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Original Research Article

Association Between Serum Vitamin D Level and Bronchial Asthma: A Cross-Sectional Study

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Conflict of interest: Nil

Abstract

Background: Vitamin D has immunomodulatory actions that may influence airway inflammation, but evidence linking vitamin D status to asthma control and lung function in adults is inconsistent, and data from eastern India are scarce.

Objective: To compare pulmonary function (PEFR, FEV1, FEV1/FVC) and asthma control between adult bronchial asthma patients with adequate and deficient serum vitamin D.

Methods: This hospital-based cross-sectional study was conducted from May 2023 to April 2024 in the pulmonary medicine outpatient department of VIMSAR, Burla. Ninety non-smoking adults (>18 years) with bronchial asthma on formoterol–budesonide were enrolled by convenience sampling and allocated to adequate (>30 ng/mL, n = 45) or deficient (<30 ng/mL, n = 45) vitamin D groups (chemiluminescence immunoassay). Spirometry was performed before and after bronchodilator, and asthma control was assessed with the Asthma Control Test (ACT). Groups were compared using the unpaired t-test, one-way ANOVA with post hoc testing, and chi-square test (SPSS).

Results: Mean age was 45.4 ± 17.8 years (adequate) and 43.6 ± 14.9 years (deficient). No significant between-group differences were found in pre- or post-bronchodilator PEFR, FEV1, or FEV1/FVC (all $p > 0.05$); pre-bronchodilator PEFR showed the largest, non-significant, difference (74.6% vs 86.4%, $p = 0.059$). Serum vitamin D did not differ across ACT categories ($F = 1.644$, $p = 0.199$). PEFR (pre, post) and FEV1 (pre, post) differed significantly across ACT categories ($p = 0.003$–0.014), with the highest values in the "not well controlled" group. FEV1/FVC was not associated with ACT category (chi-square $p = 0.487$).

Conclusion: In this sample of adult asthma patients, serum vitamin D level was not significantly associated with spirometric indices or ACT-defined asthma control. Larger, adequately powered studies with prospective follow-up are needed to clarify the relationship.

Keywords: bronchial asthma; vitamin D; 25-hydroxyvitamin D; pulmonary function tests; Asthma Control Test; India.

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Introduction

Asthma is a common type of chronic lung disease that impacts nearly three hundred million people worldwide. One thing is for sure: the condition is connected with increased hospitalisations, deaths and health-care costs.[1] It is a chronic inflammatory disease of the airways which is marked by airway hyperresponsiveness. Above all, asthma is marked by the appearance of wheeze, breathlessness, chest tightness and cough.[2] Further, the ailment is generally worse at night or in the early morning hours.[3] Type-2 cytokines (IL-4, IL-5 and IL-13) get upregulated in the asthmatic airway.4 Such upregulation is associated with eosinophilia, mast-cell degranulation and raised IgE.2 Persistent inflammation leads to airway remodelling.[5] Further, it leads to smooth-muscle hypertrophy and goblet-cell hyperplasia. In the long run, it causes fixed airflow obstruction.[6]

Vitamin D is a group of fat-soluble secosteroids mainly obtained from cutaneous synthesis under ultraviolet-B radiation. Serum 25-hydroxyvitamin D [25(OH)D] is the accepted marker of status.6 Besides its classical role in calcium homeostasis, vitamin D has non-classical actions, which include immunomodulation of lymphocytes, macrophages and dendritic cells.7,8 It up-regulates the antimicrobial peptide cathelicidin and modifies Th1/Th2 cytokine expression, thereby providing a biological rationale for an effect on airway disease.[9,10].

According to observational studies, when 25(OH)D is less than or equal to 25 nmol/L, patients may show more frequent exacerbations, poor asthma control, lower lung function and lower corticosteroid responsiveness.[11–15] Impaired lung function and asthma in offspring have also been linked to maternal vitamin D deficiency mid-pregnancy.[16] Some settings reported that vitamin D supplementation may lead to reduced exacerbations.[17,18] However, the Cochrane review of vitamin D for asthma found benefit largely limited to reduced exacerbations, with no clear effect on symptom control or lung function.[19] Reviews of the relationship between 25(OH)D and spirometry are also inconsistent.[20,21] Most evidence base comes from children or from Western populations. To our knowledge, no study from Odisha has investigated vitamin D status in adult asthma. As a result, we undertook a cross-sectional investigation that was aimed at assessing pulmonary function and asthma control among asthma cases having adequate and deficient serum vitamin D in a tertiary hospital. The null hypothesis states that serum vitamin D and bronchial asthma are not related to each other.

Materials and Methods

Study Design, Setting and Period: This hospital-based cross-sectional study was carried out in the outpatient department of Pulmonary Medicine, in collaboration with the Department of Pharmacology, V.S.S. Institute of Medical Sciences and Research (VIMSAR), Burla, Sambalpur, Odisha, from May 2023 to April 2024.

