

Comparison of Vitamin D Levels in Children with Recurrent Respiratory Tract Infections with Normal Children

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ABSTRACT

Objective: To compare Vitamin D levels in children with recurrent respiratory tract infections with normal children.

Study Design: Case-control study.

Place and Duration of Study: Department of Paediatrics, Combined Military Hospital, Kharian, from Nov 2018 to Dec 2019.

Methodology: Sixty children fulfilling the inclusion criteria from the indoor department of Paediatrics, Combined Military Hospital, Kharian were included in the study. Thirty patients were in the recurrent respiratory tract infections-group (cases), while 30 were in the normal children- group (control). The blood sample was drawn from all the children included in the study to analyze serum 25 (OH) D levels. Data regarding Vitamin D levels were noted from both groups as per operational definition on an especially designed proforma.

Results: The mean age of cases was 5.63 ± 2.82 years, and controls were 5.66 ± 2.44 years. In cases-group, 20 (66.7%) cases had low vitamin D levels, and 10 (33.3%) cases had normal vitamin D levels, while in control subjects, 11 (36.7%) children had low vitamin D levels and 19 (63.3%) children had average vitamin D level. Cases with low vitamin D levels were statistically higher than controls, with the *p*-value of 0.02 with a significant odds ratio = 3.455 (95% CI: 1.95–9.99).

Conclusion: This study concludes that children with recurrent respiratory tract infections had low vitamin D levels compared with normal children.

Keywords: Respiratory tract infection, Nourishment, Odds ratio, Vitamin D.

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INTRODUCTION

Respiratory tract infections are one of the most common childhood illnesses (RTIs) globally, with an incidence of 17.8% to 18.7%. RTIs are more common in developing and third world countries with the population having a low socioeconomic status. Respiratory infections in children cause high mortality and morbidity.¹ If a child has more than six lower respiratory infections per year, then the child is said to have recurrent respiratory tract infections (RRTISs).² There are many risk factors that make infants and children prone to RRTIs, among them the small size of the airway, immune system immaturity and poor cough mechanism noteworthy.³ Recurrent respiratory tract infections adversely affect not only the health of a child but also have a substantial social and economic impact not only for the children but for the whole family in the form of hospitalization costs, school absenteeism, and the loss of working days among parents and

caregivers of affected individuals.⁴ Apart from genetic factors, certain environmental factors such as smog and nutritional deficiencies such as zinc deficiency can also weigh RRTIs. Both genetic and environmental factors weaken the host defense in addition to genetic factors and contribute to RRTIs.⁵

Vitamin D is essential for health. It is a lipid-soluble molecule that performs various functions. The important functions are bone health, muscle functions and immunity. It also helps to prevent chronic diseases by acting as an antioxidant.⁵ Vitamin D deficiency is associated with rickets, immune dysfunction and various chronic conditions.^{6,7}

Various studies confirm the role of vitamin D in reducing the effects of many illnesses such as oncological illnesses, autoimmune conditions, certain infections and some cardiovascular diseases.⁸ Some studies confirm that vitamin D deficiency is a significant risk factor for the development of diseases such as tuberculosis, otitis media and upper respiratory tract infections.⁹ Over the past few years the prevalence of RRTIs is gradually increasing. Vitamin D is implicated as a

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possible risk factor. This prompted us to compare the vitamin D levels in children with recurrent respiratory tract infections with normal children to get local evidence on this subject. The results of our study may help in the management of such children with recurrent respiratory tract infections.

METHODOLOGY

This case-control study was carried out at the Department of Paediatrics, Combined Military Hospital, Kharian, from November 2018 to December 2019. Sample size was calculated with 95% confidence level, alpha=5% (two-sided), power=80%, expected prevalence of Vitamin D levels in group-1; p1= 86% and expected prevalence of Vitamin D levels in group-2 p2= 35% 10. We took a sample size of 60 (30 patients in each group). 30 patients were included in recurrent respiratory tract infections-group (cases) while 30 patients were included in normal children-group (control). The sampling technique was non-probability consecutive sampling.

Inclusion criteria: Patients of age 1-10 years of either gender, with recurrent respiratory tract infections were included in the cases- group, and normal children were included in the control- group.

