

## A STUDY OF VITAMIN D LEVELS IN NEWLY DIAGNOSED CASES OF CHILDHOOD TUBERCULOSIS IN THE SUB HIMALAYAN REGION

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### Abstract

**Background:** Tuberculosis (TB) impose significant treatment challenges because it requires longer treatment periods and come with high drug resistance. Vitamin D plays an important role in host defense. Vitamin D deficiency was found to be more common in untreated pulmonary and extrapulmonary TB patients than in healthy individuals without TB. This study aims to estimate the levels of serum Vitamin D in newly diagnosed cases of childhood tuberculosis and non-tuberculosis controls. We also aim to assess the potential of Vitamin D deficiency as a risk factor for childhood tuberculosis. **Materials and Methods:** The study included 41 childhood tuberculosis cases up to the age of 18 years who presented within one month of diagnosis. An equal number of age group matched non tuberculosis controls also included in the study. Subjects with Vitamin D < 50 nmol/L was considered vitamin D deficient and those with values 50-75 nmol/L was considered vitamin D insufficient. Vitamin D values between 75 – 250 nmol/L was considered sufficient. **Result:** The mean age of the tuberculosis patients was  $11.78 \pm 4.58$  years and mean age of non-tuberculosis controls was  $11.02 \pm 4.56$  years. Among total 41 tuberculosis patients, 13 (31.7%) were males and rest of 28 (68.3%) were females; whereas in non-tuberculosis controls, 20 (48.8%) were males and rest of 21 (51.2%) were females. The mean vitamin D was significantly lower in tuberculosis patients ( $34.45 \pm 11.06$  nmol/L) as compared to the non-tuberculosis controls ( $79.30 \pm 18.54$  nmol/L). This significantly indicated that Serum Vitamin D deficiency is a potential risk factor for Childhood tuberculosis. Vitamin D deficiency was significantly more prevalent in tuberculosis patients as compared to the non-tuberculosis controls. There was no significant difference in the mean vitamin D levels in pulmonary TB ( $36.55 \pm 12.34$ ) and extra pulmonary TB ( $32.80 \pm 9.91$ ). There was no significant difference in the vitamin D deficiency in pulmonary TB and extra pulmonary TB. **Conclusion:** Vitamin D Deficiency in tuberculosis patients was significantly lower compared to the non-tuberculosis controls indicating that Vitamin D deficiency as a significant risk factor for childhood tuberculosis.

## INTRODUCTION

Mycobacterium tuberculosis is the infectious agent that causes tuberculosis (TB), an illness that has proven difficult for humans to treat because it requires longer treatment periods and high drug resistance.<sup>[1]</sup> Only 61% of the 10.4 million TB cases that the WHO estimated were reported globally in 2016. The worst-affected area was South-East Asia, with 6.9% of the them being children. Approximately one-fourth of all cases worldwide were in India.

Worldwide, TB caused the deaths of over 239 000 children in 2015. In endemic countries, where children TB accounts for around 10–20% of all TB cases, paediatric TB is nevertheless a significant, albeit occasionally underappreciated, source of illness and mortality.<sup>[2]</sup>

Vitamin D is One important steroid molecule that is thought to have several biological functions in the human body. Vitamin D is known to play a function in mediating inflammatory diseases in addition to its effects on calcium and phosphorus balance. The

innate immune response is known to be significantly influenced by vitamin D, and a vitamin D deficiency may increase the chance of contracting a mycobacterial infection. Anti-microbial reaction of macrophages is mediated by a mechanism that depends on vitamin D. Moreover, it has been proposed that vitamin D influences the activation of T cells and other aspects of the adaptive immunological response to infection.<sup>[3]</sup>

Inadequate vitamin D level, vitamin D insufficiency or deficiency, is a global problem. It was estimated that one billion people globally have inadequate level of vitamin D.<sup>[4]</sup> Vitamin D deficiency was shown to be more common in untreated pulmonary and extrapulmonary TB patients than in healthy individuals without TB. There have been reports of vitamin D insufficiency among TB patients in several Asian and African nations, with prevalence rates varying from 8.5 to 62.7%. According to a research, 42% of schoolchildren do not get enough vitamin D.<sup>[5]</sup>