Participants: Adults (>18 years) with physician-diagnosed bronchial asthma attending the outpatient department and receiving formoterol–budesonide were eligible. Exclusion criteria were pregnancy or lactation, smoking, co-morbid illness, cardiac disease, sarcoidosis, raised serum calcium or phosphate, raised vitamin D levels, kidney stones or reduced renal function, and any contraindication to vitamin D supplementation. Participants were recruited by convenience sampling.

Sample Size: For comparison of two means with $\alpha = 0.05$, power of 80% ($\beta = 0.2$), an expected effect size (d) of 0.6 and an allocation ratio of 1:1, at least 45 participants per group (90 in total) were required.

Study Procedures and Variables: Written informed consent was obtained, and socio-demographic data (age, sex, education, occupation, family type, monthly income, allergy and family history) were recorded on a structured case-report form. Serum 25(OH)D was measured by chemiluminescence immunoassay. Participants were allocated to Group A (adequate vitamin D, >30 ng/mL) or Group B (deficient vitamin D, <30 ng/mL). Spirometry was used to measure peak expiratory flow rate (PEFR), forced expiratory volume in one second (FEV1) and the FEV1/forced vital capacity (FVC) ratio before and after bronchodilator, expressed as percentage of predicted.

Asthma control was assessed with the five-item Asthma Control Test (ACT; score 5–25), with categories of well controlled (20–25), not well controlled (16–19) and very poorly controlled (5–15); a score of 19 or below suggests uncontrolled asthma. Adverse drug reactions to vitamin D and to concomitant anti-asthma drugs were monitored as a secondary objective.

Statistical Analysis: Data were entered in Microsoft Excel and analysed with SPSS. Continuous variables are presented as mean ± standard deviation (SD) and categorical variables as number (%). The unpaired t-test compared spirometric indices between vitamin D groups. One-way ANOVA with post hoc comparison (homogeneous subsets, $\alpha = 0.05$) compared spirometric indices and serum vitamin D across the three ACT categories, and Pearson's chi-square test

assessed the association between FEV1/FVC (pre-bronchodilator) category and ACT category. A p-value <0.05 was considered statistically significant.

Ethics: The study was approved by the Institutional Research and Ethics Committee, VIMSAR, Burla (approval no. 170-2022/I-S-T/120, dated 22 May 2023). All participants gave written informed consent, and confidentiality was maintained using study numbers.

Results

Participant Characteristics: Ninety patients were analysed (45 per group). Mean age was 45.4 ± 17.8 years in the adequate-vitamin D group and 43.6 ± 14.9 years in the deficient group; mean monthly income was ₹13,867 and ₹13,022, respectively (Table 1).

Overall, 41.1% of participants were aged 26–45 years, 64.4% had completed higher secondary education, 68.9% had a monthly income of ₹15,000 or less, and 46.7% lived in family settings classified as "others" (Table 2, Figure 1).

Table 1: Baseline characteristics of asthma patients by vitamin D status (n = 45 per group)

Variable	Adequate vit D: range	Adequate vit D: mean ± SD	Deficient vit D: range	Deficient vit D: mean ± SD
Age (years)	18–80	45.4 ± 17.8	18–71	43.6 ± 14.9
Income (₹/month)	0–60,000	13,866.7 ± 17,983.1	0–50,000	13,022.2 ± 16,000.6
Allergy score*	0–4	1.09 ± 1.33	0–4	0.73 ± 1.21
Family history score*	0–8	1.87 ± 1.94	0–7	1.67 ± 2.29

SD, standard deviation. *Scores as coded in the study master chart.

Table 2: Socio-demographic distribution of all participants (N = 90)

Characteristic	Category	n	%
Age group (years)	18–25	14	15.6
	26–45	37	41.1
	46–60	21	23.3
	61–80	18	20.0
Education	Illiterate	8	8.9
	Primary	10	11.1
	Secondary	14	15.6
	Higher secondary	58	64.4
Family type	Nuclear	10	11.1
	Joint	24	26.7
	Extended	14	15.6
	Others	42	46.7
Monthly income (₹)	0–15,000	62	68.9
	16,000–30,000	7	7.8
	31,000–45,000	17	18.9
	45,000–60,000	4	4.4

