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Original Research Article

Levels of vitamin D in tuberculosis and comparison of vitamin D level in severe variant of tuberculosis like tubercular meningitis, miliary tuberculosis, disseminated tuberculosis with non severe variant of tuberculosis like pulmonary tuberculosis, tubercular lymphadenitis etc in paediatric age group

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ABSTRACT

Background: Tuberculosis is deadliest disease killing nearly 2 million people every year. Before the etiologic cause of TB was determined by Koch, cod liver oil and sunlight, both sources of vitamin D, were used in treatment of tuberculosis. After discovery of antibiotics, anti-infectious value of vitamin D was ignored until increasing cost of antibiotics and rise in resistance led to the need to search for alternative and antibiotic-independent therapeutic strategies. This study shed light on vitamin D, which is very safe and inexpensive by adding vitamin D to antibiotic treatment, immune system can be boosted to help body to clear TB, rather than relying on antibiotics.
Methods: A prospective, observational, comparative study in which 62 TB patients were taken and vitamin D level were estimated.
Results: The results of study show that out of total 62 patients, 31 (50.00%) had deficient(<20ng/ml) vitaminD,23(37.10%) had insufficient(20-30ng/ml) vitamin D, 8(12.90%) had sufficient (>30ng/ml) vitamin D level. Out of 62 patients, 10(62.13%) had severe variety of TB and 52(83.87%) had nonsevere TB. Among the 52 patients, 24(46.2%) had deficient vitamin D, 20(38.5%) had insufficient vitamin D and 8(15.4%) had sufficient vitamin D. Among the 10 patients with severe TB, 7(70.00%) had deficient vitamin D, 3(30.00%) had insufficient vitamin D and none had sufficient vitamin D level.
Conclusions: Majority of children with tuberculosis demonstrated low serum levels of vitamin D (deficient and insufficient levels) suggest that vitamin D deficiency is risk factor of tuberculosis and very low levels of vitamin D were noted in severe variant of TB then non severe suggest that in severe form of tuberculosis vitamin D levels were less compared to nonsevere variant.

Keywords: Tuberculosis, Non severe variant (pulmonary tuberculosis, tubercular lymphadenitis), Severe variant (Tubercular meningitis, miliary tuberculosis, disseminated tuberculosis), Vitamin D

INTRODUCTION

Tuberculosis (TB) is a chronic infectious disease caused by *Mycobacterium tuberculosis*. Tuberculosis is one of the deadliest diseases in the world killing nearly 2 million people every year. More than ninety percent of all tuberculosis cases occur in the developing countries. Tuberculosis continues to be an important cause of

morbidity and mortality for children worldwide. Several estimates make use of an arbitrary calculation assigning 10% of the tuberculosis burden to children. Tuberculosis infection and disease among children are much more prevalent in developing countries. The annual risk of tuberculosis infection in developing countries in children is 2-5%. The estimated lifetime risk of developing tuberculosis disease for a young child infected with M. tuberculosis as indicated by positive tuberculin test is about 10%. About 5% of those infected are likely to develop disease in the first year after infection and the remaining 5% during their lifetime. Nearly 8-20% of the deaths caused by tuberculosis occur in children. Approximately 40% of infected children less than 1 year of age if left untreated develop radiologically significant lymphadenopathy or segmental lesions compared with 24% of children between 1 and 10 year and 16% of children 11 and 15 year of age. In India, over 100,000 children die from tuberculosis every year.[1] The emergence of drug-resistant organisms necessitates the development of new agents to enhance the response to antimicrobial therapy for active TB.

Vitamin D is a prohormone. The best-understood function of vitamin D is in the absorption of calcium from the small intestine, which helps to prevent diseases such as osteoporosis and osteomalacia in adults and rickets in children.

In the pre-antibiotic era, the role of vitamin D in prevention of infectious diseases has been very important. The cod liver oil, one of the most important nutritional source of vitamin D, was used both for treatment of rickets and tuberculosis (TB). Vitamin D is readily metabolized in the liver, to form 25 hydroxy-vitamin D [25(OH)D], the accepted measure of vitamin D status. Calcitriol, the active metabolite of vitamin D, induces anti mycobacterial activity in vitro.[2]

This metabolite modulates the host response to Mycobacterial infection by induction of reactive nitrogen and oxygen intermediate, suppression of matrix metalloproteinase enzymes implicated in the pathogenesis of pulmonary cavitation and induction of antimicrobial peptide catheliciden which induces autophagy.[3-6] vitamin D induces the gene encoding the antimicrobial peptide LL-37.[7] This peptide has potent bactericidal capacity against a number of important bacteria and viruses, including M. tuberculosis and influenza-virus.[8]

METHODS

It is a prospective, observational, comparative study carried out in dept. of pediatrics at GMERS Medical College and Hospital, Gotri, Vadodara between March 2018 to December 2019. After ethical and scientific approval, inform consent was taken from the parents of enrolled children and patients were enrolled as per inclusion and exclusion criteria.

