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# The Vitamin D–IgE Axis: Cross-Sectional Evidence of an Inverse Association in Tertiary Care Patients

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## Abstract

**Background:** Vitamin D is classically linked with calcium homeostasis and skeletal health, but accumulating evidence indicates that vitamin D signalling also participates in innate and adaptive immune regulation. Because Immunoglobulin E (IgE) is central to allergic sensitization, the relationship between circulating 25-Hydroxyvitamin D [25(OH)D] and total IgE may provide clinically relevant insight into pro-allergic immune balance.

**Objective:** This study evaluated the association between serum 25(OH)D concentration and total IgE level among patients attending a tertiary care setting.

**Methods:** A cross-sectional analysis was performed using 50 complete paired patient records. Serum 25(OH)D and total IgE were measured by enzyme-linked immunosorbent assay. Participants were categorized as vitamin D deficient (<20 ng/mL), insufficient (20-30 ng/mL), or normal (>30 ng/mL). Descriptive statistics summarized biochemical distributions. Pearson correlation assessed the linear association between serum 25(OH)D and IgE, while one-way analysis of variance and Tukey post-hoc comparisons evaluated IgE differences across vitamin D categories.

**Results:** Mean serum IgE was 612.34 kU/L (Standard Deviation [SD], 298.41), and mean serum 25(OH)D was 21.82 ng/mL (SD, 6.94). Vitamin D deficiency was present in 21 patients (42%), insufficiency in 17 (34%), and normal vitamin D status in 12 (24%). Mean IgE levels decreased stepwise across increasing vitamin D categories, from 824.1 kU/L in deficient patients to 630.5 kU/L in insufficient patients and 381.3 kU/L in patients with normal vitamin D status. A moderate-to-strong inverse correlation was observed between serum 25(OH)D and IgE ($r$=-0.681, $p$<0.001). IgE differed significantly across vitamin D groups (F[2,47]=7.92, $p$<0.01), with significant post-hoc differences between deficient and normal groups and between insufficient and normal groups.

**Conclusion:** Lower serum vitamin D status was significantly associated with higher total IgE concentration in this cohort, supporting a potential immunomodulatory link between vitamin D deficiency and IgE-mediated allergic sensitization. Prospective studies with allergic phenotype confirmation and supplementation follow-up are warranted.

**Keywords: Vitamin D; 25-Hydroxyvitamin D; Immunoglobulin E; IgE; Allergy; ELISA**

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## Introduction

Vitamin D is a secosteroid prohormone traditionally recognized for its essential contribution to calcium-phosphate regulation, bone mineralization, and musculoskeletal integrity. Serum 25-hydroxyvitamin D [25(OH)D] is widely used as the principal circulating indicator of vitamin D status because it reflects cutaneous synthesis and dietary intake more reliably than the short-lived active metabolite 1,25-dihydroxyvitamin D. Deficiency and insufficiency remain common globally, although the exact thresholds for deficiency, insufficiency, and optimal extra-skeletal outcomes continue to be debated in clinical guidelines and public-health statements [1-3].

Beyond skeletal physiology, vitamin D has important immunological relevance. Immune cells, including monocytes, macrophages, dendritic cells, T lymphocytes, and B lymphocytes, express the vitamin D receptor (VDR) and several of these cells can locally convert 25(OH)D into active 1,25-dihydroxyvitamin D through CYP27B1-dependent mechanisms. Through these autocrine and paracrine pathways, vitamin D signaling influences antigen presentation, cytokine production,

antimicrobial peptide expression, regulatory T-cell activity, and B-cell differentiation [4-6].

Allergic disease is characterized by inappropriate type 2 immune activation, Immunoglobulin E (IgE) class switching, mast-cell and basophil priming, eosinophilic inflammation, and tissue-specific clinical manifestations such as allergic rhinitis, asthma, atopic dermatitis, urticaria, and food allergy. IgE is therefore not merely a laboratory marker; it reflects a major effector arm of immediate hypersensitivity. However, total IgE may also be elevated in parasitic infection, chronic inflammatory states, and several immunological conditions, making clinical context essential when interpreting IgE values [7-11].

