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Vitamin D Deficiency and Its Association with Metabolic Syndrome in Egyptian Patients with Psoriatic Arthritis

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ABSTRACT

Background: Vitamin D (Vit D) deficiency has been implicated in several autoimmune diseases, including psoriatic arthritis (PsA), and is considered a potential risk factor for metabolic syndrome (MetS).

Objective: This study aimed to investigate the prevalence of Vit D deficiency and its association with MetS components in Egyptian patients with PsA.

Patients and methods: In this cross-sectional study, 60 PsA patients were recruited from Tanta University Hospitals and evaluated for MetS according to established criteria. Vit D levels were measured using a CLIA kit, and disease activity was assessed via the disease activity in psoriatic arthritis "DAPSA" score.

Results: Among the 60 patients, 58.3% (35) met the criteria for MetS. Vit D deficiency (<10 ng/ml) was present in 43.3% of patients, with a significantly higher prevalence in the MetS group (54.3%) than in non-MetS patients (28%, p=0.027). Vit D levels showed a strong negative correlation with waist circumference (rs = -0.606, p < 0.001), BMI (rs = -0.552, p = 0.001), and fasting glucose (rs = -0.867, p < 0.001). Logistic regression identified Vit D deficiency as a significant risk factor for MetS (OR = 1.078, 95% CI = 1.016-1.143, p = 0.012).

Conclusion: It could be concluded that Vit D deficiency is prevalent among PsA patients and is significantly associated with MetS risk. Addressing Vit D deficiency may be essential in managing metabolic health in PsA patients.

Keywords: Vitamin D, psoriatic arthritis, metabolic syndrome.

INTRODUCTION

Psoriatic arthritis (PsA) is a chronic immunological, seronegative inflammatory disorder marked by several symptoms, including dactylitis, arthritis, enthesitis, and spondylitis [1]. It often occurs in psoriatic patients, with an incidence of around 30%, especially in those with nail or scalp psoriasis. The acknowledgment of PsA as a systemic condition underscores the heightened prevalence of its associated extra-musculoskeletal comorbidities, hence intensifying the effect on patients' quality of life. Cardiovascular disease (CVD) is acknowledged as a common comorbidity linked to PsA, affecting up to 80% of patients and leading to elevated mortality rates [2]. The European League Against Rheumatism (EULAR) promotes the screening for CVD and the therapy of its risk factors in clinical follow-up of PsA patients. CVD associated with PsA has been correlated with several cardio-metabolic risk factors, including diabetes, hypertension (HTN), obesity, hyperlipidemia, and particularly, metabolic syndrome (MetS) [3].

MetS—characterized by abdominal obesity, hyperglycemia, hypertension, and hyperlipidemia—is more commonly observed in individuals with PsA than in those with other types of inflammatory arthritis or in healthy individuals. Beyond its known association with cardiovascular disease, MetS may influence the severity, progression, and therapeutic outcomes of PsA [4]. Although the exact pathways connecting MetS and PsA remain unclear, factors such as elevated pro-inflammatory cytokines, oxidative stress, adipocytokine release from fat tissue, and gut microbiota imbalances are implicated in the development of MetS [5].

Vitamin D (Vit D), a fat-soluble steroid hormone produced in the skin through exposure to UV light, is essential in various physiological functions, notably in calcium regulation and bone health [6]. Deficiency in vit D has been associated with an array of health conditions, including osteoporosis, obesity, hypertension, diabetes, and cardiovascular disease. Additionally, low levels of vit D have been linked to an increased risk of MetS, potentially due to effects on insulin sensitivity and secretion [7]. vit D deficiency appears to raise the risk of MetS in PsA patients, especially given the higher prevalence of vit D deficiency observed in this population [8].

This study aimed to evaluate the prevalence of MetS and vit D levels in a group of Egyptian PsA patients and to explore the relationship between vit D status and various MetS components.

PATIENTS AND METHODS

This cross-sectional study included a total of 60 PsA patients diagnosed according to CASPAR criteria [9], attending at Department of Outpatient Clinic, Rheumatology, Rehabilitation and Physical Medicine, Tanta University Hospitals. This study was conducted between (mention period e.g., June 2021 and January 2023).

