

**Effect of vitamin D3 supplementation on episodes of acute respiratory tract infection in exclusively breast fed infants- a hospital based study**

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**Type of Publication:** Original Research Paper

**Conflicts of Interest:** Nil

**Abstract**

**Background :** In humans, vitamin D is synthesized in the skin from exposure to sunlight or can be obtained through dietary intake that functions as a steroidal hormone after conversion in the renal tubule to its active form 1-25-hydroxyvitamin D(25(OH)D) by 1-alpha-hydroxylase enzyme

**Methods: A randomized control study** was conducted at Department of Pediatrics, MGM hospital, Navi Mumbai after ethical clearance, during period of 7 months from 1<sup>st</sup> march 2014 to 30 September 2014 and followed up till 30 June 2015. A final sample of 200 exclusively breast fed newborns, were then randomized into two groups: **Group A:** Placebo group and; **Group B:** Vitamin D3 supplementation group (400IUOD). Both the groups were followed up at regular intervals (1.5, 2.5, 3.5, 6 and 9 months). At each visit episodes of acute respiratory tract infections were recorded. Statistical analysis was done by SPSS17. Data were analyzed by unpaired t- test.

**Results:** Mean number of acute respiratory infection episodes (3.44 vs 0.85; Median 4 vs 1) were significantly more in babies of placebo group as compared to Vitamin D group.

**Conclusion:** Frequency of Acute respiratory infection episodes were significantly less in vitamin D supplemented group as compared to Placebo group.

**Keywords:** Vitamin D deficiency, acute respiratory tract infection, exclusively breast fed infants

**Introduction:** Vitamin D deficiency considered to be most common nutritional deficiency. It is common in all age groups and both sexes across country. In humans, vitamin D is synthesized in the skin from exposure to sunlight or can be obtained through dietary intake that functions as a steroidal hormone after conversion in the renal tubule to its active form 1-25-hydroxyvitamin D (25(OH)D) by 1-alpha-hydroxylase enzyme<sup>1-5</sup>. Over the last two decades, understanding of vitamin D synthesis and its function has changed remarkably. Emerging evidence suggests that the consequences of vitamin D deficiency (VDD) extend beyond its well-known effects on bone metabolism and calcium homeostasis, and also include alterations of specific arms of immunity. The immunomodulatory properties of vitamin D may influence susceptibility to infection. Although appropriate levels for immunologic function have yet to be identified, vitamin D deficiency in relation to skeletal metabolism for children is defined as a serum 25(OH)D level <50nmol/<sup>6</sup>. Recent epidemiologic studies also indicate that low plasma

vitamin D concentrations are related to increased incidence of respiratory infections, including acute lower respiratory tract infections<sup>7-10</sup> and respiratory syncytial virus (RSV) disease<sup>11</sup> in infants and children less than 5 years of age. Furthermore, vitamin D supplementation in randomized controlled trials conducted among schoolchildren resulted in reduced incidence of influenza an infection<sup>12</sup> and acute respiratory infection<sup>13</sup>. In another trial among Afghan children less than 3 years of age, vitamin D supplementation decreased the risk of pneumonia<sup>14</sup>. The present study was conducted with aim of studying the effect of Vitamin D3 supplementation on frequency of Acute Respiratory infection episodes in infants.

### Material And Methods

A **randomized control study** was conducted at Department of Pediatrics, MGM hospital, Navi Mumbai, during period of 7 months from 1<sup>st</sup> march 2014 to 30 September 2014 and followed up till 30 June 2015. All full term newborns delivered in hospital during study period and fulfilling eligibility criteria were included in study after taking informed consent from parents. A final sample of 200 exclusively breast fed newborns, were then randomized into two groups: **Group A:** Placebo group and; **Group B:** Vitamin D3 supplementation group (400IUOD). Both the groups were followed up at regular intervals (1.5, 2.5, 3.5, 6 and 9 months) during which episodes of acute respiratory infection was recorded.