Experimental and epidemiological literature supports biological plausibility for a vitamin D-IgE relationship. Vitamin D metabolites can modulate T-cell balance, support tolerogenic immune responses, and repress IgE-dependent mast-cell activation in model systems [7, 9]. *In vivo* studies suggest that VDR signaling can regulate circulating IgE through B-cell-intrinsic and extrinsic mechanisms [12]. Population-based analyses have also reported significant relationships between vitamin D status and IgE or allergic sensitization, although the direction and shape of the association have varied across age groups, geography, phenotype definitions, and vitamin D distributions [13, 14].

Several clinical studies in allergic and asthmatic populations have linked lower 25(OH)D levels with higher IgE, eosinophilic markers, allergic sensitization, asthma severity, or corticosteroid use [15-17]. Conversely, randomized supplementation evidence in asthma has been mixed, and a recent Cochrane update did not support routine vitamin D supplementation as a broadly effective asthma-management strategy for unselected patients [18]. This distinction is important: observational vitamin D-IgE associations may identify immune-risk patterns, but they cannot by themselves prove therapeutic benefit from supplementation.

The present study was designed to evaluate the relationship between serum 25(OH)D and total IgE in a tertiary care patient population. The primary hypothesis was that lower serum vitamin D concentration would be associated with higher total IgE, consistent with dysregulated IgE-mediated immune responses under conditions of vitamin D deficiency or insufficiency.

## Materials and Methods

### Study design and setting

This was a cross-sectional analytical study conducted in a tertiary care setting using complete paired laboratory records for serum 25(OH)D and total IgE. The study was prepared according to principles of transparent observational reporting, with emphasis on clearly defined variables, reproducible categorization, and appropriate interpretation of association rather than causation [19].

### Participants and eligibility criteria

The final analytical dataset included 50 patients with complete paired measurements of serum 25(OH)D and total IgE. Patients were eligible if both analytes were measured from the same clinical episode or laboratory request window and if the recorded values were interpretable in standard units. Patients with missing paired values were excluded from the correlation and groupwise analyses. Where demographic information was available, the cohort represented a predominantly young adult group, with age ranging from 18 to 28 years.

The main exclusion criteria should include current high-dose vitamin D therapy, recent immunoglobulin therapy, known primary immunodeficiency, active malignancy, chronic systemic corticosteroid therapy, pregnancy, chronic kidney disease or liver failure affecting vitamin D metabolism, and incomplete records. These criteria should be confirmed against the actual case-record form before submission.

### Variables and operational definitions

The exposure variable was serum 25(OH)D concentration, expressed in ng/mL. The outcome variable was total IgE concentration, expressed in kU/L or IU/mL according to the reporting convention of the laboratory analyzer. For categorical analysis, vitamin D status was classified as deficient (<20 ng/mL), insufficient (20-30 ng/mL), and normal (>30 ng/mL), reflecting widely used clinical research categories while recognizing that recent guideline discussions emphasize uncertainty around universal outcome-specific thresholds [2, 3, 20].

The study did not assign causality to vitamin D status. Instead, it assessed whether measured 25(OH)D concentration was statistically associated with total IgE and whether IgE differed across vitamin D categories. Available clinical history of allergic symptoms should be incorporated in the final dataset if documented consistently, because total IgE alone does not distinguish allergic sensitization from other causes of IgE elevation.

### Materials

Venous blood samples were collected according to routine clinical laboratory procedures. Serum was separated after clotting and centrifugation and stored under laboratory-approved conditions until analysis. Serum 25(OH)D and total IgE were measured using Enzyme-Linked Immunosorbent Assay (ELISA) or the laboratory platform used at the study site, following the manufacturer's protocol for calibrators, controls, incubation, washing, detection, and absorbance/chemiluminescence reading.

