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Original Article

Association of Serum Vitamin D Levels with Disease Severity in Patients with Bronchial Asthma: A Cross-Sectional Study

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ABSTRACT

Background: Vitamin D has important immunomodulatory and anti-inflammatory properties that may influence the pathogenesis and clinical severity of bronchial asthma. However, data regarding its association with asthma severity in the Indian population remain limited. This study aimed to evaluate serum vitamin D levels in patients with different grades of bronchial asthma and to assess their relationship with disease severity.

Material and Methods: This hospital-based cross-sectional study included 100 participants comprising 60 patients with bronchial asthma and 40 healthy controls. Asthmatic patients were categorised into mild, moderate, and severe groups (n=20 each) according to Global Initiative for Asthma (GINA) guidelines. Serum 25-hydroxyvitamin D [25(OH)D], calcium, alkaline phosphatase (ALP), and magnesium levels were measured and compared among the study groups using one-way analysis of variance (ANOVA). A p-value <0.05 was considered statistically significant.

Results: The mean serum vitamin D levels were significantly lower in patients with bronchial asthma than in healthy controls and showed a progressive decline with increasing disease severity (mild: 33.20 ± 3.90 ng/mL, moderate: 23.50 ± 6.80 ng/mL, severe: 20.10 ± 7.50 ng/mL, controls: 47.30 ± 3.80 ng/mL; p<0.0001). Serum ALP levels increased significantly with asthma severity (p<0.0001), whereas serum magnesium levels showed a significant decline (p<0.0001). No significant difference was observed in serum calcium levels among the groups (p=0.385).

Conclusions: Lower serum vitamin D levels are significantly associated with increasing severity of bronchial asthma. The concomitant decrease in serum magnesium and increase in ALP further support the association between altered biochemical parameters and disease severity. Routine assessment of vitamin D status may serve as a useful adjunct in the clinical evaluation of patients with bronchial asthma. Further large-scale prospective studies are required to clarify the therapeutic role of vitamin D supplementation in asthma management.

Keywords: *Bronchial asthma; Vitamin D; 25-hydroxyvitamin D; Alkaline phosphatase; Magnesium; Asthma severity; Serum calcium.*

INTRODUCTION

Asthma represents a multifaceted and heterogeneous pulmonary disorder that imposes a substantial global health burden, affecting a diverse demographic across all age groups. Its complexity is underscored by wide variations in immunopathological mechanisms, clinical presentations, and individual responses to standard therapeutic regimens [1]. The pathophysiological foundation of asthma is primarily characterised by persistent structural and functional anomalies within the airways. These hallmark abnormalities encompass heightened bronchial hyper-responsiveness, progressive airway remodelling, and a pronounced infiltration of inflammatory cells, notably eosinophils and T-helper type 2 (Th2)

lymphocytes, into the submucosal tissue. This cascade of cellular events ultimately precipitates mucosal inflammation, bronchial wall oedema, and excessive mucus secretion, which collectively contribute to the classic clinical manifestations of the disease [2].

In recent years, the scientific community has directed considerable attention toward the extra-skeletal effects of Vitamin D, particularly its immunomodulatory and anti-inflammatory capacities, moving beyond its well-established role in calcium homeostasis and bone metabolism. Accumulating evidence suggests that Vitamin D exerts a significant influence on the structural cells of the respiratory tract by modulating critical processes such as cellular proliferation and differentiation. Furthermore, it plays a pivotal role in regulating both the innate and adaptive arms of the immune system. Consequently, a state of Vitamin D deficiency is postulated to disrupt these regulatory pathways, thereby creating a permissive environment for the exacerbation of inflammatory responses within the airways [3-5]. The etiology of such deficiency is multifactorial, with several key contributors identified in the literature, including prolonged exclusive breastfeeding without appropriate Vitamin D supplementation, maternal deficiency during gestation, inadequate dietary intake, and reduced cutaneous synthesis due to insufficient exposure to sunlight [6,7].

