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EFFECT OF HIGH-DOSE VITAMIN D ON ASTHMA CONTROL AND LUNG FUNCTION: A RANDOMIZED CONTROLLED TRIAL

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Abstract:

Background: *Asthma had remained a prevalent chronic inflammatory airway disorder characterized by recurrent episodes of wheezing, breathlessness, and reduced lung function. Despite the availability of standard therapeutic interventions, many patients had continued to experience suboptimal symptom control. Vitamin D deficiency had increasingly been recognized as a potential modifiable factor influencing asthma severity and respiratory function. High-dose vitamin D supplementation had been hypothesized to improve asthma outcomes by modulating immune responses and enhancing airway stability.*

Aim: *This study had aimed to evaluate the effect of high-dose vitamin D supplementation on asthma control and lung function among adult patients with moderate persistent asthma.*

Methods: *This randomized controlled trial had been conducted at Mayo Hospital, Lahore, from October 2024 to September 2025. The study population had comprised 90 adult patients aged 18–55 years with clinically diagnosed moderate persistent asthma. Participants had been randomly assigned into two equal groups: the intervention group, which had received high-dose vitamin D (50,000 IU weekly for 12 weeks), and the control group, which had received a placebo in addition to standard asthma therapy. Asthma control had been assessed using the Asthma Control Test (ACT) scores, while lung function parameters—Forced Expiratory Volume in one second (FEV_1) and Peak Expiratory Flow Rate (PEFR)—had been measured using standardized spirometry protocols at baseline and after 12 weeks of follow-up. Data collection had been performed by trained respiratory technicians, and statistical analysis had been carried out using independent t-tests and paired comparisons.*

Results: *The intervention group had demonstrated a significant improvement in ACT scores compared to baseline, with a mean increase of 5.2 ± 1.8 points, whereas the control group had shown a modest improvement of 1.6 ± 1.1 points. Similarly, FEV_1 values had improved by 12.4% in the intervention group compared to 4.1% in the control group. PEFR had also increased substantially in the vitamin D group by 45.6 L/min, compared to 12.3 L/min in the placebo group. The differences between groups had been statistically significant ($p < 0.05$). No major adverse events related to vitamin D supplementation had been reported.*

Conclusion: *The study had concluded that high-dose vitamin D supplementation significantly improved asthma control and lung function among adults with moderate persistent asthma. Incorporating vitamin D supplementation as an adjunct to standard asthma therapy had the potential to enhance clinical outcomes, particularly in populations with underlying vitamin D insufficiency.*

Keywords: *Asthma, Vitamin D, Lung Function, Asthma Control Test, Randomized Controlled Trial, Respiratory Health.*

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INTRODUCTION:

Asthma had been recognized as a chronic inflammatory disorder of the airways that affected millions of individuals worldwide, contributing significantly to morbidity, healthcare burden, and reduced quality of life. Characterized by variable respiratory symptoms such as wheezing, shortness of breath, chest tightness, and coughing, asthma had been associated with episodic airflow obstruction and bronchial hyperresponsiveness [1]. Despite advancements in pharmacological therapies—including inhaled corticosteroids, bronchodilators, and leukotriene modifiers—many patients had continued to experience suboptimal symptom control, frequent exacerbations, and impaired lung function. These limitations had highlighted the ongoing need to identify adjunctive therapies that could enhance disease control and improve clinical outcomes.

In recent years, vitamin D had emerged as a potential immunomodulatory agent with relevance to respiratory health. Beyond its classical role in calcium homeostasis and bone metabolism, vitamin D had been shown to influence both innate and adaptive immune responses [2]. Previous observational studies had suggested that vitamin D deficiency had been highly prevalent in individuals with asthma and had been linked to increased disease severity, higher exacerbation rates, and reduced responsiveness to standard treatments. These associations had led researchers to investigate whether vitamin D supplementation could serve as a beneficial adjunct in asthma management [3].

Biologically, vitamin D had been postulated to modulate airway inflammation by reducing pro-inflammatory cytokine production, enhancing antimicrobial peptide expression, and improving regulatory T-cell function. These mechanisms had suggested a plausible pathway through which vitamin D might enhance asthma control and reduce airway hyperreactivity. Additionally, vitamin D had been thought to play a role in lung development and repair processes, raising the possibility that supplementation could contribute to improved pulmonary function [4].

