

Association of Vitamin D level with Tuberculosis in Children: A Case Control Study

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Abstract:

Background: Tuberculosis (TB) is one of the most important public health problem affecting globally and specially South East Asia region. Several factors are associated with an increased risk of TB, including low socioeconomic status, poor nutrition, Vitamin D deficiency etc. This study tried to find out the association of Vitamin D deficiency and Tuberculosis prevalence.

Material and Methods: A Hospital based Observational study was conducted in the Department of Paediatrics, Mahatma Gandhi Medical College & Hospital, Jaipur from August 2022 to December 2023 among patients between 1-18 years diagnosed with tuberculosis (pulmonary and extra pulmonary) (cases) and compared with non TB patients (controls). Vitamin D level of both cases and control was noted.

Results: In the study majority of cases and control belonged to upper lower class and majority of cases (59.61%) were of pulmonary TB. Rest (40.38%) were of extra pulmonary TB among which TB lymphadenitis was most common (33.3%) presentation. Within the cases most of study population i.e. 21 (40.38) and 23 (44.23) fell in Vitamin D deficient and insufficient group respectively. However, most of the control i.e. 22 (42.31) fall in Vitamin D sufficient group and this difference was statistically highly significant. ($p < 0.001$).

Conclusion: Tuberculosis is more prevalent in Vitamin D deficient group linking Vitamin D deficiency a risk factor for developing TB. Hence routine Vitamin D measurement followed by Vitamin D supplementation must be done in Tuberculosis patients for rapid cure.

Keywords: Tuberculosis, Vitamin D Deficiency, Socio-economic status

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Introduction

Tuberculosis (TB) is one of the most important major challenges to global public health and the South East Asia region. According to the World Health Organization (WHO) 2023 Global Tuberculosis Report, India had the highest number of TB cases globally in 2022, accounting for 27% of all cases worldwide. [1]

Approximately 10-20% of all TB cases are reported in children and tuberculosis remains a profound health crisis, particularly affecting paediatric populations where microbiological confirmation is rare. [2] Children, especially older ones and adolescents, are one of the most common age group which is vulnerable to TB. The disease is mainly caused by *Mycobacterium tuberculosis*, with

Mycobacterium bovis and *Mycobacterium africanum* affecting less commonly. The progression of TB infection and disease is influenced by the imbalance between the virulence of the mycobacteria and the host's immune response. [3,4]

Several factors are associated with an increased risk of TB, including low socioeconomic status, poor nutrition, traditional or cultural practices, tobacco smoking, exposure to sputum smear-positive patients, and genetic susceptibility, such as vitamin D deficiency (VDD). [3]

Vitamin D supplementation has been suggested as a potential intervention for reducing the risk of acquiring latent tuberculosis infection, particularly

in populations with a high prevalence of vitamin D deficiency [5]. Furthermore, vitamin D supplementation has been reported to enhance host immunity against mycobacterial infection in individuals who are in close contact with patients with tuberculosis [6]. Vitamin D plays an important immunomodulatory role by promoting innate immune responses and enhancing the antimicrobial activity of macrophages against *Mycobacterium tuberculosis*. Therefore, vitamin D deficiency may contribute to increased susceptibility to tuberculosis and could potentially influence the clinical course of the disease. In view of the crucial role of vitamin D in immune function, the present study was undertaken to evaluate serum vitamin D levels in children and adolescents diagnosed with tuberculosis. The primary objective of the study was to estimate serum vitamin D levels among paediatric patients with tuberculosis and compare them with those of non-tubercular paediatric patients attending the outpatient department who served as controls.

Materials and Methods

A hospital-based observational study was conducted in the Department of Paediatrics, Mahatma Gandhi Medical College & Hospital, Jaipur, from August 2022 to December 2023 among patients aged 1–18 years diagnosed with pulmonary or extrapulmonary tuberculosis. Ethical approval was obtained from the Institutional Review Board, and written informed consent was obtained from the participants or their parents/legal guardians after providing complete information about the study. All eligible patients attending the hospital during the study period who fulfilled the predefined inclusion and exclusion criteria were enrolled, resulting in a total of 52 cases, along with an equal number of non-tubercular controls. Relevant demographic and clinical data were collected from all study participants using a predesigned proforma.

