

## Original Research Article

# The study of correlation between vitamin D and tuberculosis in newly detected tuberculosis: pulmonary and extra pulmonary patients attending to K R hospital, Mysuru, Karnataka, India

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## ABSTRACT

**Background:** Tuberculosis is an infectious disease caused by *Mycobacterium tuberculosis*, which has posed a constant challenge to mankind in its treatment due to increasing resistance and longer duration of treatment. The newer approach is to look towards strengthening host immune system along with suppressing the organism.

Aim of the study was to assess the existence of Vitamin D deficiency in TB patients and aid in the strategies and development of newer improvised approaches in the treatment of TB. Objectives of the study was to estimate vitamin D levels in Tuberculosis (pulmonary and extrapulmonary) patients, assess Correlation between vitamin D and pulmonary tuberculosis and to assess correlation between Vitamin D and extrapulmonary Tuberculosis.

**Methods:** This is a descriptive cross-sectional study. The study consisted of 80 tuberculosis patients both extrapulmonary and pulmonary. Blood samples were analysed for Vitamin D levels and results were compared with age and sex matched controls. Results were analysed using SPSS software.

**Results:** The cases included patient in the age group of 18-60 year with the mean age being  $42.34 \pm 14.65$  year. Of the 80 tuberculosis patients 42 were diagnosed with pulmonary tuberculosis and 38 constituted extrapulmonary tuberculosis. The mean Vitamin D in cases was  $24.82 \pm 12.33$  and controls was  $34.41 \pm 6.19$ . Among the cases 25 (31.3%) subjects had Vitamin D levels  $<20$  pg/ml and none of the controls had levels  $<20$  pg/ml. The mean Vitamin D level in pulmonary Tb patients was found to be  $24.29 \pm 11.86$  pg/ml and Extra-pulmonary Tb was  $25.40 \pm 12.96$  pg/ml. The unpaired t-test was statistically significant with p value of 0.005.

**Conclusions:** This study has emphasized on the presence of nutritional deficiency in TB patients and necessity to correct them to achieve a better cure rate.

**Keywords:** Extrapulmonary tuberculosis, Immunomodulatory effect, Tuberculosis, Vitamin D

## INTRODUCTION

Tuberculosis is an infectious disease caused by *Mycobacterium tuberculosis*, which has posed a constant challenge to mankind in its treatment due to increasing resistance and longer duration of treatment. The present TB-HIV epidemics have added to the woes of the treatment. It has been a disease of global burden with India having a significant contribution of one fourth of global TB burden.<sup>1</sup> Though the mortality and morbidity

have come down with the advent of DOTS, further research is needed to bring down the disease severity in future era.

The Discovery of *Mycobacterium Tuberculosis* dates back to 150 million years ago.<sup>2</sup> Ancient Greeks described TB as "Phtisis", the works of Hippocrates document Phtisis to be a fatal disease in young adults and his work does elaborate classical signs and symptoms along with characteristic lung lesions.<sup>3</sup> It was in 1882 that Robert

Koch isolated *Mycobacterium Tuberculosis* bacillus and started a new renaissance in the field of TB. In the pre antibiotic era TB was initially treated with the advent of sanatoriums where people were isolated. With the days many novel approaches like artificial pneumothorax, thoracoplasty, plombage and lung resection was used.<sup>4</sup> Vitamin D, a fat-soluble vitamin was one of the adjuncts in the TB treatment in pre antibiotic era. Administration of Cod liver oil which contained Vitamin D was associated with the increased cure rates.<sup>5,6</sup>

Development of streptomycin by Waksman in 1943 led to significant breakthrough into the treatment of TB.<sup>7</sup> Many other drugs like PAS, isoniazid, rifampicin were further added to the list. It was in 1962 the first TB programme was launched and underwent gradual changes until 1993 when RNTCP was launched.<sup>8</sup> This changed the outlook of dreaded TB into a controllable and curable disease. With the advent of RNTCP many newer molecules have been added to the list of drugs since then. With the increasing list of drugs there is also growing concern about increasing drug resistance.