Randomized controlled trials evaluating vitamin D supplementation in asthma had yielded mixed results. Some studies had reported reductions in exacerbation rates and improvements in asthma control, particularly among individuals with documented vitamin D deficiency. However, other trials had shown minimal or no clinical benefit. These inconsistencies had underscored the importance of further investigation, particularly regarding the optimal dose, treatment duration, and patient subgroups most likely to benefit [5]. High-dose vitamin D supplementation, in particular, had attracted considerable research interest due to its potential to rapidly restore serum vitamin D levels and exert more pronounced immunomodulatory effects.

Despite this growing body of evidence, gaps had remained in understanding the precise impact of high-dose vitamin D on both asthma control and lung function in diverse populations. Many previous studies had been limited by small sample sizes, heterogeneous dosing strategies, short follow-up durations, or lack of standardized outcome assessments [6]. As a result, there had been a need for well-designed randomized controlled trials that rigorously examined the therapeutic potential of high-dose vitamin D in asthma management.

In response to this need, the present study had been conducted to evaluate the effect of high-dose vitamin D supplementation on asthma control and lung function among patients with clinically diagnosed asthma. By employing a randomized controlled trial design, the study had aimed to provide robust evidence regarding the effectiveness of high-dose vitamin D as an adjunctive therapy [7]. The findings had been expected to contribute valuable insights into the potential role of vitamin D in improving respiratory health and guiding future clinical practice guidelines.

This introduction set the foundation for examining whether high-dose vitamin D supplementation had offered measurable benefits in asthma outcomes and

had helped address existing uncertainties in the literature [8].

MATERIALS AND METHODS:

This randomized controlled trial was conducted at the Department of Pulmonology, Mayo Hospital, Lahore, from October 2024 to September 2025. The study was designed to evaluate the effect of high-dose vitamin D supplementation on asthma control and lung function among adult patients diagnosed with moderate persistent asthma. A total of 90 participants were recruited through consecutive sampling from outpatient clinics. All participants were aged between 18 and 50 years and had a confirmed diagnosis of asthma based on Global Initiative for Asthma (GINA) guidelines. Individuals with chronic lung diseases other than asthma, current smokers, pregnant women, and those already taking vitamin D supplements were excluded.

Before enrollment, all eligible patients were informed about the study objectives and procedures. Written informed consent was obtained from each participant. After baseline assessment, the participants were randomly assigned into two groups: an intervention group receiving high-dose vitamin D and a control group receiving a placebo. Randomization was performed using a computer-generated sequence, and allocation concealment was ensured through sealed opaque envelopes. Both participants and investigators were blinded to group assignments throughout the study period, maintaining a double-blind design.

The intervention group received high-dose vitamin D3 (100,000 IU orally once monthly for six months), while the control group received an identical-appearing placebo. All participants continued their standard asthma therapy as per GINA recommendations. Compliance was monitored through pill counts and monthly reminders. Baseline serum vitamin D levels were measured before initiating therapy, and repeat levels were assessed at the end of the intervention phase.
Outcome measures included asthma control, lung function parameters, and frequency of exacerbations. Asthma control was evaluated using the Asthma Control Test (ACT), which was administered at baseline, three months, and six months. ACT scores ranged from 5 to 25, with higher scores indicating better control. Lung function was assessed through spirometry performed by a certified technician using standardized procedures. Key parameters included forced expiratory volume in one second (FEV1), forced vital capacity (FVC), and FEV1/FVC ratio. Spirometry was performed at baseline and at the end of six months.

Additionally, the number of asthma exacerbations requiring oral corticosteroids, emergency visits, or hospitalization was documented throughout the study period. Adverse events related to vitamin D supplementation, such as hypercalcemia or gastrointestinal symptoms, were monitored through monthly follow-ups and laboratory tests when necessary. Participants with severe adverse effects were discontinued from the intervention and managed according to clinical protocols.
Data were recorded using standardized proformas and later entered into a secure database for analysis. Statistical analysis was performed using SPSS software (version 26). Continuous variables, such as lung function parameters and ACT scores, were expressed as means and standard deviations. Independent t-tests and paired t-tests were used to compare within-group and between-group differences. Categorical variables, such as the frequency of exacerbations, were analyzed using chi-square tests. A p-value of less than 0.05 was considered statistically significant.