Exclusion criteria: Patients with previous vit D supplementation or those who were on corticosteroids therapy or lipid lowering drugs. Patients who were cardiac, diabetic, smoker or had any other autoimmune diseases were also excluded.

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All PsA patients were subjected to full history taking, clinical examination, assessment of disease activity, waist circumference (WC), laboratory assessment, blood pressure measurement, and body mass index (BMI).

1-Assessment of disease activity:

Disease activity was assessed using the DAPSA score, which was calculated by summing the tender joint count (TJC) (range 0–68), swollen joint count (SJC) (range 0–66), patient global visual analog scale (VAS) (range 0–10), patient pain VAS (range 0–10), and serum C-reactive protein (CRP) level (mg/dL). A DAPSA score between 0 and 4 indicates remission, 5–14 reflects low disease activity (LDA), 15–28 represents moderate disease activity, and scores above 28 denote high disease activity [10].

2-Laboratory assessment:

All PsA patients underwent laboratory testing, included measurement of C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), fasting blood glucose (FBG), lipid profile, serum 25-hydroxy vit D, and serum uric acid levels. Serum levels of vit D (25-hydroxyvitamin D) were measured using a CLIA kit, with deficiency defined as levels under 10 ng/ml, insufficiency between 10 and 30 ng/ml, sufficiency between 30 and 100 ng/ml, and toxicity above 100 ng/ml.

Criteria of MetS in PsA patients:

MetS was diagnosed in cases who met three or more of the following criteria: triglyceride levels (TG) of ≥150 mg/dl, WC of ≥102 cm in men or ≥88 cm in women, HDL levels below 40 mg/dl in men and below 50 mg/dl in women, fasting blood glucose of ≥100 mg/dl, and blood pressure of ≥130/85 mmHg[11].

***Ethical Consideration*:**

This study was ethically approved by the Ethics Committee, Faculty of Medicine, Tanta University (approval code: 36264PR919/10/24). Written informed consent of all the participants was obtained. The study protocol conformed to the Helsinki Declaration, the ethical norm of the World Medical Association for human testing.

Statistical analysis

The dataset was meticulously organized and entered into an Excel file before being processed with SPSS for Windows, version 25 (IBM Corp., Armonk, NY, USA). To evaluate the distribution of numerical data, the Shapiro-Wilk test for normality was applied. For data showing a normal distribution, values were presented as mean, standard deviation (SD), and range. In cases of nonparametric data, values were detailed as mean, SD, range, median, and IQR, covering the 25th to 75th percentiles). Qualitative data were summarized by count and percentage. To compare normally distributed quantitative data between two independent groups, the independent t-test was used, whereas the Mann-Whitney U test was chosen for comparing nonparametric quantitative data across groups. Pearson's Chi-square test assessed associations among categorical variables, and the Spearman correlation test was used to examine the direction and strength of relationships within nonparametric variables. Correlations were classified as weak for values between 0.0 and less than 0.25, moderate from 0.25 to less than 0.75, and strong from 0.75 to 1. Binary logistic regression analysis explored vit D role as a possible risk factor for MetS. Statistical significance was evaluated using the p-value: outcomes were deemed nonsignificant for p-values exceeding 0.05, significant at or below 0.05, and highly significant below 0.001.

RESULTS

This research included 60 individuals with PsA, consisting of 40 women and 20 men, with a mean age of 48.6 ± 6.89 years. The average DAPSA score was 20.0 ± 8.67, with most patients exhibiting significant disease activity, as seen in Table 1. Thirty-five patients (58.3%) fulfilled the criteria for MetS. Patients with MetS exhibited substantial differences compared to those without MetS in as regards WC, BMI, hypertension, TG, and FBG **(Table 1, 2)**. No substantial difference was seen between the two groups for disease activity and DAPSA scores.

For serum levels of vit D, according to **Table 3**, significant lower levels were noticed in MetS group compared to non-MetS group. 43.3% of total patients had vit D deficiency and 41.7% had insufficiency. Also, 54.3% of patients with MetS had deficiency compared to 28 % of non-MetS patients.