IMNCI definition of ARI: an infant with fever and/or cough or chest indrawing and/or fast breathing

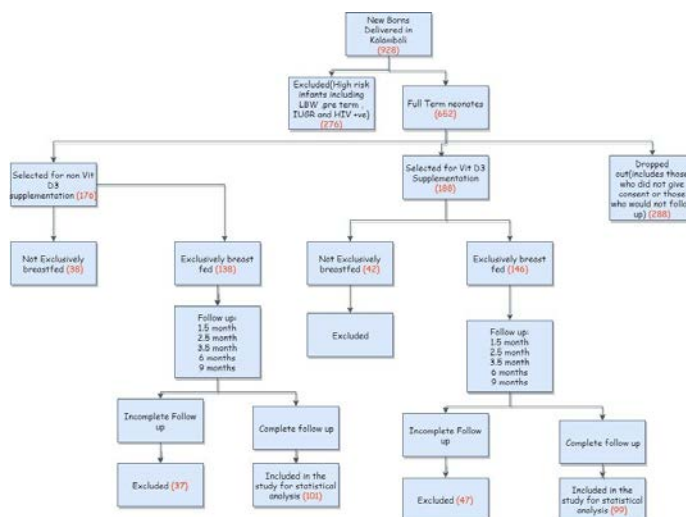
Exclusively breast fed is an infant who has been given exclusively breast milk and not even water for the first six months of life

### Justification for Sample Size

Sample size was calculated by using software PS (i.e. power and sample) version 3.1.6 and by assuming effect size 0.35, standard deviation 0.875 ,type 1 error 0.05 and type 2 error(β)= 0.2 .The sample size was worked out to be 99 in each group .The recruitment of sampling units is shown as below :

### Statistical Analysis

All the collected data was entered in Microsoft Excel sheet and then transferred to SPSS software ver. 17 for analysis. The unpaired t-test was used to test the significance of difference between the two groups. The P-value < 0.05 was taken as significant. All p-values were two tails



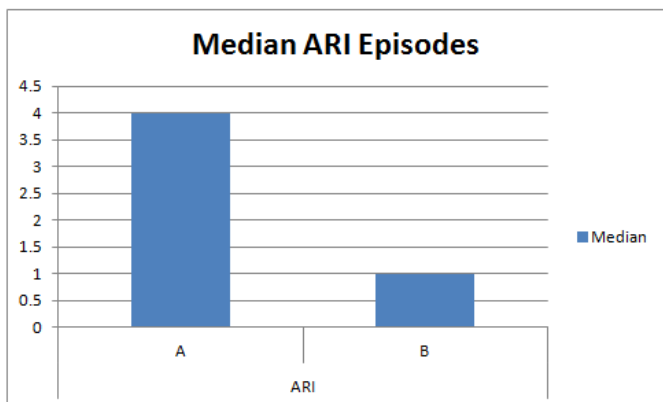
**Result:** The table depicts the comparison of Infectious episodes of ARI between group means. The mean Infection episodes of ARI in group A was (3.44 ± 0.15) and the mean infection episodes of ARI in group B was (0.85 ± 0.09).

**Table1: Comparison of mean number of Infection episodes of ARI between two groups.**

Infection Episodes	GROUP	N	Mean	Median	SE	Statistical inference	95%confidence Interval
ARI	A	101	3.44	4	0.15	t=14.71, p < 0.01	(3.15 – 3.73)
	B	99	0.85	1	0.09		(0.67 – 1.03)

t-test shows that there is a significant difference between the Infection episodes of ARI in newborn infants of two groups ( as  $p < 0.01$  ). The Infection episodes of ARI in newborn infants in group A (ie placebo group) are more as compared to group B (ie Vitamin D supplemented group).

