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**Original Research Article**

# Role of serum vitamin D levels in patients with chronic tonsillitis in paediatric age group

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## ABSTRACT

**Background:** Vitamin D has got an important role in the defence system of our body. Objective were to assess the vitamin D levels in chronic tonsillitis and to find the association between the vitamin D deficiency and chronic tonsillitis in paediatric age group.
**Methods:** A total of 325 patients aged between 5 and 15 years were enrolled in this study who were diagnosed with recurrent tonsillitis between January 2021 and December 2022. The patients were followed-up for one year and the total episodes of acute tonsillitis were recorded. Patients were divided into three groups: Those who had <5 episodes per year (Group 1), those with >5 episodes per year (Group 2) in the last two years, those who come to OPD with otological complaint, with no tonsillar involvement as a control group (Group 3). The total number of recurrent tonsillitis episodes within one year, demographic characteristics and the mean serum 25 (OH) D levels of the groups were compared.
**Results:** The tonsil size according to the Brodsky Scale and the mean 25 (OH) D levels were compared and we found, lower vitamin D levels were significantly associated with larger tonsil sizes (p=0.023).
**Conclusions:** There is a statistically significant association between vitamin D levels and recurrent episodes of tonsillitis. As the grade of tonsillar enlargement increased, the level of vitamin D were reduced significantly, thus correlating vitamin D levels not only with recurrence, but also grade of tonsillar enlargement.

**Keywords:** Vitamin D, Tonsillitis, Serum

## INTRODUCTION

Many viruses apart from bacteria like *Pneumococci*, and *Streptococci* cause common cold, pharyngitis and acute otitis media. Under the influence of vitamin D, body releases several antimicrobials, cathelicidin and defensin to which these pathogens are sensitive.[1-4] The epithelium covering the respiratory tract coming in contact with the environment directly is protected by innate immunity.[5] Over the surface of macrophages various receptors like vitamin D receptor and toll like receptor are present, which governs the innate immunity.[6-8] Vitamin D regulates the level of the enzyme CYP27B1 which ultimately causes secretion of cathelicidin, a major antimicrobial.[9] In upper respiratory tract infection it is observed that active form of 1, 25 dihydroxy Vitamin D level decreases and it is this active form of vitamin D which regulates chemotaxis of Neutrophils and monocytes.[10-11] Therefore its deficiency causes decreased immunity and thus enhancement in respiratory tract infection.[12] Due to recurrent sore throat infections during childhood, chronic tonsillitis is one of the leading cause of frequent hospitalization.[13] Exact cause for chronic tonsillitis has not been identified yet but primarily

reasons for it are noncompliance of the patient to treatment, incomplete course of antibiotics, lack of absorption of antibiotics, antibiotic resistance, high bacterial load, bacterial biofilms and immune system deficiencies.[14] Chronic tonsillitis is the major reason for the tonsillectomies and this is linked with significant morbidities and sometimes mortality.[15]

This study was planned to assess the vitamin D levels in chronic tonsillitis to find the association between the vitamin D deficiency and chronic tonsillitis in paediatric age group.

## METHODS

The present observational study was conducted among 325 children in otolaryngology-head and neck surgery department of SMGS hospital GMC Jammu, who were diagnosed with recurrent tonsillitis between January 2021 and December 2022. The age of the patients ranged between 5 and 15 years.