In 2016–18, the Ministry of Health and Family Welfare, Government of India, performed the Comprehensive National Nutrition Survey (CNNS), which included around 35,000 children from all over India, ages 1 to 19. The prevalence of vitamin D deficiency, which is defined as serum 25OHD < 12 ng/mL, was found to be lower than the proportions reported in hospital and community-based studies from India. It was found to be 14% among children aged 1-4 years, 18% among school-age children (5-9 years), and 24% among adolescents (10-19 years). The biggest gender gap was seen in teenagers, when 14% of boys and 34% of girls were found to be deficient.<sup>[6]</sup>

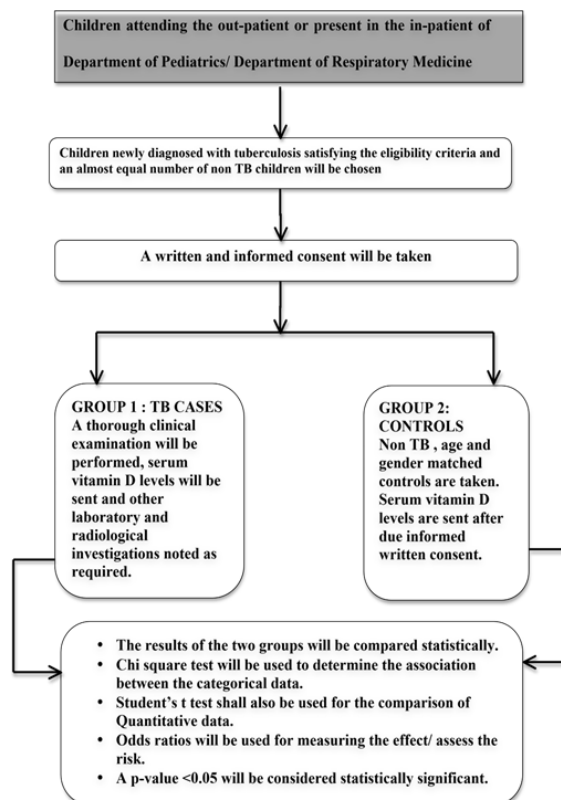
A quite a lot of studies have been conducted to find the vitamin D levels in TB patients. But not so many have been done in the childhood population and especially in India. Hence, we have particularly chosen this study. This study aims to estimate the levels of serum Vitamin D in newly diagnosed cases of childhood tuberculosis and non-tuberculosis controls. We also aim to assess the potential of Vitamin D deficiency as a risk factor for childhood tuberculosis.

## MATERIALS AND METHODS

**Study design:** Present study was an observational study that included 41 childhood tuberculosis cases up to the age of 18 years who presented within one month of diagnosis. An equal number of age group and gender-matched non tuberculosis controls also included in the study. Newly diagnosed TB patients was defined as those identified for the first time and those on Anti Tubercular Treatment (ATT) for a period of not more than 1 month [Figure 1].

**Serum Vitamin D levels:** Serum Vitamin D levels was measured in all cases as well as controls. Assessment of Vitamin D levels was done by drawing venous blood. The centrifuged sample was assessed for 25 (OH) vitamin D (active form) using

chemiluminescence method. The results were expressed in nmol/L and according to the US National Osteoporosis Foundation, those with <50 nmol/L was considered vitamin D deficient (VDD) and those with values 50-75 nmol/L was considered vitamin D insufficient. Vitamin D values between 75 – 250 nmol/L was considered sufficient.



**Figure 1: Workflow diagram of study.**

**Statistical Analysis:** The data was analyzed by SPSS software. Different statistical analysis was performed. Unpaired t test was used to compare the Serum Vitamin D levels between cases and controls. Chi square test was used for the comparison of Vitamin D deficiency amongst the tuberculosis cases and controls. Quantitative data were expressed in terms of mean  $\pm$  SD. A p-value <0.05 was considered statistically significant.