No substantial correlation was seen between serum vit D concentrations and several indicators of disease activity or MetS, including the DAPSA score, ESR, and CRP. Table 4 and figure 1 shows a substantial positive association with HDL, whereas a significant negative correlation was seen with WC, BMI, and FBG **(Figures 2, 3, 4)**.

Binary logistic regression was performed to assess vit D deficiency as a risk factor for MetS, demonstrating a significant association. **Table 5**

Table (1): Demographic and clinical & laboratory data between cases with & without MetS

	Total cases (60, 100%)		With MetS (35, 58.3%)		Without MetS (25, 41.7%)		Test of sig.	p
Age (year) Mean ± SD. Range	48.6 ± 6.89 37.0 – 66.0		48.7 ± 6.42 39.0 – 62.0		48.5 ± 7.64 37.0 – 66.0		**t** **0.107**	**0.915**
Sex Women Men	**No.** 40 20	**%** 66.7 33.3	**No.** 24 11	**%** 68.6 31.4	**No.** 16 9	**%** 64.0 36.0	χ^2 **0.137**	**0.711**
DAPSA Range Median (IQR)	5.0 – 39.0 20.0 (12.25 – 28.5)		5.0 – 35.0 20.0 (15.0 – 26.0)		6.0 – 39.0 20.0 (11.5 – 29.0)		**U** **429.0**	**0.898**
 Low disease activity > 4 - < or equal 14 High disease activity > 14 - < or equal 28 Very high disease activity > 28	**No.** 16 29 15	**%** 26.7 48.3 25.0	**No.** 8 20 7	**%** 22.9 57.1 20.0	**No.** 8 9 8	**%** 32.0 36.0 32.0	χ^2 **2.646**	**0.266**
HTN No Yes	**No.** 31 29	**%** 51.7 48.3	**No.** 14 21	**%** 40.0 60.0	**No.** 17 8	**%** 68.0 32.0	χ^2 **4.578**	**0.032***
Waist circumference (cm) Mean ± SD. Range	105.1 ± 16.64 70.0 – 133.0		114.8 ± 11.74 88.0 – 133.0		91.6 ± 12.59 70.0 – 120.0		**t** **7.322**	**<0.001***
BMI (kg/m^2) Mean ± SD. Range	29.7 ± 7.53 19.2 – 48.1		33.4 ± 6.66 20.2 – 48.1		24.6 ± 5.43 19.2 – 41.4		**t** **5.430**	**<0.001***

SD: Standard Deviation, IQR: Interquartile Range, t: Independent T Test, U: Mann Whitney U Test, χ2: Chi-Square Test, p: P-Value (Probability Value), HTN: Hypertension, BMI: Body Mass Index, DAPSA: Disease Activity in Psoriatic Arthritis, *p ≤ 0.05 (Statistically significant).

Table (2): laboratory data of patients with and without MetS

	Total cases (60, 100%)	With MetS (35, 58.3%)	Without MetS (25, 41.7%)	Test of sig.	p
HDL (mg/dl) Range Median (IQR)	20.0 – 102.0 40.0 (31.7 – 49.0)	20.0 – 102.0 39.0 (30.0 – 48.0)	21.0 – 66.0 41.0 (31.8 – 56.8)	**U** **380.5**	**0.392**
TG (mg/dl) Range Median (IQR)	49.9 – 345.0 105.0 (89.25 – 140.0)	56.0 – 345.0 110.0 (90.0 – 160.0)	49.9 – 208.0 100.0 (86.0 – 124.5)	**U** **301.5**	**0.041***
Cholesterol (mg/dl) Range Median (IQR)	48.0 – 277.0 154.0 (132.0 – 184.5)	120.0 – 277.0 155.0 (135.0 – 183.0)	48.0 – 246.0 153.0 (130.0 – 193.5)	**U** **411.5**	**0.696**
VLDL (mg/dl) Range Median (IQR)	9.0 – 55.0 20.3 (15.25 – 27.0)	11.0 – 55.0 21.0 (17.0 – 29.0)	9.0 – 42.0 19.0 (13.0 – 25.5)	**U** **336.5**	**0.129**
LDL (mg/dl) Range Median (IQR)	61.0 – 201.0 100.0 (85.25 – 121.2)	61.0 – 178.0 100.0 (84.0 – 116.0)	70.0 – 201.0 110.0 (84.5 – 128.0)	**U** **381.0**	**0.397**
ESR Range Median (IQR)	6.0 – 110.0 30.0 (20.0 – 40.0)	6.0 – 100.0 30.0 (20.0 – 35.0)	10.0 – 110.0 30.0 (20.0 – 60.0)	**U** **411.5**	**0.696**
CRP Range Median (IQR)	1.0 – 66.09 6.0 (2.0 – 10.75)	1.0 – 63.0 6.0 (3.0 – 11.0)	1.0 – 66.09 5.0 (2.0 – 10.0)	**U** **420.5**	**0.798**
FBG (mg/dl) Mean ± SD.	103.9 ± 23.23	116.5 ± 21.25	86.3 ± 11.46	**T 6.464**	**<0.001***
Uric acid (mg/dl) Mean ± SD.	4.6 ± 1.22	4.5 ± 1.14	4.8 ± 1.31	**t** **1.009**	**0.317**