The inclusion criteria included-age 5-15 years with recurrent tonsillitis, children who had not received vitamin D in the depot or daily basis within the past three months. The exclusion criteria included-patients with blood sample inadequate for Vitamin D testing and Patients with immunological diseases. The patients were followed-up for at least one year and the total episodes of acute tonsillitis were recorded. Serum 25 (OH) D levels were determined using enzyme linked immunosorbent assay (ELISA) method. According to Hollis et al and Brodsky et al 25 (OH) D levels below 50 nmol/l was defined as a deficiency, between 50 to 80 nmol/l as inadequacy, between 80 to 250 nmol/l as normal, between 250 to 325 nmol/l as excessiveness, and greater than 325 mol/l as toxicity.[16,17] According to the number of recurrent tonsillitis episodes they underwent, the patients were divided into three groups: Those who had <5 episodes of tonsillitis per year (Group 1), those with >5 episodes of tonsillitis per year (Group 2). Group 1 and Group 2 were considered as case group and Group 3 (with no tonsillar involvement) as a control group. Age, sex, chronic diseases, total number of recurrent tonsillitis episodes per year, serum 25 (OH) D levels, body mass index (BMI), tonsil size were recorded. The total number of recurrent tonsillitis episodes within 1-year, demographic characteristics and the mean serum 25 (OH) D levels of groups were compared. All patient's parents/guardian were informed about the study and written consent was obtained. The study protocol was approved by the institutional ethical committee.

### *Statistical analysis*

All data was entered in the MS excel sheet and was analysed using SPSS software. Appropriate statistician tool was used as per advice of statistician ($p<0.05$ considered significant).

## RESULTS

A total of 325 patients were examined in this study. Group 1 consisted of 112 patients (mean age7.23±3.12 years), while group 2 consisted of 146 patients (mean age 7.31 years±2.88 years). Group 3 consisted of 67 patients (mean age 7.27 years±3.41 years). In all groups, there was female preponderance.

The mean serum vitamin D levels of group 1, group 2, group 3 were 54.22±16.33 nmol/l, 49.17±15.11 nmol/l and 91.23±14.31nmol/l respectively (Table 1). Upon comparison, the serum vitamin D level in group 1 was statistically significant (p=0.0034) as compared to group 3 as well in group 2 as compared to group 3 (p=0.0023). The vitamin D level between group 1 was also statistically significant (p=0.0044) as compared to group 2.

**Table 1: Serum vitamin D levels in three groups.**

| Groups | Mean serum vitamin D levels (nmol/l) | P value |
|---|---|---|
| **Group 1** | 54.22±16.33 | |
| **Group 2** | 49.17±15.11 | <0.05 |
| **Group 3** | 91.23±14.31 | |

On comparing the size of tonsil with vitamin D levels we found that as the grades of tonsil size increased, vitamin D also decreased significantly in group 1 and group 2. Out of 112 patients in group 1, 52 patients had grade 1 Tonsil size with vitamin D levels of 58.2 nmol/l, 16 patients had grade 2 tonsil size with vitamin D levels of 51.4 nmol/l, 20 patients had grade 3 tonsil size with vitamin D levels of 52.7 nmol/l and 24 patients had grade 4 tonsil size with vitamin D levels of 53.1 nmol/l. Likewise out of 146 patients in group 2, 28 patients had grade 1 tonsil size with vitamin D levels of 48.22 nmol/l, 71 patients had grade 2 tonsil size with vitamin D levels of 49.1 nmol/l, 16 patients had grade 3 tonsil size with vitamin D levels of 49.7 nmol/l and 31 patients had grade 4 tonsil size with vitamin D levels of 49.4 nmol/l (Table 2).

On comparing cases (group 1 and 2) and controls (group 3) clinically and demographically we found that the mean age in case group was 7.23 years±3.12 years where as in control group it was 7.27 years±3.41 years with female to male ratio in case group 1.33:1 and in control group 1:1. The number of patients with deficiency of vitamin D in case group was ninety-nine and in the control group equal to twenty-two. The number of patients with inadequate vitamin D in case group was eighty-four and in the control group equal to twenty. The number of patients with sufficient vitamin D in case group was seventy-five and in the control group equal to twenty-five, their corresponding percentage and p values have been shown in (Table 3).

