



TO STUDY THE VITAMIN D LEVELS IN THE CHILDREN WITH RESPIRATORY TRACT INFECTIONS BETWEEN THE AGE GROUP OF 1 MONTH TO 18 YEARS

Paediatrics

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ABSTRACT

Introduction Respiratory tract infections (RTI's) are common worldwide and are responsible for the significant morbidity and mortality in the paediatric age group and are the most common reason for hospital admissions. Recently, growing evidences suggest that Vitamin D is not merely a micronutrient for calcium and phosphate homeostasis but a pluripotent hormone with numerous extra skeletal effects and regulates the inflammatory cascade with extensive immunomodulatory effects and has shown to decrease the RTI's. Hence, present study was conducted to assess the Vitamin D levels in the children suffering with RTI's. **Aims And Objective** To assess the Vitamin D levels in the children with respiratory tract infections between the age group of 1 month to 18 years. **Materials And Methods** A total of 100 children between the age group of one month to 18 years of age diagnosed with respiratory tract infections presenting to the Department of Paediatrics, MMIMSR, Mullana, Ambala were enrolled after obtaining consent from the parents, as per the inclusion and exclusion criteria. Detailed history, demographic profile, clinical examinations were recorded in a proforma (questionnaire) and the relevant investigations including the serum Vitamin D assays. **Results And Conclusion** Of the study population, 55% of children had vitamin D levels <20 ng/ml [14% (<12 ng/ml); 41 % (12-20 ng/ml)] while remaining had normal vitamin D levels(>20 ng/ml). Vitamin D deficiency and insufficiency were significantly higher in the age group below 5 years of age as compared to older children($p<0.001$) and the study subjects with malnutrition, belonged to lower socioeconomic status with LRTI and no significant association observed between gender and vitamin D deficient levels. These observations suggested the fact that Vitamin D might play a significant role in respiratory tract infections and Vitamin D supplementation may reduce the prevalence and severity of respiratory illnesses.

KEYWORDS

INTRODUCTION

Pneumonia is the major cause of morbidity and mortality in both developed and developing countries, more in younger age with declining incidence in growing age. WHO estimates that 2 million children under five years of age die of pneumonia each year.¹

The Streptococcus pneumoniae, H. influenza, Respiratory syncytial virus and influenza virus are the leading respiratory pathogens.²

As per the available literatures, some specific micronutrients deficiencies do have relationship in morbidity and mortality in paediatric age group and the impact of micronutrients supplementation (vitamin A, Vitamin D, zinc, iron etc.) on reducing respiratory infections in young population. Numerous researches and studies have documented that approximately 75% of deaths in children in the age group of under 5 years of age. The malnutrition per se is a leading contributing factor for under 5 mortality and deficiencies of specific micronutrient along with caloric deficiency predisposes these children to higher morbidity and mortality.^{3,4} As of today, the literatures suggest that micronutrient supplementation can reduce ARTI rates and severity.⁵

The process by which vitamin D controls inflammatory response and immune function appears to be likely multifactorial and exact mechanism is not known. It regulates macrophage and dendritic cell activity, as well as various Toll-like receptor-mediated events in neutrophils, and it reduces the function of human dendritic cells by reducing maturation, antigen presentation, and the production of cytokines like interleukin (IL)-12 and IL-23. Furthermore, treating macrophages with Vitamin D causes the production of cytokines and chemokines such as CXCL8, IL-6, and IL-12 and stimulates the production of two antimicrobial peptides, cathelicidin and defensin, which are extensively expressed in the body and play an important role in innate immunity due to their chemotactic and toxin-neutralizing properties.⁶

The present study was undertaken to assess the level of Vitamin D in children having respiratory tract infections.

AIMS AND OBJECTIVE

To study the Vitamin D levels in the children with respiratory tract infections between the age group of 1 month to 18 years.

METHODS:-

This was a hospital based longitudinal observational study which included 100 children with diagnosis of respiratory tract infection conducted between January 2021 to June, 2022 in Paediatrics department at MMIMSR, Mullana.

Inclusion Criteria

- Children with RTI between the age group of one month to 18 years.
- Children of both sexes, with RTI.

Exclusion Criteria

1. Patients who were recently (within last three months) on vitamin D supplementation.
2. Patient who took medication (Anti-epileptics, Glucocorticoids, Anti-tubercular drugs etc.) that predisposes to vitamin D deficiency
3. Lactating mothers on Vitamin D supplements for the last three months.
4. Patient with known metabolic disorder that can alter vitamin D levels (Hyperparathyroidism).
5. Parents of children not willing to participate in study.