A growing body of epidemiological and clinical research indicates that suboptimal levels of Vitamin D, defined as deficiency (<20 ng/mL) or insufficiency (<30 ng/mL), are not only prevalent but are also significantly associated with an increased susceptibility to various pulmonary afflictions. These include a higher incidence of respiratory tract infections, both bacterial and viral, as well as diminished lung function and heightened airway inflammation. Such physiological derangements are frequently linked to adverse clinical outcomes and poorer disease control in asthmatic populations [6-9]. Despite these compelling observational associations, the findings from interventional clinical trials remain inconclusive, failing to provide definitive and consistent evidence for a universally beneficial role of Vitamin D supplementation in asthma management. This ambiguity underscores the need for further investigation, particularly in diverse geographic and ethnic settings. In the Indian context, there is a notable paucity of comprehensive studies that systematically evaluate the relationship between circulating Vitamin D levels, pulmonary function parameters, and the clinical trajectory of asthma. To address this significant knowledge gap, the present study was designed with a dual purpose: first, to compare serum Vitamin D concentrations between asthmatic patients and non-asthmatic healthy controls, and second, to ascertain whether a correlation exists between Vitamin D deficiency and the graded severity of the disease. The primary objective, therefore, is to quantitatively assess serum 25-hydroxyvitamin D [25(OH)D] levels across a spectrum of asthmatic patients, encompassing those with mild, moderate, and severe forms of the condition.

MATERIALS AND METHODS

Study Design and Setting:

This investigation was designed as a hospital-based, cross-sectional observational study with a case-control component. The research was conducted within the Department of Biochemistry at the Birsa Institute of Medical Sciences and Research, Khunti, Jiarapa, Jharkhand, India. The study protocol received prior approval from the institutional ethics committee, and all procedures were performed in accordance with the ethical standards laid down in the Declaration of Helsinki.

Sample Size Calculation:

The required sample size was calculated by using G*Power software (version 3.1.9.7; Heinrich Heine University, Düsseldorf, Germany) to ensure adequate statistical power for detecting clinically meaningful differences in serum 25-hydroxyvitamin D [25(OH)D] levels across the study groups. The calculation was performed for a one-way analysis of variance (ANOVA) with a fixed effects, omnibus, and one-way design. Based on previous literature reporting differences in mean serum Vitamin D levels between asthmatic patients and healthy controls, an effect size (Cohen's f) of 0.35 was assumed, which corresponds to a medium-to-large effect. The following parameters were employed for the sample size estimation:

- Statistical test: One-way ANOVA (fixed effects, omnibus, one-way)
- Effect size (f): 0.35
- α-error probability: 0.05
- Power (1 - β error probability): 0.80 (80%)
- Number of groups: 4 (Control Group, Mild Asthma, Moderate Asthma, Severe Asthma)

The analysis yielded a total sample size of 84 participants to detect a significant difference among the groups. To account for an anticipated attrition rate of approximately 15–20% due to incomplete data, missing laboratory results, or withdrawal from the study, a final sample size of 100 participants was enrolled. This comprised 40 healthy controls (Group A) and 60 asthmatic patients (Group B), with the latter further subdivided into three severity subgroups (n = 20 each for mild, moderate, and severe asthma) to maintain balanced group sizes and maximise the statistical efficiency of the ANOVA.

Study Population and Sampling:

A total of 100 participants, comprising both males and females within the age bracket of 15 to 50 years (mean age: 37.40 ± 9.46 years), were enrolled in the study. Participants were allocated into two principal groups:

- **Group A (Control Group):** This group consisted of 40 age- and sex-matched healthy, non-asthmatic individuals (22 males and 18 females), recruited from the general population and hospital staff, with no documented history of respiratory or systemic illness.
- **Group B (Case Group):** This group comprised 60 patients with a confirmed clinical diagnosis of bronchial asthma (34 males and 26 females), attending the outpatient and inpatient departments of the hospital. Based on the severity of their disease, Group B was further stratified into three subgroups according to the Global Initiative for Asthma (GINA) guidelines, utilising both the percentage of predicted forced expiratory volume in the first second (FEV1%) and the frequency of daytime/nighttime symptoms [10]:
  - **Subgroup B1 (Mild Asthma):** Patients with FEV1 > 80% of the predicted value, with symptoms occurring less than twice a week (n = 20).
  - **Subgroup B2 (Moderate Asthma):** Patients with FEV1 between 60% and 80% of the predicted value, with daily symptoms and occasional nocturnal awakenings (n = 20).
  - **Subgroup B3 (Severe Asthma):** Patients with FEV1 < 60% of the predicted value, presenting with continuous daily symptoms, frequent nocturnal exacerbations, and limited physical activity (n = 20).