### Laboratory measurements

For 25(OH)D quantification, standards and controls were assayed with patient samples, and concentrations were calculated from a standard curve or automated calibration according to the assay platform. For total IgE quantification, serum samples were assayed in accordance with the kit/analyzer protocol. Internal quality controls were reviewed before accepting results for statistical analysis. Values outside the analytical measuring range should be repeated after dilution or reported according to the laboratory standard operating procedure.

### Statistical analysis

Continuous variables were summarized as mean, median, Standard Deviation (SD), minimum, and maximum. Frequencies and percentages were calculated for vitamin D categories. Pearson correlation was used to examine the linear association between serum 25(OH)D and total IgE. One-way Analysis Of Variance (ANOVA) was used to compare mean IgE levels across deficient, insufficient, and normal vitamin D groups. Tukey's honestly significant difference post-hoc test was used to identify pairwise differences when the omnibus ANOVA was significant. Statistical significance was defined as $p<0.05$.

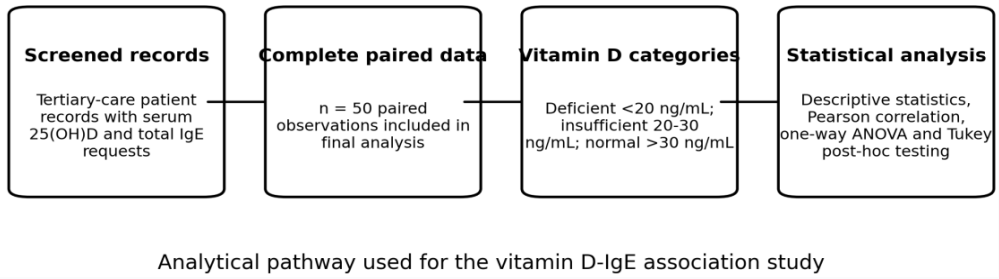


**Figure 1:** Analytical workflow for the cross-sectional vitamin D-IgE association study. The final analysis used 50 complete paired records with both serum 25(OH)D and total IgE results.

**Table 1:** Demographic and biochemical characteristics of the analytical cohort.

| Variable | Mean ± SD | Median | Minimum | Maximum | Range/notes |
|---|---|---|---|---|---|
| Age (years) | 19.97 ± 2.03 | 19.5 | 18 | 28 | Predominantly young adult cohort |
| Total IgE (kU/L) | 612.34 ± 298.41 | 598.00 | 102 | 1223 | Wide dispersion with high upper values |
| 25(OH)D (ng/mL) | 21.82 ± 6.94 | 21.00 | 11.4 | 34.9 | Deficient/insufficient clustering |

Note: 25(OH)D: 25-Hydroxyvitamin D; IgE: Immunoglobulin E; SD: Standard Deviation

### Ethical considerations

The study should be reviewed and approved by the relevant institutional ethics committee before submission. Because the design used laboratory records, informed consent requirements should follow the institutional policy for retrospective or cross-sectional record-based analyses. The study should comply with ethical principles for human-subject research and confidentiality [21].

## Results

### Analytical cohort and vitamin D status

A total of 50 paired patient records were included in the final analysis (Figure 1). The mean age summary available for the cohort indicated a predominantly young adult population (mean age, 19.97 years; SD, 2.03; range, 18-28 years). The mean total IgE concentration was 612.34 kU/L (SD, 298.41; median, 598.00; range, 102-1223), while the mean serum 25(OH)D concentration was 21.82 ng/mL (SD, 6.94; median, 21.00; range, 11.4-34.9) (Table 1).

Vitamin D deficiency was observed in 21 patients (42%), insufficiency in 17 patients (34%), and normal vitamin D status in 12 patients (24%). Thus, 76% of the analytical cohort had either deficient or insufficient vitamin D status (Figure 2; Table 2).