The newer approach is to look towards strengthening the host immune system along with suppressing the organism. Vitamin D supplementation in TB is one such approach. The role of Vitamin D in bone metabolism and calcium homeostasis is well known. In addition, Vitamin D is known to have certain cellular activity and immunomodulatory effect.<sup>9,10</sup> Vitamin D is known to enhance both cellular and adaptive immunity thereby strengthening the host immune system.

Thus, the study was conducted in order to assess the existence of Vitamin D deficiency in TB patients and aid in the strategies and development of newer improvised approaches in the treatment of TB.

## METHODS

This is a descriptive cross-sectional prospective study conducted in the department of medicine, K R hospital Mysuru. The study duration period included from May 2019 to August 2019. The study consisted of 80 tuberculosis patients both extrapulmonary and pulmonary and 20 age and sex matched healthy controls.

All newly diagnosed TB patients attending to the hospital during the above said period giving informed consent were enrolled in the study. Newly diagnosed TB patients were defined as those identified for the first time and those on ATT for a period of 1 month. Diagnosis of TB was done with the help of sputum AFB, CBNAAT, pleural fluid analysis, CSF analysis, Ascitic fluid analysis, FNAC, lymph node biopsy and imaging techniques wherever required.

### Inclusion criteria

- Age >18 year.

- Newly diagnosed Sputum positive/radiologically proven pulmonary tuberculosis.
- Newly diagnosed Tubercular pleural effusion.
- Newly diagnosed lymph node Tuberculosis and Extrapulmonary TB.
- Patients on ATT for 1 month.

### Exclusion criteria

- Recurrent/reactivation of TB.
- Chronic lung disease.
- Chronic kidney disease patients.
- Diabetes/Hypertensive.
- Other immune compromised states.
- Pregnancy.

All newly diagnosed TB patients were further subjected to assessment of Vitamin D levels by drawing 2ml of venous blood. The centrifuged sample was assessed for 25 (OH) vitamin D (active form) using chemiluminescence method. The results were expressed in pg/ml and those with <20 pg/ml were considered to be vitamin D deficient (VDD) and those with values 20-30pg/ml were considered to be vitamin D insufficient. The patients suffering from chronic lung disease, Chronic renal and liver disease were excluded from the study population.

### Data analysis and interpretation

Data was entered into Microsoft Excel (Windows 7; Version 2007) and analyses were done using the Statistical Package for Social Sciences (SPSS) for Windows software (version 22.0; SPSS Inc, Chicago). Descriptive statistics such as mean and Standard Deviation (SD) for continuous variables, frequencies and percentages were calculated for categorical variables. Association between variables was analyzed by using Chi-Square test for categorical variables. Comparison of mean of quantitative variables were analyzed using unpaired t test. Bar charts and Pie charts were used for visual representation of the analyzed data. Level of significance was set at 0.05.

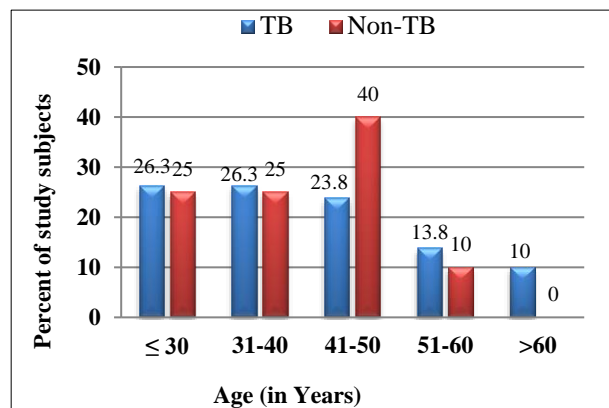
## RESULTS

The study consisted of 100 study subjects, 80 cases and 20 healthy controls. The cases included patients in the age group of 18-60 years with the mean age being 42 years. (Figure 1) The demographic details of both cases and controls are tabulated as follows (Table 1).

