

## The Prevention of Acute Respiratory Infection and Vitamin D Supplementation

Biswas B K

Among the leading causes of under 5 mortality and morbidity in Bangladesh, Acute respiratory infections (ARI) are at the top of the list. These are a major cause of global mortality and morbidity and are responsible for 10% of ambulatory and emergency department visits in the USA<sup>1</sup> and an estimated 2.65 million deaths worldwide in 2013<sup>2</sup>. Observational studies report consistent independent associations between the low serum concentrations of 25-hydroxyvitamin D (the major circulating Vitamin D metabolite) and susceptibility of acute respiratory tract infections<sup>3,4</sup>. This Article highlights the indication of vitamin D supplementation in the prevention of acute respiratory Infection.

Vitamin D, or the “sun-shine vitamin”, is not just as a vitamin; it is also prohormone with numerous functions in the body<sup>5</sup>. ”Prohormone “refers to a group of fat soluble seco-steroids. The best-understood function of Vitamin D is in the absorption of calcium from the small intestine, which helps to prevent diseases such as rickets in children and osteoporosis and osteomalacia in adults<sup>6</sup>. In addition to causing rickets, vitamin D deficiency has been linked to respiratory infection such as tuberculosis and Bronchiolitis along with pneumonia<sup>7</sup>. The effects of Vitamin D are mediated by a cytosolic receptor called Vitamin D Receptor (VDR). VDR is ubiquitously expressed, and this ubiquity accounts for the numerous and varied mechanisms that are regulated by vitamin D<sup>8</sup>. The VDR gene, which is located on chromosome 12q13.1, has several polymorphic regions, some of which are associated with predisposition of certain diseases. This means that not only is vitamin D deficiency is associated with considerable risk of diseases, but there is wide interindividual variation in vitamin D sensitivity, which may influence risk<sup>9</sup>.

Vitamin D has an important influence on the host's immune system, modulating both innate and adaptive immunity and regulating the inflammatory cascade. Vitamin D supports induction of antimicrobial peptides in response to both viral and bacterial stimuli, suggesting a potential mechanism by which vitamin D inducible protection against respiratory pathogens might be mediated<sup>10-12</sup>. Vitamin D metabolites have also been reported to induce other innate antimicrobial effector mechanisms, including synthesis of reactive nitrogen intermediates and reactive oxygen intermediates. These epidemiological and in vitro data have prompted numerous randomized controlled trials to determine whether vitamin D can decrease the risk of

ARI. A total of five aggregate data meta-analyses incorporating data from up to 15 primary trials have been conducted to date, of which two reports statistically significant protective effects and three not statistically significant<sup>13</sup>.

This heterogeneity might have arisen as a result of variation in participant characteristics and dosing regimens between trials, either of which may modify the effects of vitamin D supplementation on immunity of respiratory pathogens<sup>14</sup>. In this regard, it is very important to understand the definition of deficiency and insufficiency of vitamin D and how to treat this condition. Unfortunately, there is no consensus, although a level of at least 10ng/ml 25(OH)D is thought to be necessary to promote bone mineralization and calcium homeostasis and a concentration between 20ng/ml and 50 ng/ml is considered adequate to provide an immunomodulatory effect<sup>15</sup>. Overall, in children as well as in adults, the term “Vitamin D deficiency” indicates values <20ng/ml, whereas insufficiency is defined as between 20ng/ml and 30ng/ml, with at least 30ng/ml required for optimal health benefits<sup>16-18</sup>. Although hypervitaminosis D is arbitrarily defined as 25 (OH) D concentrations >100ng/ml, symptoms of vitamin D intoxication typically do not manifest until circulating 25 (OH) D concentrations rise above 150ng/ml<sup>19</sup>.

Now, a major role of vitamin D supplementation for the prevention of acute respiratory infections should be considered seriously specially for children, the most vulnerable group of population of the developing nations.