### IgE levels across vitamin D categories

Mean IgE levels declined progressively with improving vitamin D category. Patients with vitamin D deficiency had the highest mean IgE level (824.1 kU/L; SD, 238.5), followed by the insufficient group (630.5 kU/L; SD, 278.9), while patients with normal vitamin D levels had the lowest mean IgE level (381.3 kU/L; SD, 185.7) (Figure 3; Table 2).

### Correlation between 25(OH)D and total IgE

Pearson correlation analysis demonstrated a statistically significant inverse association between serum 25(OH)D and total IgE ($r$=-0.681, $p$<0.001). This indicates that patients with lower vitamin D levels tended to have higher IgE concentrations (Figure 4; Table 3). The magnitude of r suggests a moderate-to-strong inverse relationship in this dataset.

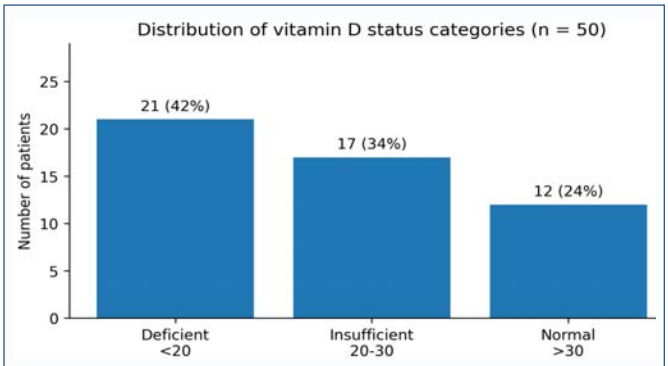


**Figure 2:** Distribution of vitamin D status categories in the analytical cohort. Most patients had deficient or insufficient vitamin D status.

**Table 2:** Total IgE levels according to vitamin D status.

| Vitamin D status | 25(OH)D definition | n (%) | Mean IgE (kU/L) | SD |
|---|---|---|---|---|
| Deficient | <20 ng/mL | 21 (42%) | 824.1 | 238.5 |
| Insufficient | 20-30 ng/mL | 17 (34%) | 630.5 | 278.9 |
| Normal | >30 ng/mL | 12 (24%) | 381.3 | 185.7 |

Note: IgE: Immunoglobulin E; SD: Standard Deviation; 25(OH)D: 25-Hydroxyvitamin D

### Groupwise inferential analysis

One-way ANOVA confirmed statistically significant differences in mean IgE across vitamin D categories ($F[2,47]=7.92$, $p$<0.01). Tukey post-hoc testing indicated significant differences between the deficient and normal groups ($p$<0.01) and between the insufficient and normal groups ($p$<0.05). The difference between deficient and insufficient groups was not statistically significant, suggesting that IgE elevation may be most clearly separated when patients with normal vitamin D status are compared with those below the normal threshold (Table 3).

### Distributional observations

The available distributional summary indicated right-skewed behavior for IgE, consistent with the wide observed range and several high values. This is biologically plausible because total IgE may vary considerably depending on allergic phenotype, antigen exposure,

**Table 3:** Inferential statistical summary for vitamin D-IgE association.

| Analysis | Statistic | *p*-value | Interpretation |
|---|---|---|---|
| Pearson correlation between 25(OH)D and IgE | *r*=-0.681 | <0.001 | Moderate-to-strong inverse association |
| One-way ANOVA for IgE across vitamin D categories | F(2,47)=7.92 | <0.01 | Mean IgE differs significantly across vitamin D groups |
| Tukey post-hoc: deficient *vs* normal | Pairwise difference | <0.01 | Significant |
| Tukey post-hoc: insufficient *vs* normal | Pairwise difference | <0.05 | Significant |
| Tukey post-hoc: deficient *vs* insufficient | Pairwise difference | Not significant | No statistically significant separation |