The clinical profile of the study population is depicted in the table as follows (Table 2).

Unpaired t-test was used to compare the clinical parameters among cases and controls. Total WBC count and albumin levels had a statistically significant difference between two groups indicating the presence of

significant infection as indicated by increased WBC count and a lower albumin level indirectly indicating a chronic malnourished state.



**Figure 1: Age distribution of study population.**

**Table 1: Demographic parameters of study population.**

Parameters	Case	Control
Age	42.34±14.65	39.5±9.58
Sex		
Male	58(72.5%)	5(25%)
Female	22 (27.5%)	15(75%)
BMI	20.38±4.89	23.76±3.25
Tobacco exposure	48%	40%
Alcohol	27.5%	35%
Diabetic	5 (6.3%)	-

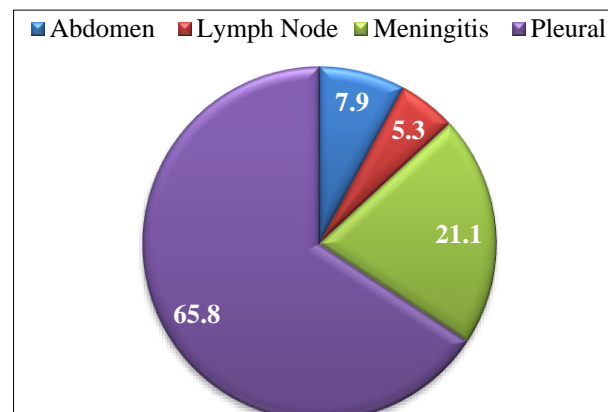
**Table 2: Clinical profile of study population.**

Parameters	Cases Mean (SD)	Controls Mean (SD)	p value
Haemoglobin	10.66(12.5)	11.05(1.60)	0.42
Oxygen saturation	94.69(4.22)	97.32(3.99)	0.45
WBC count	7673(2729)	5883(909)	0.005
Albumin	3.39(0.97)	3.92(0.74)	0.026

Of the 80 tuberculosis patients 42 were diagnosed with pulmonary tuberculosis (radiologically/microbiologically) and 38 constituted extrapulmonary tuberculosis. Of the 38 EPTB patient pleural effusion constituted 65% of EPTB followed by meningitis (21.1%), TB abdomen (7.9%) and lymph node (5.3%) (Figure 2).

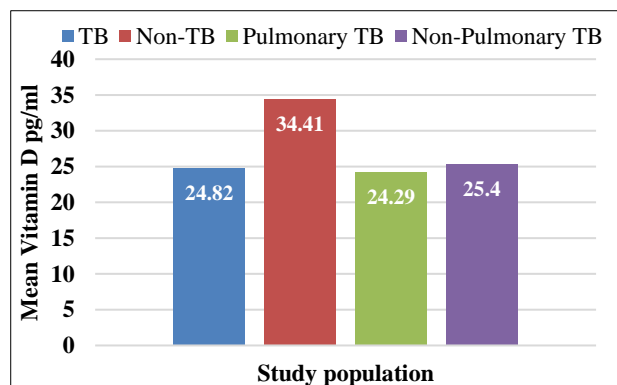
The vitamin D levels were assessed in both TB and Non-TB controls and those with values less than 20 pg/ml were considered to be Vitamin D deficient in both cases and controls. The mean Vitamin D in cases was 24.82±12.33 and controls was 34.41±6.19. Among the cases 25(31.3%) subjects had Vitamin D levels <20 pg/ml and none of the controls had levels <20 pg/ml. when unpaired-t test was carried out there was a

statistical significant difference between Vitamin D levels between cases and controls (p value-0.001), indicating a significant Vitamin D deficiency among cases.