## RESULTS

Total 82 individuals were enrolled in the study among which 41 (50%) were tuberculosis patients and 41 (50%) were non-tuberculosis controls. The mean age of the tuberculosis patients was  $11.78 \pm 4.58$  years and mean age of non-tuberculosis controls was  $11.02 \pm 4.56$  years with no significant difference between the two. In both tuberculosis and non-tuberculosis group, 7 (17.07%) patients belong to age group of 0-5 years, 8 (19.51%) patients belong to age group of 6-10 years, 16 (39.02%) patients belong to age group of 11-15 years and 10 (24.39%) patients belong to age group of 16-18 years. Among total 41 tuberculosis patients, 13 (31.7%) were male and rest

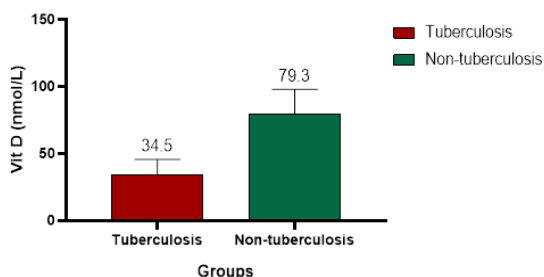
of 28 (68.3%) were female; whereas in non-tuberculosis controls, 20 (48.8%) were male and rest of 21 (51.2%) were female with no significant difference between the two groups in terms of gender distribution. In tuberculosis patients, monthly family income was  $\geq 15,197$  in 5 (12.2%) patients, 7,595-15,196 in 10 (24.4%) patients, 5,694-7,594 in 16 (39%) patients, 3,793-5,693 in 7 (17.1%) patients and 2,273-3,792 in 3 (7.3%) patients. In non-tuberculosis controls, monthly family income was  $\geq 15,197$  in 16 (39%) cases, 7,595-15,196 in 12 (29.3%) cases, 5,694-7,594 in 10 (24.4%) cases, and 3,793-5,693 in

3 (7.3%) cases. According to the Modified Kuppuswamy scale, in tuberculosis patients, 1 (2.4%), 2 (4.9%), 6 (14.6%), 20 (48.8%), and 12 (29.3%) patients belongs to upper, upper middle, lower middle, upper lower, and lower socioeconomic class respectively. In non-tuberculosis controls, 7 (17.1%), 18 (43.9%), 10 (24.4%), and 6 (14.6%) cases belongs to upper, upper middle, lower middle, and upper lower socioeconomic class respectively. Socioeconomic status was significantly high in the non-tuberculosis controls [Table 1].

**Table 1: Socioeconomic determinants of tuberculosis patients and non-tuberculosis controls.**

Variable	Domain	Tuberculosis (n = 41)	Non-tuberculosis (n = 41)	P value
Mean age		11.78 $\pm$ 4.58	11.02 $\pm$ 4.56	0.963
Age groups	0-5 years	7 (17.07 %)	7 (17.07 %)	0.999
	6-10 years	8 (19.51 %)	8 (19.51 %)	
	11-15 years	16 (39.02 %)	16 (39.02 %)	
	16-18 years	10 (24.39 %)	10 (24.39 %)	
Gender	Male	13 (31.7%)	20 (48.8%)	0.115
	Female	28 (68.3%)	21 (51.2%)	
Monthly income	$\geq 15,197$	5 (12.2%)	16 (39%)	0.017*
	7,595-15,196	10 (24.4%)	12 (29.3%)	
	5,694-7,594	16 (39%)	10 (24.4%)	
	3,793-5,693	7 (17.1%)	3 (7.3%)	
	2,273-3,792	3 (7.3%)	0	
Socioeconomic class	Upper	1 (2.4%)	7 (17.1%)	0.001*
	Upper middle	2 (4.9%)	18 (43.9%)	
	Lower middle	6 (14.6%)	10 (24.4%)	
	Upper lower	20 (48.8%)	6 (14.6%)	
	Lower	12 (29.3%)	0	

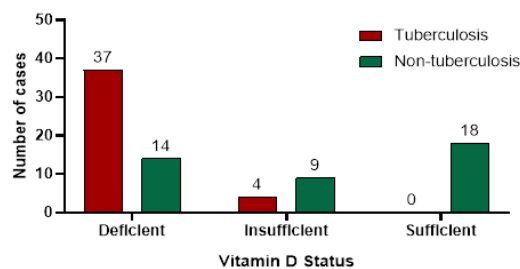
The mean vitamin D was significantly lower in tuberculosis patients (34.45  $\pm$  11.06) nmol/L as compared to the non-tuberculosis controls (79.30  $\pm$  18.54) nmol/L indicating that Vitamin D deficiency is a significant risk factor for childhood tuberculosis [Figure 2].