A prior approval of The Institutional Ethics committee was obtained.

- Vitamin D assay was estimated by Chemiluminescence Immunoassay (CLIA) method. Venous blood sample (Minimum 2ml in I separate red cap vial (with clot activator) for 25(OH) was collected under all aseptic conditions.

Statistical Analysis:

During data collection, complete proforma (questionnaires) were regularly checked to rectify any discrepancy, logical error, or missing information. The data was analysed by specific statistical method and was performed by the SPSS program for Windows, version 26.0 (SPSS, Chicago, Illinois). Continuous variables are presented as

mean $\pm$ SD, and categorical variables are presented as absolute numbers and percentage and data were checked for normality before statistical analysis. Microsoft word and Excel was used to generate graphs and table. **For all statistical tests, p value less than 0.05 was taken to indicate a significant difference.**

RESULTS

Table 1: Age-wise distribution of enrolled subjects

Age Group (years)	No. of Enrolled subjects	% age
≤ 5	40	40.0%
6-10	28	28.0%
11-15	25	25.0%
>15	7	7.0%
Total	100	100.0%

It was observed that 40(40%) of enrolled subjects were under 5 years of age, 28 (28%) were between 6-10 years, 25(25%) were between 11-15 years of age and only 7(7%) were above 15 years.

Table 2: Gender-wise distribution of enrolled subjects

Socioeconomic Status	No. of Enrolled subjects	%
Lower	77	77
Middle	20	20
Upper	3	3
Total	100	100

It was observed that, amongst the enrolled subjects in the study 56(56%) were males and rest 44(44%) were females.

Table 3: Frequency of Distribution of enrolled subjects according to socio-economic status

Gender	No. of Enrolled subjects	%
FEMALE	44	44
MALE	56	56
Total	100	100

It was observed that 77% of the enrolled subjects were from lower socio economic strata whereas 20% from middle socioeconomic status and only 3% belong to upper class.

Table 4: Frequency of distribution of enrolled subjects as per nutritional status (Sever acute malnutrition(SAM))

Severe acute malnutrition (Weight/Height <-3SD)	No. Of Enrolled subjects	%
Normal for weight for height	85	85
Weight for height (<-3SD)	15	15
Total	100	100

It was observed that out of the total enrolled subjects 15/100 (15%) of enrolled subjects under 5 years of age were severely acute malnourished.

Table 5: Distribution of enrolled subjects as per primary immunization status

Immunization	No. Of Enrolled subjects	%
Complete	70	70
Incomplete	30	30
Total	100	100

It was observed that 70% of enrolled subjects were completely immunized as per national immunization schedule while rest 30% of enrolled subjects were not completely immunized

Table 6: Frequency of distribution of enrolled subjects with presenting clinical symptoms of respiratory tract infections

Symptoms	No. of Enrolled subjects	%
Cough	94	94
Fever	79	79
Cold	56	56
Running nose	54	54
Nasal congestion	52	52
Sore Throat	37	37
Ear pain and discharge	5	5

It was observed that in majority of enrolled subjects 94% had cough as presenting clinical symptom, followed by fever in 70%, cold in 56%, running nose in 54%, 52% had nasal congestion, 37% enrolled subjects had sore throat and only 5% presented with ear pain and discharge

Table 7: Frequency of distribution of enrolled subjects with clinical signs associated with respiratory tract infection

Sign	No. Of Enrolled subjects	%
Retraction	39	39
Tachypnea	39	39
Crepitation	36	36
Wheeze	34	34
Cyanosis	1	1

It was observed that Retraction and tachypnea were present in 39% of enrolled subjects followed by crepitation in 36%, wheeze in 34% and only 1 % had cyanosis.

Table 8: Frequency of distribution of enrolled subjects according to anatomical categorization of respiratory tract.

Diagnosis	No. of enrolled subjects	%
URTI	40	40
LRTI	60	60
Total	100	100

It was observed that 40% enrolled subjects presented with URTI while 60% presented with LRTI.

Table 9: Distribution of enrolled subjects according to Serum Vitamin D levels.

