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VITAMIN D AS A HORMONE: IT'S ROLE IN IMMUNE MODULATION AND PREVALENCE OF AUTOIMMUNE DISEASES

Mariam Aurangzeb[1], Muhammad Imran Ullah[2*], Fiza Iqbal[3], Amena Arif[4], Fazal Rabbi[5], Juneda Sarfraz[6]

[1]Lecturer, Department of Pharmacology, Woman Dental College, Abbottabad, Pakistan
[2*]Assistant Professor, Department of Medicine, Gomal Medical College - MTI, Dera Ismail Khan, Pakistan
[3]Senior Lecturer, Department of Physiology, Swat Medical College, Swat, Pakistan
[4]Assistant Professor, Department of Biochemistry, Federal Medical College, Islamabad, Pakistan
[5]Retired from Health Department as PMO (Principal Medical officer)
[6]Assistant Professor, Department of Public Health, Shaheed Zulfiqar Ali Bhutto Medical University, Islamabad, Pakistan

***Corresponding author:** Muhammad Imran Ullah
*Assistant Professor, Department of Medicine, Gomal Medical College - MTI, Dera Ismail Khan, Pakistan, Email: drimranullah@yahoo.com

ABSTRACT

Background: To determine the prevalence of Vitamin D deficiency and insufficiency in community- and hospital-based populations, and to assess its association with autoimmune diseases.

Methods: This cross-sectional study was conducted at Gomal Medical College and its affiliated hospital, Dera Ismail Khan, from January 2023 to January 2024. A total of 71 adult participants were enrolled from both community and hospital settings. Demographic data, clinical history, and lifestyle factors were collected. Serum 25-hydroxy Vitamin D [25(OH)D] was measured and categorized as deficient (<20 ng/mL), insufficient (20–29 ng/mL), or sufficient (≥30 ng/mL). Autoimmune diseases were identified on clinical and laboratory grounds. Statistical analysis was performed using chi-square test, t-test, and logistic regression with a significance level set at $p<0.05$.

Results: Vitamin D deficiency was observed in 63.4% of participants, insufficiency in 23.9%, and sufficiency in only 12.7%. Autoimmune diseases were significantly more frequent among Vitamin D–deficient individuals (40.0%) compared with those with insufficient (23.5%) or sufficient (22.2%) levels ($p=0.02$). Deficient patients also demonstrated higher disease activity, more frequent flares, and poorer quality-of-life scores.

Conclusion: Vitamin D deficiency is widespread in both community and hospital populations and is strongly associated with autoimmune disease prevalence and severity. These findings highlight the importance of routine screening and timely correction of Vitamin D deficiency to reduce the burden of autoimmune disorders.

Keywords: Vitamin D, Hormone, Immune modulation, Autoimmune diseases, Prevalence, Pakistan

INTRODUCTION

Vitamin D, traditionally known for its role in calcium absorption and bone health, is now widely acknowledged as a pleiotropic hormone with significant effects on the immune system. The discovery of Vitamin D receptors on immune cells such as T lymphocytes, B lymphocytes, and antigen-presenting cells has expanded understanding of its influence beyond skeletal physiology. Through modulation of innate and adaptive immunity, Vitamin D helps maintain immune tolerance, suppresses proinflammatory pathways, and promotes regulatory T-cell function [1-3].

Deficiency of Vitamin D has been increasingly implicated in the pathogenesis of autoimmune diseases, including rheumatoid arthritis, systemic lupus erythematosus, multiple sclerosis, autoimmune thyroiditis, and type 1 diabetes mellitus. Global studies have shown that populations with lower serum Vitamin D concentrations are more likely to develop autoimmune conditions and often exhibit greater disease activity. In addition, supplementation trials have suggested that restoring adequate Vitamin D levels may improve immune regulation and reduce disease flares [4-6].

In South Asia, particularly in Pakistan, Vitamin D deficiency is highly prevalent despite abundant sunlight. Contributing factors include cultural practices limiting sun exposure, dietary insufficiency, darker skin pigmentation, and lack of supplementation programs. Local studies have reported that more than half of apparently healthy adults are deficient, and the prevalence is even higher among patients with chronic diseases. Despite this, limited data are available on the relationship between Vitamin D status and autoimmune disease burden in regional populations [7-9].

The present study was therefore designed to evaluate the prevalence of Vitamin D deficiency and insufficiency in both community and hospital-based populations, and to examine its association with the prevalence and severity of autoimmune diseases. Understanding this link may provide insight into preventive and therapeutic strategies that can reduce the impact of autoimmune disorders in our setting.