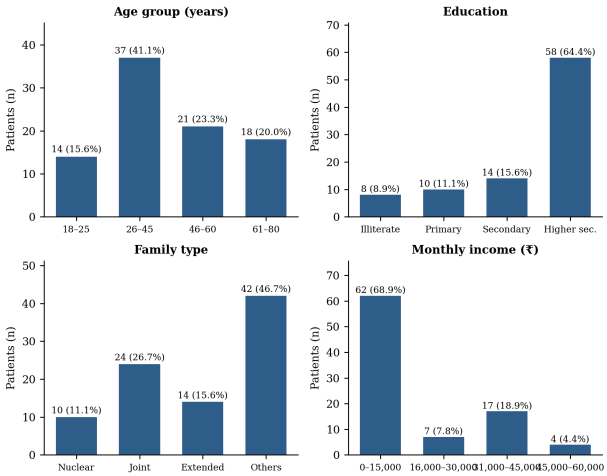


Figure 1: Distribution of study participants by age group, education, family type and monthly income (N = 90)

Pulmonary function by vitamin D status: There were no statistically significant differences in any spirometric index between patients with adequate and deficient vitamin D (all $p > 0.05$; Table 3, Figure 2). The largest difference was in pre-bronchodilator PEFR (74.6% vs 86.4%, $t = -1.917$, $p = 0.059$), which was numerically higher in the vitamin D-deficient group, i.e. opposite to the direction predicted by the study hypothesis.

Table 3: Comparison of pulmonary function (% predicted) between vitamin D groups (unpaired t-test)

Parameter	Adequate (>30 ng/mL), mean	Deficient (<30 ng/mL), mean	t	p
PEFR pre-bronchodilator	74.556	86.378	−1.917	0.059
PEFR post-bronchodilator	73.622	79.578	−1.367	0.175
FEV1 pre-bronchodilator	74.089	74.511	−0.095	0.924
FEV1 post-bronchodilator	77.533	79.733	−0.548	0.585
FEV1/FVC pre-bronchodilator	89.978	90.822	−0.359	0.720
FEV1/FVC post-bronchodilator	90.178	92.444	−1.129	0.262

n = 45 per group. No comparison reached $p < 0.05$.

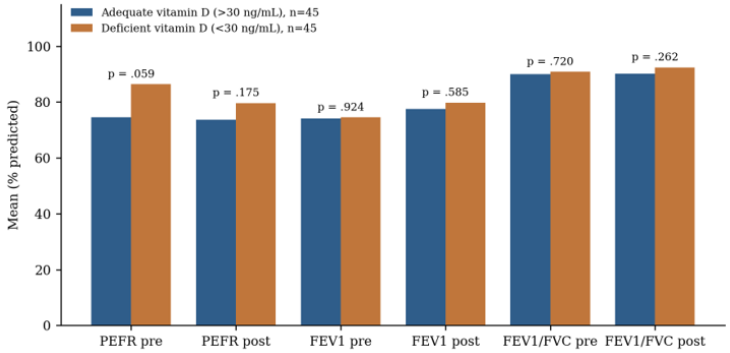


Figure 2: Mean pulmonary function indices (% predicted) in asthma patients with adequate versus deficient serum vitamin D. p-values from unpaired t-tests

Asthma control (ACT), pulmonary function and vitamin D: By ACT score, 25 patients (27.8%) were well controlled, 38 (42.2%) not well controlled and 27 (30.0%) very poorly controlled. Serum vitamin D did not differ significantly across ACT categories ($F = 1.644$, $p = 0.199$); mean levels were 25.2, 23.3 and 27.2 ng/mL in the well, not well and very poorly controlled groups, respectively (Table 4, Figure 3). PEFR and FEV1, before and after bronchodilator, differed significantly across ACT categories ($p = 0.003$ to 0.014). In post hoc analysis the "not well controlled" group formed a separate subset with the highest mean values, whereas the well and very poorly controlled groups did not differ from each other for pre-bronchodilator indices. FEV1/FVC (pre and post) was not significantly associated with ACT category on ANOVA ($p = 0.074$ and 0.102). Pearson's chi-square test likewise showed no association between FEV1/FVC category (pre-bronchodilator) and ACT category ($\chi^2 = 1.440$, df = 2, $p = 0.487$; Table 5).

Table 4: One-way ANOVA of pulmonary function and serum vitamin D across ACT control categories (mean values)

Parameter	Well controlled (n = 25)	Not well controlled (n = 38)	Very poorly controlled (n = 27)	F	P
PEFR pre (%)	73.800	92.316	69.963	5.937	0.004
PEFR post (%)	73.840	83.711	69.148	4.520	0.014
FEV1 pre (%)	66.600	82.921	69.296	6.373	0.003
FEV1 post (%)	76.520	85.000	71.630	4.457	0.014
FEV1/FVC pre (%)	92.640	91.789	86.370	2.688	0.074
FEV1/FVC post (%)	92.680	92.737	88.037	2.342	0.102
Serum vitamin D (ng/mL)	25.227	23.286	27.215	1.644	0.199

ACT categories: well controlled 20–25; not well controlled 16–19; very poorly controlled 5–15.