SD: Standard Deviation, IQR: Interquartile Range, U: Mann Whitney U Test, p: P-Value (Probability Value), HDL: High-Density Lipoprotein, TG: Triglycerides, VLDL: Very Low-Density Lipoprotein, LDL: Low-Density Lipoprotein, ESR: Erythrocyte Sedimentation Rate, CRP: C-Reactive Protein, FBG: Fasting Blood Glucose, t: Independent T Test, *p ≤ 0.05 (Statistically significant)

Table (3): Vitamin D level in psoriatic arthritis patients with & without MetS

	Total cases (60, 100%)		With MetS (35, 58.3%)		Without MetS (25, 41.7%)		Test of sig.	p
Vit. D (ng/ml) Range Median (IQR)	4.0 – 35.2 10.0 (7.25 – 21.6)		4.0 – 35.2 9.0 (7.0 – 15.0)		5.0 – 35.1 15.0 (8.5 – 31.8)		**U** **279.5**	**0.018***
	No.	**%**	**No.**	**%**	**No.**	**%**		
Deficiency <10	26	43.3	19	54.3	7	28.0	χ^2 **7.210**	**0.027***
Insufficient 10 – 30	25	41.7	14	40.0	11	44.0		
Sufficient 30 – 100	9	15.0	2	5.7	7	28.0		

SD: Standard Deviation, IQR: Interquartile Range, U: Mann Whitney U Test, χ2: Chi-Square Test, p: P-Value (Probability Value), Vit. D: Vitamin D, *p ≤ 0.05 (Statistically significant).

Table (4): Correlation between vitamin D & other parameters in patients with MetS (n=35)

	Vitamin D	
	r_s	**p**
DAPSA	0.178	0.307
HTN	0.168	0.334
ESR	-0.013	0.940
CRP	0.033	0.850
S. uric acid	-0.012	0.948
LDL	0.010	0.952
HDL	0.638	<0.001*
Triglycerides	-0.062	0.724
Cholesterol	-0.187	0.281
VLDL	-0.014	0.935
Waist circumference	-0.606	<0.001*
BMI	-0.552	0.001*
Fasting glucose	-0.867	<0.001*

rs: Spearman Correlation Coefficient, p: P-Value (Probability Value), DAPSA: Disease Activity in Psoriatic Arthritis, HTN: Hypertension, ESR: Erythrocyte Sedimentation Rate, CRP: C-Reactive Protein, LDL: Low-Density Lipoprotein, HDL: High-Density Lipoprotein, VLDL: Very Low-Density Lipoprotein, BMI: Body Mass Index, *p ≤ 0.05 (Statistically significant).