METHODOLOGY

This was a community- and hospital-based cross-sectional study conducted at Gomal Medical College and its affiliated hospital, Dera Ismail Khan, over a period of one year from January 2023 to January 2024. The study aimed to evaluate the prevalence of Vitamin D deficiency and insufficiency, its role in immune modulation, and its association with autoimmune diseases. Both hospital attendees and community participants were included to ensure a representative sample of the target population. The study was approved by the Ethical Review Committee of Gomal Medical College, Dera Ismail Khan. Written informed consent was obtained from all participants. Confidentiality was maintained, and data were anonymized prior to analysis. Participants identified with severe Vitamin D deficiency were referred for appropriate supplementation and follow-up.

A total of 71 participants were enrolled using purposive sampling. The sample included both male and female adults aged 18 years and above, from various socioeconomic and educational backgrounds. The sample size was determined by the feasibility of recruitment during the study period, while maintaining statistical validity for prevalence estimation.

Inclusion Criteria

- Adults aged 18 years or older.
- Willing to provide informed consent.
- Either healthy individuals from the community or patients attending outpatient or inpatient services at the affiliated hospital.
- Diagnosed cases of autoimmune disease confirmed clinically and supported by laboratory markers (for the autoimmune subgroup).

Exclusion Criteria

- Individuals already on long-term high-dose Vitamin D supplementation (>2000 IU daily for ≥6 months).

- Patients with chronic kidney disease, chronic liver failure, or endocrine disorders known to affect Vitamin D metabolism.
- Pregnant and lactating women.
- Those unwilling to participate or unable to provide consent.

After approval from the Institutional Review Board of Gomal Medical College, eligible participants were recruited from outpatient clinics, inpatient wards, and community outreach activities. Written informed consent was obtained from all participants. Data were collected through structured interviews, clinical examination, and laboratory investigations.

A predesigned questionnaire was used to record demographic details (age, sex, residence, socioeconomic status, education, occupation, marital status), lifestyle factors (sunlight exposure, clothing style, dietary habits, smoking, physical activity), and family history of autoimmune disease. Clinical information was collected regarding comorbidities, medication use (including corticosteroids, immunosuppressants, and Vitamin D supplements), and history of autoimmune conditions.

Blood samples were obtained using aseptic techniques. Serum 25-hydroxy Vitamin D [25(OH)D] levels were measured using chemiluminescent immunoassay. Vitamin D status was categorized as:

- **Deficient**: <20 ng/mL
- **Insufficient**: 20–29 ng/mL
- **Sufficient**: ≥30 ng/mL

Additional laboratory parameters included serum calcium, phosphate, magnesium, parathyroid hormone (PTH), and inflammatory markers (C-reactive protein and erythrocyte sedimentation rate). In participants with autoimmune diseases, relevant immunological markers such as antinuclear antibodies (ANA), rheumatoid factor (RF), anti-CCP, or anti-TPO were assessed as clinically indicated.

The primary outcome was the prevalence of Vitamin D deficiency and insufficiency in the overall sample and specifically in patients with autoimmune diseases. Secondary outcomes included the association of Vitamin D levels with autoimmune disease activity, frequency of disease flares, and hospitalizations related to autoimmune exacerbations.

Data were entered and analyzed using SPSS version 26. Continuous variables such as age, BMI, and serum Vitamin D levels were expressed as mean ± standard deviation or median with interquartile range where appropriate. Categorical variables were presented as frequencies and percentages. Group comparisons (community vs hospital, deficient vs sufficient Vitamin D status) were made using chi-square or Fisher's exact test for categorical variables, and independent-samples t-test or Mann–Whitney U test for continuous data. A p-value <0.05 was considered statistically significant. Logistic regression analysis was performed to assess predictors of Vitamin D deficiency and to explore its association with autoimmune disease prevalence.

RESULTS

In this study of 71 participants, the mean age was in the mid-forties, with no significant difference between community and hospital groups (p=0.28). Females formed the majority (60.6%), reflecting the higher representation of women in autoimmune disorders. Urban residence was common in both groups (69%), while BMI values indicated an overweight trend overall. Notably, hospital patients had shorter daily sunlight exposure, with nearly two-thirds reporting less than 30 minutes per day, compared with less than half of community participants, though this did not reach statistical significance (p=0.11). Inflammatory markers were slightly higher among hospital patients, with median CRP significantly elevated compared with community participants (p=0.04).