Inclusion criteria

- All patients aged below 18 years who presented with symptoms and signs of Tuberculosis and in whom the diagnosis was documented by laboratory findings both indoor and outdoor patient.
- All newly diagnosed cases of Tuberculosis.

Exclusion criteria

- All patients above 18 years of age presented with Tuberculosis.
- All patients presented with tuberculosis with HIV.
- Refusal of the patients or parents to be included in the study.

All sputum or alternative specimens (Gastric lavage, Induced sputum, bronchoalveolar lavage) microscopy acid fast bacilli positive tuberculosis, all CBNAAT positive tuberculosis, patient diagnosed as TB clinically by radiological findings with blood investigations and histopathology finding etc. were enrolled and blood samples, details such as age, sex, demographic data, personal and family history, immunization history, nutritional supplementation history and detailed history of clinical features of tuberculosis were recorded on pre-designed and pre – tested proforma. Anthropometric measurement like weight, height were recorded in all cases. Venous blood samples were collected for 25 (OH) D3 levels estimation. Patient was not pricked separately for Vitamin D levels. Patients who were deficient in vitamin D were given standard regimen for treatment of vitamin D deficiency.

Data was entered in Microsoft excel sheet computer program and analysis was done using SSPS statistical package. Parameters such as rate, ratio and percentage were calculated. To test the significance suitable statistical test like chi square was applied. A probability of less then 0.05 was considered for a statistically significant association for all the analyses.

RESULTS

Out of 62 patients, 31 (50.00%) had deficient (<20 ng/ml) vitamin D level, 23 (37.10%) patients had insufficient (20-30ng/ml) vitamin D level and only 8 (12.90%) patients had sufficient (>30 ng/ml) vitamin D levels (Table 1).

Table 1: Distribution of the patients according to level of vitamin D.

Level of vitamin D	No. of patient	Percentage
Deficient (<20ng/ml)	31	50.00%
Insufficient (20-30ng/ml)	23	37.10%
Sufficient (>30ng/ml)	8	12.90%
Total	62	100.00%

Out of total 62 patients, 29 (46.77%) patients were females and 33 (53.23%) were males. Among these 29 female patients, 13 (44.83%) had deficient (<20 ng/ml) vitamin D level, 11 (37.93%) had insufficient (20-30 ng/ml) vitamin D level and 5 (17.24 %) had sufficient (>30 ng/dl) vitamin D level. Out of 33 male patients, 18 (54.55%) had deficient (<20 ng/ml) vitamin D level, 12 (36.36%) patients had insufficient (20-30 ng/ml) vitamin D level and only 3 had sufficient (>30 ng/ml) vitamin D level (Table 2).

Table 2: Distribution of the patients according to levels of vitamin D and gender profile.

Level of vitamin D	Male	Percentage	Female	Percentage
Deficient (<20ng/ml)	18	54.55%	13	44.83%
Insufficient (20-30ng/ml)	12	36.36%	11	37.93%
Sufficient (>30ng/ml)	3	9.09%	5	17.24%
Total	33	100.00%	29	100.00%

Chi square-1.096; Degree of freedom-2; p>0.05(0.5)

Table 3: Distribution of the patients according to level of Vitamin D and age groups.

Age Group		Vitamin D Level			
		Deficient (<20ng/ml)	Insufficient (20-30ng/ml)	Sufficient (>30ng/ml)	Total
0-5yr	Count	4	2	2	8
	% within age group	50.0%	25.0%	25.0%	100.0%
5-10yr	Count	7	4	0	11
	% within age group	63.6%	36.4%	.0%	100.0%
>10yr	Count	20	17	6	43
	% within age group	46.5%	39.5%	14.0%	100.0%
Total	Count	31	23	8	62
	% within age group	50.0%	37.1%	12.9%	100.0%