Eligibility Criteria:

To ensure the internal validity of the study and minimise confounding variables, stringent inclusion and exclusion criteria were established.

- **Inclusion Criteria:** All participants were required to be between 15 and 50 years of age, of either gender, and willing to provide written informed consent. For the case group, a definitive diagnosis of bronchial asthma based on standard clinical and spirometric criteria was mandatory.
- **Exclusion Criteria:** The following individuals were systematically excluded from the study to avoid potential biases:
  - Participants under 15 years of age.
  - Patients with coexisting renal or hepatic disorders, diabetes mellitus, or any known endocrine dysfunction.
  - Pregnant or lactating women.
  - Individuals with a history of other pulmonary pathologies (e.g., chronic obstructive pulmonary disease, tuberculosis, interstitial lung disease), cardiovascular disease, or any systemic condition that could secondarily affect respiratory function.
  - Participants with significant neuromuscular disorders or a history of recent abdominal or thoracic surgery.
  - Active or former smokers (to eliminate the confounding effect of smoking on both lung function and Vitamin D metabolism).
  - Patients receiving medications known to interfere with serum 25-hydroxyvitamin D [25(OH)D] levels, including but not limited to anticonvulsants, systemic corticosteroids, vitamin D supplements, or calcium preparations.

Data Collection and Clinical Assessment:

All enrolled subjects underwent a comprehensive evaluation, which was carried out by a qualified physician and trained laboratory personnel. The assessment protocol was standardised for all participants and included the following components:

1. **Detailed Medical History:** A thorough history was obtained, focusing on respiratory symptoms (cough, wheeze, dyspnea, and chest tightness), duration of illness, frequency of exacerbations, medication history, and any relevant family history of atopy or asthma.
2. **Complete Clinical Examination:** A systematic general and systemic physical examination was performed, with special emphasis on the respiratory system (inspection, palpation, percussion, and auscultation) to assess for signs of airway obstruction, wheezing, or prolonged expiration.
3. **Radiological Investigation:** A plain chest radiograph (postero-anterior view) was obtained for all participants to rule out any underlying structural lung pathologies, infections, or other thoracic abnormalities.
4. **Laboratory Investigations:** Venous blood samples (approximately 5 mL) were collected under aseptic conditions from all subjects following an overnight fast of 8–10 hours. The samples were processed and analysed for the following parameters:
   - Complete blood count (CBC) using an automated haematology analyser.
   - Liver function tests (serum bilirubin, alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase).
   - Kidney function tests (serum creatinine and blood urea nitrogen).
   - Random blood sugar (RBS) to exclude undiagnosed diabetes mellitus.
5. **Pulmonary Function Testing (Spirometry):** Spirometric measurements were performed using a calibrated, computerised spirometer, following the American Thoracic Society (ATS) guidelines. For each participant, the FEV1 and forced vital capacity (FVC) were recorded, and the FEV1/FVC ratio was calculated. The best of three reproducible manoeuvres was used for analysis, and the results were expressed as a percentage of the predicted values based on age, sex, height, and ethnicity.

6. **Serum Vitamin D Assay:** The serum concentration of 25-hydroxyvitamin D [25(OH)D] was quantitatively measured using a commercially available enzyme-linked immunosorbent assay (ELISA) kit, following the manufacturer's instructions [11]. The assay exhibited high sensitivity and specificity, and all samples were run in duplicate to ensure precision. Based on the results, Vitamin D status was categorised as deficient (<20 ng/mL), insufficient (20–29 ng/mL), or sufficient (≥30 ng/mL).

Ethical Considerations:
Before participation, all individuals were provided with a detailed explanation of the study's objectives, procedures, potential risks, and benefits. Written informed consent was obtained from every participant (or from a legal guardian for minors) prior to enrollment. Confidentiality of all personal and clinical data was strictly maintained throughout the study and in subsequent publications.