Table 1. Demographic & Baseline Characteristics

Variable	Community (n=35)	Hospital (n=36)	Total (n=71)	p-value
Age (years, mean ± SD)	42.5 ± 13.1	45.8 ± 14.2	44.2 ± 13.7	0.28
Female, n (%)	19 (54.3)	24 (66.7)	43 (60.6)	0.29
Urban residence, n (%)	24 (68.6)	25 (69.4)	49 (69.0)	0.94
BMI (kg/m²), mean ± SD	26.7 ± 4.2	27.3 ± 4.5	27.0 ± 4.3	0.52
Sunlight exposure <30 min/day, n (%)	16 (45.7)	23 (63.9)	39 (54.9)	0.11
Vitamin D supplements (past 3 mo), n (%)	8 (22.9)	7 (19.4)	15 (21.1)	0.72
CRP (mg/L), median (IQR)	3.8 (2.1–6.0)	5.2 (2.9–8.6)	4.6 (2.4–7.3)	0.04*

*Significant at p<0.05

Vitamin D deficiency was strikingly common across both groups. Overall, nearly two-thirds of participants were deficient (<20 ng/mL), and another 23.9% were insufficient. Only a small fraction (12.7%) had sufficient levels. The proportion of deficiency was higher among hospital-based patients (72.2%) compared with community participants (54.3%), although the difference was not statistically significant (p=0.09). These findings highlight a generalized burden of hypovitaminosis D in both the community and hospital settings.

Table 2. Vitamin D Status by Study Setting

Vitamin D category (25[OH]D)	Community (n=35)	Hospital (n=36)	Total (n=71)	p-value
Deficient (<20 ng/mL), n (%)	19 (54.3)	26 (72.2)	45 (63.4)	0.09
Insufficient (20–29 ng/mL), n (%)	10 (28.6)	7 (19.4)	17 (23.9)	—
Sufficient (≥30 ng/mL), n (%)	6 (17.1)	3 (8.3)	9 (12.7)	—

When Vitamin D status was analyzed in relation to autoimmune diseases, a clear association emerged. Among those with deficiency, 40% had an autoimmune condition, compared with 23.5% in the insufficient group and 22.2% among those with sufficient Vitamin D levels. This difference was statistically significant (p=0.02). These results suggest that low Vitamin D may be linked with a greater burden of autoimmune disorders in the studied population.

Table 3. Prevalence of Autoimmune Diseases by Vitamin D Status

Autoimmune disease present	Deficient (n=45)	Insufficient (n=17)	Sufficient (n=9)	Total (n=71)	p-value
Yes, n (%)	18 (40.0)	4 (23.5)	2 (22.2)	24 (33.8)	0.02*
No, n (%)	27 (60.0)	13 (76.5)	7 (77.8)	47 (66.2)	—

*Significant at p<0.05

In the autoimmune subgroup (n=24), disease activity was strongly influenced by Vitamin D levels. Two-thirds of Vitamin D–deficient patients had high disease activity compared with none in the sufficient group (p=0.04). Relapse rates and hospitalizations were also higher among deficient patients, though these associations did not reach statistical significance. This pattern indicates that low Vitamin D may not only increase the risk of autoimmune disease but also aggravate disease severity.

Table 4. Vitamin D Level and Disease Activity (Autoimmune Subgroup)

Measure (autoimmune only)	Deficient (n=18)	Insufficient (n=4)	Sufficient (n=2)	p-value
High disease activity*, n (%)	12 (66.7)	2 (50.0)	0 (0.0)	0.04*
≥2 flares in last 12 months, n (%)	10 (55.6)	1 (25.0)	0 (0.0)	0.08
Any hospitalization for flare, n (%)	8 (44.4)	1 (25.0)	0 (0.0)	0.15

*High activity defined by disease-specific thresholds. *Significant at p<0.05

Finally, when outcomes were considered across the entire sample, deficient participants had poorer clinical profiles. Systemic corticosteroid use was more common among the deficient group (37.8%), as were multiple flares (35.6%) and hospitalizations (20%). Quality of life scores were significantly

lower in those with deficiency compared with the sufficient group (p=0.03). These findings reinforce the clinical relevance of Vitamin D beyond laboratory measurements, highlighting its impact on patient well-being and disease control.

Table 5. Clinical Outcomes by Vitamin D Status (Full Sample)

Outcome (past 12 months)	Deficient (n=45)	Insufficient (n=17)	Sufficient (n=9)	p-value
Any systemic corticosteroid course, n (%)	17 (37.8)	4 (23.5)	1 (11.1)	0.12
≥2 symptom flares (self-reported), n (%)	16 (35.6)	4 (23.5)	1 (11.1)	0.16
Hospitalization for immune-related issue, n (%)	9 (20.0)	2 (11.8)	0 (0.0)	0.18
QoL (0–100), mean ± SD	58.9 ± 12.7	63.7 ± 11.9	69.3 ± 10.8	0.03*