Inclusion criteria for cases included 1 to 18 year age of patients of either clinically diagnosed (on the basis of clinical features and radiography and/or contact history and/or Mantoux test) or microbiologically confirmed (on the basis of smear and/or culture and/or nucleic acid amplification test) involving lungs (Pulmonary TB) or involving organs other than lungs (Extra pulmonary TB). Patients already on vitamin D supplements, chronic renal diseases, chronic liver diseases, antiepileptic drugs affecting vitamin D metabolism or malabsorption syndromes were excluded from study. Non-Tubercular paediatric patients attending OPD were taken as control.

A detailed medical history was taken and physical examination was done. Necessary tests such as sputum for AFB/ NAAT, Mantoux test, chest X ray, CSF examination, lymph node biopsy etc necessary for diagnosis of Pulmonary TB or Extra Pulmonary TB was done and Vitamin D level was measured by lab test. Vitamin D level < 20 ng/ml, 20-30 ng/ml and >30 ng/ml were categorised as in Vitamin D deficient, insufficient and sufficient group.

Data was collected in MS Excel and analysed by statistical analysis (Statistical Package of Social Services version 20). The student's test (T) and Pearson Chi-square were done and the level of significance was set at $p < 0.05$.

Results

Majority of cases (51.9%) and controls (46.2%) belonged to age group 5-12 yrs. Least number of both cases (15.4%) and controls (19.2%) belonged to 13-18 years group. Male were predominant both in cases (61.53%) and controls (63.5%). Majority of study subject in both groups were male, with 61.53% in cases and 63.5% in controls. Females were 38.47% of the cases and 36.5% of the controls.

Table 1 Distribution of Cases and Control According to Socio-Economic Status (N=52)

Socio-Economic Status	Cases N (%)	Control N (%)	P
Upper	4 (7.69)	6 (11.53)	p>0.05
Upper middle	6 (11.53)	5 (9.61)	
Lower middle	11 (21.15)	12 (23.07)	
Upper lower	22 (42.30)	19 (36.53)	
Lower	9 (17.30)	10 (19.23)	
Total	52 (100)	52 (100)	

When categorising the study subject according to modified Kuppaswamy scale (2024 update) it was found that most of the study subjects both for cases (42.30%) and controls (36.53%) belonged to upper lower class followed by lower middle class with 21.15% and 23.07% population for cases and control respectively. But the distribution of study subject did not differ significantly among cases and control as per SES ($p>0.05$). On seeking contact history with TB patients, it was found that among cases 44.23% and among controls 26.92% reported having contact history. (Table 1)

Table 2: Distribution of Cases According to Type of Tuberculosis (N=52)

Diagnosis	Number (%)	Sub Type	Number (%)
Pulmonary	31 (59.61)	-	-
Extra Pulmonary	21(40.38)	TB Lymphadenitis	7 (33.33)
		CNS TB	5 (23.81)
		Pleural Effusion	4 (19.04)
		Abdominal TB	4 (19.04)
		Skeletal TB	1 (4.76)
Total	52 (100)	Total	21 (100)

Among the cases majority i.e. 31 (59.61%) were diagnosed with pulmonary TB and 21 (40.38%) were diagnosed with extra pulmonary TB. TB lymphadenitis was most common (33.3%) and

Skeletal TB was the least common (4.76%) extra pulmonary TB cases. (Table 2)

