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ORIGINAL RESEARCH

To evaluate the role of vitamin D in Lower Respiratory tract Infection Among Children ages 6 Months To 5 Years: A Study at Tertiary Care Hospital in Central Uttar Pradesh

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Abstract

Background: Lower respiratory tract infection (LRTI) has long been a leading cause of morbidity and mortality in infancy. Any promising strategies for the prevention of LRTI should be explored extensively and as early as possible. Vitamin D has shown to possess immunomodulatoryproperties and mediate the immune responses to infections.

Methodology : A cross-sectional observational study was performed over 177 patients diagnosed with lower respiratory tract infection in the Department of Pediatrics of a tertiary care hospital during the study period of 14 months duration from December 2022 to February 2024 after obtaining consent from the patients.Patients were selected based on clinicaland radiological findings indicative of lower respiratory tract infection, utilizing bothoutpatient department (OPD) and inpatient department (IPD) records while adheringto predefined inclusion and exclusion criteria. Samples were collected for vitamin D measurement using 25(OH) D ELISA. Other investigations like x ray chest and mantoux also done.

Results: The data comprised a total of 177 cases, majority of patients' fathers belonged to the lower socio-economic status, accounting for 71 patients (40.1%). The most common symptom was a cough, reported by 174 patients (98.3%) followed by fever, which affected 157 patients (88.7%); cold, reported by 151 patients (85.3%); difficulty in breathing, experienced by 106 patients (59.9%); and other symptoms, which were present in 88 patients (49.7%).The majority of patients were in the insufficient category (12-20 ng/mL), accounting for 118 patients (66.7%) followed by the deficient category (<12 ng/mL), which included 32 patients (18.1%) and sufficient category (21-100 ng/mL) comprised 27 patients (15.3%).Age-wise, 13 patients (40.6%) in the deficient group were aged 6 months to 1 year. Meanwhile, 19 patients (59.4%) in the deficient group were aged1 year to 5 years, compared to 61 patients (51.7%) in the insufficient group and 10 patients (37.0%) in the sufficient group. Gender-wise, 19 male patients (59.4%) were in the Deficient group, compared to 78 male patients (66.1%) in the insufficient group and 18 male patients (66.7%) in the sufficient group. Female patients included 13 (40.6%) in the Deficient group, 40(33.9%) in the Insufficient group, and 9 (33.3%) in the Sufficient group. Although deficient and insufficient levels of Vitamin D are more in male patientscompared to 57 patients (48.3%) in the Insufficient group and 17 patients (63.0%) in sufficient group. Most common diagnosis in deficient group was bronchiolitis 12(37.5%), pneumonia 52(44.1%) in insufficient and sufficient group 52(44.1%) and 11(40.7%) respectively. Sun exposure was adequate in sufficient group while inadequate in both deficient and insufficient group.

Conclusion : This study showed children with LRTIs exhibited a higher proportion of vitamin D deficient subjects leading to reduced lung functions. Our research highlights the need to measure blood vitamin D levels in a variety of

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respiratory conditions in order to start appropriate and prompt treatment interventions that reduce morbidity and death in children under-five. The exposure to the sun and its importance (30 min a day for 5-6 days/week between 10A.M -3 P.M) should be educated. Routine vitamin D supplementation should be advised from birth onwards.