**Figure 2: Distribution of EPTB in cases.**

The mean Vitamin D levels as depicted in Above graph (Figure 3) indicates a significant lower values of vitamin D when considered to controls. The mean Vitamin D level in pulmonary Tb patients was found to be 24.29±11.86 pg/ml and Extra-pulmonary Tb was 25.40±12.96 pg/ml. The unpaired t-test was statistically significant with p value of 0.005.



**Figure 3: Mean Vitamin D.**

Among the 25 study subjects with Vitamin D deficiency 13 had pulmonary TB and 12 had extra pulmonary TB. Those with Vitamin D insufficiency that is levels 20-30 Pg/ml where 17(40.5%) and 13(34.2%) in pulmonary and extrapulmonary TB respectively (Table 3).

**Table 3: Vitamin D levels in TB and EPTB.**

Vitamin D (pg/ml)	Pulmonary TB n (%)	Extra-Pulmonary TB n (%)
<20	13 (31.0)	12 (31.6)
20-30	17 (40.5)	13 (34.2)
>30	12 (28.6)	13 (34.2)
Mean (SD)	24.29 (11.86)	25.40 (12.96)
Range	5.25-55.29	0.80-59.35

Unpaired t Test, p Value = 0.005, Significant

Vitamin D levels were further evaluated in different forms of EPTB. It was found that the mean Vitamin D levels in case of tubercular meningitis ( $9.95 \pm 5.74$ ) was significantly lower when compared to other forms of EPTB (Table 4).

**Table 4: Mean Vitamin D levels in EPTB.**

Extra pulmonary TB	Mean Vitamin D levels Mean (SD)
Meningitis	9.95( $\pm 5.74$ )
Abdomen	18.31( $\pm 5.17$ )
Lymph node	37.52( $\pm 8.77$ )
Pleural effusion	30.23( $\pm 11.01$ )

## DISCUSSION

There is presence of Vitamin D deficiency in TB patients, the deficiency is more in pulmonary TB patients compared to extra-pulmonary TB patients. This study included predominantly male patients with mean BMI of 20 and presence of hypoalbuminemia, this shows the presence of malnourishment which might lead to nutritional deficiency of Vitamin D including many other nutrients which has made individuals more susceptible to the disease. The presence of disease itself forms a state of nutritional deficiency, this forms a vicious cycle which hampers the cure rate.

Similar studies have been conducted across the country however most of the studies included only pulmonary TB; study involved both pulmonary and extrapulmonary TB patients.<sup>11-14</sup>

The mean Vitamin D levels in Tubercular meningitis had significantly lower values when compared to other forms of TB indicating higher vitamin D deficiency associated with more severe disease.

A similar study was conducted by Karoli et al, which stated that hypovitaminosis was prevalent in pulmonary tuberculosis patient and prompt treatment and vitamin D supplementation would lead to early sputum negativity.<sup>15</sup>

Vitamin D tend to possess immunomodulatory activity. The active form of Vitamin D tends to act on VDRE (Vitamin D receptor element) which are present in respiratory epithelium and distributed all over the body. Vitamin D acting through them bring about increased expression of cathelicidin which bring about release of cytokines and activates macrophages leading to antibacterial and antiviral activity. Deficiency of this leads to increased respiratory tract infections.<sup>10,16-18</sup>

Study has certain limitations in that it couldn't follow up the patients and also interventions in the form of vitamin D supplementation to assess sputum conversions were not done. The study was conducted on a smaller

population which therefore might not represent the entire community.

## CONCLUSION

In conclusion study proves the presence of Vitamin D deficiency in both pulmonary and extrapulmonary TB patients. Study has emphasized on the presence of Low Vitamin D Levels in TB patients and necessity to correct them to achieve a better cure rate. Further interventional studies are required to assess sputum conversion rates with supplementation of Vitamin D.

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