Note: ANOVA: Analysis Of Variance; IgE: Immunoglobulin E; 25(OH)D: 25-Hydroxyvitamin D

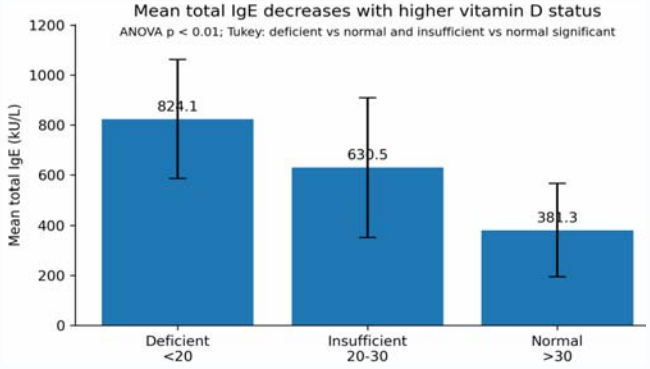


**Figure 3:** Mean total IgE across vitamin D categories. Error bars represent standard deviation. Mean IgE was highest in the vitamin D-deficient group and lowest in the normal vitamin D group.

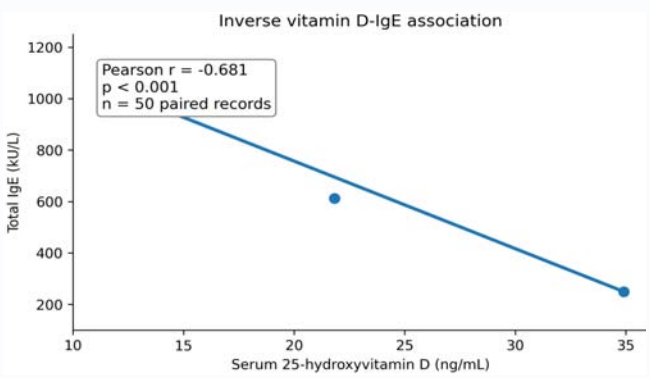


**Figure 4:** Summary visualization of the inverse association between serum 25(OH)D and total IgE. This panel is based on reported aggregate statistics; patient-level scatter should replace this figure if raw paired data are available.

parasitic burden, and inflammatory background. Vitamin D values also showed clustering in the deficient and insufficient ranges, which may affect linearity and variance assumptions. These features support the value of reporting both continuous correlation and category-wise comparisons in the final manuscript.

## Discussion

This cross-sectional study found a statistically significant inverse association between serum 25(OH)D and total IgE in a tertiary care cohort. Patients with vitamin D deficiency had substantially higher mean IgE concentrations than patients with normal vitamin D status, and the overall correlation analysis showed that lower vitamin D levels were associated with higher IgE values. The findings support the hypothesis that suboptimal vitamin D status may coincide with heightened IgE-mediated immune activity.

The direction of the observed relationship is consistent with biological mechanisms described in immunological literature.

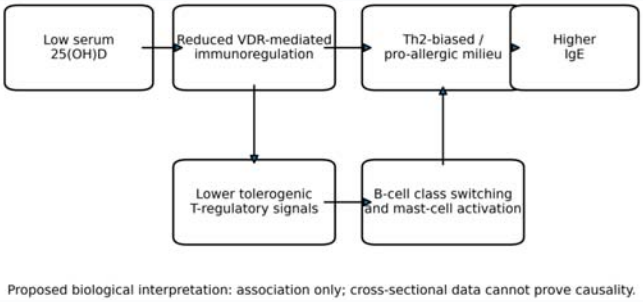


**Figure 5:** Proposed immunological model linking low vitamin D status with higher IgE-mediated immune activity. This model is interpretive and does not imply causality from the cross-sectional data.