### References:

1. Grijalva CG, Nuroti JP, Griffin MR. Antibiotic prescription rates for acute respiratory tract infections in US ambulatory settings. *JAMA* 2009;356:758-766. doi:10.1001/jama.2009.1163.
2. GBD Mortality and Causes of Death Collaborators. Global, regional and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: a systematic analysis for the Global Burden of Diseases Study 2013. *Lancet* 2015;356:117-71.
3. Cannell JJ, Vieth R, Umhau JC, et al. Epidemic influenza and vitamin D. *Epidemiol Infect* 2006; 356:1129-40.
4. Jolliffe DA, Griffiths CJ, Martineau AR. Vitamin D in the prevention of acute respiratory infections: systematic review of clinical studies. *J Steroid Biochem Mol Biol* 2013;356:321-9.

### Correspondence to:

Professor Dr. Barun Kanti Biswas  
Professor and Head, Department of Paediatrics,  
Diabetic Association Medical College, Faridpur.  
Email: drbarun2008@yahoo.com

5. Holick MF. Sunlight and vitamin D for bone health and prevention of autoimmune diseases, cancers, and cardiovascular disease. *Am J Clin Nutr.*2004;80 Suppl 6:1678S–88.
6. Holick MF. Resurrection of vitamin D deficiency and rickets. *J Clin Invest.* 2006; 116:2062–72.
7. [www.who.int/Elena/titles/vitaminD\\_pneumonia\\_children/en/Feb23,2017](http://www.who.int/Elena/titles/vitaminD_pneumonia_children/en/Feb23,2017)
8. Miyamoto K, Kesterson RA, Yamamoto H, Taketani Y, Nishiwaki E, Tatsumi S, et al. Structural organization of the human vitamin D receptor chromosomal gene and its promoter. *Mol Endocrinol.* 1997;11:1165–79.
9. Labuda M, Fujiwara TM, Ross MV, Morgan K, Garcia-Heras J, Ledbetter DH, et al. Two hereditary defects related to vitamin D metabolism map to the same region of human chromosome 12q13-14. *J Bone Miner Res.*1992;7:1447-53.
10. Hansdottir S, Monick MM, Hinde SL, Lovan N, Look DC, Hunninghake GW. Respiratory epithelial cells convert inactive vitamin D to its active form: potential effects on host defense. *J Immunol*2008;356:7090-9.
11. Olliver M, Spelmink L, Hiew J, Meyer-Hoffer U, Henriques-Normark B, Bergman P. Immunomodulatory effects of vitamin D on innate and adaptive immune responses to *Streptococcus pneumoniae*. *J Infect Dis*2013;356:1474-81. doi10.1093/infdis/jit355pid:23922371.
12. Greiller CL, Martineau AR. Modulation of the immune response to respiratory viruses by vitamin D. *Nutrients*2015;356:4240-70.
13. Martineau AR, Jolliffe DA, Hooper RL, Greenberg L, Aloia JF, Bergman P et al. Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta analysis of individual participant data. *BMJ*2017;356:i6583.
14. Martineau AR. Bolus-dose vitamin D and prevention of childhood pneumonia. *Lancet*2012;356:1373-5..
15. Cranney A, Horsley T, O'Donnell S, Weiler H, Puil L, Ooi D, et al. Effectiveness and safety of vitamin D in relation to bone health. *Evid Rep Technol Assess (Full Rep)*.2007;158:1-235.
16. Ross AC, Taylor CL, Yaktine A, Del Valle HB. Committee to review dietary reference intakes for vitamin D and calcium. Institute of Medicine: Dietary Reference Intakes for Calcium and Vitamin D. Washington, DC: National Academic Press; 2001.
17. Urashima M, Segawa T, Okazaki M, Kurihara M, Wada Y, Ida H. Randomized trial of vitamin D supplementation to prevent seasonal influenza A in schoolchildren. *Am J Clin Nutr.*2010;91:1255-60.
18. Inamo Y, Hasegawa M, Saito K, Hayashi R, Ishikawa T, Yoshino Y, et al. Serum vitamin D concentrations and associated severity of acute lower respiratory infections in Japanese hospitalized children. *Pediatr Int.*2011,53:199-201.
19. Hollick MF, Binkley NC, Bishoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.*2011;96:1911-30. practice guideline. *J Clin Endocrinol Metab.*2011;96: 1911-30.