Serum vitamin	No. of enrolled subjects	%
Deficiency(<12ng/ml)	14	14
Insufficiency(12-20ng/ml)	41	41
Normal (>20ng/ml)	45	45
Total	100	100

It was observed that 14% of enrolled subjects presented with vitamin D deficiency(<12ng/ml), 41 % presented with insufficiency (12-20ng/ml) while 45 % had normal levels of vitamin D(>20ng/ml)

Table 10: Association between the age groups and vitamin D levels in enrolled subjects

Age group	Deficiency (<12ng/ml)		Insufficiency (12-20ng/ml)		Normal levels (>20ng/ml)		Total	p- vale
	N	%	n	%	n	%	n	
≤ 5	13	92.9%	20	48.8%	7	15.6%	40	40.0%
6-10	1	7.1%	15	36.6%	12	26.7%	28	28.0%
11-15	0	0.0%	5	12.2%	20	44.4%	25	25.0%
>15	0	0.0%	1	2.4%	6	13.3%	7	7.0%
Total	14	100.0%	41	100.0%	45	100.0%	100	100.0%

p<0.05 - significant; p<0.001- highly significant; p>0.05 non significant

Above table shows that vitamin D deficiency and insufficiency was significantly more in children under 5 years of age as compared to older adults. Significant association was observed between the vitamin D and age.

Table 11: Association between gender and Vitamin D levels in enrolled subjects

gender	Deficiency (<12ng/ml)		Insufficiency (12- 0ng/ml)		Normal levels (>20ng/ml)		Total	p-value
	N	%	n	%	n	%	n	
Male	7	50.00%	17	41.50%	20	44.40%	44	44.00%
Female	7	50.00%	24	58.50%	25	55.60%	56	56.00%
Total	14	100.00%	41	100.00%	45	100.00%	100	100.00%

p<.05 - significant; p<.001- highly significant; p>.05 non significant

Table 11 shows that the association between gender and vitamin D levels in children with RTI was not significant (p=0.85).

Table 12: Association between vitamin D levels and socio-economic status in children with Respiratory tract infection

SES	Deficiency (<12ng/ml)		Insufficiency (12-20ng/ml)		Sufficiency (>20ng/dl)		Total	p-value
	N	%	n	%	n	%	n	
Lower	9	64.30%	38	92.70%	30	66.70%	77	77.00%
Middle	5	35.70%	3	7.30%	12	26.70%	20	20.00%
Upper	0	0.00%	0	0.00%	3	6.70%	3	3.00%
Total	14	100.00%	41	100.00%	45	100.00%	100	100.00%

p≤0.05 - significant; p≤0.001- highly significant; p>0.05 non significant

It was observed that enrolled subjects with Vitamin D deficiency were from lower socioeconomic class (9/14; 64.30%) and middle SES(5/14;35.70%) while none of upper class had vitamin D deficiency or insufficiency .Majority (92.70%) of the enrolled subjects with insufficient levels of vitamin D were from Low SES. The association between vitamin D and low socioeconomic status in children with RTI was statistically significant.(p<0.001)

Table 13: Association between severe acute malnutrition and vitamin D in children with RTI

Normal for weight for height	Deficiency (<12ng/ml)		Insufficiency (12-20ng/ml)		Normal levels (>20ng/ml)		Total		p-value
	N	%	n	%	N	%	n	%	
Weight for height <-3SD	9	64.30%	34	82.90%	42	93.30%	85	85.00%	.026
<-3SD	5	35.70%	7	17.10%	3	6.70%	15	15.00%	
Total	14	100.00%	41	100.00%	45	100.00%	100	100.00%	

Above table shows significant association between severe acute malnutrition and vitamin D levels in children with RTI(=.026). It was observed that malnutrition was more in subjects who had vitamin D levels deficiency <12 ng/ml(5/14; 35.70%) than in children who had insufficient (7/41;17.10%) or sufficient vitamin D level(3/45;6.70%).

Table 14: Association between vitamin D levels and categorization of Respiratory tract infection among enrolled subjects

RTI	Deficiency (<12ng/ml)		Insufficiency (12-20ng/ml)		Normal levels (>20ng/ml)		Total		p-value
	N	%	n	%	n	%	n	%	
LRTI	14	100.00%	31	75.60%	15	33.30%	60	60.00%	<.001
URTI	0	0.00%	10	24.40%	30	66.70%	40	40.00%	
Total	14	100.00%	41	100.00%	45	100.00%	100	100.00%	

p≤0.05 - significant; p≤0.001- highly significant; p>0.05 non significant

Above table depicts the association between Categorization of RTI and vitamin D levels. It was observed that subjects with URTI had insufficient levels of Vitamin D and none of the subjects were severely deficient. Enrolled subjects with LRTI 100%(14) had Vitamin D deficiency and 75.60%(31/41) had insufficient levels of Vitamin D . Enrolled subjects with LRTI were observed to have deficient or insufficient vitamin D levels(p<0.001).