Statistical Analysis:
The collected data were compiled, coded, and entered into a Microsoft Excel spreadsheet. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) software, version 24.0 for Windows (IBM Corp., Armonk, NY, USA). Descriptive statistics were employed to summarise the quantitative variables, which were expressed as mean ± standard deviation (SD). Categorical data were presented as frequencies and percentages. For comparative analysis, the one-way analysis of variance (ANOVA) test was utilised to evaluate the differences in mean serum Vitamin D levels and other continuous variables across the four study groups (control, mild asthma, moderate asthma, and severe asthma). Post-hoc comparisons, when applicable, were performed using Tukey's Honestly Significant Difference (HSD) test to identify specific group differences. A two-tailed *p*-value of less than 0.05 was considered to indicate statistical significance, with a 95% confidence interval.

RESULTS
A total of 100 participants were included in the study, comprising 60 patients with bronchial asthma (20 each with mild, moderate, and severe asthma) and 40 healthy controls. The overall study population consisted of 58 males (58%) and 42 females (42%), with a mean age of 37.15 ± 9.28 years.

As shown in Table 1, the mild asthma group included 11 males and 9 females, the moderate asthma group comprised 10 males and 10 females, and the severe asthma group consisted of 14 males and 6 females. The control group included 23 males and 17 females. The mean age was 34.20 ± 10.12 years in the mild asthma group, 37.85 ± 9.45 years in the moderate asthma group, 40.90 ± 8.97 years in the severe asthma group, and 36.10 ± 8.25 years among healthy controls. Although patients with severe asthma tended to be older than those with mild or moderate disease, the demographic characteristics were generally comparable across the study groups.

The biochemical parameters evaluated among the different study groups are presented in Table 2 and Figure 1. Serum 25-hydroxyvitamin D [25(OH)D] levels showed a progressive decline with increasing asthma severity. The highest mean vitamin D concentration was observed in the control group (47.30 ± 3.80 ng/mL), followed by the mild asthma group (33.20 ± 3.90 ng/mL), moderate asthma group (23.50 ± 6.80 ng/mL), and severe asthma group (20.10 ± 7.50 ng/mL). This difference was highly statistically significant ($p < 0.0001$). In contrast, serum calcium levels remained relatively constant across all groups, with mean values ranging from 9.48 to 9.55 mg/dL, and the difference was not statistically significant ($p = 0.385$). A significant increase in serum alkaline phosphatase (ALP) levels was observed with increasing asthma severity. The mean ALP level was 49.50 ± 6.90 U/L in healthy controls, increasing to 78.50 ± 5.80 U/L in patients with mild asthma, 175.20 ± 13.90 U/L in those with moderate asthma, and 252.40 ± 15.80 U/L in patients with severe asthma. The intergroup difference was highly significant ($p < 0.0001$). Similarly, serum magnesium levels demonstrated a significant declining trend with increasing disease severity. Healthy controls had the highest mean serum magnesium concentration (2.30 ± 0.07 mg/dL), followed by patients with mild asthma (1.85 ± 0.10 mg/dL), moderate asthma (1.72 ± 0.06 mg/dL), and severe asthma (1.55 ± 0.04 mg/dL). These differences were also highly statistically significant ($p < 0.0001$).

Overall, the findings demonstrate that increasing severity of bronchial asthma is associated with significantly lower serum vitamin D and magnesium levels, together with significantly higher alkaline phosphatase levels, whereas serum calcium concentrations remain unaffected across the study groups.

Table 1: Baseline demographic characteristics of the study population stratified by asthma severity

Grade of Asthma	Gender		Age (Years) [Mean ± SD]
	Male	Female	
Mild (n=20)	11	9	34.20 ± 10.12

Moderate (n=20)	10	10	37.85 ± 9.45
Severe (n=20)	14	6	40.90 ± 8.97
Control (n=40)	23	17	36.10 ± 8.25
Total (n=100)	58	42	37.15 ± 9.28

Abbreviations: SD, Standard Deviation; n, number of subjects

Table 2: Serum levels of Vitamin D, calcium, alkaline phosphatase, and magnesium across asthma severity groups and healthy controls