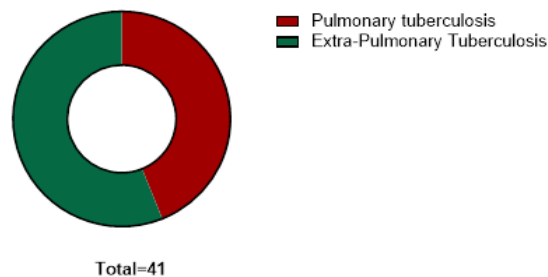
**Figure 2: Vitamin D level in tuberculosis patients and non-tuberculosis controls and Vitamin D deficiency as a risk factor for childhood tuberculosis.**

In tuberculosis patients, Vitamin D was deficient in 37 (90.24%) patients and insufficient in 4 (9.8%) patients; whereas in non-tuberculosis controls, vitamin D was deficient in 14 (34.1%) cases, insufficient in 9 (22%) cases and Sufficient in 18 (43.9%) cases. Vitamin D deficiency was significantly more prevalent in tuberculosis patients as compared to the non-tuberculosis controls [Figure 3].

Among total 41 cases of tuberculosis, there were 18 (49.90%) patients of pulmonary tuberculosis and 23 (56.10%) patients of extra-pulmonary tuberculosis [Figure 4].



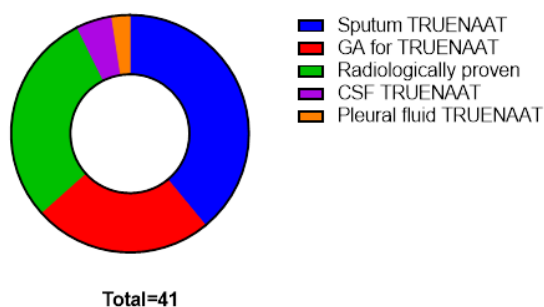
**Figure 3: Prevalence of Vitamin D deficiency in tuberculosis patients.**



**Figure 4: Types of Tuberculosis cases**

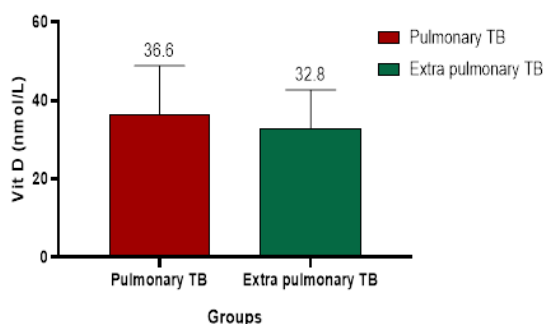
In the tuberculosis (cases) group, sputum Truenat positive was 16 (39%) cases, CSF Truenat positive

was 2 (4.9%) case, GA for Truenat positive was 10 (24.4%) case, pleural fluid Truenat positive was 1 (2.4 %) case, and radiologically proven were 12 (29.3%) cases [Figure 5].



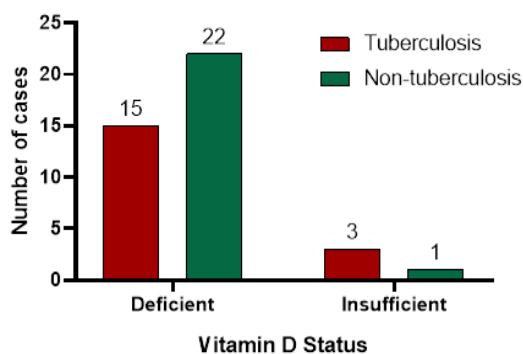
**Figure 5: Evidence of Tuberculosis (Test used: chi-square).**

There was no significant difference in the mean serum vitamin D levels in pulmonary TB ( $36.55 \pm 12.34$ ) and Extra pulmonary TB ( $32.80 \pm 9.91$ ) [Figure 6].



