Original Research Article

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Association of infant and maternal serum 25-hydroxy vitamin d levels with severity of pneumonia in infants

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ABSTRACT

Background: Vitamin D is a prohormone essential for normal absorption of calcium from the gut. Solar UVB radiations transform pre-vitamin D in the skin to vitamin D3. The aim was to find out association of infant and maternal serum 25 (OH) D levels with severity of pneumonia in infants.

Methods: In this prospective cross sectional study conducted in a tertiary care centre of Northern India during 2014-2015, a total of 160 subjects were enrolled; the study group involved infants with pneumonia of varying severity and their mothers while normal infants and their mothers were included in control arm of the study. This was followed by quantitative estimation of 25 (OH) D3 of all the enrolled infants along with their mothers.

Results: Among 40 infants presenting with variable severity of ARI taken as cases, the median 25 (OH) D levels was 12.55 ng/ml and 40 healthy infants taken as controls was 12.70 ng/ml. The median 25 (OH) D levels of mothers of infants enrolled as cases and controls were 13.00 ng/ml and 11.15 ng/ml respectively. The observations showed vitamin D deficiency in majority (78.75%) of our studied subjects although we could not find any statistically significant difference between the study group and control group.

Conclusions: This study showed vitamin D deficiency in both the studied groups although there was no causal relation between the vitamin D levels and severity of pneumonia. This study also showed that vitamin D levels were not statistically significant in infants presenting with variable severity of ARI and healthy infants. The observations of the study indicate that vitamin D deficiency is prevalent in high risk population group in Himachal Pradesh.

Keywords: 25 (OH) D, Vitamin D, Vitamin D deficiency

INTRODUCTION

Vitamin D is a prohormone essential for normal absorption of calcium from the gut. Solar UVB radiations transform pre-vitamin D in the skin to vitamin D3. Studies in recent years have demonstrated many nonclassical roles for vitamin D in the immune, cardiovascular, muscular, reproductive integumentary systems, as well as in cancer prevention.¹⁻⁵

Nuclear receptors of vitamin D have been identified in many tissues, with best-characterized target organs being intestine, kidney and bone. Growing evidence of association of vitamin D deficiency with acute lower respiratory tract infections (ALRTI), neurological function and possibly mental health conditions, namely schizophrenia has been noted in children. 64.0% in children younger than 5 years died of infectious causes (WHO report, 2010).

Of all infectious disorders, pneumonia, diarrhea and malaria were the leading causes of death worldwide. As high morbidity and mortality in infants due to pneumonia has been noted, this study was undertaken to find out the correlation between infant and maternal 25 (OH) D3 levels with risk of pneumonia in infants.

METHODS

This was a case control study (2014-15) in which we studied 2 groups of population. The studied population was divided into 2 groups (study group (group A) and control group (group B)). Group A was further subdivided into 2 groups (group A1 and group A2). Group A1 included all infants aged less than 1 year with clinical diagnosis of pneumonia, severe pneumonia or very severe pneumonia. Group A2 included all mothers of infants enrolled in group A1 (with pneumonia, severe pneumonia or very severe pneumonia). Group B was further subdivided into 2 groups (group B1 and group B2). Group B1 included 40 healthy infants aged less than 1 year reporteded for routine health check-up. Group B2 included all mothers of healthy infants enrolled in group B1 (Figure 1).

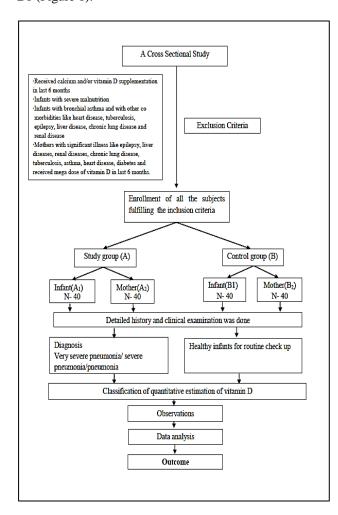


Figure 1: Methodology.

Inclusion criteria

- For study group (group A1), infants aged less than 1 year with clinical diagnosis of pneumonia, severe pneumonia and very severe pneumonia as per WHO classification of acute respiratory infections (ARI)
- For study group (group A2), mothers of infants enrolled in group A1 (suffering from pneumonia, severe pneumonia or very severe pneumonia)
- For control group (group B1), equal number of age matched healthy infants aged less than 1 year reporting for routine health check up
- For study group (group B2), all mothers of healthy infants enrolled in group B1
- Willingness to participate in the study
- Informed written parental/ guardian consent.

