ORIGINAL ARTICLE

Bali Medical Journal (*Bali Med J)* 2020, Volume 9, Number 3: 668-671
P-ISSN.2089-1180, E-ISSN: 2302-2914

Published by DiscoverSys

Correlation of plasma vitamin d receptors with the severity of psoriasis vulgaris

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ABSTRACT

Introduction: Psoriasis vulgaris is still a major problem in the field of dermatology. Until recently, the exact cause of psoriasis is still being debated. In recent years research has been carried out on vitamin D and its role in the immune system, especially in psoriasis. Vitamin D cannot be separated from the role of VDR. The study aims to evaluate correlation between VDR plasma levels and the severity of psoriasis vulgaris.

Method: Study design using a cross-sectional design to determine the correlation of vitamin D levels in plasma with the severity of psoriasis vulgaris calculated using the Psoriasis Area and Severity Index (PASI) score.

Result: This study included 47 study participants who had psoriasis vulgaris, consisting of 30 (63.8%) men and 17 (36.2%) women with a mean age of 44.66 years. The mean PASI score was 6.904, while the mean plasma VDR level was 30.328 ng/ml. Spearman correlation shows a strong negative correlation (r = - 0.979; p <0.001) between plasma VDR levels and PASI scores in psoriasis vulgaris patients.

Conclusion: Vitamin D plays a role in regulating the growth and differentiation of keratinocytes and influences dendritic cells and T lymphocytes' immune function so that low vitamin D levels have essential implications in the pathogenesis of psoriasis vulgaris. In performing its function, vitamin D must bind to VDR and form a complex. In this study, it was found that there was a strong negative correlation between plasma VDR levels and PASI scores, so it can be concluded that low plasma VDR levels correlate with high degrees of psoriasis vulgaris severity and vice versa.

Keywords: atrial fibrillation, spontaneous, conversion, acute coronary syndrome
Cite this Article: Adiguna, M.S., Rusyati, L.M.M., Sudarsa, P.S.S. 2020. Correlation of plasma vitamin d receptors with the severity of psoriasis vulgaris. *Bali Medical Journal* 9(3): 668-671. DOI: 10.15562/bmj.v9i3.2013

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Received: 2020-08-14
Accepted:2020-10-07
Published: 2020-10-20

INTRODUCTION

Psoriasis is a chronic autoimmune skin disease that results in excessive proliferation of the epidermis. Normally a person experiences skin change every 3-4 weeks, but psoriasis patients will experience a relatively fast changeover period between 2-3 days and unevenly causing the appearance of red spots on the skin. The clinical picture of psoriasis is in the form of silver scale layered skin, with a red base accompanied by itching or burning. Patients with severe psoriasis tend to feel embarrassed in their social environment and develop a fear of contagion, rejection and avoidance from people who are not used to seeing it.

Psoriasis is found throughout the world with a prevalence that varies from 0.1 percent to 11.8 percent. The highest incidence reported in Europe was in Denmark at 2.9 percent.[1] The prevalence of psoriasis in caucasians ranges from 1.5 to 3 percent, while in Asia it ranges from 0.1% to 0.3%. The incidence of psoriasis at the Central General Hospital (RSUP) Dr. Cipto Mangunkusumo during 2000 to 2001 reached 2.3 percent.[11] The age of onset of psoriasis varies with two peaks of incidence, the earlier onset type (16-22 years) and the late-onset type (57-60 years). Psoriasis is equally distributed between men and women but in women it tends to develop earlier.[2]

Until recently, the exact cause of psoriasis is still being debated. In recent years studies have been carried out on vitamin D, its role in the immune system and psoriasis.[3] Vitamin D performs different functions apart from its well-known role in calcium and phosphorus metabolism, such as the discovery of vitamin D receptors (VDR) and CYP271 (an enzyme responsible for the synthesis of 25-hydroxyvitamin D) in other tissues. There are at least 60 cell types known to express VDR and more than 200 genes modulated by vitamin D.[4] Vitamin D in the immune system is acted on by VDR on activated T lymphocytes as well as the suppressive or inhibitory effect of 1,25-dihydroxyvitamin D. In vivo and in vitro findings indicate that vitamin D causes changes in the immune system.[5] The available evidence also suggests that vitamin D plays a role in modulating dendritic cell function and regulating keratinocyte and T cell function so

that it may have important implications in psoriasis pathogenesis.[6]

Study conducted by Orgaz-Molina et al.[5] in Spain showed significantly lower outcomes in psoriasis patients than controls. Similar to a study conducted in Egypt by Gutte et al. Vitamin D levels in psoriasis patients were significantly lower than controls with an OR value of 27.58.[7] However, the role of vitamin D cannot be separated from the VDR expression, so in this study we would like to evaluate relationship between VDR expression and the severity of psoriasis vulgaris.