Table (5): Binary logistic regression for vitamin D deficiency as a risk factor for MetS

	Wald	Sig.	OR	95% C.I. for OR	
				Lower	**Upper**
Vit. D	6.277	0.012*	1.078	1.016	1.143

Wald: Wald Test, Sig.: Significance, OR: Odds Ratio, C.I.: Confidence Interval, Vit. D: Vitamin D, *p ≤ 0.05 (Statistically significant)

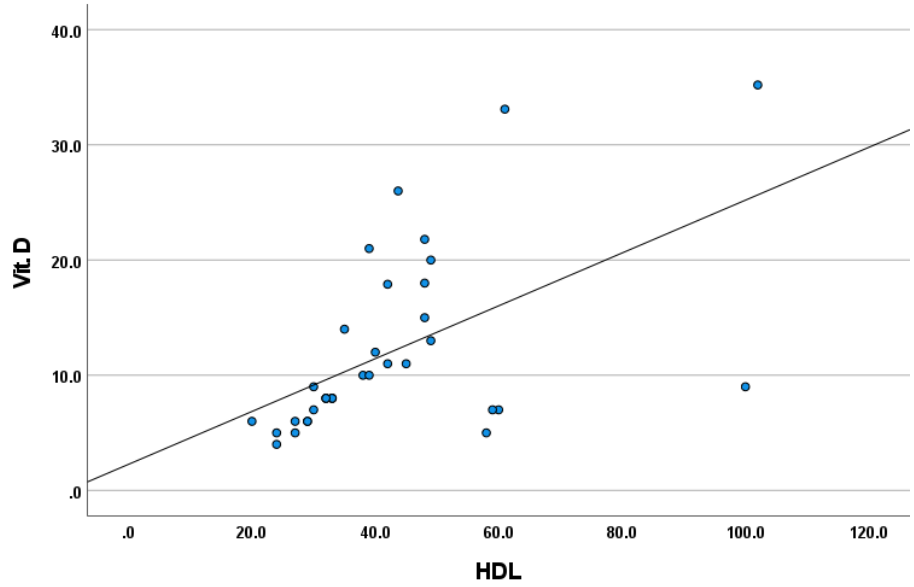

Figure 1: Vit. D and HDL correlation

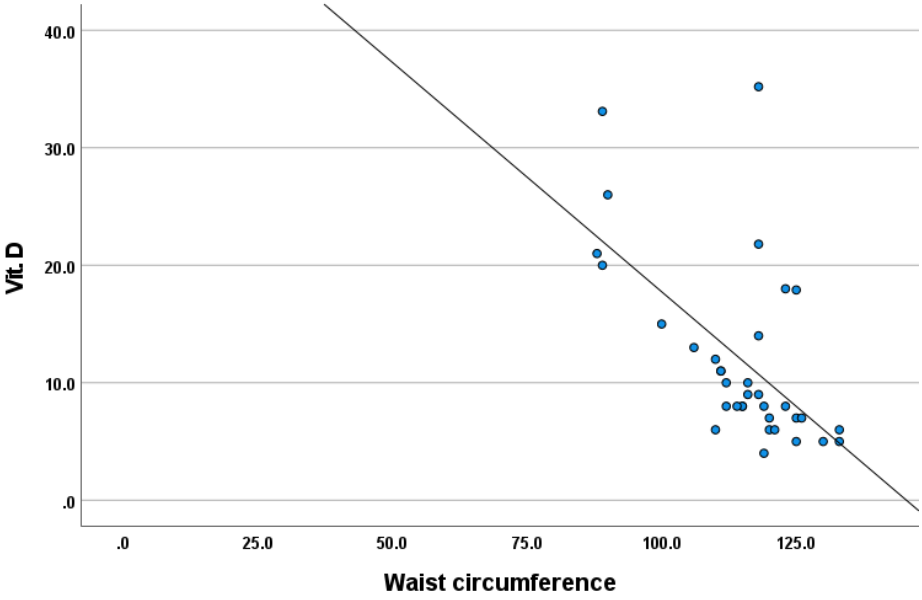

Figure 2: Vit. D and waist circumference correlation

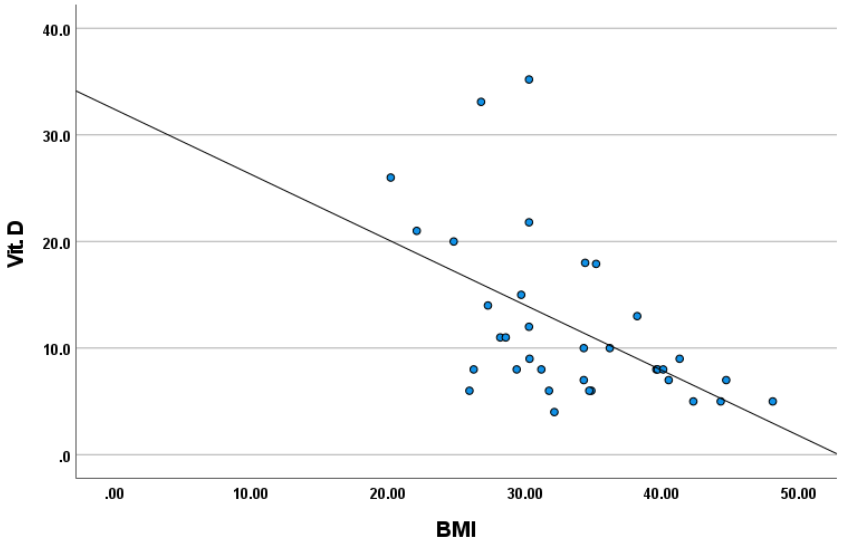

Figure 3: Vit. D and BMI correlation

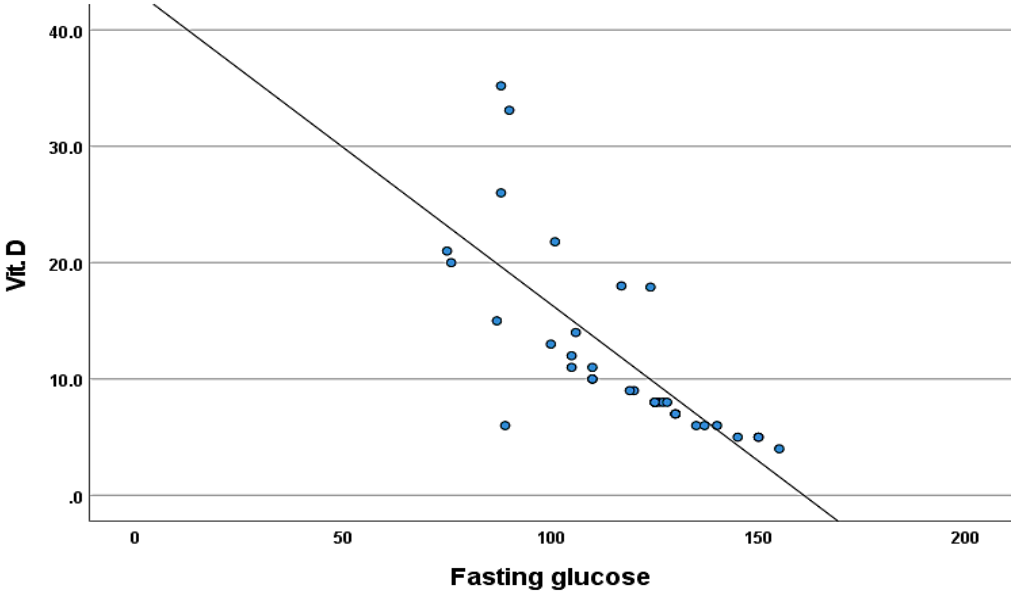

Figure 4: Vit. D and Fasting glucose correlation.

DISCUSSION

Vit D deficiency is now widely regarded as a global epidemic, significantly impacting public health, particularly concerning cardiovascular and metabolic diseases. In this study, we included 60 PsA patients to investigate the relationship between serum vit D levels and MetS and. More than half (58.3%) of the study participants were diagnosed with MetS. This high prevalence of MetS among PsA patients showed no significant association with age, sex, or disease activity measures such as DAPSA score, ESR, and CRP levels. Similar findings were reported by **Raychaudhuri *et al.*** [12], who found a 58.1% prevalence of MetS. **Haroon *et al.*** [13] observed a MetS prevalence of 44% in PsA patients, also noting no link to inflammatory markers. Urruticoechea- **Urruticoechea-Arana *et al.*** [14] indicated in their systematic review that MetS prevalence in PsA varies widely, ranging from 23.5% to 62.9%. Additionally, multiple studies have shown that MetS is more common in PsA populations than in patients with psoriasis, rheumatoid arthritis, ankylosing spondylitis, and non-inflammatory rheumatologic conditions [15-17].

