

Vitamin D in chronic obstructive pulmonary disease and asthma in Indian population

In 2016, the prevalence of chronic obstructive pulmonary disease (COPD) and asthma in India was 4.2% and 2.9%, respectively.^[1] The leading risk factors were ambient and household air pollution, tobacco use, and occupational exposure. The control and management of both these chronic respiratory diseases requires a strict adherence to medications and follow-up guidelines. Recent evidence suggests that Vitamin D can play a role in the control of exacerbations of COPD and asthma.

In India, recent decades show an epidemic of Vitamin D deficiency from community-based studies, with the prevalence ranging from 50% to 90%.^[2] Vitamin D and its metabolites have a significant clinical role because of their interrelationship with calcium homeostasis and bone metabolism. Vitamin D may also regulate many other cellular functions such as muscle and bone strength and immune and cardiovascular system. The primary source of Vitamin D is sunlight, and all other dietary sources provide <10% of the daily requirement.^[3]

Should Vitamin D levels be routinely measured in all patients of COPD and asthma? What role does the supplementation of Vitamin D play in reducing the exacerbation of COPD and asthma? How does the genetic polymorphism in Vitamin D metabolic pathway affect the control of asthma? The current issue of the journal carries two original articles which address these questions.^[4,5] Mishra *et al.* in a hospital-based case-control study among persons >40 years old demonstrated a positive linear relation between serum concentration of Vitamin D and lung function (forced vital capacity and forced expiratory volume in 1 s), after controlling for confounders such as age, sex, body mass index, and smoking-matched participants. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines do not support the supplementation of Vitamin D for the prevention of exacerbations of COPD in unselected patients.^[6] A systematic review and meta-analysis of individual participant data from three randomized controlled trials by Jolliffe *et al.* concluded that Vitamin D supplementation safely and substantially reduced the rate of moderate-to-severe COPD exacerbations in patients with baseline 25-hydroxyvitamin D levels <20 nmol/L but not in those with higher levels.^[7] These three randomized controlled trials were conducted among European participants at the secondary care level using a GOLD spirometry grading system.^[8-10] They differed in the dosage

and schedule of Vitamin D supplementation. The study findings support routine testing of 25-hydroxyvitamin D among COPD patients who experience exacerbations. It also supports giving Vitamin D supplementation to those COPD patients with 25-hydroxyvitamin D levels <25 nmol/L.

Rajaram *et al.* in their hospital-based study among 18–50-year-old South Indian patients with bronchial asthma demonstrated the effects of genetic polymorphisms in Vitamin D metabolic pathway on Vitamin D level and asthma control.^[5] They concluded that Vitamin D receptor polymorphism (rs2228570) was found to be protective against asthma exacerbations. There were poor correlations and insignificant associations of single-nucleotide polymorphisms and serum 25-hydroxyvitamin D levels among asthma patients and healthy controls. The Global Initiative for Asthma guidelines do not support the supplementation of Vitamin D for the prevention of exacerbation of asthma.^[11] A systematic review and meta-analysis of individual participant data from seven randomized controlled trials by Jolliffe *et al.* studied the pooled estimate of the protective effects of Vitamin D against asthma exacerbations requiring treatment with systemic corticosteroids.^[12] It also investigated the effect of Vitamin D supplementation on risk of asthma exacerbation according to baseline 25-hydroxyvitamin D concentrations. All these seven randomized controlled trials were conducted at secondary and tertiary care levels, among children and adults. The Vitamin D supplementation dosage and schedule varied among the studies. All the studies gave oral Vitamin D₃ supplementation to participants in the intervention arm. Minimum dose given was 500 IU/day to a maximum of 4000 IU/day. Three of the randomized controlled trials also gave a bolus dose of Vitamin D₃ ranging from 100000 IU to 120000 IU.^[13-15] The authors concluded that Vitamin D supplementation reduced asthma exacerbations treated with oral corticosteroids when compared with placebo. Nevertheless, differences across subgroups, including baseline 25-hydroxyvitamin D status, did not reach statistical significance. Therefore, which group of patients will have preventive effects of Vitamin D supplementation is still not known.

The Indian Chest Society and National College of Chest Physicians, along with the Postgraduate Institute of Medical Education and Research, Chandigarh, framed

guidelines for the diagnosis and management of COPD and bronchial asthma.^[16,17] These guidelines were made to bridge the gaps in recognition and management of COPD and asthma in India due to the differences in availability and affordability of health-care facilities across the country. None of these guidelines recommends the role of Vitamin D supplementation for the prevention of exacerbations in COPD and asthma patients. These guidelines require an update based on recent evidence from India.

The patients with COPD had an increased risk for Vitamin D deficiency when compared to their controls.^[18] The prevalence of Vitamin D deficiency increases as the severity of COPD increases.^[19] COPD can also lead to osteoporosis and osteopenia.^[20] These evidence were from cross-sectional and case-control studies. The casual association of COPD leading to Vitamin D deficiency has not been established. A systematic review and meta-analysis of observational studies by Jat and Khairwa studied the association of Vitamin D and asthma in children.^[21] It concluded that asthmatic children had lower Vitamin D levels than nonasthmatic children. With the available data from India, the evidence is equivocal on the usefulness of routine measurement of Vitamin D levels among patients with COPD or asthma. However, patients with exacerbations can be followed up with measurement of 25-hydroxyvitamin D levels. This would provide an evidence base for initiating Vitamin D supplementation to them, as well as assist in planning future course of action.

The Indian Council of Medical Research guidelines on recommended dietary allowance for Vitamin D are set at 400 IU/day. With the recent epidemic of Vitamin D deficiency among all age groups and the supplementation of Vitamin D being inexpensive, supplementation programs may be beneficial for reducing exacerbations in COPD and asthma patients. As correctly stated by Mishra *et al.* in their article in this issue of the journal, it is not clear whether abnormal level of Vitamin D is a consequence of COPD or a contributor to COPD.^[4] Even if it is a consequence of COPD, its supplementation in the Vitamin D-deficient individual would have a positive effect on other systems of the body as well.

India is a country of diversity with different ethnicity and origin. The genetic polymorphisms that lead to changes in the Vitamin D metabolic pathway need to be researched. Further genetic sequencing studies are required to understand the role of genetic polymorphisms in understanding the metabolism of Vitamin D and its effect on bronchial asthma. Randomized controlled trials and cohort studies in the Indian settings are required to understand the role of vitamin D supplementation in the prevention of exacerbation among COPD and asthma patients.

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