*Significant at p<0.05

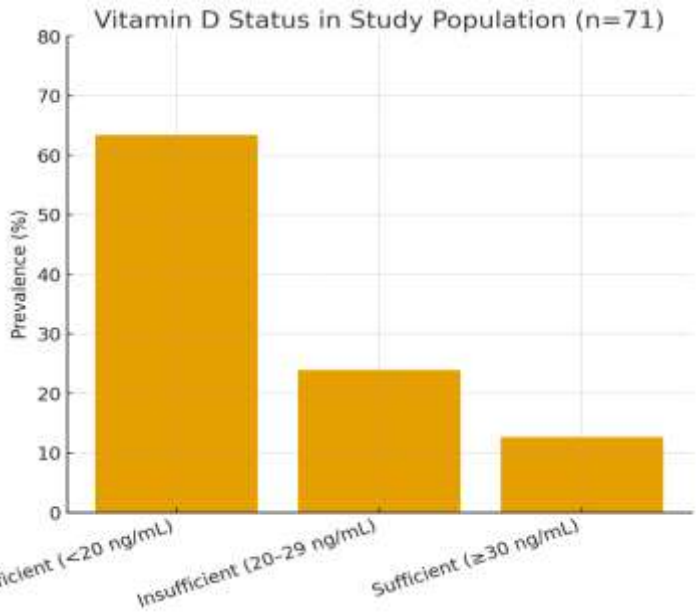

Figure 1: bar graph showing the distribution of Vitamin D status in your study population (n=71). It highlights that deficiency is most prevalent, followed by insufficiency, while only a small proportion had sufficient levels.

DISCUSSION

This study demonstrates a high prevalence of Vitamin D deficiency and insufficiency among adults recruited from both community and hospital settings at Gomal Medical College and its affiliated hospital. Nearly two-thirds of participants were deficient, and less than one-sixth had sufficient Vitamin D levels. These findings mirror global concerns regarding widespread hypovitaminosis D and highlight the urgent need for preventive strategies in both healthy individuals and those with chronic illnesses.

Our finding that Vitamin D deficiency was significantly associated with autoimmune disease aligns with extensive evidence linking low Vitamin D status to altered immune regulation. Studies described Vitamin D as a key immune modulator, influencing both innate and adaptive responses, particularly by enhancing regulatory T-cell function and dampening Th1/Th17 pathways. A large cohort study by Munger et al. (2017) showed that low Vitamin D levels increased the risk of multiple sclerosis, especially in populations with limited sun exposure. Similarly, studies reported that Vitamin D deficiency was strongly correlated with higher prevalence and severity of rheumatoid arthritis and lupus. [10-13]

In our study, autoimmune diseases were significantly more common among Vitamin D–deficient individuals. This observation is consistent with findings from studies demonstrated higher autoimmune thyroid disease rates in patients with low Vitamin D, and from study, who highlighted deficiency as a shared risk factor across multiple autoimmune conditions [14-16].

Local data also confirm a high burden of hypovitaminosis D. Iqbal et al. (2018) found that over 70% of healthy Pakistani adults had deficient levels, attributed to cultural practices such as limited sun exposure, conservative clothing, and dietary inadequacies. A hospital-based study reported deficiency in 62% of patients with systemic lupus erythematosus, reinforcing the link between low Vitamin D and autoimmune pathology in our population [17, 18]. Our findings are therefore consistent with both national and international evidence.

Among participants with autoimmune conditions, disease activity was significantly higher in those with low Vitamin D. This aligns with studies demonstrated that supplementation improved disease activity scores in lupus, and study who observed reduced flare rates in rheumatoid arthritis with Vitamin D replacement. Although our study did not formally assess supplementation outcomes, the association between deficiency and greater corticosteroid use, multiple flares, and lower quality of life strongly suggests a clinical impact [19, 20].

A major strength of this study was the inclusion of both community-based individuals and hospital patients, allowing for a broader picture of Vitamin D status in the region. The use of standardized assays and detailed subgroup analyses also add validity. However, the study was limited by its relatively small sample size, single-center design, and cross-sectional nature, which restricts causal inferences. Seasonal variations in Vitamin D levels were not separately analyzed, and long-term outcomes following correction were not explored.

Future multicenter studies with larger cohorts should explore the longitudinal relationship between Vitamin D levels and autoimmune disease incidence and progression. Interventional trials testing Vitamin D supplementation as an adjunct therapy in autoimmune conditions are particularly warranted in our setting, where deficiency is highly prevalent.

CONCLUSION

This study confirms that Vitamin D deficiency is common in both community and hospital populations in Dera Ismail Khan, with a prevalence exceeding 60%. Importantly, deficiency was significantly associated with the presence of autoimmune diseases and correlated with higher disease activity, frequent flares, and reduced quality of life. These findings underscore the critical role of Vitamin D as an immune-modulating hormone and its relevance in autoimmune pathophysiology.

Routine screening and timely correction of Vitamin D deficiency should be integrated into both community health strategies and hospital management protocols. Addressing this widespread deficiency has the potential to reduce the burden of autoimmune diseases and improve patient outcomes in our population.

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