Introduction

Acute lower respiratory infections (ALRI), such as pneumonia and bronchiolitis, are a leading cause of morbidity and mortality in young children.[1-3] By 2030, the Sustainable Development Goals (SDGs) aim to eradicate avoidable disease-related mortality among infants and children under five, ARI being serious public health issue in India.[6] A person's health and development can be negatively impacted not just in their early years but also in their later years if they have a poor quality of life throughout this crucial time in their life. Any viable LRTI preventive techniques must be thoroughly investigated as soon as feasible.[7]LRTIs are caused by several factors, such as age (<1year), low birth weight, early delivery, malnutrition, underlying morbidity, inability to breastfeed, low socioeconomic status, crowded living circumstances (big family, daycare, etc.), mother age and education, indoor and outdoor air pollution (primarily from passive smoking), insufficient immunization, and vitamin D deficiency.[9]Fat-soluble vitamin D is necessary for immune system control, bone metabolism, and the control of inflammatory processes.[10] Lack of vitamin D is becoming more widely acknowledged as a global public health concern. It has been connected to a wide range of acute and chronic conditions, such as autoimmune disorders, cardiovascular illnesses, and some forms of cancer.[12,13] The scientific community has become more interested in vitamin D's possible involvement in the prevention and treatment of infectious illnesses, particularly respiratory infections, in recent years.[14] People who live at high altitude are more likely to experience seasonal vitamin D deficiency in the winter. This is because sunshine does not encourage the skin's conversion of vitamin D precursors throughout the winter.[15] Recent research has linked vitamin D insufficiency to a wide range of illnesses, including cancer, cardiovascular disease, autoimmune disorders, and type 2 diabetes.[16] Very few foods naturally contain vitamin D. Foods high in vitamin D include egg yolks, fish liver oils, and some fatty fish (mackerel, salmon, and sardines). Certain cereals and dairy products, for example, are fortified foods and are additional sources of vitamin D.[17,18]

Vitamin D: Research showedthat vitamin D has role in calcium metabolism, bone formation, and immunesystem interaction. Vitamin D receptors are expressed invarious tissues, including the brain, heart, skin, bowel, gonads, prostate, breasts,immune cells, bones, kidneys, and parathyroid glands.[19] Numerous epidemiological studies have demonstrated the critical role that vitamin D plays in several important physiological processes, includingimmunological control, cellular proliferation and differentiation, central nervous systemfunction, and cardiovascular health.[22-24] Besides regulating calcium and phosphorushomeostasis vitamin D is also enhance immunity against microbial pathogens.It also has role in autoimmune and metabolicdisorders. Many research groups haveinvestigated the potential of vitamin D in the managing and combating TB.[25,26]

Role of vitamin D in respiratory illness[37]

Vitamin D boosts the generation of natural antibodies, which strengthens immunity. It inhibits the overproduction of inflammatory cytokines and promotes macrophage activity. When a pathogen is encountered then vitamin D and its receptors works atthe alveolar macrophages, dendritic cells, and the epithelium of the airways. As a result, locally produced vitamin D reduces inflammation and tissue damage in the respiratory tract. The airway epithelium expresses high levels of 1 alpha hydroxylase, which converts it to active form. This conversion initiates the secretion of cathelicidin and other peptides in the epithelial cells that protect against infections. Alveolar macrophages express the enzyme 1 a-hydroxylase, which produces active vitamin D.Given that both T and B cell lymphocytes express VDR and 1 ahydroxylase, this active form also directly affects these cells. Interleukin (IL)-10, a cytokine with anti-inflammatory and immunosuppressive properties, is produced with the aid of vitamin D. Vitamin D produced by dendritic cells originating from monocytes inhibits the maturation and differentiation of cells while increasing the release of IL-10.

Considering the substantial effects RTI has on public health and the potentialadvantages of vitamin D as a cheap, secure, and easily accessible intervention, it is crucial to evaluate and compile the current data.[42,43] Comprehensive knowledge of the link between vitamin D deficiency and RTI should influence public health initiatives and clinical practices targeted at lowering the incidence of these diseases in young people.[45]Children's respiratory infections are the most prevalent illnesses and community exposure to respiratory infections ends at the preschool age. Thus, a thorough and up-to-date assessment of the literature is required due to the

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continually changing body of information.[46] In newborns and kids under five, low blood vitamin D levels are linked to a higher risk of respiratory infections and respiratory syncytial virus illness."

Material and methods

This cross-sectional observational study was performed over 177 patientsdiagnosed with a clinical diagnosis of lower respiratory tract infection in the Department of Pediatrics, at a tertiary center in Lucknow with study period of 14 months duration from December 2022 to February 2024 afterobtaining consent from the patients.

