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Original Article

Evaluation of Serum Vitamin D Levels Among Patients with Viral Warts

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ABSTRACT

Objective: To evaluate serum levels of 25-hydroxyvitamin D (25-OHD) in patients with viral warts.
Study Design: Comparative cross-sectional study.
Place and Duration of Study: Dermatology Department, Fauji Foundation Hospital, Rawalpindi Pakistan, from Jul to Dec 2020.
Methodology: One hundred patients were included in the study, 50 with viral warts (Group-1) and 50 without warts (Group-2). Our study included both male and female patients of 10 to 60 years of age. Three categories were made according to their serum vitamin D levels. First, all participants were tested for serum vitamin D levels using ELISA.
Results: In Group-1, 20(40%) had insufficient, and 25(50%) had deficient vitamin D levels. A statistically significant decrease in serum 25-OHD levels (p = 0.004) was found in patients with viral warts. In Group-2, 9(18%) had insufficient, and 2(4%) had deficient vitamin D levels. The mean serum vitamin D level was 22.61±10.11 in Group-1 and 45.12±24.60 in Group-2, resulting in a significant difference between patients with viral warts and those without viral warts regarding serum vitamin D levels (p=0.004).
Conclusion: Patients with viral warts have deficient vitamin D levels.

Keywords: Benign proliferation, Viral Warts, Vitamin D.

How to Cite This Article: *Kanwal S, Rehman F, Fatima B, Qureshi SW, Jmail S, Khan RN. Evaluation of Serum Vitamin D Levels Among Patients with Viral Warts. Pak Armed Forces Med J 2023; 73(2): 402-404. DOI: https://doi.org/10.51253/pafmj.v73i2.7412*

INTRODUCTION

Warts (verrucae) are the benign proliferation of the skin and mucosa caused by human papillomavirus (HPV).[1] Verrucae are rough, thick, skin-coloured or grey-brown lesions present mostly over hands, feet, face and knees, which can be single or multiple. Genital and non-genital are the two main types of warts. Non-genital is classified as common, planar, palmoplantar, mosaic, and digitate/filiform.[2] Verrucae are a common viral infection of the skin.[3,4]

Topical drugs (5-Flurouracil, Formaldehyde, Trichloroacetic acid, Podophyllotoxin, Salicylic acid, Imiquimod), surgical procedures (surgical excision, electrocautery, cryotherapy, laser ablation), photodynamic treatment, Intralesional interferons, topical and systemic Immunotherapy (Rubella, Mumps and Measles vaccine, BCG vaccine, Human papillomavirus vaccine, Tricophyton antigen, Tuberculin, Zinc and Vitamin D) and oral medicines (Cimetidine and Levamisole) are used in the treatment of warts.[5,6] Warts are frequently resistant to treatment, resulting in recurrence. Resistant warts persist after several months of conventional treatment like chemical peels, surgery, freezing, and laser. Low serum 25-OHD levels were seen in patients with viral warts in many studies, indicating the importance of vitamin D in treatment.[7,8]

Epidemiological studies revealing a strong link between deficient vitamin D levels and the occurrence of several infectious illnesses, such as respiratory infection, septic shock, and influenza, prompted researchers to link vitamin D signalling to protection against infection.[9,10] This study aims to identify vitamin D deficiency in patients of verruca and address the role of vitamin D in treating viral warts.

METHODOLOGY

The comparative cross-sectional study comprising 100 participants, 50 of whom had viral warts and 50 without viral warts, attending the Dermatology Outpatient Department, Fauji Foundation Hospital, Rawalpindi Pakistan, from July to December 2020. The study was approved by the Ethical Committee of Fauji Foundation Hospital Rawalpindi Pakistan (Ref No 495/RC/FFH/RWP). The sample size was calculated using the WHO sample size calculator, keeping the population proportion of warts at 7%.[4]

Inclusion Criteria: Both male and female patients from 10 to 60 years of age with verrucae were diagnosed based on their clinical appearance.

Exclusion Criteria: Patients who took topical and systemic treatments for warts prior to the research, systemic disorders with deficient serum 25-OHD levels (liver and kidney disease); autoimmune disorders like

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Received: 26 Sep 2021; revision received: 01 Jan 2022; accepted: 05 Jan 2022

vitiligo; and patients taking supplements containing vitamin D, medicines that influence vitamin D levels, for example, cytostatic agents, lipidlowering medicines, antiretroviral medications, antiestrogens, glucocorticoids and antiepileptic; pregnant and lactating females were excluded from the study.

Informed written consent was taken from all participants. In addition, a non-probability consecutive sampling technique was carried out in data collection. Both Groups were classified based on age as Children (10 to 16 years), Young (17-25), Middle age (26 to 45) and Elderly (46 and above). The participants' complete medical history was obtained, including course and duration of disease, a history of diseases that affect blood 25-OHD levels, a history of drug use, and length and frequency of sun exposure. The number and distribution of warts were taken into account.

Vitamin D levels were tested in the Fauji Foundation Hospital laboratory using an enzymelinked immunosorbent assay after five cc of venous blood was obtained under aseptic conditions. The tests were free of cost. Participants were grouped based on their 25-OHD levels: 1) Deficient: Vitamin D levels less than 20 ng/ml; 2) Insufficient: Vitamin D levels 20–25 ng/ml; 3) Sufficient: Vitamin D levels greater than 25 ng/ml.