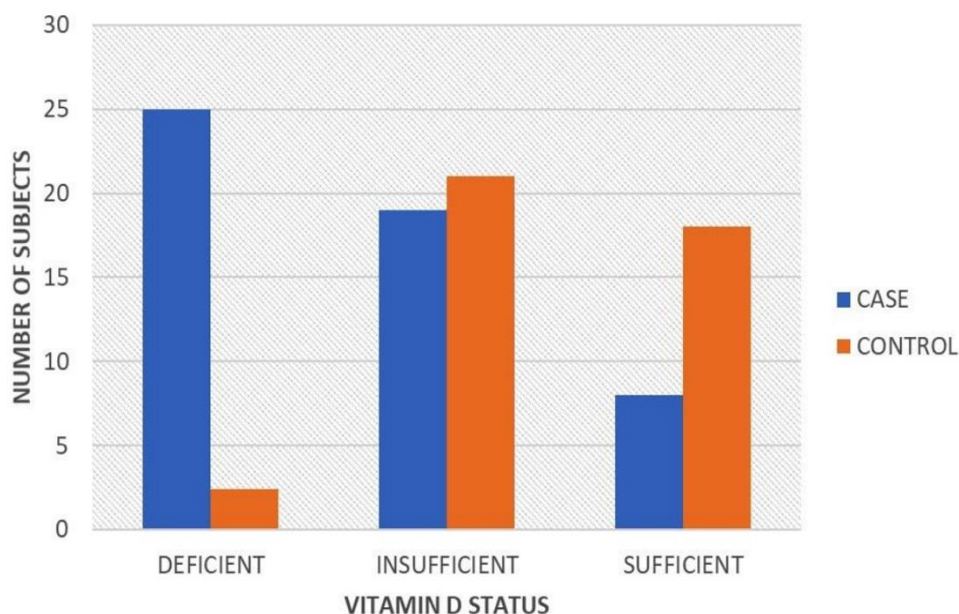
The mean vitamin D levels in case group was 22.59 ng/mL (SD 8.64), while the control group had a mean of 33.09 ng/mL (SD 11.69)

Table 3 Distribution of cases and control according to Vitamin D Level (N=52)

Vitamin D Level (ng/ml)	Cases N (%)	Control N (%)	P
Deficient (<20)	21 (40.38)	11 (21.15)	P<0.001 (S)
Insufficient (20-30)	23 (44.23)	19 (36.53)	
Sufficient (>30)	8 (15.38)	22 (42.31)	
Total	52 (100)	52 (100)	

Among the cases most of the study subject i.e. 21 (40.38) and 23 (44.23) fell in Vitamin D deficient and insufficient group respectively. However, most of the control i.e. 22 (42.31) fall in Vitamin D sufficient group and this difference was statistically

highly significant. ($p<0.001$). It means tuberculosis is more prevalent in Vitamin D deficient group linking Vitamin D deficiency a risk factor for developing TB. (Table 3) (Figure 1)

**Figure 1- Bar Diagram showing distribution of cases and control according to Vitamin D Level**

Discussion

This study tried to measure the level of Vitamin D among TB patients to find out the association of

Vitamin D levels with TB prevalence and its protective role in preventing its occurrence by comparing it with patients not suffering from TB.

The majority of both cases and controls fall within the "Upper Lower" class, with 42.30% of cases and 36.53% of controls. The "Lower" class includes 17.30% of cases and 19.23% of controls. This showing no significant difference (p -value > 0.05) in socio-economic status of subjects of case and control group. Similar was the result observed by Ageeru K et al [7], (2023 in India), 48.6% cases and 42.9% controls in upper lower class. Both groups were statistically similar in terms of their socioeconomic status, with a p -value of 0.281. Contrasting observations were found Aygun D et al, (2019 in Turkey) [8] 59.5% cases from lower socio-economic status.