**Table 2: Correlation between tonsil size and mean 25 (OH) vitamin D levels.**

| Group/tonsil size | Grade 1, N (%) | Grade 2, N (%) | Grade 3, N (%) | Grade 4, N (%) | P value |
|---|---|---|---|---|---|
| **Group 1, 112** | 52 (58.2) | 16 (51.4) | 20 (52.7) | 24 (53.1) | <0.05 |
| **Group 2, 146** | 28 (48.22) | 71 (49.1) | 16 (49.7) | 31 (49.4) | |

**Table 3: Demographic and clinical comparison of case and control.**

| Variables | Case (Group 1 and 2), n=258 (%) | Control (Group 3), n=67 (%) | P value |
|---|---|---|---|
| **Mean age (years)** | 7.23±3.12 | 7.27±3.41 | 0.088 |
| **Female: male** | 1.33:1 | 1:1 | 0.061 |
| **Number of patients with deficiency of vitamin D** | 99 (38.37) | 22 (32.83) | 0.00047 |
| **Number of patients with inadequate vitamin D** | 84 (32.55) | 20 (29.85) | 0.0096 |
| **Number of patients with sufficient vitamin D** | 75 (29.06) | 25 (37.31) | 0.00029 |

**Table 4: Demographic and clinical comparison of group 1 and 2.**

| Variables | Group 1, n=112 (%) | Group 2, n=146 (%) | P value |
|---|---|---|---|
| **Mean age (years)** | 7.23±3.12 | 7.31±2.88 | 0.0721 |
| **Female: male** | 1.1:1 | 1.3:1 | 0.057 |
| **Number of patients with deficiency of vitamin D** | 42 (37.50) | 57 (39.04) | 0.00086 |
| **Number of patients with inadequate vitamin D** | 39 (34.82) | 45 (30.82) | 0.00053 |
| **Number of patients with sufficient vitamin D** | 31 (27.67) | 44 (30.13) | 0.00082 |

On comparing group 1 and 2 clinically and demographically we found that the mean age in group 1 was 7.23±3.12 years where as in group 2, it was 7.31±2.88 years with female to male ratio in group 1was 1.1:1 and in group 2 was 1.3:1. The number of patients with deficiency of vitamin D in group 1 group was 42 and in the group 2 group equal to 57. The number of patients with inadequate vitamin D in group 1 group was 39 and in the group 2 group equal to 45. The number of patients with sufficient vitamin D in group 1 group was 31 and in group 2 group equal to 44, their corresponding percentage and p values has been shown in (Table 4).

## DISCUSSION

Tonsil's mass of lymphoid tissue presents in oropharynx which prevent micro-organisms invasion into our body system through its surveillance mechanism. In children's tonsils are important; for many reasons such as size and position of tonsils may interferes with the phonation, therefore in early life, it has essential relationship with processing of words, respiration, nutrition, and if it gets infected, it affects mental physical development.

Tonsillitis is one of the leading causes of hospital OPD visits, and recurrent tonsillitis is the most common indication of tonsillectomy among children.[18,19] The exact cause and pathogenesis of recurrent acute tonsillitis are still not fully understood.[15]

Vitamins can be synthesized by the body, sometimes it must be provided through dietary supplements. Among fat soluble vitamins, vitamin D has got unique characteristics in the body.[20] Vitamin D deficiency is associated with diseases like autoimmune diseases, cardiovascular diseases, upper respiratory infection.[14] Vitamin D has got vital role in maintaining adaptive immunity.[15] Studies have shown the association between vitamin D levels and recurrent tonsillitis, adenotonsillar hypertrophy, tonsillopharyngitis, otitis media with effusion.[15,21,22] Factors which influences the vitamin D levels in children are maternal factors, environmental factors, dietary factors, exposure to sunlight, regional clothing habits.[22,23]