Grade of Asthma	Vit D (ng/ml)	S. Ca^{2+} (mg/dl)	ALP (U/L)	S. Mg^{2+} (mg/dl)
Mild (n=20)	33.20 ± 3.90	9.50 ± 0.45	78.50 ± 5.80	1.85 ± 0.10
Moderate (n=20)	23.50 ± 6.80	9.52 ± 0.14	175.20 ± 13.90	1.72 ± 0.06
Severe (n=20)	20.10 ± 7.50	9.48 ± 0.11	252.40 ± 15.80	1.55 ± 0.04
Control (n=40)	47.30 ± 3.80	9.55 ± 0.07	49.50 ± 6.90	2.30 ± 0.07
P Value	< 0.0001	0.385	< 0.0001	< 0.0001

[Data are expressed as Mean ± Standard Deviation (SD). Abbreviations: Vit D, Vitamin D; S. Ca^{2+}, Serum Calcium; ALP, Alkaline Phosphatase; S. Mg^{2+}, Serum Magnesium. P value < 0.05 was considered statistically significant (One-way ANOVA)].

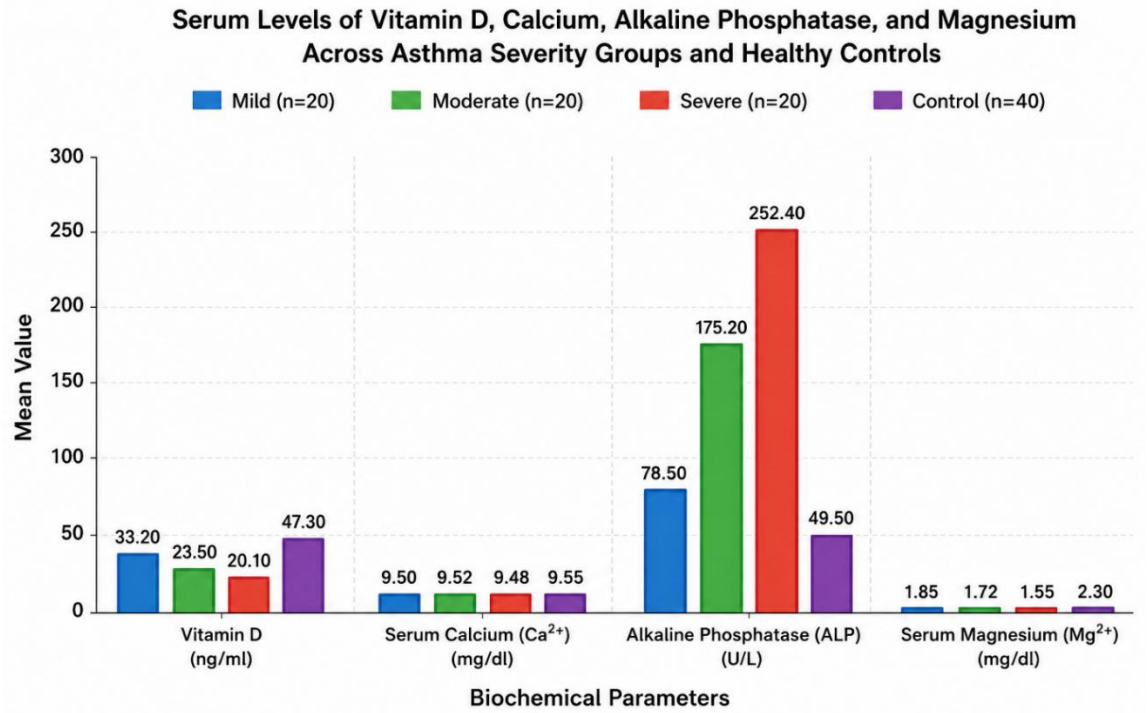

Figure 1. Mean serum levels of Vitamin D, calcium, alkaline phosphatase (ALP), and magnesium among patients with different grades of bronchial asthma and healthy controls.