**Figure 1: Showing comparison of median ARI episodes in both groups.**



From the Table: 1 and Figure: 1 it is seen that there is a significant difference between the infection ARI episodes in the two groups

**Discussion**

Vitamin D is well known for its role in calcium metabolism and bone health<sup>15</sup> In addition, vitamin D is active in the immune system.<sup>16</sup> Low plasma levels of calcidiol, the accepted marker of vitamin D status, are associated with increased infectious disease, especially respiratory tract infections, in several

populations,<sup>7,18,19</sup> including young Indian children<sup>19</sup>. A low plasma calcidiol level is widespread, even among populations at low latitude. In India, vitamin D deficiency is common among women and children<sup>20-21</sup>. Low birth weight is also common in India and these infants are at high risk of respiratory tract infections and other morbidity.<sup>22</sup> Low cost interventions such as improving vitamin D status are needed to improve the health and survival of these infants.

We thus conducted this randomized control study with the hypothesis that Vitamin D3 supplementation in infant’s results in reducing the of frequency infectious diseases like ARIs. In present study, mean number of ARI (3.44 vs 0.85; Median 4 vs 1) was significantly more in babies of placebo group as compared to Vitamin D group. So, Vitamin D supplementation significantly increases disease resistance as shown by reduced frequency of infection episodes. These results reflect the role of vitamin D in immunity as reported by other studies. Airway epithelial cells have been found to express high levels of 1 $\alpha$ -hydroxylase, converting 25-hydroxyvitamin D to its active form, leading to the increased production of both cathelicidin and the Toll-like receptor co receptor CD14, important in the recognition of Grampositiveand negative bacteria<sup>7</sup>. It enhances the differentiation and recruitment of macrophages, which may lead to an increased ability to fight infection<sup>23</sup>. Several recent epidemiology studies have observed the association between inadequate vitamin D concentrations and hospitalization and/or respiratory infection among children. Williams *et al.* determined the vitamin D status of 64 children infected with TB. Eighty-six percent of their patients had inadequate vitamin D stores<sup>24</sup>. Although TB is the prototypical association of vitamin D deficiency and infectious disease, other infectious diseases have also been linked to inadequate

vitamin D stores in children. Mazary et al.<sup>25</sup> conducted a study to examine the effect of vitamin D supplementation in the first 6-months of life on the immunity and risk of infections during the first year in infants. They observed that incidence of infections were less common in infants supplemented with daily vitamin D than those not supplemented (p value = 0.01). There were significant negative correlations between the incidence of respiratory and gastrointestinal infections and maternal vitamin D levels (p value = 0.001, r= -0.65, versus p value = 0.001, r= -0.61 respectively). Lies K et al. investigated a possible association between vitamin D deficiency and respiratory infection. Their findings suggest that the immunomodulatory properties of vitamin D influence ALRI disease severity<sup>26</sup>. Muhe *et al.* examined the risk for developing pneumonia among Ethiopian children with nutritional rickets. This case-control study found a strong positive correlation between vitamin D deficiency and respiratory compromise<sup>24</sup>. Devereux et al, 2007<sup>27</sup> reported that vitamin D deficiency increased the risk of wheezy chest during the first year of life and they attributed this to the immune regulatory effect of vitamin D in preventing respiratory tract infections that lead to wheezy chest. Many studies reported that vitamin D deficiency is more common in asthmatic children which may be due to two mechanisms; the immune prophylactic effect of vitamin D against respiratory infections which may be triggering factors for precipitation of asthma and to the direct immune regulatory effect of vitamin D that control asthma

### Conclusion

vitamin D supplementation after birth should be recommended as it is associated with lower frequency of acute respiratory infection during the first year of life. The findings support the importance of vitamin D

supplementation in full term infants who are exclusively breast fed, not only for its importance for the skeletal system but also for potential immune functions.

In this study infections were studied among the control and study subjects. Other parameters have also been studied, which are not included in this paper and will be put in subsequent papers.

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