Exclusion criteria

- Infants who had received calcium and/or vitamin D supplementation in last 6 months
- Infants with severe malnutrition (grade III and IV as per IAP classification of protein energy malnutrition (PEM))
- Infants with bronchial asthma and with other comorbidities like heart disease, tuberculosis, epilepsy, liver disease, chronic lung disease and renal disease
- Mothers of infants having any significant illness like epilepsy, liver diseases, renal diseases, chronic lung disease, tuberculosis, asthma, heart disease, diabetes and received mega dose of vitamin D in last 6 months based on history and clinical examination
- Non- willingness to participate in the study
- Failure to get informed written consent.

Collection of data

After taking approval from the institutional ethics committee, the study was commenced with enrolment of all the subjects fulfilling the inclusion criteria in 2 groups. Detailed history and clinical examination of all enrolled infants and mothers was done. History of breastfeeding, initiation of complimentary feeding and exposure to sunlight for infants was taken. Clinical examination was done to find out status of pneumonia as per WHO classification or to find out any other significant finding. This was followed by quantitative estimation of 25 (OH) D3 of all the enrolled infants along with their mothers. Classification of vitamin D status as sufficient/insufficient/ deficient was done as suggested by Veith et al (Table 1).

Collection and storage of samples

3 ml blood was collected by venipuncture in properly covered test tube to avoid sunlight exposure. Then it was allowed to clot and serum from it was separated after centrifugation at room temperature.

This serum was subjected for quantitative analysis of serum 25 (OH) D by chemiluminiscence macro-particle enzyme immunoassay (CMIA).

Statistical analysis

Results obtained were analyzed statistically. Continuous variables were presented as mean or median. Chi square test was used for categorical variables. Analysis of variance (ANOVA) was used to analyse the differences among group means. A p-value of less than 0.05 was considered significant.

Ethics

There was no drug trial or human/animal experiment involved. All the subjects were counselled and results informed.

RESULTS

We have enrolled total of 160 subjects. In group A, total of 80 subjects were enrolled of which group A1 had 40 infants and group A2 had 40 mothers. In group B, total of 80 subjects was enrolled of which group B1 had 40 healthy infants and group B2 had 40 mothers. In group A1, out of 40 infants, there were 21 males and 19 females with mean age of 5.55 months. In controls group B1, there were 20 males and 20 females with mean age of 6.07 months. The mean age of mothers in group A2 was 26.33 years. The mean age of mothers in group B2 was 26.93 years. As per modified kuppuswamy scale, in group A, 2.5% subjects belonged to class I, 30% subjects to class II, 52.5% subjects to class III and 15% subjects to class IV. In group B, 15% subjects belonged to class IV.

In group A1, the mean duration of sunlight exposure with clothes during summers and winters in age group 0-2 months was 2.75 hours and 2.50 hours respectively, in age group 2-6 months, 3.15 hours and 3.72 hours respectively and in age group 6-12 months, 5.64 hours and 6.27 hours respectively. In group B1, the mean duration of sunlight exposure with clothes during summers and winters in age group 0-2 months was 2.50 hours and 3.50 hours respectively, in age group 2-6 months, 4.40 hours and 4.50 hours respectively and in age group 6-12 months, 5.08 hours and 6.23 hours respectively.

Table 1: Classification of quantitative estimation of vitamin D.

Vitamin D status	Serum 25(OH) D level		
Vitaliili D status	(ng/ml)	(nmol/l)	
Deficiency	<20	< 50	
Insufficiency	20-<30	50-<75	
Sufficiency	30-<100	75-<250	
Toxic	<u>≥</u> 100	<u>≥</u> 250	

Vitamin D deficiency was observed in 26 (65%) infants and vitamin D insufficiency in 7 (17.50%) infants out of 40 infants in group A1. Whereas out of 40 infants in Group B1, vitamin D deficiency was observed in 32 (80%) infants and vitamin D insufficiency in 4 (10%) infants. Similarly vitamin D deficiency was observed in 33 (82.50%) mothers and vitamin D insufficiency in 6 (15%) mothers out of 40 mothers in group A2. Whereas vitamin D deficiency was observed in 35 (87.50%) mothers and vitamin D insufficiency in 3 (7.50%) mothers out of 40 mothers in Group B2 (Table 3).

Table 2: Characteristics of the subjects.

Characteristics	Cases	Controls
Age (months) of infants		
0-2	10	10
2-6	13	11
6-12	17	19
0-12 (total)	40	40
Mean age of infants	5.55	6.07
Sex		
Males	21	20
Females	19	20
Mean age (years) of mothers	26.33	26.93
Socioeconomic status		
Type I	1	0*
Type II	12	6
Type III	21	28
Type IV	6	6
Feeding		
Exclusive breast feeding	18	19
(EBF)	10	19
Top feeding (TF)**	2	0*
Breast feeding with complimentary feeding (BF with CF)	14	13
Mixed feeding (MF)***	6	8

*There were no subjects in this group; **Infants who were top fed (animal milk or formula milk) alone or top fed along with breast feeding till 6 months of age.; ***Infants who were top fed alone or top fed along with breast feeding till 6 months of age and continued with it along with complimentary feeds.