Exclusion criteria: Patients with a history of congenital disease on medical record and those who had received vitamin D supplementation within the last four weeks were excluded from the study.

Recurrent respiratory tract infections were defined as any of the following presented on medical records; ≥6 RTIs per year, ≥1 URTI per month from September to April and ≥3 LRTIs per year. Normal children were defined as those who did not fulfill the criteria of having recurrent respiratory tract infections. Respiratory tract infection was defined as children presented with fever >1000 F and any three of the following; nasal congestion (stuffy or congested nose), rhinorrhea, nasal discharge (may change from clear to white to green), nasal breathing, sneezing, sore throat and painful swallowing (odynophagia) (VAS>2) and vitamin D levels of <20 ng/ml by laboratory test.^{11,12} Sixty children fulfilled the inclusion criteria from the inpatient department of Paediatrics, CMH, Kharian and were included in the study after permission from the Institutional Review Board. Informed consent was taken from the parents or legal guardian after explaining the benefit of the study. Basic demographics like age, gender, and weight were noted on the weighing machine. The blood sample was drawn from all the children included in the study to analyze serum 25

(OH) D levels. Samples were sent to the same hospital laboratory. Data regarding Vitamin D levels were noted from both groups on the proforma.

Statistical Package for Social Sciences (SPSS) version 24.0 was used for the data analysis. Mean ± SD was presented for quantitative variables like age, vitamin D levels and weight. Frequency and percentage were calculated for a qualitative variables like gender and low Vitamin D levels. A chi-square test was applied to compare vitamin D levels in both groups, with p-value of ≤0.05 as significant. The odds ratio was calculated with the 95% confidence level.

RESULTS

We studied 60 patients, i.e. 30 patients in the case-group and 30 patients in the control-group. The mean age of cases was 5.63 ± 2.82 years, and controls were 5.66 ± 2.44 years. In cases, the mean weight was 16.20 ± 5.07 kg, and in controls, the mean weight was 17.22 ± 5.39 kg. The mean Vitamin D levels in cases were 21.490 ± 12.81 and in controls was 41.53 ± 31.12.

Among the case-group, 20 (66.7%) children were found to have low vitamin D levels, and 10 (33.3%) had normal vitamin D levels. In cases with low vitamin D levels statistically higher than controls, the p-value was 0.02 with the significant Odds ratio=3.455 (1.95-9.990), as shown in Table-I.

Table-I: Comparison of Low vitamin D levels in both study groups.

		Study Group	
		Case	Control
Low Vitamin D Levels	Yes	20 (66.7%)	11(36.7%)
	No	10(33.3%)	19(63.3%)

Table-II: Comparison of Low vitamin D levels in both study groups with respect to age groups (years).

Age (years)	Low Vitamin D levels	Study Group		p-value	Odds Ratio (95% CI)
		Case	Control		
1-5	Yes	8 (47.1%)	7 (43.8%)	0.849	1.143 (0.290-4.507)
	No	9 (52.9%)	9 (56.2%)		
6-10	Yes	12 (92.3%)	4 (28.6%)	0.001	30.00 (2.871-313.470)
	No	1 (7.7%)	10 (71.4%)		

In cases, 20 (66.7%) the cases had low vitamin D levels, and 10 (33.3%) cases had normal vitamin D levels, while in control subjects, 11 (36.7%) of the cases had low vitamin d levels and 19 (63.3%) of the cases had average vitamin D level. Vitamin D levels were significantly lower in cases in the age group 6-10 years. A comparison of low vitamin D levels in both study

groups with respect to age groups WAS shown in Table-II. Vitamin D levels were found to be significantly lower in female cases as compared to males. The frequency of low vitamin D levels in males and females WAS shown in Table-III.

Table-III: Comparison of Low vitamin D levels in both study groups with respect to gender.

Gender	Low vitamin D levels	Study Group		p-value	OR (95% CI)
		Case	Control		
Male	Yes	11 (55%)	8 (40%)	0.342	1.833 (0.522-6.434)
	No	9 (45%)	12 (60%)		
Female	Yes	9 (90%)	3 (30%)	0.006	21.00 (1.777-248.103)
	No	1 (10%)	7 (70%)		

DISCUSSION

This study showed that children with recurrent respiratory tract infections had low vitamin D levels compared with normal children. Hence, in managing children with recurrent respiratory tract infections, vitamin D supplementation is mandatory to improve their outcomes. Vitamin D supplementation is also mandatory for rickets, ataxia, diarrheal diseases, type-1 diabetes, tuberculosis, and coronary heart disease.