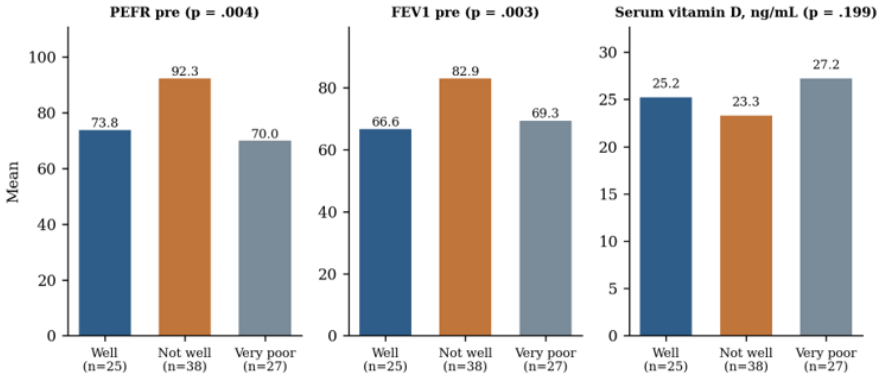


Figure 3: Mean pre-bronchodilator PEFR, pre-bronchodilator FEV1 and serum vitamin D across ACT control categories. p-values from one-way ANOVA

Table 5: Cross-tabulation of pre-bronchodilator FEV1/FVC category and ACT category (Pearson χ^2 = 1.440, df = 2, p = 0.487)

ACT category	FEV1/FVC pre: category 1	FEV1/FVC pre: category 2	Total
Well controlled	4	21	25
Not well controlled	11	27	38
Very poorly controlled	6	21	27
Total	21	69	90

Discussion

Our cross-sectional study of 90 adults with asthma revealed no significant differences in spirometric indices between patients with adequate and deficient levels of serum vitamin D. Additionally, the serum vitamin D levels did not significantly vary across ACT categories. The results do not indicate that vitamin D status is associated with lung function or symptom control in this cohort, and they are consistent with the inconsistent literature on this question.[19–21]. The age of about 44-45 years of the participants is in accord with asthma in adults being a disease of working age [22]. It is different from the literature, which is largely paediatric in which vitamin D deficiency has been associated with asthma severity more strongly [23,24]. A wide range of income, with 68.9% earning ₹ 15,000 or less, is relevant as lower socio-economic status is connected with an increase in the burden of asthma through environmental exposure and limited access to care [25].

Socio-economic factors may affect vitamin D status and so residual confounding cannot be considered unlikely. Earlier research, including a meta-analysis and several observational studies, shows positive relationships between serum 25(OH)D with lung function and low 25(OH)D with severe or uncontrolled asthma.[15,24,26] Our null findings might be due to cohort characteristics: all patients were on formoterol-budesonide, and mean FEV1/FVC values were high (around 90%), suggesting a predominantly mild airflow limitation in which any vitamin D effect would prove difficult to observe. Steroid-related immune associations of vitamin D have also been reported to be weaker in adults than children.[27] FEV1/FVC mainly reflects fixed structural obstruction, and diagnostic thresholds for it have been debated;[28] additionally, ACT score correlations with spirometry are known to be weak, especially with mild-to-moderate disease.[29,30].

The finding which was unexpected is PEFR and FEV1 values differed significantly among ACT groups with the highest values seen in not well-controlled group instead of the well-controlled group. The pattern in question is not one that is intuitive biologically and consequently warrants a rather cautious interpretation.

According to ACT, spirometry measures airflow at a point in time, and the two are only modestly related. There may therefore be differences in perception of symptoms, treatment effect, and chance findings in uneven small subgroups.[29,30] This should be taken as hypothesis-generating rather than evidence of a real relationship.

Strengths and limitations

Strengths include measurement of serum vitamin D by a standardised immunoassay, use of a validated control questionnaire and spirometry, and a pre-specified sample size in an under-studied population. Limitations include the cross-sectional design, which precludes causal inference; single-centre convenience sampling; reliance on a single 30 ng/mL cut-off; no adjustment for confounders such as body mass index, sun exposure, season, diet, asthma duration and severity; and multiple

comparisons without correction. The study was powered for a medium effect (d = 0.6), so smaller associations may have been missed. Adverse drug reaction data, a secondary objective, are not reported here.

Conclusion

Serum vitamin D level was not significantly associated with pulmonary function indices (PEFR, FEV1, FEV1/FVC) or with ACT-defined asthma control in adult asthma patients attending a tertiary care centre in Odisha. Although PEFR and FEV1 differed across ACT categories, this was independent of vitamin D status. Larger multicentre studies, adjusted for confounders and with longitudinal follow-up or supplementation trials, are required before conclusions can be drawn on the clinical role of vitamin D in adult asthma.

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