The median vitamin level in Group A1 was 12.30 ng/ml (deficient) and in Group B1 was 12.45ng/ml (deficient). The p value among vitamin D levels among cases and controls in infants was not significant (p-value = 0.45). The median vitamin D level in group A2 was 13.00 ng/ml (deficient) and in group B2 was 11.15 ng/ml (deficient). The p value among median levels among cases and controls in mothers was not significant (p value 1.00).

Out of 40 infants, 14 had very severe pneumonia, 14 had severe pneumonia and 12 had pneumonia in Group A1. All 40 infants in Group B1 had no pneumonia. In Group

A1, the median vitamin D level among very severe pneumonia was 12.45 ng/ml (deficient), among severe pneumonia was 12.40ng/ml (deficient) and among pneumonia was 16.55ng/ml (deficient). In Group B1, the median vitamin D level among no pneumonia was 12.70ng/ml (deficient). The p value among vitamin D levels was not significant (p value = 0.874). In group A2,

the median vitamin D level in mothers of infants with very severe pneumonia was 12.15ng/ml (deficient), with severe pneumonia was 13.40ng/ml (deficient) and with pneumonia was 17.40 ng/ml (deficient). In group B2, median vitamin D level in mothers of healthy infants was 11.15 ng/ml (deficient). The p-value among vitamin D levels was not significant (p-value 0.638).

Table	3:	Vitamin	D	level	distribution.
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Vitamin D levels	Study group (A	A)	Control group	Control group (B)	
Vitanini Dieveis	Infants(A ₁)	Mothers (A ₂)	Infants(B ₁)	Controls (B ₂)	
Deficiency(<20 ng/ml)	26 (65%)	33 (82.50%)	32 (80%)	35 (87.50%)	
Insufficiency(20-<30 ng/ml)	7 (17.50%)	6 (15%)	4 (10%)	3 (7.50%)	
Total (deficiency+insufficiency)	33 (82.50%)	39 (97.50%)	36 (90%)	38 (95%)	
Sufficient/ excess (>30 ng/ml)	7 (17.50%)	1 (2.50%)	4 (10%)	2 (5%)	
Total (n-160)	40	40	40	40	

In group A1 in infants aged 0-6 months, 18 (90%) infants were EBF and in infants aged 6-12 months, 14 (70%) were BF with CF. In group B1 in infants aged 0-6 months, 19 (100%) were EBF whereas in infants aged 6-12 months, 13 (61.90%) were BF with CF (Table 2).

DISCUSSION

This preliminary study revealed that there was no causal relation between the vitamin D levels and severity of pneumonia as vitamin D deficiency was present in both the studied groups. This study also showed that vitamin D levels were not statistically significant in infants presenting with variable severity of ARI and healthy infants. To our knowledge, this is the first study conducted in India comparing the status of vitamin D levels with severity of pneumonia in infants aged till 12 months. Also this is the first study comparing vitamin D levels of infants having ARI and healthy infants. Also vitamin D status of their mothers were also compared which was also deficient in both the groups and serum vitamin D level in mothers were not significantly different between cases and controls.

There were no baseline differences in the age characteristics in infants of study group and control group in our study when compared with study conducted by Zuo et al in children from 6-36 months in which case to control ratio was 2:1 and there was male predominance.⁸

In our study there was no difference between the mean age of mothers in groups A2 and B2 as far as age was concerned. These findings were very similar to the study conducted by Mirzaei et al where they compared the 25 (OH) D levels between mothers and their appropriate for gestational age (AGA) newborns and between mothers and their small for gestational age (SGA) newborns with mothers.⁹

The majority of our subjects belonged to class III followed by class II and class IV in our study which shows the strata of population coming to our hospital.

From our study, it is evident that duration of sun exposure in both groups was more during winters. The duration of sun exposure also increased with the increasing age of infants. This can be explained with cultural practice of less exposure to the young infant as compared to the older infants.

It has been observed that in our study population, the infants in age group 0-6 months were on EBF in cases (90%) and controls (100%). The infants in age group 6-12 months were predominantly on breast feeding with complimentary feeds in both cases (70%) and controls (61.90%). So more controls were given breastfeeding when compared with cases. This may suggest more ARI among infants in cases. Wayse et al studied 150 Indian children aged 2-60 months as part of a case control study. They reported that subclinical vitamin D deficiency and non-exclusive breast feeding on the first 4 months of life as significant risk factors for severe ALRTI in Indian children. ¹⁰