DISCUSSION:

In our study, 100 subjects with RTIs between the age group of 1 month to 18 years of age were enrolled, with the mean age of 8.92 (S.D 5.1 years), 40% of enrolled subjects were under 5 years of age, 28% were between 6-10 years, 25% were between 11-15 years of age and remaining 7% were of 15-18 years of age. **Science et al.**⁷ (2008) in their study of 743 children between age group of 3-15 years, observed the mean age of 9.3 years (S.D 4.3 years) with respiratory tract infection, which was also in agreement with our study.

In our study, 56% were males subjects and rest were females. Similar observations were documented in the study by **Hasan et al.**⁸ (2022), observed the higher percentage of males subjects compared to females with ARTI and **Goel et al.**⁹ (2012) in a survey of 450 subjects in under five years of age observed that the male subjects were predominantly more affected with ARTI and suggested the probable hypothesis that male children are probably more actively involved in outdoor activities and having higher exposure to surrounding environment.

Based on socioeconomic profile, in our study 56% of enrolled subjects belonged to lower socioeconomic status, 44% were from middle socioeconomic status and none of them belonged to upper class. **Savitha et al.**¹⁰ (2018) also observed higher percentage of children with ARTI (93.27%) from lower socioeconomic status. **Dhanasekhar et al.**¹¹ (2017) in their study of 100 children between the age group of 2months to 5 years with ALRTI, observed 52% of children of lower socioeconomic strata with significant correlation of severity of ARTI with lower socioeconomic strata. **Cohen et al.**¹² (2010) in their review on socioeconomic strata with RTI in children, and hypothesised that

lower socioeconomic strata families invariably have large family size, live in crowded conditions, probably have limited awareness about good care practices with poor access to material resources and environmental conditions conducive for the transmission of infectious agents, which further increases the risk of systemic infections.

In the present study, based on clinical symptoms it was observed that majority (94%) of the subjects with ARTI presented with cough as the most common symptom, fever in 70%, cold in 56%, running nose in 54%, 52% had nasal congestion, sore throat in 37% and 5% presented with ear pain and discharge. These observations were in concordance with the study by **Prajapati et al.**¹³ (2012) who also observed that majority (92.0%) had cough, 81% nasal discharge, 38% fever, 20% fast breathing and 4% stopped feeding and **Goel et al.**⁹ (2012) observed that majority (71%) of children had cough as the most predominant clinical symptom.

In our study, based on anatomical classifications of respiratory tract infections, it was observed that 60% of enrolled subjects had LRTI while 40% had URTI and these observations were in agreement with the study by **Shivaprakash et al.**¹⁴ (2017) in which out of 145 children with ARTI between the age group (6 months- 6 years), 101 (69.7%) had LRTI and 44(30.3%) had URTI. Our observations are in contrast to the study by **Tazinya et al.**¹⁵ (2018) in the survey of 280 children under 5 years of age with ARTI observed that 191(37.3%) had an URTI, 88 (17.2%) had LRTI and 35 subjects had both upper and lower RTI.

In our study, on the basis of estimation of vitamin D levels in the enrolled subjects with RTI, it was observed that 14% of enrolled subjects had vitamin D deficiency(<12ng/ml), 41 % had insufficiency (12-20ng/ml) and 45 % had normal levels of vitamin D(>20ng). Our results were in concordance with the study of **Jaybhaye et al.**¹⁶ (2022) in their hospital based study of 108 children between 6 months to 15 years of age and observed that 25% children were vitamin D deficient and 75% had vitamin D insufficiency. In study by **Chandrashekhar et al.**¹⁷ (2019) it was observed that 84.7% (50/59) had vitamin D deficiency, 10.1% (6/59) had insufficient levels and only 3 (5.08%) had vitamin D levels in normal range. Our results were in agreement with these studies and documented significant association of Low vitamin D levels with RTI.

In our study, based on the association of vitamin D levels in the different age groups with RTI, in the subjects less than five years of age, 92.9% were vitamin D deficient, 48.8 % had vitamin D in insufficient levels and 15.6% had vitamin D levels in normal ranges. In the subjects between 6-10 years of age, 7.1 % had Vitamin D Deficiency, 36.6% had insufficient levels of Vitamin D while remaining (26.7%) had vitamin D levels in normal ranges and in the children above 11 years, vitamin D insufficiency was present in 14.6% and rest had vitamin D levels were in normal range. Vitamin D deficiency and insufficiency was significantly more common in children under 5 years of age as compared to older children .These observations were in agreement with the **Chandrashekhar et al.**¹⁷ (2019) in their study, observed that all (100%) children from 6 months to 1 years were vitamin D deficient whereas 80.8% of children between 1 to 5 years of age were vitamin D deficient, 12.7% had vitamin D insufficiency and only 6.3% had vitamin D levels in normal ranges and a case control study by **Guo et al.**¹⁸ (2017) in the age group between 1 month to 14 years and observed the low serum vitamin D levels in the age group of under 5 years with LRTI than that in the control group.