Inclusion and exclusive criteria: -

We included all children between 6 months to 5 years of age report to the hospital (OPD and IPD) with a clinical diagnosis of lower respiratory tract infection, radiologically confirmed cases of LRTI and Recurrent chest infections.

We excluded all children who are recipients of vitamin D supplementation within the last 4 Weeks, children with the presence of non-specific symptoms like poor growth, gross motor developmental delay and unusual irritability,children with suspected rickets and osteoporosis,chronic kidney disease or congenital cardiac disease,hepatic failure, malabsorption syndromes like cystic fibrosis and inflammatory bowel disease and on medication like anticonvulsants, glucocorticoids, and AIDS medication.

The study included detailed personal and present histories, with emphasis on symptoms such as fever, cough, dyspnoea, grunting, cyanosis, and feeding difficulties. Additional information gathered included feeding history, sun exposure, and socioeconomic status, which was categorized into very low, low, middle, and high levels. Adequate sun exposure was defined as spending more than 30 minutes per day outdoors between 10 AM and 3 PM. A complete clinical examination was performed, with specific attention given to chest examinations, anthropometric measurements, and signs of respiratory distress based on the child's age. Laboratory methods involved obtaining a 3 ml blood sample via venepuncture using trace element-free tubes under aseptic conditions. Samples were collected in a plain vial for vitamin D measurement using 25(OH) D ELISA. For this study, a cut-off value of >20 ng/ml was considered indicative of optimal vitamin D status.

Statistical analysis

All patient data were analysed using Statistical Package for Social Sciences (SPSS) version 23.0 for Windows. Quantitative data were presented as arithmetic mean ± standard deviation. Qualitative data was presented as frequencies (percentages). The chi-square test was used to compare categorical variables between the groups of lower respiratory tract infection patients and to find the association. A Probability (P) was calculated and considered as-value <0.05 was statistically significant.

Results

The data comprised a total of 177 cases, the most prevalent category was

Of Employed fathers, accounting for 66 (37.3%) of the group. Shopkeepers were the nextmost common at 51 (28.8%), followed by fathers in the labour sector (27 - 15.3%).Business owners and farmers made up the remaining portions, at 16 (9.0%) and 17(9.6%) respectively

The majority of patients' fathers belonged to the Lower socio-economic status,accounting for 71 patients (40.1%). This was followed by the Upper socio-economicstatus with 28 patients (15.8%), the Upper middle status with 27 patients (15.3%), theUpper lower status with 26 patients (14.7%), and the Lower middle status, whichincluded 25 patients (14.1%). Most of the children (6months to 5 years) had cough(98.3%) followed by fever, cold, difficulty in breathing and others as the presenting complaint. Pneumonia was the most common diagnosis followed by bronchiolitis. Most of the children were categorized as insufficient (66.75%).

Table 1: Distribution of the studied patients based on their symptoms

Symptoms	Number of patients (n=177)	Percentage (%)
Fever	157	88.7%
Cough	174	98.3%
Cold	151	85.3%
Difficulty in breathing	106	59.9%
Others	**88**	49.7%

Others =body-ache (1), chest pain (1), excessive crying (1) fast breathing (3), less oral intake (16), less urine output (2), loose stool (2), mucus in stool (1), noisy breathing (34) not gaining weight (1), pain abdomen (1), poor oral intake (1), post tussive vomit (23), puffiness over body (1)

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Table2: Prevalence of vitamin D deficiency in children with lower respiratory tract infections

Grade	Number of patients (n=177)	Percentage(100%)
Deficient (<12 ng/mL)	**32**	**18.1**
Insufficient (12-20 ng/mL)	**118**	**66.7**
Sufficient (21-100 ng/mL)	**27**	**15.3**
Toxic (>100 ng/mL)	**0**	**0**
Total	**177**	**100**