The vitamin D deficiency was observed in 26 (65%) infants and vitamin D insufficiency in 7 (17.50%) infants among cases whereas vitamin D deficiency was observed in 32 (80%) infants and vitamin D insufficiency in 4 (10%) infants among controls. This suggests the magnitude of the problem of vitamin D deficiency in infants present in our society. In a prospective observational study, Prasad et al observed vitamin D deficiency in 67 (83.8 %) out of 80 children aged 2 month to 12 years admitted with medical conditions including pneumonia admitted at the pediatric intensive care unit of a tertiary care hospital. In a case control study conducted by Roth et in Bangladesh found that in subgroup of 29 community control participants aged 1-6

months were all either vitamin D deficient or insufficient. Ritu et al reported that vitamin D deficiency prevails in epidemic proportions all over the Indian subcontinent, with a prevalence of 70%-100% in the general population. They also reported that subclinical vitamin D deficiency is highly prevalent in both urban and rural settings and across all socioeconomic and geographic strata.

The vitamin D deficiency and insufficiency was observed in 33 (82.50%) mothers and 6 (15%) infants respectively in group A2 whereas in group B2, vitamin D deficiency and insufficiency was observed in 35 (87.50%) mothers and (7.50%) mothers respectively. This suggests that vitamin D deficiency is prevalent among mothers in our society. The lower levels of vitamin D in infants can be correlated with the lower levels of vitamin D in mothers as suggested by the study conducted by Sachan et al. Sachan et al studied 207 urban and rural pregnant women at term in India. 138 out of 207 (66.67%) of women were vitamin D deficient (<15 ng/ml) and maternal serum 25 (OH) D correlated positively with cord blood 25(OH)D. They observed a high prevalence of vitamin D deficiency among pregnant women and their newborns. 14 The vitamin D levels were not significantly different between cases and controls in our study. This finding was similar to the case control study was conducted by McNally et al on 197 children to find out the role of vitamin D in increased occurrence of acute lower respiratory tract infections and observed that there was no difference was observed in vitamin D levels between the entire ALRI group and control groups. 15

Our finding that serum vitamin D level in mothers were not significantly different between cases and controls was not consistent with the studies done by Dinlen et al and Mirzaei et al. Dinlen et al conducted a case control study consisting of 30 term newborns with ALRTI who were admitted at neonatal intensive care unit as cases and 30 healthy newborns with the same age as controls along with their mothers in the same respective groups. They concluded that the median serum 25 (OH) D levels in the mothers of the study group were also lower than those in the mothers of the control group. 16 Mirzaei et al compared the 25-hydroxy vitamin D levels between mothers and their small for gestational age (SGA) newborns with mothers and their appropriate for gestational age (AGA) newborns. Vitamin D deficiency was statistically higher in women with SGA newborns in comparison to women with AGA newborns. The relationship of vitamin D deficiency levels between mothers and infants in both the SGA group and the AGA group was significant.9

There was no statistically significant difference between vitamin D level distribution according to socioeconomic status in cases and controls in infants. Vitamin D levels in socioeconomic class I was 41.70 ng/ml (sufficient). There was only 1 infant out of 40 infants among cases who belonged to socioeconomic class I and hence it does not

reflect the exact nature of vitamin D distribution. Also there was no significant difference between vitamin D level distribution according to socioeconomic status in cases and controls in mothers. Ritu et al reported that subclinical vitamin D deficiency is highly prevalent in both urban and rural settings, and across all socioeconomic and geographic strata.¹³

Infants in both group A1 and group B1 were having vitamin deficiency but there was no statistically significant association was found between vitamin D levels and severity of pneumonia. Also mothers in group A2 and group B2 were having vitamin D deficiency but there was no statistically significant association between vitamin D levels and severity of pneumonia.

Our observations showed deficient vitamin D levels in 78.75% of population and insufficient vitamin D levels in 12.50% of population in the whole studied population which suggests the high prevalence of vitamin D deficiency in our high risk population group (mothers and their infants).

CONCLUSION

In this case control study, association of infant and maternal serum 25 (OH) D levels in relation to severity of pneumonia in infants was evaluated. The vitamin D levels were not statistically significant in the studied population. This study showed vitamin D deficiency in both the studied groups although there was no causal relation between the vitamin D levels and severity of pneumonia. This study also showed that vitamin D levels were not statistically significant in infants presenting with variable severity of ARI and healthy infants. The observations of the study indicate that vitamin D deficiency is prevalent in high risk population group in Himachal Pradesh and as a consequence this must be taken into consideration with future planning of strategies to prevent vitamin D deficiency during antenatal period in mothers and during infancy. However keeping in view the role of vitamin D in preventing many infectious, inflammatory and neoplastic diseases, a screening programme of this high risk group can be undertaken. Limitations of the study was that sample size was small and hence a population based study is required to find out prevalence of vitamin D deficiency in high risk population to formulate the strategy to prevent it.

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Ethical approval: The study was approved by the

Institutional Ethics Committee

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