**Figure 6: Association between Vitamin D level and the type of tuberculosis and Vitamin D deficiency in pulmonary TB and extra pulmonary TB**

In pulmonary TB, Vitamin D was deficient in 15 (83.3%) patients and insufficient in 3 (16.7%) patients; whereas in extra pulmonary TB, Vitamin D was deficient in 22 (95.7%) patients and insufficient in 1 (4.3%) patient. There was no significant difference in the vitamin D deficiency in pulmonary TB and extra pulmonary TB [Figure 7].



**Figure 7: Vitamin D deficiency in pulmonary TB and extra pulmonary TB**

## DISCUSSION

Deficiency of vitamin D, an immunomodulator agent, is associated with increased susceptibility to tuberculosis in adults, but only limited studies are available in the Pediatric age group, especially regarding association of vitamin D with type and outcome of tuberculosis. We conducted this study to determine the vitamin D levels in children newly diagnosed with tuberculosis and its association with type of tuberculosis and to determine the potential of Vitamin D deficiency as a risk factor for Childhood tuberculosis.

In present study, the mean vitamin D was significantly lower in tuberculosis patients ( $34.45 \pm 11.06$  nmol/L) as compared to the non-tuberculosis controls ( $79.30 \pm 18.54$  nmol/L). Vitamin D deficiency in our study was significantly more prevalent in tuberculosis patients as compared to the non-tuberculosis controls. Results of present study was similar to most of the studies conducted in adult population that have suggested that 25-hydroxy vitamin D levels are lower in individuals with tuberculosis.<sup>[7-9]</sup>

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,<sup>[10]</sup> which again correlates with our study depicting Vitamin D deficiency as a risk factor for Childhood TB. A study done by Ho-Pham et al on Vietnamese population showed that prevalence of vitamin D insufficiency was 35.4 and 45.3 per cent in men and women with TB, respectively,<sup>[7]</sup> which again correlates with our study where 90.24 per cent of the Children with Tuberculosis were Vitamin D deficient. Other studies done on Africans, Pakistani, Ugandan, Gujarati Asians in West London and immigrant population from Sub-Saharan Africa living in Australia also suggested that 25-hydroxy vitamin D levels were low in adult TB patients.<sup>[8,9]</sup> Even in India, a case-control study done by Sashidharan et al. in Kerala observed very low levels of vitamin D in tuberculosis patients compared to healthy controls,<sup>[11]</sup> which is again similar to our study showing significant Vitamin D deficiency amongst children with Tuberculosis in the Sub Himalayan region. In the study by Nouri-Vaskeh et al., the prevalence of subnormal vitamin D levels in patients with TB was significantly higher than the control group. around 13.3% of patients were vitamin D deficient while 70% were vitamin D insufficient,<sup>[12]</sup> which is similar to the results of our study where 90.24% of the cases are Vitamin D deficient which was significantly higher than our control group which showed a 34.1% Vitamin D deficiency.

Studies from Pediatric population are scarce, but those available show lower 25-hydroxy vitamin D levels in children with tuberculosis as compared to controls.<sup>[10,13]</sup> A study done by Ganmaa et al showed

that 25-hydroxy vitamin D levels were low (<20 ng/ml) (or <50 nmol/L) in Mongolian children with tuberculosis ( $7 \pm 4$  ng/ml) (or  $17.5 \pm 10$  nmol/L) which is similar to the mean Vitamin D levels ( $34.45 \pm 11.06$  nmol/L) of the children with tuberculosis (cases group) in this present study from the Sub Himalayan region in India.<sup>[13]</sup> Likewise, another study which was done in Australia included refugee children and showed that 25-hydroxy vitamin D levels were significantly lower in children with latent tuberculosis and TB infection (35.9 nmol/L and 81.8%, respectively), the findings of which are again consistent with this present study from the Himalayan foothills of India, where mean Vitamin D levels in the children with TB group was ( $34.45 \pm 11.06$  nmol/L) and 90.24% of the cases (TB group) were Vitamin D deficient.<sup>[14]</sup> 73.6% of patients with Childhood Tuberculosis and 47.1% of controls had low Vitamin D levels (deficiency and insufficiency) in the study by Ahmad and Aslam,<sup>[15]</sup> which fall in line with this present study where 90.24% children of the Tuberculosis group and 34.1% of the control group had Vitamin D deficiency.