Table 3: Correlation between age and vitamin D deficiency and Gender and vitamin D deficiency

Category	Deficient(n=32)	Insufficient(n=118)	Sufficient(n=27)	p-value
6 months to 1year	13(40.6%)	57 (48.3%)	17 (63.0%)	0.220
1 year to 5years	19(59.4%)	61 (51.7%)	10 (37.0%)	
Male	19 (59.4%)	78 (66.1%)	18 (66.7%)	0.763
Female	13 (40.6%)	40 (33.9%)	9 (33.3%)	

Table 4: Correlation between diagnosis with vitamin D deficiency

Diagnosis	Deficient (n=32)	Insufficient (n=118)	Sufficient (n=27)	P value
Bronchiolitis	12 (37.5%)	31 (26.3%)	6 (22.2%)	0.725
Pneumonia	11 (34.4%)	52 (44.1%)	11 (40.7%)	
WALRI	5 (15.6%)	28 (23.7%)	7 (25.9%)	
HRAD	3 (9.4%)	6 (5.1%)	2 (7.4%)	
PulmonaryTB	1 (3.1%)	1 (0.8%)	1 (3.7%)	
Total	**32(100%)**	**118(100%)**	**27(100%)**	

WALRTI= Wheeze associated lower respiratory tract infection, HRAD= hyper-reactive airway disease

Table 5: Association of vitamin D deficiency in recurrent and non-recurrentlower respiratory tract infections and Association of Sun exposure and Vitamin D deficiency in lower respiratory tract infections

Variable	Category	Deficient (n=32)	Insufficient (n=118)	Sufficient (n=27)	p-value
H/o Previous Illness	**NRRTI**	6 (18.75%)	52 (44.1%)	12 (44.4%)	**0.029**
	RRTI	26 (81.25%)	66 (55.9%)	15 (55.6%)	
	Total	**32(100%)**	**118(100%)**	**27(100%)**	
Sun exposure	**Adequate**	10 (31.2%)	32(27.1%)	26 (96.3%)	**<0.001**
	Inadequate	22 (68.8%)	22 (68.8%)	1(3.7%)	
	Total	**32(100%)**	**118(100%)**	**27(100%)**	

RRTI=recurrent respiratory tract infections
NRRTI= non-recurrent respiratory tract infections

Discussion

The skin's natural production of vitamin D occurs when it is exposed toultraviolet B (UV-B) radiation, which has a wavelength of between 290 and 320 nm.The widespread perception is that India has an abundance of sunshine, which makes vitamin D deficiency and rickets rare there. That is untrue, though, as evidence indicates that vitamin deficiencies are very common.[18]According to recent research, vitamin D may aid in lung development, maintain lungfunction, and guard against pulmonary infections.[48]In the biggest investigation, data from the Third National Health and Nutrition Examination Survey (NHANES III) were used to compare FVC and FEV1 across healthy persons with varying levels of 25- (OH)-vitamin D (25-OHD). The results indicated that those with the highest 25-OHD levels had considerably higher baseline values.[49]**Garg D et al**[8]reported that the majority of the cases were from urban areas (58.75%) followed byrural (41.25%).Chandrashekhara and Pampana **S**[11]in their study found that 76.2%were from the lower class followed by class 3 and class 5 with 11.86% cases in eachclass.The most common symptom was a cough, reported by 174 patients (98.3%).This was followed by fever, which affected 157 patients (88.7%); cold, reported by 151patients (85.3%); difficulty in breathing, experienced by 106 patients (59.9%); andother symptoms, which were present in 88 patients (49.7%). **Raju A et al**[20]reported that based on observation, it appears that symptoms like fever and cough require a high enough level of vitamin D, raising the possibility that vitamin D levels play a part in immunological and