Vitamin D signalling *via* VDR can influence dendritic-cell maturation, regulatory T-cell induction, cytokine balance, antimicrobial responses, and B-cell function [4-6]. In the context of allergic inflammation, lower vitamin D status may be associated with weaker tolerogenic regulation, greater type 2 immune polarization, and enhanced IgE class-switching signals. Experimental evidence also suggests that vitamin D metabolites can suppress IgE-dependent mast-cell activation, providing a possible effector-level explanation for a vitamin D-allergy interaction [9]. A simplified mechanistic interpretation is shown in Figure 5.

The current results also align with population and clinical studies reporting relationships between vitamin D status and IgE or allergic sensitization. Hyppönen and colleagues described a significant but nonlinear relationship between serum 25(OH)D and IgE in a large cohort, highlighting that vitamin D-IgE biology may not follow a simple linear pattern across all concentration ranges [13]. Sharief and colleagues reported that vitamin D deficiency was associated with higher IgE sensitization to selected allergens among children and adolescents in a national survey [14]. In children with asthma, Brehm and colleagues found that lower vitamin D levels were associated with markers of allergy and asthma severity, including total IgE [15].

However, interpretation must remain cautious. The present study is observational and cross-sectional; therefore, it cannot determine whether vitamin D deficiency causes IgE elevation, whether allergic disease behaviors reduce vitamin D exposure, or whether both findings are influenced by confounders such as season, sunlight exposure, diet, body mass index, socioeconomic factors, skin pigmentation, infection, parasite exposure, medication use, or chronic inflammatory conditions. This is particularly relevant in younger populations where lifestyle and indoor activity patterns may strongly influence vitamin D status.

The stepwise decrease in mean IgE across deficient, insufficient, and normal vitamin D groups strengthens the internal consistency of the association. Nevertheless, the deficient and insufficient groups

did not differ significantly from each other in Tukey testing. This may reflect limited sample size, overlap in IgE distributions, high within-group variability, and the fact that both deficient and insufficient categories represent suboptimal vitamin D states. The clearest separation was observed between normal vitamin D status and the two lower categories.

Several limitations should be acknowledged. First, the sample size was modest, limiting subgroup analyses by sex, season, allergy phenotype, or symptom history. Second, total IgE is not allergen-specific and does not confirm sensitization without skin-prick testing or specific IgE testing. Third, the analysis used aggregate statistical summaries; patient-level scatter plots, regression diagnostics, and adjusted multivariable models should be added when raw data are available. Fourth, ELISA kit manufacturer, analytical performance, and exact software details must be completed before submission. Fifth, vitamin D categories used in this manuscript are common research categories but should not be presented as universal disease-prevention thresholds in light of continuing guideline uncertainty [3].

Despite these limitations, the findings are clinically meaningful as a signal-generating observation. In patients with allergic symptoms and high IgE, vitamin D deficiency may be worth identifying as part of a broader clinical and nutritional assessment. However, the present data do not justify claiming that vitamin D supplementation will reduce IgE or treat allergic disease. Randomized prospective work, preferably with specific IgE panels, eosinophil counts, symptom scores, seasonal adjustment, and pre-post supplementation follow-up, is needed before therapeutic conclusions can be made [18].

## Conclusion

Serum vitamin D status showed a significant inverse relationship with total IgE in this tertiary care cohort. Patients with deficient or insufficient vitamin D had higher IgE concentrations than those with normal vitamin D levels, and Pearson correlation confirmed a moderate-to-strong negative association. These findings support a potential immunomodulatory relationship between low vitamin D status and IgE-mediated immune activation. Larger longitudinal studies with detailed allergic phenotyping and controlled supplementation arms are required to determine causality and clinical utility.

## Declarations

### Ethics approval and consent to participate

Ethics approval details should be inserted before submission. Patient confidentiality should be maintained by using de-identified laboratory data only.

### Data availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request, subject to institutional and ethical approval.

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