Research Article

Comparison of Serum Vitamin D Levels in Individuals with and without Dupuytren's Disease -A Case Control Study

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Abstract: Background: It is a benign fibroproliferative illness of the hand known as Dupuytren's disease (DD). The precise etiology of the illness is yet unknown. Many studies have been conducted on vitD (Vitamin D) anti-fibrotic effects in chronic non-malignant disorders. However, little study has been done on measuring vitD (vitD) levels in both healthy people and DD patients.

Objective: To compare serum vitD in individuals with and without DD presenting to a tertiary care hospital in Karachi, Pakistan.

Materials & Methods: This case-control study was performed in Department of Plastic surgery, Civil Hospital, Karachi, Pakistan during November 2023 to August 2024. Patients were enrolled from outpatients' clinics whereas healthy controls were enrolled from Plastic & Reconstructive Department of Civil Hospital. Serum 25(OH)D (25-hydroxyvitD) levels were assessed as part of a standard laboratory evaluation for controls and all DD patients. The analysis of the data was done with SPSS 27.

Result: A total of 60 subjects were enlisted with 1:1 ratio of cases and controls. All of the patients were males. Age and body mass index were not significantly different among cases and control. Median vitD level among cases and controls was 18.4 (IQR=17.6-24.1) ng/mL and 26.1 (IQR=18.9-28.4) ng/mL respectively. The vitD levels of the patients and controls differed considerably ($p<0.001$).

Conclusion: The current investigation showed a considerably lesser level of vitD in cases compared to controls, indicating a connection between vitD and DD.

Keywords: Dupuytren's disease, Fibroproliferative disorder, VitD deficiency, Myofibroblasts, Etiology, Epidermal growth factor.

INTRODUCTION

A proliferative fibroplasia of the subcutaneous tissue, which can manifest as nodules or cords, causes palmar fascia hypertrophy in Dupuytren's disease (DD), a benign fibroproliferative illness of the hand. The cords, which are composed of normal fascia and connect the nodules to the skin and surrounding tissues, are what cause the nodules, which are locations of active contraction of the tissues. This causes contractures, which cause the finger joints to flex in a gradual and irreversible manner [1, 2].

A recent meta-analysis estimated the prevalence to be around 8% globally [3]. Africa has the highest recorded prevalence rates (17%), followed by Asia (15%), Europe (10%), and the Americas (2%). The incidence per ten thousand people rises with age, starting at about 5 in the age range under 50 and ranging up to 15-40 for age range of 50–79 years. Men are three to four times more likely than women to be afflicted [3, 4].

The first clinical sign is a hard lump that forms in the hand and grows into fibrous collagenous strands that reach into the fingers. The cords mature, thicken, and compress as the condition worsens, resulting in long-term flexion abnormalities. Although the course of the disease varies, 20 to 40 percent of patients eventually experience flexion deformity to some extent, which can cause functional impairments to the hands [5].

The precise etiology of the illness is yet unknown. The pathological changes linked to DD include aberrant myofibroblast proliferation, which results in uncontrollably growing palmar fascia. Type III collagen makes up the majority of these myofibroblasts. This procedure involves numerous mediators. These consist of platelet-derived growth factor, epidermal growth factor, connective tissue growth factor, transforming growth factor beta-1, transforming growth factor beta-2, and interleukin-1 [6]. Many studies have been conducted on vitD's anti-fibrotic effects in chronic non-malignant disorders. Numerous investigations have demonstrated that the primary target cells of 1,25(OH)2D3 inhibitory activity are myofibroblasts [7,8]. In many different types of cells, calcitriol represses the synthesis of collagen through an inhibitory action. Elevation of TGF-β1 in serum is caused by vitD (vitD) deficiency [9]. Thus, we hypothesized that vitD deficiency is involved in pathophysiology of DD. However, literature is lacking regarding this association. To the best of our knowledge, we have found a single study evaluating vitD deficiency and comparing it among DD patients and healthy

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controls [10]. Thus, we planned a current study to compare vitD levels among DD patients with their healthy counterpart.

MATERIALS AND METHODS

This case-control study was performed in Plastic & Reconstructive Department of Civil Hospital during November 2023 to August 2024. The study was commenced after acquiring formal approval from Hospital ethics committee (IRB-3200/DUHS/Approval/2023/421). Prior to their involvement, patients provided written informed consent. Cases were patients with confirmed diagnosis of DD. Age and gender match healthy controls were enrolled from waiting areas of hospital who were attendants. Patients with arthritis, chronic liver disease, kidney disease, thyroid disorders, and malnourished, using proton pump inhibitors were excluded.

Sample size was estimated using online available calculator Open-epi. Statistics considered for calculations are; mean serum vitD levels in DD was 19.33 ± 6.28 ng/mL, and in controls was 25.13 ± 8.35 ng/mL [10]. Power of test as 80% and confidence level was set at 95%. The estimated sample size was 26≈30 in each group. Non-probability consecutive sampling technique was employed to enlist participants.