Rayaz et al. investigated the Vitamin D levels of children with tuberculosis and it was observed that 34% cases with severe vitamin D deficiency and 32% with mild vitamin D deficiency. The study of Rayaz et al. shows a certain variation from this present study where 90.24% of the children with Tuberculosis have Vitamin D deficiency which is significantly lower than the control group as opposed to the study by Rayaz et al. which shows only 34% cases with severe Vitamin D deficiency and 32% with mild Vitamin D deficiency.<sup>[16]</sup>

The median Vitamin D of the present study is 35.2 nmol/L (IQR: 26.18 – 40.08 nmol/L). This correlates similarly to the study by McArdle et al. McArdle et al. reported that median 25-OHD levels were higher in non-infected children (45.5 nmol/l) than in those with tuberculous infection (36.2 nmol/l) and TB disease (20.0 nmol/l).<sup>[17]</sup> Dabla et al. found that out of 25 cases of osteoarticular tuberculosis, there were 14 (56%) with deficiency of vitamin D.<sup>[18]</sup> A study evaluating vitamin D levels in bronchial asthma cases in 44 children (Bangalore, India) revealed similar findings with majority of controls (84%) having insufficiency of vitamin D.<sup>[19]</sup>

In present study, 37 (90.24%) patients were Vitamin D deficient and 4 (9.8%) patients were Vitamin D insufficient. In this present study among the children with pulmonary TB, Vitamin D was deficient in 83.3% patients and insufficient in 16.7% patients; whereas in extra pulmonary TB, Vitamin D was deficient in 95.7% patients and insufficient in 4.3% of the patients. Khandelwal et al. reported that most of the children with intrathoracic tuberculosis were either vitamin D deficient (69.9%) or insufficient (20.7%).<sup>[20]</sup> The findings of Khandelwal et al. are similar to this present study where, in the Children with Tuberculosis group, 83.3% of those having Pulmonary Tuberculosis had deficiency in the serum Vitamin D levels. Shah et al. also reported the similar

results indicating 85.3% of children with tuberculosis were found to have either insufficiency or deficiency of vitamin D.<sup>[21]</sup> Williams et al. also reported that vitamin D deficiency or insufficiency occurred in 80% of children with tuberculosis.<sup>[22]</sup> The studies of Shah et al,<sup>[21]</sup> and Williams et al,<sup>[22]</sup> are consistent with the results of the present study which shows 90.24% children in the Tuberculosis group to have Vitamin D deficiency. Parameswaran et al. conducted a cross-sectional observational study at a tertiary care teaching hospital in North-India over a period of one year and found that Vitamin D deficiency, insufficiency and sufficiency occurred in 70%, 17.5% and 12.5% children, respectively.<sup>[23]</sup> Tha et al. reported that 49.46% of children suffering tuberculosis had vitamin D deficiency.<sup>[24]</sup>

Many studies have evaluated the association of tuberculosis with low serum vitamin level and the immunomodulatory effects of vitamin D. But there are no reports available on association of severity of vitamin D deficiency and types of tubercular disease in children. A study conducted on South Korean adults showed that baseline serum 25-hydroxy vitamin D levels were low in all patients with tuberculosis and levels did not differ between patients with pulmonary and extrapulmonary tuberculosis (25). Similar results were observed in present study where there was no significant difference in the mean vitamin D levels in pulmonary TB ( $36.55 \pm 12.34$  nmol/L) and Extra pulmonary TB ( $32.80 \pm 9.91$  nmol/L). Also, there was no significant difference in the vitamin D deficiency in pulmonary TB and extra pulmonary TB in current study. Findings of this study is also similar to those reported by the Khandelwal et al. which did not observe any difference in the serum levels of 25-hydroxy vitamin D in the three types of the tuberculosis. The three types of intrathoracic tuberculosis described by Khandelwal et al. are Primary Pulmonary complex (PPC), Progressive Pulmonary Disease (PPD) and Pleural effusion (PE) (20). In the Khandelwal et al. study, the Primary Pulmonary Complex, Progressive Pulmonary Disease (PPD) and Pleural effusion (PE) showed 75%, 67% and 69% Vitamin D deficiency respectively which is quite similar to our present study where 83.3% of the children with pulmonary TB and 95.7% of the children with Extra Pulmonary TB had Vitamin D deficiency and there was no significant difference in the Vitamin D deficiency levels between these groups (20). Pareek et al. showed that the patients with extrapulmonary TB had lower mean vitamin D (25-OH D) concentration as compared with pulmonary TB and doubling in serum vitamin D concentration significantly reduced the risk of extrapulmonary TB, whereas our present study did not report any significant difference in the Vitamin D deficiency levels between the Pulmonary and Extra Pulmonary Tuberculosis group ( $p = 0.571$ ).<sup>[26]</sup>