DISCUSSION

Since India is a tropical nation with abundant sunlight throughout the year, it was traditionally believed that vitamin D insufficiency was not a significant public health concern in this region [12]. However, accumulating evidence from

published research has challenged this assumption, demonstrating that vitamin D deficiency is remarkably prevalent across both sexes and all age groups in the Indian population [13-15]. The precise reasons underlying this widespread deficiency remain incompletely understood. Nevertheless, Webb et al. have identified several key contributory factors, including reduced outdoor activity and consequent limited sun exposure, suboptimal dietary intake, seasonal variations, advancing age, skin pigmentation, and cultural practices of skin coverage. These factors collectively create a predisposition toward the development of allergic disorders, including asthma [16]. It is well documented that individuals who spend prolonged periods indoors or who routinely employ ultraviolet (UV) protective clothing and sunscreen exhibit significantly diminished cutaneous synthesis of vitamin D. Consequently, vitamin D insufficiency has been recognised in numerous populations worldwide, including India [17], irrespective of geographic latitude or ambient sunlight availability. Despite this recognition, only a limited number of Indian studies have directly investigated the role of vitamin D in the pathogenesis and clinical course of bronchial asthma.

In the present study, we observed a progressive and statistically significant decline in mean serum vitamin D levels across the spectrum of asthma severity. The mean serum 25-hydroxyvitamin D [25(OH)D] concentrations were 33.20 ± 3.90 ng/mL in the mild asthma group, 23.50 ± 6.80 ng/mL in the moderate asthma group, and 20.10 ± 7.50 ng/mL in the severe asthma group, compared with 47.30 ± 3.80 ng/mL in healthy controls. The intergroup differences were highly significant (*p* < 0.0001). This graded reduction in serum vitamin D levels with increasing disease severity strongly suggests an inverse relationship between vitamin D status and the clinical severity of bronchial asthma. In other words, lower serum vitamin D levels are associated with more severe disease manifestations, whereas higher levels appear to confer a protective effect or at least correlate with milder disease.

Our findings are consistent with the seminal work of Litonjua and Weiss [18], who demonstrated that low vitamin D levels were significantly associated with reduced pulmonary function tests and worsening respiratory symptoms in patients with bronchial asthma. Similarly, Somashekar et al. [19] conducted a cross-sectional study on 44 asthmatic children in Bangalore, India, and reported that 31.28% of the asthmatic children had insufficient serum vitamin D levels (>15 ng/mL to <20 ng/mL), while a striking 68.18% had deficient levels (≤15 ng/mL). Alarmingly, this indicates that 100% of the asthmatic children in their study population had suboptimal serum vitamin D levels, underscoring the near-universal prevalence of vitamin D inadequacy among asthmatic individuals in the Indian context.

Our results also resonate with the findings of Bener et al. [20], who reported a high prevalence of vitamin D deficiency in asthmatic patients and identified vitamin D as a strong predictor of asthma in their study population. Furthermore, Columbo et al. [21] investigated the role of vitamin D in elderly patients with asthma and other respiratory diseases, confirming that vitamin D deficiency was highly prevalent in this demographic and was associated with poorer clinical outcomes. In a large population-based study, Ginde et al. [22] demonstrated that low serum vitamin D levels were independently associated with an increased risk of upper respiratory tract infections, which are known to exacerbate asthma and contribute to disease worsening. Brehm et al. [23] extended these observations by reporting a higher frequency of both asthma and allergic rhinitis in individuals with vitamin D insufficiency, further strengthening the epidemiological link between vitamin D deficiency and atopic diseases.

Pathophysiological Mechanisms Linking Vitamin D Deficiency and Asthma Severity

The biological plausibility of the observed association between vitamin D deficiency and asthma severity is supported by a growing body of mechanistic evidence. Vitamin D exerts its immunomodulatory effects through the vitamin D receptor (VDR), which is expressed on a wide array of immune cells, including T lymphocytes, B lymphocytes, dendritic cells, and macrophages. Vitamin D has been shown to suppress the production and release of Th1-associated cytokines and pro-inflammatory molecules, including interleukin-17 (IL-17), thereby attenuating the inflammatory cascade that characterises asthmatic airways [24, 25]. Conversely, vitamin D deficiency creates a permissive immunological environment that promotes the expansion of Th2-mediated responses, which are central to the pathogenesis of allergic asthma. Recent studies have established a correlation between vitamin D deficiency and elevated expression of tumour necrosis factor-alpha (TNF-α), a potent pro-inflammatory cytokine that is particularly upregulated in patients with poorly controlled asthma [24, 26]. Additionally, vitamin D enhances the synthesis of the anti-inflammatory cytokine interleukin-10 (IL-10) and supports the differentiation and function of regulatory T cells (Tregs), which are crucial for maintaining immune tolerance and suppressing aberrant inflammatory responses in the airways [24]. Collectively, these immunoregulatory actions underscore the critical role of vitamin D in modulating airway inflammation, bronchial hyper-responsiveness, and airway remodelling—all of which are hallmark features of asthma pathogenesis.