Serum 25(OH)D (25-hydroxyvitD) levels were assessed as part of a standard laboratory evaluation for controls and all DD patients. There were two categories for vitD levels: insufficient (<20 ng/mL) and non-deficient (≥20 ng/mL). Investigations were also conducted into the patients' age, body mass index, length of illness, history of diabetes and hypertension, smoking status, history of prior surgery, involvement of both hands, and employment status. Every patient's characteristic was noted on a study proforma that had been pre-planned.

STATISTICAL ANALYSIS

SPSS version 27 was used to enter data and do statistical analysis. For categorical variables, percentages and frequencies were calculated. If the numerical variables were normally distributed, they were reported as mean ± standard deviation; if not, they were expressed as median with interquartile range. To compare categorical features between cases and controls, the chi-square test was utilized. Under the supposition of normality, the independent t-test or Mann-Whitney U test was used to compare numerical variables between cases and controls. Utilizing the Shaprio-Wilk test, the normality assumption was evaluated. P-value less than or equal to 0.05 was deemed as statistically significant.

RESULT

Total 60 patients were enrolled into the study with equal allocation in cases and control. Average age among cases and controls was 54.2 ± 7.8 years and 55.5 ± 9.1 years respectively. Average weight of cases of controls was 71.8 ± 5.4 Kg and 69.4 ± 6.7 Kg correspondingly. Mean height of controls was 1.7 ± 0.1 meter. Mean BMI for cases was 24.8 Kg/m^2 and for controls was 24.2 ± 1.7 Kg/m^2. Cases and controls did not differ on the basis of age (p=0.564), weight (p=0.149), height (p=0.553) and BMI (p=0.183) (Fig. **1**).

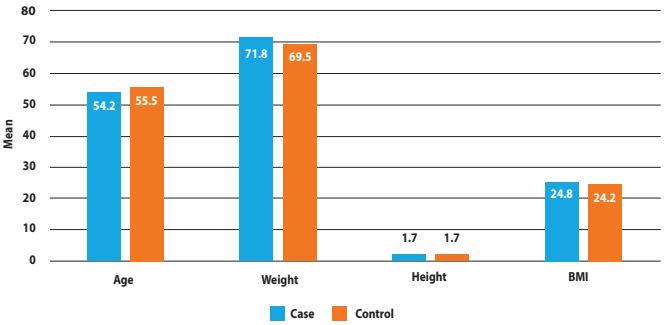

Fig. (1). Comparison of Patient's Age and Body Mass Index (BMI) among Cases and Controls.

The cases and control did not differ on the basis of work status (p=0.774) and sun exposure (p=0.371). Frequency of bilateral hand involvement (p=0.026) and past surgery (p=0.002) was significantly higher in cases than controls (Table **1**).

Table 1. Comparison of Patients' Features among Cases and Control.

Variables	Cases n(%)	Control n(%)	p-value
Gender			
Male	30(100)	30(100)	-
Female	0(0)	0(0)	
Working Status			
Employed	21(70)	22(73.3)	0.774
Unemployed	9(30)	8(26.7)	
Sun Exposure			
Yes	24(80)	21(70)	0.371
No	6(20)	9(30)	
Bilateral Hand Involvement			
Yes	8(26.7)	1(3.3)	*¥0.026
No	22(73.3)	29(96.7)	
Past Surgery			
Yes	9(30)	0(0)	*¥0.002
No	21(70)	30(100)	

¥Fisher-excat test is reported, *Significant at p<0.05.

Median vitD level among cases and controls was 18.4 (IQR=17.6-24.1) ng/mL and 26.1 (IQR=18.9-28.4) ng/mL respectively. The difference in vitD levels among cases and controls was significantly different (p<0.001).

Table **2** displays comparison of vitD levels among cases and control based on stratification of patients' features. Significantly lower levels of vitD was seen n cases among sub-group of

≥ 50 years (p=0.011), employed individuals (p=0.003), having sun exposure (p=0.003) and who did not undergo past surgery (p=0.002).

Table 2. Comparison of vitD Levels among Cases and Control Based on Stratification of Patients' Features.

Variables	Cases	Control	p-value
Age Groups			
<50 years	18.3 (17.8-22.7)	26.7 (18.9-27.7)	0.054
≥ 50 years	18.7 (17.3-24.8)	25.9 (18.8-28.9)	*0.011
Working Status			
Employed	18.9 (17.7-24.2)	25.8 (18.8-28.5)	*0.008
Unemployed	18.3 (15.9-24.9)	26.4 (20.1-30.3)	0.059
Sun Exposure			
Yes	18.3 (17.1-23.1)	25.8 (18.5-28.7)	*0.003
No	26.2 (18.7-26.7)	26.8 (24.8-27.5)	0.456
Bilateral Hand Involvement			
Yes	18.3 (16.7-22.7)	24.3	-
No	18.6 (17.6-25.0)	26.2 (18.8-28.5)	*0.005
Past Surgery			
Yes	19.0 (17.9-23.7)	-	-
No	18.3 (17.2-25.1)	26.1 (18.8-28.5)	*0.002

*Significant at p<0.05, Data is expresses as median (IQR).