The strengths of this study included use of a sensitive technique for 25-hydroxy vitamin D level estimation. But the study had some limitations. In the present

study, an adequate sample size was not achieved as the survey was time-bound. Hence, it is difficult to generalize the study findings. Further prospective studies with larger sample size are required to understand the relation between vitamin D and tuberculosis. We did not estimate vitamin D intake, duration of sun exposure and degree of skin pigmentation, all of which might have helped in explaining the low serum 25-hydroxy vitamin D levels. Patients were given a therapeutic dose of vitamin D, and they were not followed up. Further studies are required to study vitamin D's role in the prognosis and outcome of pulmonary tuberculosis.

## CONCLUSION

The vitamin D was significantly lower in tuberculosis patients as compared to the non-tuberculosis controls. Vitamin D deficiency was significantly more prevalent in tuberculosis patients as compared to the non-tuberculosis controls. However, there was no significant difference in the mean vitamin D levels in pulmonary TB and Extra pulmonary. Vitamin D levels in tuberculosis patients were significantly lower compared to the non-tuberculosis control indicating that Vitamin D deficiency as a significant risk factor for childhood tuberculosis. However, Vitamin D Deficiency did not differ significantly in pulmonary TB and extra pulmonary TB. Present study is a single-centric study, and it reflects a population of the foothills of the Himalayas in the Northern part of India. This justifies the need for future large-scale multi-centric studies at various parts of our country to see for the Vitamin D levels in a larger population of Childhood tuberculosis in India and to develop a greater association between Vitamin D deficiency and childhood tuberculosis which would aid clinicians in the management of childhood tuberculosis. Thus, to generalize the associations of this study we need larger multi - centric randomize controlled trials in different populations of our country.

## REFERENCES

1. WHO. Global tuberculosis report 2021. World Health Organization. 2022.
2. Kashyap B, Gupta N, Dewan P, Hyanki P, Singh NP. Hypovitaminosis D in pediatric tuberculosis: a clinicomicrobiological study. *The Egyptian Journal of Chest Diseases and Tuberculosis*. 2022;71(1):9-14.
3. Junaid K, Rehman A. Impact of vitamin D on infectious disease-tuberculosis-a review. *Clinical Nutrition Experimental*. 2019;25:1-10.
4. Wakayo T, Belachew T, Vatanparast H, Whiting SJ. Vitamin D deficiency and its predictors in a country with thirteen months of sunshine: the case of school children in central Ethiopia. *PLoS One*. 2015;10(3):e0120963.
5. Aranow C. Vitamin D and the immune system. *J Investig Med*. 2011;59(6):881-6.
6. UNICEF. Comprehensive national nutrition survey: 2016–2018. 2019.