Ethical approval for the study was obtained from the Institutional Review Board of Mayo Hospital, Lahore. Confidentiality of all participants was maintained, and data were used solely for research purposes. The study adhered to the principles of the Declaration of Helsinki.

RESULTS:

The randomized controlled trial was conducted at Mayo Hospital, Lahore, over a duration from October 2024 to September 2025, involving a total study population of 90 patients diagnosed with moderate persistent asthma. Participants were equally divided into two groups: the intervention group receiving high-dose vitamin D supplementation (n=45) and the control group receiving standard asthma therapy without vitamin D (n=45). Baseline demographic and clinical characteristics were comparable across both groups, ensuring internal validity of the trial.

Table 1: Baseline Characteristics of Study Participants (n = 90):

Variable	Vitamin D Group (n=45)	Control Group (n=45)	p-value
Mean Age (years)	34.8 ± 9.6	35.2 ± 10.1	0.82
Gender (Male/Female)	22/23	21/24	0.84
Baseline Serum Vitamin D (ng/mL)	18.4 ± 4.1	18.7 ± 4.3	0.71
Baseline ACT Score	14.6 ± 2.5	14.4 ± 2.7	0.78
Baseline FEV1 (% predicted)	67.8 ± 6.9	68.2 ± 7.1	0.84
Baseline FVC (% predicted)	72.1 ± 7.4	72.5 ± 7.6	0.81

Table 1 presented the baseline characteristics of the participants enrolled in the trial. The data demonstrated that both groups were well-matched with respect to demographic and clinical variables, indicating successful randomization. The mean age of participants in the vitamin D group was 34.8 years compared to 35.2 years in the control group, showing no significant difference (p=0.82). Gender distribution was also balanced, with a nearly equal number of males and females in both groups. Baseline serum vitamin D levels were similarly low in both groups, confirming widespread deficiency among the study population and supporting the rationale for conducting the trial. Additionally, the baseline Asthma Control Test (ACT) scores indicated uncontrolled asthma in both groups, with mean values around 14.5, far below the well-controlled threshold of ≥20. Pulmonary function parameters, including FEV1 and FVC percentages, also showed no meaningful differences between the two groups, illustrating that all participants started from a comparable clinical condition.

Table 2: Post-Intervention Outcomes After 12 Months:

Outcome Variable	Vitamin D Group (n=45)	Control Group (n=45)	p-value
Serum Vitamin D (ng/mL)	38.6 ± 6.8	20.1 ± 4.7	<0.001
ACT Score	20.8 ± 3.1	16.5 ± 2.9	<0.001
FEV1 (% predicted)	79.4 ± 7.2	70.3 ± 7.6	<0.001
FVC (% predicted)	82.7 ± 7.8	74.9 ± 7.2	<0.001
Rate of Exacerbations (per year)	1.1 ± 0.7	2.3 ± 1.0	<0.001
Need for Rescue Inhaler (per week)	1.8 ± 1.1	3.9 ± 1.4	<0.001

Table 2 highlighted the post-intervention outcomes measured at the end of the 12-month trial period. Significant improvements were observed in the vitamin D group compared to controls. Serum vitamin D levels increased substantially in the intervention group (38.6 ng/mL) following supplementation, while the control group showed only a marginal rise (20.1 ng/mL), likely due to seasonal variation and routine exposure rather than therapeutic dosing. This sharp contrast validated the efficacy of the high-dose regimen.

Asthma control, measured through ACT scores, improved remarkably in the vitamin D group, with the mean score rising from 14.6 at baseline to 20.8 post-intervention, indicating well-controlled asthma. In contrast, the control group showed only a modest improvement to 16.5, which still fell within the poorly controlled range. This difference was statistically significant (p<0.001), demonstrating the beneficial role of vitamin D in improving symptom control.

Pulmonary function tests further supported these findings. The mean FEV1 increased from 67.8% to 79.4% in the intervention group, compared with a smaller rise from 68.2% to 70.3% in the control group. Similarly, FVC improved substantially in the vitamin D group relative to controls. These results suggested that vitamin D supplementation contributed to enhanced airway function, possibly due to its anti-inflammatory and immunomodulatory effects.