Significance of Elevated Alkaline Phosphatase Levels

An additional noteworthy finding of our study is the progressive and highly significant elevation in serum alkaline phosphatase (ALP) levels with increasing asthma severity. The mean ALP level was lowest in the mild asthma group (78.50 ± 5.80 U/L), followed by the moderate asthma group (175.20 ± 13.90 U/L), and highest in the severe asthma group (252.40 ± 15.80 U/L), compared with the control group (49.50 ± 6.90 U/L). The difference was highly statistically significant (*p* < 0.0001). This marked elevation in ALP levels likely reflects increased osteoid tissue turnover and bone remodelling, which may be attributable to secondary hyperparathyroidism resulting from chronic vitamin D deficiency [27]. Vitamin D

deficiency leads to impaired intestinal calcium absorption, which in turn triggers compensatory hypersecretion of parathyroid hormone (PTH). Chronic secondary hyperparathyroidism stimulates osteoclastic bone resorption and increases osteoblast activity, both of which contribute to elevated serum ALP levels. The observation of progressively higher ALP levels in patients with more severe asthma suggests that vitamin D deficiency may have significant skeletal consequences in this population, particularly in those with long-standing or poorly controlled disease. This finding carries important clinical implications, as it underscores the need for routine bone health assessment in patients with severe asthma and chronic vitamin D deficiency.

Significance of Reduced Serum Magnesium Levels

Our study also revealed a significant progressive decline in serum magnesium levels with increasing asthma severity. Healthy controls had the highest mean serum magnesium concentration (2.30 ± 0.07 mg/dL), followed by patients with mild asthma (1.85 ± 0.10 mg/dL), moderate asthma (1.72 ± 0.06 mg/dL), and severe asthma (1.55 ± 0.04 mg/dL). The intergroup differences were highly significant (*p* < 0.0001). This finding is particularly noteworthy given the well-established role of magnesium as a physiological calcium antagonist and its importance in maintaining bronchial smooth muscle tone. Magnesium deficiency can potentiate bronchial hyperreactivity by enhancing calcium influx into smooth muscle cells, thereby promoting bronchoconstriction. Moreover, magnesium acts as a cofactor for numerous enzymatic reactions involved in energy metabolism and has been shown to possess anti-inflammatory properties. The progressive decline in serum magnesium levels with increasing asthma severity observed in our study may be explained by several mechanisms. First, inadequate dietary intake of magnesium is common in asthmatic patients, who often have suboptimal nutritional status. Second, chronic use of medications commonly employed in asthma management, including theophylline, corticosteroids, and β2-agonists, has been shown to increase renal magnesium excretion, thereby depleting systemic magnesium stores [26, 27]. Third, genetic factors may predispose certain individuals to magnesium deficiency. The parallel decline in both vitamin D and magnesium levels across the asthma severity spectrum suggests a potential synergistic relationship between these two essential micronutrients in the pathophysiology of asthma.

