ROLE OF VITAMIN D IN PREVENTION OF ACUTE EXACERBATION OF BRONCHIAL ASTHMA IN ADULTS
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INTRODUCTION
Bronchial asthma is the chronic inflammation of the airways and their hyper responsiveness that leads to symptoms of shortness of breath, cough, wheeze and chest tightness¹. Approximately 5% of the world population is having bronchial asthma². The prevalence of asthma is increasing day by day and it has increased by more than 75% over the last two decades³.

Bronchial asthma is an ever increasing epidemic and it has been found that morbidity of asthma patients is increased by its exacerbations so early treatment of these patients is helpful in prevention of its exacerbations and complications⁴. It has been found that vitamin D supplementation is effective in prevention of exacerbations in asthmatic patients.

As of 2014, prevalence of asthma is around 334 million people worldwide⁵, and mortality rate is 2 per 100,000 patients per year⁶. 84.3% of Pakistani population is deficient in vitamin D⁷. Interest is growing in the world to see the effect of vitamin D in pulmonary disorders specially asthma. The beneficial effect of vitamin D in bronchial asthma triggered by respiratory viral infections has been pointed out in quite a few clinical trials and a good number of observational studies¹,³,⁷. Vitamin D has significant immune modulatory effects and it is one of the essential nutrient⁸. Previously it was thought that vitamin D has role only in bone physiology and calcium metabolism but now it is also believed that vitamin D metabolism, specifically its conversion to activated form, is important for innate and adaptive immunity⁹.

Li et al¹⁰ reported the correlation of lung function with vitamin D status and they stated that a large number of asthmatic patients in China were vitamin D deficient. Studies suggest that therapeutic potential of vitamin D supplementation in asthma patients as a steroid-enhancing agent. In a study by Majak et al¹ it was found that exacerbation in bronchial asthma caused by respiratory tract infections can be prevented by vitamin D supplementation. Only 17% children who were supplemented with Vitamin D, suffered from asthma exacerbation as compared to 46% asthma exacerbation in children who were not supplemented with vitamin D¹. Asthma control may be improved by supplementation of vitamin-D through its effect on inhibition of the in-
flux of cytokines within the lungs and by increasing the secretion of interleukin 10 by dendritic and T cells. The induction of innate antimicrobial mechanism, maintenance of regulatory T-cells and inhibition of inflammation are the major roles played by vitamin D in respiratory disorders.

Emerging studies also show an association between poor clinical responsiveness to glucocorticoids and poor vitamin D status in asthmatic patients. Vitamin D supplementation can enhance the action of steroids on inflammatory cells taken from patients with asthma by tenfold. Vitamin D and asthma are thought to have some indirect association owing to the susceptibility to infections.

There is high rate of asthma exacerbations in adults in the world. It was planned to check the role of vitamin D supplement to prevent its exacerbation. This study and future studies will set a new horizon for role of novel treatments like vitamin D in the treatment of bronchial asthma.

**METHODOLOGY**

It was a randomized controlled trial done in Services Hospital, Lahore for a period of 6 months. Sampling technique was non-probability consecutive sampling. Patients having age ranging from 16 to 46 years and bronchial asthma diagnosed for at least 1 year with vitamin D levels less than 30 ng/ml were included in the study. While patients with intake of vitamin D 6 months before the trial, Ischemic heart disease or other chronic diseases like chronic liver disease, chronic kidney disease, chronic obstructive pulmonary disease were excluded from the study. Patients fulfilling inclusion criteria mentioned above, were assigned two groups randomly, by using computer generated random number table, group A and group B. Sample size was calculated using WHO sample size calculator for 2 sided proportions taking proportions 17% and 46%, power of study 80%, level of significance 5%. It turned out to be 80 (40 for each group separately).

Bronchial asthma was operationally defined as shortness of breath associated with wheezing in the chest and improvement in forced expiratory volume in one second (FEV1) of ≥15% following administration of 2 puffs (180µg) of salbutamol inhaler. Exacerbation of bronchial asthma was operationally defined as acute onset of shortness of breath in already diagnosed asthmatic patients who are having all of the following: tachycardia more than 100/min., respiratory rate more than 25/min., inability to complete a sentence in one breath and wheezing or reduce air entry on chest auscultation.