7. Ho-Pham LT, Nguyen ND, Nguyen TT, Nguyen DH, Bui PK, Nguyen VN, et al. Association between vitamin D insufficiency and tuberculosis in a Vietnamese population. *BMC Infect Dis*. 2010;10:1-8.
8. Banda R, Mhemedi B, Allain T. Prevalence of vitamin D deficiency in adult tuberculosis patients at a central hospital in Malawi. *The International journal of tuberculosis and lung disease*. 2011;15(3):408-10.
9. Wilkinson RJ, Llewelyn M, Toossi Z, Patel P, Pasvol G, Lalvani A, et al. Influence of vitamin D deficiency and vitamin D receptor polymorphisms on tuberculosis among Gujarati Asians in west London: a case-control study. *The Lancet*. 2000;355(9204):618-21.
10. Nnoaham KE, Clarke A. Low serum vitamin D levels and tuberculosis: a systematic review and meta-analysis. *Int J Epidemiol*. 2008;37(1):113-9.
11. Sasidharan P, Rajeev E, Vijayakumari V. Tuberculosis and vitamin D deficiency. *The Journal of the Association of Physicians of India*. 2002;50:554-8.
12. Nouri-Vaskeh M, Sadeghifard S, Saleh P, Farhadi J, Amraii M, Ansarin K. Vitamin D deficiency among patients with tuberculosis: a cross-sectional study in Iranian-Azari population. *Tanaffos*. 2019;18(1):11.
13. Ganmaa D, Giovannucci E, Bloom BR, Fawzi W, Burr W, Batbaatar D, et al. Vitamin D, tuberculin skin test conversion, and latent tuberculosis in Mongolian school-age children: a randomized, double-blind, placebo-controlled feasibility trial. *The American journal of clinical nutrition*. 2012;96(2):391-6.
14. Gray K, Wood N, Gunasekera H, Sheikh M, Hazelton B, Barzi F, et al. Vitamin D and tuberculosis status in refugee children. *The Pediatric infectious disease journal*. 2012;31(5):521-3.
15. Ahmed MI, Aslam M. A study of vitamin D status in children with tuberculosis in Peterborough, United Kingdom. *Int J Contemp Pediatr*. 2015;2(2):69-71.
16. Rayaz S, Bizenjo A, Hussain M, Iqbal M. Frequency of Vitamin D Deficiency in Children with Tuberculosis. *Pakistan Journal of Medical & Health Sciences*. 2022;16(11):302-.
17. McArdle A, Keane D, Seddon J, Bernatoniene J, Paton J, McMaster P, et al. Vitamin D deficiency is associated with tuberculosis disease in British children. *The International Journal of Tuberculosis and Lung Disease*. 2020;24(8):782-8.
18. Dabla PK, Agarwal A, Mishra M, Sharma S. Vitamin D deficiency among pediatric osteoarticular tuberculosis patients. *Journal of Clinical Orthopaedics and Trauma*. 2016;7:147-9.
19. Somashekar A, Prithvi AB, Gowda MV. Vitamin D levels in children with bronchial asthma. *Journal of Clinical and Diagnostic Research: JCDR*. 2014;8(10):PC04.
20. Khandelwal D, Gupta N, Mukherjee A, Lodha R, Singh V, Grewal HM, et al. Vitamin D levels in Indian children with intrathoracic tuberculosis. *Indian J Med Res*. 2014;140(4):531-7.
21. Shah I, Tolani D, Bansal N, Shetty NS. Vitamin D Status in Children with Tuberculosis. *The Indian Journal of Pediatrics*. 2019;86:1146-.
22. Williams B, Williams AJ, Anderson ST. Vitamin D deficiency and insufficiency in children with tuberculosis. *The Pediatric infectious disease journal*. 2008;27(10):941-2.
23. Parameswaran P, Vaidya PC, Attri SV, Angurana SK, Vignesh P, Singh M. Vitamin D Deficiency: Prevalence and Association with Intrathoracic Tuberculosis in Indian Children. *The Indian Journal of Pediatrics*. 2021;88:276-.
24. Tha STM, Rasheed S, Mukhtar A, Rasheed M, Naz S, Javaid MF. Vitamin D Deficiency in Children with Tuberculosis: A Cross Sectional Study. *Pakistan Journal of Medical & Health Sciences*. 2022;16(09):604-.
25. Kadam NS, Chiplonkar SA, Khadilkar AV, Fischer PR, Hanumante NM, Khadilkar VV. Modifiable factors associated with low bone mineral content in underprivileged premenarchal Indian girls. 2011.
26. Pareek M, Innes J, Sridhar S, Grass L, Connell D, Woltmann G, et al. Vitamin D deficiency and TB disease phenotype. *Thorax*. 2015;70(12):1171-80.