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inflammatory responses. **Garg D et al**[8]reported that of 80 cases, 42 had sufficient vitamin D levels, 31 had insufficient and 7 had deficient levels. Chandrashekhara, Pampana **S**[11] reported that 50 (84.7%) of the 59 children with LRTI who were recruited in the research had vitamin D insufficiency. Only 3 (5.08%) had adequate vitamin D levels, while 6 (10.1%) were insufficient. In this study, age-wise, 13 patients (40.6%) in the Deficient group were aged 6 months to 1 year, compared to 57 patients (48.3%) in the Insufficient group and 17 patients (63.0%) in the Sufficient group. Meanwhile, 19 patients (59.4%) in the Deficient group were aged 1 year to 5 years, compared to 61 patients (51.7%) in the Insufficient group and 10 patients (37.0%) in the Sufficient group. Gender-wise, 19 male patients (59.4%) were in the Deficient group, compared to 78 male patients (66.1%) in the Insufficient group and 18 male patients (66.7%) in the Sufficient group. Female patients included 13 (40.6%) in the Deficient group, 40 (33.9%) in the Insufficient group, and 9 (33.3%) in the Sufficient group. There was a statistically non significant correlation between age or gender and vitamin D deficiency among the patients (P>0.05). Our findings were similar to the findings of Chandrashekhara Pampana **S**[11]who reported that under a year-old children and male children are more likely to suffer from vitamin D insufficiency. **Esposito S and Lelii M**[21]after a review of the research on vitamin D and respiratory infections, it was discovered that a vitamin D deficiency increases the chance of developing TB, bronchiolitis, and recurrent otitis media. They concluded that keeping vitamin D levels in check would be an inexpensive and practical way to stop certain respiratory tract infections. **Afridi JK et al**[50]reported that children aged 1 to 3 years had 60.0% vitamin D deficiency and that of 4 to 5 years the deficiency was 60.3% and the difference was statistically insignificant (p>0.05). Based on gender 55.1% of males had vitamin D deficiency and 70.6% of females had vitamin D deficiency but the difference was statistically insignificant (p>0.05). Research by **Yakoob MY et al[38]**, Results showed that children who took vitamin D supplements had less recurrent wheezing. Notable is also the finding that vitamin D administration has been linked to a decrease in the severity of respiratory infections. As an example, research by **Bergman P et al[39]** discovered that vitamin D supplementation was linked to a lower incidence of severe bronchiolitis in babies.

Strengths and limitations

This study is an effort to establish correlation between the lower respiratory tract infections with vitamin D deficiency along with the clinical features, probable diagnosis and demography in this regard.This study was conducted on a very small group of children in a single area so findings couldn't be generalized. Limited literature is available in this regard.

Conclusion

Through this study, we can conclude that children with LRTIs exhibited a significantly higher proportion of vitamin D deficient subjects. Reduced blood vitamin D levels are a contributing factor in lower respiratory tract infections (LRTIs) because they are linked to reduced lung function. Vitamin D levels should be evaluated in children with recurrent RTIs and treated timely for better management of the problem. Our research highlights the need to measure blood vitamin D levels in a variety of respiratory conditions in order to start appropriate and prompt treatment interventions that reduce morbidity and death in children under five. The exposure to the sun at the appropriate time and its importance (30 min a day for 5-6 days/week between 10A.M -3 P.M) should be educated. Routine vitamin D supplementation should be advised from birth onwards.

Additional information

Disclosures

Human subjects: consent was taken from all participants' parents in the study. Prasad institute of medical sciences, Lucknow, Institutional Ethics Committee approved IEC/PIMS/10/2021-22. **Animal subjects:** all authors have confirmed that this study did not involve animal subjects or tissues. **Conflicts of interest:** In compliance with the ICMJIE uniform disclosure form, al, authors declare the following: **Payment/services info:** Authors declare that no financial support was received from any organization for the subjected work. **Financial relationship:** All authors have declared that they have no financial relationship at present or within the previous 3 years with any organizations that might have an interest in the subjected work. **Other relationships:** All authors have declared that there no other relationship or activities that could appear to have influenced the submitted work.

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