The findings of the present study carry several important clinical implications. First, the strong and consistent association between lower serum vitamin D levels and increasing asthma severity suggests that routine assessment of vitamin D status should be considered as a valuable adjunct in the comprehensive clinical evaluation of patients with bronchial asthma. Such assessment may help identify patients who are at higher risk of severe disease and who may benefit from targeted nutritional intervention. Second, the significant elevation in ALP levels observed in patients with severe asthma highlights the potential skeletal consequences of chronic vitamin D deficiency in this population. Clinicians should be vigilant about the bone health of asthmatic patients, particularly those receiving long-term corticosteroid therapy, and consider periodic monitoring of bone turnover markers and bone mineral density when clinically indicated. Third, the progressive decline in serum magnesium levels with increasing asthma severity underscores the importance of evaluating and correcting magnesium status in asthmatic patients. Magnesium supplementation may have a role in improving bronchodilator response and reducing airway hyperreactivity, particularly in patients with moderate-to-severe disease. Fourth, the results of this study support the need for larger, well-designed prospective studies and randomised controlled trials to establish a causal relationship between vitamin D deficiency and asthma severity and to determine whether vitamin D supplementation can improve clinical outcomes, reduce exacerbation rates, and enhance quality of life in asthmatic patients. Finally, given the high prevalence of vitamin D deficiency in the Indian population, public health strategies aimed at improving vitamin D status through safe sunlight exposure, food fortification, and targeted supplementation may have a significant impact on reducing the burden of asthma and other allergic diseases in the country.

Our findings are consistent with several international studies that have explored the relationship between vitamin D status and asthma severity. In a Costa Rican study, Brehm et al. [23] demonstrated that lower vitamin D levels were associated with increased asthma severity, reduced lung function, and higher levels of total serum IgE. Similarly, Sutherland et al. [26] reported that vitamin D insufficiency was associated with reduced lung function and impaired corticosteroid responsiveness in adult asthmatic patients. Montero-Arias et al. [25] extended these observations by showing that vitamin D insufficiency was significantly correlated with worse asthma control and increased healthcare utilisation in adult patients. These international studies, together with our findings, provide compelling evidence for a consistent association between vitamin D deficiency and adverse asthma outcomes across different geographic regions, ethnic groups, and age populations.

Strengths and Limitations of the Study

The present study has several strengths, including its well-defined case-control design, rigorous use of GINA guidelines for asthma severity classification, comprehensive biochemical assessment, and careful exclusion of potential confounders such as smoking, comorbidities, and medications that could affect vitamin D metabolism. However, several limitations must be acknowledged. First, the cross-sectional design precludes the establishment of a causal relationship between vitamin D deficiency and asthma severity. Second, the relatively small sample size and single-centre setting may limit the generalizability of the findings. Third, factors known to influence vitamin D status, including dietary intake, sunlight exposure, seasonal variation, body mass index, and physical activity, were not systematically assessed. Fourth, vitamin D levels were measured at a single time point, without follow-up evaluation or assessment of the effects of vitamin D supplementation. Fifth, inflammatory biomarkers, such as serum IgE, eosinophil count, and fractional exhaled nitric oxide

(FeNO), were not correlated with vitamin D levels, which could have provided additional mechanistic insights. Despite these limitations, the study provides important and clinically relevant evidence supporting the association between vitamin D deficiency and asthma severity in the Indian population.

Future Research Directions

Future research should focus on large-scale, multi-centre prospective cohort studies to confirm the association between vitamin D status and asthma severity and to elucidate the underlying pathophysiological mechanisms. Randomised controlled trials are urgently needed to evaluate the therapeutic efficacy of vitamin D supplementation in improving asthma control, reducing exacerbation rates, and modifying disease progression. Additionally, studies examining the interaction between vitamin D and other micronutrients, such as magnesium and calcium, in the context of asthma pathogenesis may provide valuable insights into potential combination nutritional interventions. Finally, research exploring the genetic determinants of vitamin D metabolism and VDR polymorphisms may help identify subgroups of asthmatic patients who are most likely to benefit from vitamin D supplementation, paving the way for personalised medicine approaches in asthma management.

CONCLUSIONS

The present study demonstrates a significant association between serum vitamin D deficiency and increasing severity of bronchial asthma. Patients with moderate and severe asthma exhibited progressively lower serum vitamin D and magnesium levels, along with significantly higher alkaline phosphatase levels, compared with healthy controls, whereas serum calcium levels remained comparable across all groups. These findings suggest that vitamin D deficiency may be linked to disease severity and could serve as a useful biochemical marker in the clinical assessment of patients with bronchial asthma. Routine evaluation of vitamin D status may help identify patients at greater risk of severe disease and support individualised management strategies. However, large-scale prospective studies and randomised controlled trials are warranted to establish a causal relationship and to determine the therapeutic role of vitamin D supplementation in improving asthma outcomes.

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