Statistical software for Social Sciences (SPSS), version 23, was used to code and enter the data. Mann–Whitney test was used to make comparisons between quantitative variables. To calculate correlations between quantitative variables, Spearman's correlation coefficient was used. The *p*-value of ≤0.05 was considered statistically significant.

RESULTS

Only 5(10%) patients with viral warts and 39 (78%) without viral warts had sufficient vitamin D levels. 20(40%) patients with viral warts had insufficient 25-OHD levels while 9(18 %) patients without viral warts had insufficient 25-OHD levels. The mean age was 26.98±15.17 years in Group-1 and 25.76±7.75 years in Group-2. Vitamin D deficiency was found in 25(50%) in Group-1 and 2(4%) in Group-2. Both Group-1 and Group-2 comprised of 36(72%) females and 14(28%) males. The mean serum vitamin D level was 22.61±10.11 in the patient Group and 45.12±24.60 in Group-2, resulting in a statistically significant difference between patients with viral warts and patients without viral warts regarding serum vitamin D levels (*p*=0.004). In Table-I, the Mann-Whitney U test has been used for comparison between vitamin D levels of males and females. Table-II shows a comparison of vitamin D levels between Group 1 and Group 2 using Spearman correlation.

Table-I: Comparison of Vitamin D levels of Males and Females (n=100)

Parameters	Study Groups		*p*-value
	Males (n=28)	Females (n=72)	
Vitamin D levels (ng/ml)	30.46 (10.22- 71.18)	27.66 (10.43- 128.26)	0.017

Table-II: Comparison of Vitamin D levels of Group-1 and Group-2 (n=100)

Factors	Group-1	Group-2	Spearman Correlation	*p*-value
Vitamin D levels(ng/ml)	21.0850 (10.22 - 44.35)	41.22 (18.44-128.26)	-0.398	0.004

DISCUSSION

The study showed that patients with verruca had deficient 25-OHD levels compared to patients with viral warts. Numerous studies in different countries have evaluated the correlation between vitamin D levels and viral warts with varying results.

Though the specific function of vitamin D against warts is yet to be discovered, the action of vitamin D is thought to be due to its immunoregulatory properties, an important function in epidermal cell proliferation and differentiation, and the production of cytokine.[11,12] Vitamin D is important in developing autoimmune disorders like type-1 diabetes, multiple sclerosis, systemic lupus erythematosus, autoimmune thyroid disease, psoriasis, and Sjogren's syndrome. Most research demonstrates that sufficient supplementation can help prevent and treat some of these disorders.[13] The primary treatment for viral warts is local destruction of warts using cryotherapy and electrocautery. However, all these primary treatments are painful and cause scarring. Moreover, the chances of recurrence also increase. Therefore, by establishing a relationship between deficient serum vitamin D levels and the occurrence of viral warts, we can justify topical and intra-lesional vitamin D injections as an efficient treatment mode for viral warts.[14]

Tamer *et al*. concluded that patients with viral warts had lower levels of serum 25-OHD, ferritin, folate and vitamin B12.[15] In another study done by Aktas *et al*., the effect of vitamin D injection on warts was investigated, showing that patients with viral warts had lower levels of serum vitamin D and used intralesional vitamin D that resulted in complete resolution (80%) in 60 patients with one or more refractory warts.[16] Moscarelli *et al*.[17] published a case

study conducted in Italy to see if warts might be successfully treated with local vitamin D activation in a kidney transplant patient. After some time, they discovered that active vitamin D considerably impacted the treatment.

In a study by Raghukumar *et al*., twenty plantar warts patients were treated with intralesional vitamin D3, with recovery in 80% of patients without adverse effects or recurrence.[18] However, a study conducted in 2021 in Egypt revealed significantly lower vitamin D levels in patients of verrucae.[19] All the studies conducted in the past in Pakistan show the relationship between intralesional vitamin D injection and the resolution of viral warts.

Vitamin D levels may vary depending on the patient's lifestyle, such as sunscreen use, regular sun exposure, diet consumption, and skin colour. In addition, seasonal variations, air pollution levels, latitude, cultural differences and type of clothing can all impact vitamin D production.

ACKNOWLEDGMENTS

The authors thank Allah Almighty for His blessings in this research work. Secondly, we thank our parents and family for being very supportive

LIMITATIONS OF STUDY

Limitations of the study include the confounding variables which were not studied, such as sunscreen use, regular sun exposure, vitamin D consumption in the diet, skin colour, seasonal variations, cultural differences, type of clothing and use of veil. Larger sample size studies are required to corroborate the findings and to monitor out-comes over a longer period (samples collected at different times of year to study seasonal variations). Vitamin D plays a vital role in warts, but more research on a broader scale is needed.

CONCLUSION

Vitamin D levels are deficient in patients with warts.

Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

SK: Conception, interpretation of data, drafting the manuscript, approval of the final version to be published.

FR: Study design, data analysis, drafting the manuscript, cri-tical review, approval of the final version to be published.

BF:, SWQ: Data acquisition, interpretation of data, approval of the final version to be published.

SJ:, RNK: Study design, Drafting the manuscript, interpre-tation of data, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated & resolved.

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