Our study shows the distribution of vitamin D levels among paediatric tuberculosis (TB) cases and controls, were categorized into deficient (< 20 ng/ml), insufficient (20-30 ng/ml), and sufficient (> 30 ng/ml). In the case group, 40.38% of children (21 out of 52) have deficient vitamin D levels, compared to 21.15% of children (11 out of 52) in the control group. This indicates that vitamin D deficiency is significantly more prevalent among paediatric TB cases. Conversely, sufficient vitamin D levels are observed in only 15.38% of TB cases (8 out of 52), compared to 42.31% of the controls (22 out of 52). This significant disparity underscores that a much lower proportion of TB cases have adequate vitamin D levels. Ageeru k et al [7] (2023 in India) in a similar study found that among the cases, 74.3% (52 individuals) had vitamin D levels below 10 ng/mL, compared to 21.4% (15 individuals) in the control group. For the category of more than 20 ng/mL, 15.7% (11 individuals) of cases had sufficient levels, contrasted with 54.3% (38 individuals) of the controls. They found the mean vitamin D level in paediatric TB cases to be 10.4 (SD 6.74), while in controls it was 22.8 (SD 12.13) with the difference being statistically significant ($p = 0.001$). In our study the mean vitamin D levels in case group was 22.59 ng/mL (SD 8.64), while the control group had a mean of 33.09 ng/mL (SD 11.69) which is similar finding.

In a similar study done by Banerjee et al [9] (2024) found that the mean vitamin D was significantly lower in tuberculosis patients (34.45 ± 11.06 nmol/L) as compared to the non-tuberculosis controls (79.30 ± 18.54 nmol/L). This significantly indicated that Serum Vitamin D deficiency is a potential risk factor for Childhood tuberculosis. In our study we found tuberculosis to be more prevalent in Vitamin D deficient group.

Similar to our study Ahmed et al [10] (2015) in their retrospective study found that 73.6% of patients with Childhood Tuberculosis and 47.1 % of controls had low Vitamin D levels (deficiency and insufficiency) and concluded that children with evidence of exposure to Tuberculosis were more

likely to be associated with lower levels of vitamin D than control population. Again, Yani Fitry F et al (2017, Indonesia) [11], in their study on 276 paediatric tubercular patients (under 5 year of age) observed deficiency Vitamin D deficiency in 23.3 %, insufficiency in 43.5% and sufficiency in 33.3%.

Khandelwal D. et al (2014) [12] enrolled 266 paediatric tubercular children and evaluated them for vitamin D levels. They classified the study subject into 3 groups (deficient < 12 ng/ml, insufficient 12-20ng/ml, sufficient > 20 ng/ml) and concluded that 75% of paediatric tubercular patient were vitamin D deficient similar to our study.

Ludmir J. et al (2016, Gaborone, Botswana) [13] in their study divided the study subjects into 2 groups according to vitamin D levels below 20ng/ml and below 30 ng/ml. They found the median vitamin D level of 33.2ng/ml in cases and 30.9 ng/ml in controls which shows no significant difference between cases and controls. Though the finding of this study is in contrast to our study but the reason may be the fact that the study subjects were only under 2 year of age.

Vitamin D contributes to protection against TB inducing antimicrobial peptides and boosting concentrations of the antimicrobial peptide LL37 (cathelicidin) in human neutrophils. Vitamin D exerts its effects on innate immune responses by the promotion of autophagy and the suppression of tissue remodelling and lung matrix breakdown. A systematic review and meta-analysis on low serum vitamin D levels and tuberculosis in 2008 had included 7 studies with 531 participants and reported that low serum vitamin D levels were associated with a higher risk of active TB. Talat et al.¹⁴ (2010) investigated the role of vitamin D in TB progression and revealed that low serum vitamin D levels were associated with a five-fold increased risk for progression to TB. However, there is paucity of relevant epidemiological data regarding vitamin D deficiency in paediatric tuberculosis. [15]

Conclusion

The results of the present study indicate that children with tuberculosis (TB) exhibited a higher prevalence of vitamin D deficiency. This study provides new evidence supporting the idea that vitamin D deficiency was significantly associated with TB in the paediatric population and suggested that all children diagnosed with TB should be screened for vitamin D deficiency, although larger prospective studies are needed to determine whether supplementation improves clinical outcomes.

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