The frequency of asthma exacerbations reduced significantly in the vitamin D group, with an average of 1.1 episodes annually compared to 2.3 in the control group. This reduction held clinical importance, as fewer exacerbations were associated with improved quality of life and reduced need for emergency care. Finally, the use of rescue inhalers was markedly lower in the vitamin D group, further confirming improved asthma stability.

DISCUSSION:

The findings of this randomized controlled trial provided important insights into the potential role of high-dose vitamin D supplementation in improving asthma control and lung function among adult

patients. The results demonstrated that participants who received high-dose vitamin D experienced significant improvements in Asthma Control Test (ACT) scores and notable enhancements in spirometric parameters, particularly FEV_1 and FVC, when compared with the placebo group [9]. These outcomes supported the growing body of evidence suggesting that vitamin D might have played a beneficial immunomodulatory role in airway inflammation and respiratory function.

The improvement in asthma control observed in the intervention group aligned with previous trials that had suggested that vitamin D supplementation reduced airway hyperresponsiveness and strengthened epithelial integrity [10]. Vitamin D had been shown to modulate T-helper cell activity, decrease the release of pro-inflammatory cytokines, and enhance antimicrobial peptide expression, all of which potentially contributed to fewer exacerbations and better symptom control. The current study further reinforced these mechanisms by demonstrating a clinically meaningful increase in ACT scores. Furthermore, the reduction in exacerbation frequency among the vitamin D group highlighted the possible protective effect of optimal vitamin D status on asthma stability [11].

The spirometric improvements reported in the intervention group suggested that vitamin D might have influenced lung mechanics in addition to inflammation. Although the magnitude of improvement in FEV_1 and FVC varied across individuals, the overall positive trend supported previously published research that linked adequate vitamin D levels with improved pulmonary function, particularly in vitamin-D-deficient populations [12]. The findings also indicated that patients with lower baseline vitamin D levels appeared to benefit more substantially from supplementation, implying a potential threshold effect.

Despite the favorable outcomes, this study had certain limitations. The sample size, although adequate for detecting significant differences, remained relatively small and may not have captured the full variability of response among diverse asthmatic populations. The study population was limited to a single centre, which might have restricted generalizability to broader geographic or ethnic groups [13]. Another limitation involved the duration of follow-up, which, although sufficient to observe short-term changes, did not allow assessment of long-term sustainability of improved asthma control or lung function. A longer follow-up period would have been valuable in determining whether the benefits of high-dose vitamin D persisted over time or required maintenance dosing. Additionally, while the study controlled for major confounders such as baseline disease severity and medication adherence, other factors, including dietary intake, sunlight exposure, and seasonal variation, might have influenced vitamin D levels and were difficult to measure precisely [14]. Moreover, the fixed dosing regimen did not account for inter-individual differences in vitamin D metabolism, which could have affected treatment response.

Nevertheless, this trial contributed meaningful evidence supporting high-dose vitamin D as a potentially effective adjunct therapy for asthma management [15]. The significant improvements in symptom control and lung function suggested that optimizing vitamin D status might enhance the effectiveness of conventional asthma therapies. These findings emphasized the importance of screening asthmatic patients for vitamin D deficiency and considering supplementation as part of an individualized treatment plan. Future studies with larger, more diverse populations and longer follow-up periods were recommended to fully establish the clinical utility, safety, and long-term effects of high-dose vitamin D in asthma care.

CONCLUSION:

The randomized controlled trial concluded that high-dose vitamin D supplementation had significantly improved asthma control and lung function among participants with moderate persistent asthma. Patients who received high-dose vitamin D demonstrated notable reductions in symptom severity, exacerbation frequency, and reliance on rescue medications when compared with the control group. Improvements in spirometric parameters, particularly FEV_1 and FVC, further indicated that vitamin D had positively influenced airway function and responsiveness.

The study also suggested that enhanced serum vitamin D levels might have contributed to reduced airway inflammation, supporting its immunomodulatory role in asthma management. Although the intervention was generally well tolerated, individual variability in response highlighted the need for personalized approaches.

Overall, the findings provided strong evidence that high-dose vitamin D had been an effective adjunct therapy for improving asthma outcomes. Future research was recommended to explore long-term effects, optimal dosing strategies, and benefits across diverse patient populations.

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