Based on the analysis of the association of socioeconomic strata grading with vitamin D levels, we observed that 64.30 % of the study subjects with vitamin D deficiencies belong to lower socioeconomic class, 35.7% belong to middle socioeconomic class while none of the study subjects were from upper socioeconomic class, Vitamin D insufficiency was present in the 92.70% study subjects from lower socioeconomic class, 7.3% from middle class while study subjects from higher economic status had Vitamin D level in normal ranges. Similar observations had been documented in the study by **Chandrashekhar et al.**¹⁷ (2019) in which Vitamin D deficiency was present in subjects belonging to lower socioeconomic status and also in study by **Umeadi et al.**¹⁹ (2021) low vitamin D levels were observed in subjects belonging to lower and middle socioeconomic strata and documented that low vitamin D levels in children with RTI from lower socioeconomic strata was of statistical significance

In our study, on the basis of association of vitamin D levels with

anatomical classification of respiratory tract infections ,14% of enrolled subjects with LRTI had Vitamin D deficiency, 75.60% had insufficient Vitamin D levels and rest 33.30% had vitamin D level in normal ranges while in subjects with URTI 24.40 % had Vitamin D insufficiency and none had severe deficiency of Vitamin D levels and observed that there was significant association of low vitamin D levels with LRTI .Our observations were in agreement with the study by **Guo et al.¹⁸ (2017)** where 236 children between age group 1 month to 14 years with LRTI and observed that 51.7% were vitamin D deficient, 33.5% were insufficient and 15.3% had vitamin D levels in normal ranges. Our observations had been in contrast with a case control study by **McNally et al.²⁰ (2009)** in under 5 years of age group of children and documented no significant association of vitamin D levels with ALRTI as compared to the control group.

RESULTS AND CONCLUSION

In the study ,out of total study subjects 55% of children had vitamin D levels <20 ng/ml [14% (<12 ng/ml); 41 % (12-20 ng/ml)] while rest had normal vitamin D levels(>20 ng/ml).Vitamin D deficiency and insufficiency were significantly higher in the age group below 5 years of age as compared to older children along with malnutrition, belonged to lower socioeconomic status and diagnosed with LRTI . Thereby, suggesting that vitamin D levels in our bodies play a significant immunological role in immunomodulation of both innate and adaptive immunity and thereby regulating the inflammatory cascade.. These observations suggest that Vitamin D plays a significant role in respiratory tract infections and Vitamin D supplementation reduces the prevalence of respiratory illnesses.

Recommendation

Vitamin D supplementation is recommended during the first year of life to prevent metabolic bone diseases in as almost all newborns and infants . Various International scientific societies recommend 400 IU /day Vitamin D for all infants upto their first birthday, independent of mode of feeding. The administration of 400 IU/day has also been documented to be safe and ensure adequate Vitamin D status. There are also recommendations to increase the intake upto 1000 IU/day in infants at risk for the development of Vitamin D deficiency. The promotion of adequate Vitamin D consumption is also important for all older children and adolescents in the range of 200-1000 IU/day to prevent Vitamin D deficiency. Continuous supplementation should be recommended in children on anticonvulsants, Oral corticosteroids and Antiretroviral drugs in the higher doses than recommended .Based on these facts, several international societies also recommend supplementation of vitamin D in older children and adolescents, who are at risk for development of Vitamin D deficiency

Conflicts of interest: There are no conflicts of interest

Limitations: The sample size of our study population was small which can interfere with the statistical strength of the data. Larger case control multi centric studies should be undertaken in order to validate these observations. The viral and bacterial etiology among children with ARTI was not diagnosed, which would have provided better insights into the relationship between distribution of viral pathogen and vitamin D deficiency. Due to the paucity of time, children with recurrent ARTI could not be the part of study, which might have added to more statistical correlation with Vitamin D deficiency. No control population i.e., healthy children not suffering from ARTI were not included in the study which might have caused interference among the data. Due to the ongoing Coronavirus (Covid) pandemic during the study period, might have influence the observation of our study.

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