METHOD

The study design used was an analytic cross-sectional design aimed at determining the relationship between plasma VDR levels and the incidence and severity of vulgaris psoriasis as assessed using the psoriasis area severity index (PASI) score. This study's population was all psoriasis vulgaris patients in Dermatology and Venereology Outpatient Clinics at Sanglah General Hospital between October 2017 to January 2018. This study's inclusion criteria were psoriasis patients in good general condition and willing to participate after obtaining a brief informed consent. The exclusion criteria in this study were patients who had just received therapy for less than two weeks, were receiving NB-UVB therapy in the last 4 weeks, took supplements containing vitamin D, had acute or chronic infectious diseases such as upper respiratory tract infections and tuberculosis infection or systemic diseases such as systemic lupus erythematosus, rheumatoid arthritis, diabetes mellitus, malignancy, multiple sclerosis, cardiovascular disease, being pregnant, breastfeeding, menstruation, thyroid disease, parathyroid disease, ovarian tumors, and a history of taking anti-seizure drugs and antibiotics such as phenobarbital, phenytoin, carbamazepine and rifampin in the long term. Samples were recruited through consecutive methods, patients who met the inclusion and exclusion criteria were included in this study. Patients selected to be the sample in this study will be subjected to focused interviews, physical examinations, and blood sampling. The examination of vitamin D receptors using the ELISA (Kit By Elabscience) method with a detection ability of 0.63-40 ng/mL, and a sensitivity of 0.38 ng/mL.

Statistical analysis

The research analysis in this study used SPSS version 25.0 (IBM Corporation, Armonk, NY, USA). Numerical data are presented as mean and standard deviation, and categorical data are presented in frequency and percentage. The normality test using Saphiro-Wilk test. Correlation in this study was assessed using the Pearson Correlation test if the data were normally distributed and the Spearman correlation test if the data were not normally distributed. All values are considered significant if $p<0.05$.

RESULTS

characteristics of research participants

This study involved 47 psoriasis vulgaris patients, consisting of 30 (63.8%) men and 17 (36.2%) women. The study participants' mean age was 44.66 years, with the youngest being 17 years and the oldest being 65 years. Based on the degree of severity calculated using the PASI score, the mean PASI score was 6.904, while the mean plasma VDR level was 30.328 ng/ml (Table 1).

Table 1. Sample characteristics

Characteristics	Psoriasis Vulgaris (n= 47)	Percentage (%)
Sex		
Male	30	63.8
Female	17	36.2
Age (years)		
1 - 20	1	2.1
21 - 40	16	34.0
41 - 60	24	51.1
61 – 80	6	12.8
Mean PASI score		6.904
Mean VDR score		30.328 ng/ml

Data Normality Test

In the normality test carried out on the research data on VDR levels and PASI scores, the results are presented in Table 2. Based on Table 2, it is found that the data on VDR levels and PASI scores using the Shapiro-Wilk test is not normally distributed because the p-value = 0.000 (p <0, 05).

Table 2. Normality plot with test

No	Variable	p
1.	VDR serum	0.000
2.	PASI score	0.000

Normal distribution p>0,05

Correlation of VDR plasma levels with vulgaris psoriasis

The mean VDR level among study participants was 30.328 ng/ml, with the lowest level being 19.39 ng/ml and the highest being 36.54 ng/ml. To determine the correlation between plasma VDR levels and bacterial indexes, a correlation analysis

was performed using the Spearman Correlation method because the VDR level data were not normally distributed. Based on the statistical analysis, it was found that a strong negative correlation (r = - 0.979; p<0.001) between plasma VDR levels and PASI scores in psoriasis vulgaris patients. The results of the correlation can be seen in Table 3.The scatter plot graph shows a negative correlation (direction of the correlation line towards the bottom), with a linear R^2 value of 0.996 (Figure 1).

Table 3. Correlation between VDR serum and PASI

		PASI score
Plasma VDR	r	- 0,979
	p	<0.001
	n	47

DISCUSSION

This study showed that psoriasis vulgaris was more common in men as much as 63.8% compared to women as much as 36.2%. In general, it is known that psoriasis incidence in men and women is almost the same. There is no evidence to show a phenotypic difference between the sexes of psoriasis vulgaris.[1] Research by Kurd and Gefland conducted in the United States showed that there was no difference in the incidence of psoriasis between men and women.[8]

Recently, several studies have found that psoriasis incidence in men is slightly higher than in women. A hospital-based study conducted in Taiwan found the ratio of the incidence rate of psoriasis in men to women was 2.17:1.[9] Meanwhile, the population-based study in Taiwan which involved 5864 psoriasis sufferers, found a significantly higher prevalence of psoriasis in male than female.[10] The same results were obtained in research by Setyorini at dr. Cipto Mangunkusumo and in a private clinic, which shows the proportion of psoriasis in men and women is 1.5: 1.[11] The variation in results obtained in these studies is strongly influenced by the sampling technique and variables used in the study, and as is known psoriasis is a complex disease, with genetic and environmental factors playing an important role.[1]