A cough lasting for more than four weeks is defined as a chronic cough. Chronic cough is a significant cause of childhood morbidity, parental concerns, and healthcare resources burden.^{13,14} Chronic cough affects 22% of the children. Depending upon the age, chronic cough has got a variety of causes. In pre-schoolers, the most common cause was persistent bacterial bronchitis (40%), followed by prolonged upper respiratory tract infection (URTI), while asthma, upper airway cough syndrome or gastroesophageal reflux disease constituted 10% of cases. In school children, the most common causes include asthma (25%), persistent bacterial bronchitis (23%), upper airways syndrome (20%) and gastro oesophageal reflux disease (5%).¹⁵ Inflammation of the airways increases the cough sensitivity and airway hyperactivity that causes chronic cough and may lead to bronchial asthma, which has gradually increased over the past decades.^{16,17} There is scarce data available on the therapeutic role of vitamin D in such diseases.¹⁸

Alladi *et al*, has showed in another study that the frequency of low Vitamin D levels in children with recurrent respiratory tract infections was 86% versus 35% in control groups.¹⁰ In the current study, we also

found similar statistics, i.e. among cases, 20 (66.7%) of the cases had low vitamin D levels, and 10 (33.3%) cases had normal vitamin D levels while in control subjects 36.7% had low vitamin D levels, and 63.3% had normal vitamin D level. In cases low vitamin D levels were statistically higher than controls, *p*-value <0.05 with significant Odds ratio = 3.455 (1.95-9.99).

Weinberger *et al*, has shown in a study that means vitamin D levels were 11.97 ± 4.04 ng/ml in children with recurrent respiratory tract infections as compared to 21.91 ± 18.79 ng/ml in control groups.¹³ We also found lower vitamin D levels in cases when compared with controls, i.e. the mean Vitamin D levels in cases were 21.490 ± 12.81 and in controls was 41.53 ± 31 .

In 2016, a prospective observational study was performed to determine the effect of serum vitamin D levels in RRTIs and chronic cough and its therapeutic role in preventing the recurrence of these conditions. Patients with low serum vitamin D levels were divided into two groups. The control group was started with vitamin D supplementation in addition to the conventional treatment and was followed for up to 6 months. The results showed that the mean serum 25(OH) vitamin D level in the recurrent respiratory infections group was 11.97 ± 4.04 ng/ml, the chronic cough group was 13.76 ± 4.81 ng/ml, and the control group was 31.91 ± 18.79 ng/ml. A statistically significant difference was found between the groups (*p*<0.05), and it was concluded that vitamin D deficiency has a role in RRTIs and chronic cough in children hence proving the therapeutic role of vitamin D administration in preventing the recurrence of these conditions.¹⁷

Recently a study was conducted to evaluate the vitamin D levels in patients with RRTIs with or without congenital or acquired immune deficiency and find a correlation between the vitamin D concentration and the immunoglobulin levels and response to hepatitis B vaccination. The study included 730 patients with RRTIs. The concentration of vitamin D, immunoglobulin levels and anti-Hbs Ab was determined. The study demonstrated that 11% of patients had IgG levels below the age-related reference values. Children with reduced IgG concentration were also found to have significantly lower vitamin D concentrations than children with normal IgG. However, there was no correlation between vitamin D levels and anti-Hbs Ab levels.¹⁸ After this study, it was added to the Central European practice guidelines that vitamin D levels should be monitored in patients with immunoglobulin deficiency, and intervention with vitamin-D

supplementation must be started in children with immune deficiency.

CONCLUSION

This study concludes that children with recurrent respiratory tract infections had low vitamin D levels compared with normal children.

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LIMITATIONS OF STUDY

This was a single-centre study with limited sample size. There is a requirement for a multicenter trial to validate the findings of this study further.

Conflict of Interest: None.

Authors' Contribution

SZ: Original research work, UA: Assistance in research work, SAS: Writing article, MM: Literature review, SN: Data collection, LG: Help in article submission.

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