%)
Female	128(91.5%)	146(79.7%)

Table 2 Serum vitamin D level.

Variable	Mean		P value
Serum vitamin D level mean±SD	Group A	Group B	
	41.47±19.6	21.83±8.5	0.05

Table 2 show the mean and standard deviation of serum vitamin D level in both. The mean serum vitamin D level in group A is 41.47 and mean vitamin D in group B is 21.83.

Regarding correlation of serum vitamin D level to psoriasis and acne, it is seen that there is a significant negative relation of serum vitamin D level to psoriasis (r=0.13, p=0.05) and there is non-significant correlation of serum vitamin D level to acne (r=1, p=>0.05) as shown in **Table 3**.

Values of one paired t test show that there is significant difference between the mean of vitamin D level of acne (M=41.47, SD=19.6) and vitamin D level of psoriasis (M=21.83, S. D=8.5). Regarding correlation of serum vitamin D level to psoriasis and acne, it is seen that there is a significant negative relation of serum vitamin D level to psoriasis (r=0.13, p=0.05) and there is non-significant correlation of serum

Table 3 Correlation of vitamin D level.

Correlations			
		Vitamin D level in acne	Vitamin D level in psoriasis
Vitamin D level in acne	Pearson Correlation	1	-0.139
	Sig. (1-tailed)		0.050
	N	140	140
Vitamin D level in psoriasis	Pearson Correlation	-0.139	1
	Sig. (1-tailed)	0.050	
	N	140	183

Table 4 Paired Sample Test.

	Paired Differences							*Significance*	
	Mean	*Std. Deviation*	*Std. Error Mean*	*95% Confidence Interval of the Difference*		*t*	*df*	*One-Sided p*	*Two-Sided p*
				Lower	*Upper*				
Vitamin D level in acne - Vitamin D level in psoriasis	19.64579	22.50901	1.90236	15.88448	23.40709	10.327	139	<.001	<.001

vitamin D level to acne (r=1, p=>0.05) as shown in **Table 4**.

Table 5 shows that out of 140 people having acne, 59 people (35%) had serum vitamin D level less than normal. And out of 183 people having psoriasis 107 (58.5%) had vitamin D level less than normal.

Skin conditions like psoriasis and acne have a great impact on various metabolic aspects. This includes synthesis and activation of vitamins D having skin as the source. Since acne does not affect keratinocyte proliferation until severe, it is not influenced vitamin D absorption as much as psoriasis which directly impacts keratinocyte proliferation and hence disrupts the formation and activation of vitamin D.

This study shows that more than half of psoriasis patients have Vitamin D deficiency i.e., <30ng/ml. The study conducted by Angela Filon *et al*. provides similar results that aimed to compare the levels of vitamin D in healthy populations and patients with psoriasis as well. The levels of serum in healthy individuals were greater than the levels of serum instigated in psoriatic patients.[26]

Vitamin D deficiencies are found to impact psoriatic patients more than acne patients. The people suffering from acne were found to have lower than average levels of serum vitamin D.

Similar was the result of a study conducted by Ghadah Alhetheli to evaluate serum levels of vitamin D of patients with acne vulgaris by comparing serum levels of acne patients with normal population show a significant deficiency in vitamin D level of people having acne.

Table 5 Category of Vitamin D level in patients of psoriasis and acne.

Vitamin D level	*Group A (acne)*	*Group B (psoriasis)*
Deficiency >20ng/ml	9 (6.4%)	67(36.6%)
Insufficiency 21-29ng/ml	50 (28.6)	40(21.9%)
Sufficiency 30-100 ng/ml	116 (65.0%)	72(39.3%)

In a comparison conducted to analyze the difference in levels of serum levels in acne patients with healthy individuals where some individuals had suffered from acne vulgaris and some were completely healthy, the results indicated that vitamin D deficiencies were more common in patients suffering from acne vulgaris (P value=0.003). But there was not an established relationship found between the deterioration of acne vulgaris with the levels of 25-hydroxyVitamin D [25 (OH) D].[27]

Research study depicts that the levels of vitamin D serum are significantly impactful in psoriasis but there are no such signs of the serums in acne vulgaris. Rohini Sharma *et al*. conducted an analysis that interrogated the regulation of vitamin D levels in dermatology. The findings of the review suggested that there is a direct impact of LL37's overexpression on the secretion of Vitamin D3, the overexpression also promulgates the secretion of cAMP which is dysfunctional and is released by epidermal keratinocytes, assisting in the manufacturing and activation of vitamin D leading to Vitamin D deficiency. There are fewer impacts of expression on the inflammation of cytokines that can benefit acne treatment, but their insufficiency is not significant.[25]

Similar results regarding the relation of vitamin D with psoriasis are shown in a study, by Masoud Maleki, and Yalda Nahidi to investigate serum Vitamin D levels in psoriasis by comparing their mean vitamin D levels with that of the healthy control group, showing that psoriasis patients have vitamin D deficiency (m=12.52 ± 4.54) as compared to healthy control group 14.92±6.31.[28]

Recommendation

It is recommended for future researchers to consider the relation of Vitamin D with the severity of disease to get a better insight regarding and assessment of other genetic and biological factors that affect diseases should be considered.

Conclusion

The study exhibits that the deficiency of Vitamin D is significantly related to psoriasis, whereas deficiency of vitamin D does not have a significant relation to acne. This shows that due to greater area of skin involvement, there are more chances of development of vitamin D deficiency in psoriasis patients whereas acne disease itself does not have an important impact on vitamin D deficiency. This finding can help in the development of treatment of psoriasis and acne. Since there is a chance of vitamin D deficiency, it provides better results with topical and oral intake of vitamin D based on the required dosage.

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