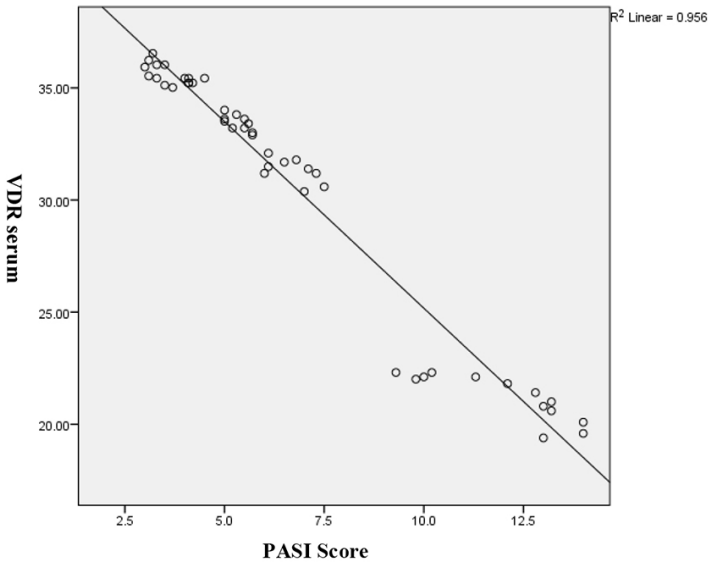

Figure 1. Correlation between serum VDR and PASI in psoriasis vulgaris

In this study, it was found that the research subject with the youngest age was 17 years and the oldest age was 65 years. The mean age in the cases was 44.66 years. In this study, age grouping showed that psoriasis vulgaris was found to be more in the age range 41-60 years as much as 51.1%. Based on research conducted by Gisondi et al.[12] in 338 psoriasis vulgaris patients, the mean age distribution was 42.1. The results of this study are also consistent with previous studies showing that psoriasis is rare in children and tends to occur in adulthood, although the incidence rate may vary according to geographic area. Several previous studies have shown an increased incidence of psoriasis with increasing age. The incidence of psoriasis increases over 39 years of age and the incidence of psoriasis is estimated to decrease in the elderly.[13]

Vitamin D plays an important role as a regulator of the immune system in CD4+ T lymphocytes and several cytokines' production and action. There is some convincing evidence for vitamin D function in the formation and/or maintenance of immunological self-tolerance, so that more and more studies are evaluating the relationship between vitamin D and chronic plaque psoriasis.[12] The exact mechanism of vitamin D deficiency contributing to psoriasis' complex pathogenesis is not yet fully understood. Several pathways have been suggested including loss of the anti-proliferative function of vitamin D, as it has been suggested that human keratinocyte cultures exposed to calcitriol showed growth inhibition and maturation speed.[14]

Inflammation and angiogenesis are also pillars in the pathogenesis of psoriasis, loss of anti-inflammatory and antiangiogenic activity of vitamin D could represent another explanation for the contribution of vitamin D deficiency in psoriasis.[15] 1,25-dihydroxyvitamin D3 is known to suppress the proliferation of Th1 and Th17 cells, and induce Treg, this is an alternative pathway, vitamin D deficiency can occur in psoriasis with the proliferation of Th1 and Th17 cells on the one hand and inhibition of Treg cells on the other.[16]

Vitamin D3 via vitamin D receptor (VDR) regulates the growth and differentiation of

keratinocytes. It also influences the immune function of dendritic cells and T lymphocytes so that low vitamin D levels may also have important implications in the pathogenesis of psoriasis.[17] Vitamin D receptors are a part of a large group of steroid/thyroid hormone receptors. The existence of a bond between the receptor and this hormone will form a complex that will bind to the target gene's regulatory region so that it can modulate the transcription of the gene. In previous studies, it was found that the amount of intracellular VDR protein was correlated with cellular response to vitamin D3 and the induction of VDR mRNA in patients with psoriasis was a sign of a clinical response to therapy using vitamin D derivatives.[18]

Recently, it has been found that there is a strong possible genetic background to psoriasis incidence. In addition to the commonly discussed disruption in human leukocyte antigen, the presence of polymorphisms in the VDR gene is associated with psoriasis incidence. In a study by Zhou et al.[19] in 2014, it was found that polymorphisms in the VDR gene were related to the incidence of psoriasis vulgaris in the Han population in Southeast China.

CONCLUSION

There was a strong negative correlation between plasma VDR levels and the severity of psoriasis vulgaris calculated using the PASI score. In further research, genetic level evaluation to assess the relationship between VDR mRNA expression and psoriasis vulgaris might prove the correspondence between the decreased VDR mRNA expression and plasma VDR levels in psoriasis.

CONFLICT OF INTEREST

All authors declare there is no conflict of interest regarding publication of this article.

FUNDING

This research received grant funding from the post doctoral research grant scheme (HPPD) Universitas Udayana.

ETHICAL CONSIDERATION

This study has been approved by Ethical Committee Faculty Medicine/Sanglah General Hospital, Bali-Indonesia. All study procedures in accordance to declaration of Helsinki (declaration of human right).

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