In our analysis, 43.3% of participants had vit D deficiency, while 41.7% exhibited vit D insufficiency, indicating that approximately 85% of patients had serum vit D levels below 30 ng/ml. However, no correlation was observed between vit D levels and disease activity indices such as DAPSA, ESR, or CRP. Similar high rates of vit D inadequacy (82.2%, 81%, and 87%) were documented in studies by **Gamonal *et al.*** [8], **Petho *et al.*** [18], and **Grazio *et al.*** [19]. **El Tawab *et al.*** [20] conducted a study in Egypt, finding that 87.5% of PsA patients were vit D deficient, with no significant link to DAPSA scores. Likewise, **Elhelaly *et al.*** [21] and **Braun-Moscovici *et al.*** [22] also reported no association between disease activity and 25(OH)D levels in PsA patients. **Radić *et al.*** [23] conducted a meta-analysis indicating that PsA patients tend to have lower vit D levels compared to the general population, although further research is necessary to clarify any potential correlation with disease activity and severity.

Vit D has a substantial impact on autoimmune diseases such as PsA, as lower levels promote the expansion of self-reactive T cells that attack the body's tissues and increase the production of pro-inflammatory cytokines (IL-12 and IFN-γ), thus raising susceptibility to autoimmune disorders. Additionally, vit D may reduce levels of the pro-inflammatory cytokines IL-17A and IL-23, which are particularly relevant in PsA [24]. Vit D also influences both adaptive and innate immunity by regulating the proliferation and maturation of immune cells, including macrophages, T and B lymphocytes, and dendritic cells [23].

In our analysis, a significant relationship was observed between vit D levels and MetS, with MetS patients showing considerably lower vit D levels and a higher frequency of vit D deficiency and insufficiency compared to those without MetS. Serum vit D levels demonstrated a notable inverse association with several MetS indicators, including WC, BMI, and fasting blood glucose, along with a positive association with HDL. Additionally, vit D deficiency was strongly associated with MetS, as confirmed by binary logistic regression analysis. Previous studies, such as those by **Patil *et al.*** [25] and **Orgaz-Molina *et al.*** [26], had also shown an association between vit D deficiency and MetS and its components, especially in cases with psoriasis rather than PsA. **Patil *et al.*** [25] found that 7% of participants had PsA, although the findings were constrained by a small sample size. A significant negative correlation between vit D levels and BMI in PsA patients was also reported by **Kincse *et al.*** [27].

Gao and Kou [28] highlighted a correlation between vit D deficiency, MetS, and central obesity in studies of the general population, aligning with our findings. Similarly, **Hajhashemy *et al.*** [29], through their meta-analysis, confirmed an association between

reduced blood vit D levels and an increased risk of MetS across the adult population. Consistent with our results, **Schmitt *et al.* [30]** also found a relationship between low vit D levels, MetS, and decreased HDL levels. **Pathania *et al.* [31]** observed a high prevalence of vit D deficiency in MetS patients and noted a significant negative correlation between vit D levels and fasting blood glucose.

Vit D deficiency has been suggested as an early contributor to metabolic disorders. By binding to its receptors, vit D activates gene expression to produce proteins that help regulate blood pressure through modulation of the renin–angiotensin system, reduce inflammation from oxidative stress, and impact lipid levels and insulin resistance (IR) [32]. Additionally, vit D enhances insulin receptor expression and increases the glucose transporters' responsiveness to insulin. It may also activate enzymes such as calpain and caspase-12, which are involved in the apoptosis of fat tissue [33]. Low vit D may further influence adipose tissue growth and differentiation, thereby contributing to obesity through effects on gene expression and regulation of parathyroid hormone, calcium, and leptin [34]. As a result, inadequate vit D levels may contribute to obesity, IR, diabetes, and hypertension, which collectively lead to MetS [32].

Our study thus provides evidence supporting the association between MetS and vit D deficiency in PsA patients. However, certain limitations are present including the absence of a control group and being a cross-sectional study making vit D deficiency role in MetS development cannot be completely evaluated and other studies are recommended.

CONCLUSION

It could be concluded that vit D may be involved in obesity, diabetes and MetS development in patients with PsA which enhance the risk for cardiovascular morbidity and mortality among those patients. Regular monitoring with immediate correction of serum vit D is recommended in PsA.

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