All the findings were recorded in Proforma. Group A was given vitamin D3 50,000 units fortnightly for a period of three months in addition to standard treatment (Salmeterol/fluticasone inhaler preparation Salmicort 25/250µg twice daily, Montelukast Montika 10mg at night) for bronchial asthma. Group B was given standard treatment (Salmeterol/fluticasone inhaler preparation Salmicort 25/250µg twice daily, Montelukast Montika 10mg at night) of bronchial asthma treatment only. Patients had an enrollment visit and follow up was done monthly or as needed. Treatment was given to all patients depending on clinical situation and severity of asthma. Vitamin D levels were measured before treatment and after completion of treatment period of 3 months. Efficacy was measured in terms of decrease in number of exacerbations. SPSS ver. 20 was used. We calculated mean and standard deviation for variables like age and number of exacerbations (quantitative variables) and frequency and percentage for variables like gender and asthma exacerbation (qualitative variables). Chi-square test was applied to compare the number of asthma exacerbations in both groups.

**RESULTS**

There were total 80 cases with a mean age of 29.56 ±8.06. Baseline demographics were noted and presented in Table 1. Prevention in asthma exacerbations were in 31(77.5%) in Group A and 19(47.5%) in Group B (p value <0.05) as shown in Table 2.

Mean serum vitamin D level before supplementation with vitamin D were 13 ±3.45ng/ml and Mean serum vitamin D levels after 3 months of supplementation with vitamin D were 35 ±4.5ng/ml.

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Group A (Vitamin D Supplement added)</th>
<th>Group B (Vitamin D Supplement Not added)</th>
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</thead>
<tbody>
<tr>
<td>Age</td>
<td>29.70±7.74</td>
<td>29.43±8.47</td>
</tr>
<tr>
<td>Gender</td>
<td>25(62.5%)</td>
<td>21(52.5%)</td>
</tr>
<tr>
<td>Female</td>
<td>15(37.5%)</td>
<td>19(47.5%)</td>
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**DISCUSSION**

Our present study showed that vitamin D supplementation reduces exacerbation of asthma in 77.5% of patients as compared to 47.5% patients without supplementation which is quite significant. This fact has been demonstrated in several other studies. A meta-analysis was conducted in 2016 including 7 studies in children and 2 studies in adults to evaluate the efficacy of supplementation with vitamin D in reducing severe exacerbation of asthma. Vitamin D supplementation decreased exacerbations rate effectively reducing systemic steroids requirement and decreased the risk of exacerbations leading to hospitalization. These results support our study which also support the use of vitamin D supplementation to decrease asthma exacerbation.

Arshi et al conducted a study to evaluate the effects of vitamin D supplementation along with controller medications for asthma (inhaled corticosteroids or inhaled corticosteroids + long-acting β-agonist) on functions of airways. A randomized clinical controlled trial of 130 individuals 10-50 years of age in Tehran was conducted during a period of 6 months. One group received vitamin D supplementation along with controller medications for asthma. Improvement in FEV1 after 2 months was significant in two groups. The results of the study are in support of our study suggesting that vitamin D supplementation can be a valuable tool for decreasing asthma exacerbation hence asthma management.

Studies also noted that vitamin D deficiency is associated with blunted glucocorticoid responsiveness. This fact supports the notion that vitamin D supplementation can decrease the need for systemic steroids for asthma exacerbation and enhance steroids response as suggested in our study.

Brehm et al noted that vitamin D deficiency was linked to increased eosinophil counts, IgE concentrations and airway hyper-responsiveness so leading to increased symptoms of asthma as well as its exacerbations. This also supports the results of our study. Similarly, in Italian studies, increased airway hyper responsiveness and lung functions were inversely related to serum vitamin D levels. This fact explains the reason of vitamin D supplementation effectiveness in decreasing asthma exacerbation as demonstrated in our study.

Searing et al also found an increase in corticosteroid requirements and sensitivity to aeroallergens in children having low vitamin D levels. Majak P et al also noticed that vitamin D deficiency is associated with increase in number of asthma exacerbations and vitamin D supplementation reduces these exacerbations.

Menon B et al demonstrated improvement in control of asthma after vitamin D supplementation and vitamin D deficiency was associated with poor asthma control in these patient. This is in keeping with the results of our study that vitamin D supplementation improves asthma control and decreases asthma exacerbations. But there are more studies needed on the same pattern to confirm these results. Once a sufficient literature will be available then the related guidelines could be developed and it will put health care professional to a new way of preventing asthma related complications by adding vitamin D to the treatment of bronchial asthma.

**CONCLUSION**

Vitamin D was efficacious in bronchial asthma in terms of prevention in number of exacerbations when added to standard treatment.

**REFERENCES**

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2012; 7:e33452.


15. Sutherland ER, Goleva E, Jackson LP, Stevens AD, Leung DY. Vitamin D levels, lung function, and steroid response in adult asthma. Am J Respir Crit Care Med 2010; 181:699-704.


CONTRIBUTORS
MUM conceived the idea, planned the study, and drafted the manuscript. MUM and MFR helped acquisition of data and did statistical analysis. GAS critically revised the manuscript. All authors contributed significantly to the submitted manuscript.