In present study the mean serum vitamin D levels of group 1-3 were 54.22±16.33 nmol/l, 49.17±15.11 nmol/l and 91.23±14.31nmol/l respectively. None of the patients had a serum 25 (OH) D level at toxic levels. The tonsil size according to the Brodsky scale and the mean 25 (OH) D levels have been shown in Table 2.[17] Based on our results, lower 25 (OH) D levels were significantly associated with larger tonsil sizes (p=0.023). Vitamin D deficiency causes an increase in VEGF expression in the tonsillar tissue which plays a role in the pathogenesis of recurrent/chronic tonsillitis. Moreover, it has been proposed that vitamin D inhibit the biofilm formation associated with recurrent tonsillitis. Gombart et al revealed that 1, 25 (OH) D increased the production of

cathelicidin peptides.[10] These peptides have been demonstrated to have a protective role against URTIs in the previous studies.[24-26] In another study, Ball et al compared tonsillectomies for recurrent tonsillitis and obstructive sleep apnea syndrome and concluded that AMPs of the tonsil surface epithelium, beta-defensin 1, 3- and cathelicidin decreased in the recurrent tonsillitis group.[17] Nseir et al found a positive correlation between recurrent group A *Streptococci* (GAS) tonsillitis and vitamin D deficiency.[14] In their study, the mean vitamin D level was 26±7 ng/ml (64.7±17.4 nmol/l) in the control group and 11.5±4.7 ng/ml (28.6±11.7 nmol/l) in the recurrent GAS group. Reid et al found that low vitamin D levels were linked with dark skin, high body mass index, and large tonsil sizes.[15] Although, this may be a potential explanation, further studies are required to assess the association of larger tonsil sizes with lower 25 (OH) vitamin D status. In another study, Esteitie et al measured the mean vitamin D levels as 28.4±7.7 ng/ml (70.7±19.2 nmol/l) in children undergoing adenotonsillectomy and 27.1±7.1 ng/ml (67.5±17.7 nmol/l) in the control group, suggesting no significant vitamin D deficiency between the two groups.[28] In addition, Yıldız et al measured serum vitamin D levels as 142.7±68.1 nmol/l in patients with recurrent tonsillitis and 192.3±56.1 nmol/l in healthy controls.[22] The authors concluded that the recurrent tonsillitis group had significantly lower vitamin D levels, compared to healthy children. This study results are consistent with our study. In all groups, there was female preponderance. While comparing the male and female with tonsillitis, it was found that in male and female of same age, females had more lower serum vitamin D levels than males. In randomized-controlled studies, vitamin D supplementation was shown to reduce the incidence of URTI.[29-30] On the contrary, Li-Ng et al was unable to retrieve any data indicating that the supplementation therapy reduces the incidence of URTIs.[31] In another study, Robertson et al reported that there was no relationship between vitamin D levels and URTIs and concluded that vitamin D supplementation did not reduce the incidence of URTIs in the Norwegian population.[32] On the other hand, there are some limitations to this study. Firstly, the seasonal changes of vitamin D levels were ignored. Secondly, the vitamin D levels were measured only once. An ideal study should encompass vitamin D level measurements at the same seasonal period. Although our laboratory test results are consistent with the studies conducted worldwide, we obtained different results from other studies of Yıldız et al and Aydın et al which were carried out among the Turkish children.[22,33] The reason behind this difference in results may be ignorance of the seasonal changes, laboratory testing and also not measuring VDR polymorphism.

### *Limitations*

In the current study we have not considered role of vitamin D receptor gene polymorphism, serum IgE levels and anti-streptolysin O titre which might be associated with an increase in risk of recurrent tonsillitis. The seasonal changes of vitamin D levels were ignored. So further studies are needed to assess the association of vitamin D deficiency with recurrent tonsillitis.

## CONCLUSION

The vitamin D levels of children who are potential candidates for recurrent tonsillitis and tonsillectomy were significantly lower than those with tonsillitis episodes less than five within one year. Evaluation of vitamin D levels in candidates for tonsillectomy may reduce the rates of tonsillectomy operations. Further studies with large sample size are needed to investigate the association between the vitamin D deficiency and chronic tonsillitis in paediatric age group.

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