DISCUSSION

Due to an increased deposition of collagen, DD is a benign fibroproliferative disease causing unalterable flexion finger contracture. It's interesting to note that vitD insufficiency is interrelated to some causes of DD, including diabetes and hypertension [11, 12]. More and more research is revealing that vitD has anti-inflammatory and anti-fibrotic consequences in addition to regulating cell division and proliferation. It has been thoroughly investigated in a number of chronic illnesses as an anti-fibrotic agent [13]. The vitD receptor (VDR) has been shown to block TGF-β signaling [14]. Reduced expression of VDR and low amounts of vitD may exacerbate impaired VDR signaling, which in turn may lead to uncontrollably high fibroblast activation in systemic sclerosis [15]. The present study found that vitD levels were significantly lesser in DD patients compared to their healthy controls. Consistent with this study, Par JW *et al.*'s [10] data demonstrate that the vitD concentrations in the disease group were significantly lower (mean 19.33 ± 6.28 ng/mL) than in the healthy control group (mean 22.89 ± 7.89 ng/mL).

According to published research, DD typically appears in people between the ages of 50 and 60 [16]. The study's DD patients were 54.2 ± 7.8 years old on average. A population-based study conducted in the Netherlands found that the median age was 63 years at the time of diagnosis. Additionally, the age group of 65 to 75 years old was when the prevalence of DD peaked [17]. The Swedish population likewise reached this high, but a little bit later [18]. Nevertheless, a meta-analysis also shown that the condition increases in frequency as people age. The mean prevalence of DD of age 55, 65, and 75 years was found to be 12%, 21%, and 29%, respectively, in a systematic review and meta-analysis [19]. Additionally, our research revealed that vitD levels differed considerably between cases and controls only in cases involving elderly individuals.

Greater serum levels of the substrate (25-hydroxyvitD) can counteract the reduction in lung epithelial cells' synthesis of the active form of vitD (1,25-dihydroxyvitD) caused by cigarette smoke. Furthermore, the expression vitD receptor may be impacted by cigarette smoke [20]. Furthermore, it has been established that drinking alcohol and smoking are frequent risk factors for a number of diseases [21, 22]. Nonetheless, a number of lifestyle decisions, such as smoking and alcohol consumption, have been linked to an increased risk of dementia. Numerous studies have demonstrated that the prevalence of DD is higher in individuals with a history of smoking than in the general population. Additionally, because there is a correlation between lifetime cigarette consumption and lifetime alcohol consumption, individuals with DD also consume more alcohol on average each week than people without the condition [23, 24]. Nevertheless, there is still disagreement over the causal association between these behaviors and DD, and further investigation is needed to get a firm conclusion. Since every patient who presented with DD did not smoke, our investigation did not uncover any connection between smoking and DD.

Research indicates that patients with co-occurring conditions like diabetes mellitus (DM) and alcoholism are more likely to experience DD. Since hypertension and diabetes typically coexist, hypertension is a significant risk factor for diabetic kidney disease. According to one study, individuals receiving antihypertensive treatment experienced a later onset of dementia relative to those without hypertension [25]. Additionally, other research has linked antihypertensive drugs to DD. Beta-blockers, for instance, have been shown to decrease human fibroblast proliferation by obstructing the production of endogenous beta adrenergic agonists, which prevent fibrosis [26]. There is also substantial evidence in the literature linking these two underlying diseases to vitD insufficiency [27, 28]. However, since none of the study's cases had hypertension or diabetes, we were unable to find any such association. Despite being older than fifty years, none of the study participants had hypertension or diabetes, which is a surprising finding. This unlikely finding may have arisen from the study's enrollment of a small number of patients.

CONCLUSION

The current investigation showed a considerably lesser level of vitD in cases compared to controls, indicating a connection between vitD and DD.

ABBREVIATIONS

25(OH)D: 25-hydroxyvitD.

DD: Dupuytren's disease.

DM: Diabetes Mellitus.

VitD: Vitamin D.

VDR: vitD Receptor.

AUTHORS' CONTRIBUTION

Seema: Conceptualization, Study Design, Writing draft, Critical Review and Revision the Manuscript.

Faisal Akhlaq Ali Khan: Study Design, Critical Review and Revision the Manuscript, Final approval, final proof to be published.

Waqas Sami and **Sana Shoukat**: Writing draft, Final approval, final proof to be published.

Erum Naz and **Hiba Moazam**: Methodology, Data analysis and Interpretation, Final approval, final proof to be published.

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Declared none.

DECLARATIONS

Data Availability

Data will be available from the corresponding author upon a reasonable request

Ethical Approval

The study was commenced with the approval of Institutional Review Board of Civil Hospital (IRB-3200/DUHS/Approval/2023/421).

Consent to Participate

All the study participants were enlisted with their written informed consent.

Consent for Publication

All authors give consent for the publication of this work.

Conflict of Interest

Declared none.

Competing Interest/Funding

Declared none.

Use of AI-Assisted Technologies

The authors declare that no generative artificial intelligence (AI) or AI-assisted technologies were utilized in the writing of this manuscript, in the creation of images/graphics/tables/captions, or in any other aspect of its preparation.

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