Chi square-3.263; Degree of freedom-4; p= 0.515

Out of total 62 patients, 8 (12.90%) were in the age group 0-5 years, 11 (17.74%) were in the age group 6-10 years and 43 (69.35%) were of age >10 years. Among the 8 patients in 0-5 years of age group, 4 (50.00%) of them had deficient (<20 ng/ml) vitamin D level, 2 (25.00%) had insufficient (20-30 ng/ml) vitamin D level and 2 (25.00%) had sufficient (>30 ng/ml) vitamin D level. Among the 11 patients in 6-10 years age group, 7(63.6%) had deficient (<20 ng/ml) vitamin D level, 4(36.4%) had insufficient (20-30 ng/ml) vitamin D level and none of them had sufficient (>30 ng/ml) vitamin D level. Among the 43 patients of >10 years, 20 (46.5%) had deficient (<20 ng/ml) vitamin D level, 17 (39.5%) had insufficient (20-30ng/ml) vitamin D level and 6 (14%) had sufficient (>30 ng/ml) vitamin D level. Age group and vitamin D levels were significantly not associated (p=0.5) (Table 3).

Out of total 62 patients, 11 (17.74%) were pre-term and 51 (82.26%) were full term deliveries. Among the 11 patients with pre-term delivery, 5 (45.5%) had deficient (<20ng/ml) vitamin D level, 5 (45.5%) had insufficient (20-30ng/ml) vitamin D level and 1 (9.1%) had sufficient (>30ng/ml) vitamin D level. Among the 51 patients with full term delivery, 26 (51%) had deficient (<20ng/ml) vitamin D level, 18 (35.3%) had insufficient (20-30ng/ml) vitamin D level and 7 (13.7%) had sufficient (>30ng/ml) vitamin D level (Table 4).

Table 4: Distribution of the patients according to level of Vitamin D and gestational age.

Level of vitamin D	Gestational age			
	Pre term	Percentage	Full term	Percentage
Deficient (<20ng/ml)	5	45.45%	26	50.98%
Insufficient (20-30ng/ml)	5	45.45%	18	35.29%
Sufficient (>30ng/ml)	1	9.09%	7	13.73%
Total	11	100.00%	51	100.00%

Chi square-0.458; Degree of freedom-2; p= 0.795

Out of 62 patients, 40 (64.52%) were of low birth weight <2.5 kg and 22 (35.48%) were of birth weight >= 2.5kg. Among the 40 patients with low birth weight <2.5kg, 23 (57.50%) had deficient (<20ng/ml) vitamin D level, 12 (30.00%) had insufficient (20-30ng/ml) vitamin D level and 5 (12.50%) had sufficient (>30ng/ml) vitamin D level. Among the 22 patients with >=2.5kg birth weight, 8 (36.4%) had deficient (<20ng/ml) vitamin D level, 11 (50.00%) had insufficient (20-30ng/ml) vitamin D level and 3 (13.6%) had sufficient (>30ng/ml) vitamin D level. Birth weight and level of vitamin D were not significantly associated p=0.245 (Table 5).

Table 5: Distribution of the patients according to level of vitamin D and birth weight.

Birth weight		Vitamin D Level			Total
		Deficient (<20ng/ml)	Insufficient (20-30ng/ml)	Sufficient (>30ng/ml)	
Normal (>=2.5 kg)	Count	8	11	3	22
	% within Bwt group	36.4%	50.0%	13.6%	100.0%
LBW (<2.5)	Count	23	12	5	40
	% within Bwt_group	57.5%	30.0%	12.5%	100.0%
Total	Count	31	23	8	62
	% within Bwt_group	50.0%	37.1%	12.9%	100.0%

Chi square-2.813; Degree of freedom-2; p= 0.245

Table 6: Distribution of the patients according to level of vitamin D and nutrition status.

Nutrition	Status		Vitamin D Level			Total
			Deficient (<20ng/ml)	Insufficient (20-30ng/ml)	Sufficient (>30ng/ml)	
	Normal (Median to -1SD)	Count	2	8	6	16
		% within nutrition status	12.5%	50.0%	37.5%	100.0%
	Mild (>1SD to -2SD)	Count	8	4	2	14
		% within nutrition status	57.1%	28.6%	14.3%	100.0%
	Moderate (>2SD to -3SD)	Count	17	5	0	22
		% within nutrition status	77.3%	22.7%	.0%	100.0%
	Severe (<-3SD)	Count	4	6	0	10
		% within nutrition status	40.0%	60.0%	.0%	100.0%
Total		Count	31	23	8	62
		% within nutrition status	50.0%	37.1%	12.9%	100.0%

Chi square-23.398; Degree of freedom-6; p= 0.001

Out of total 62 patients, 16 (25.81%) had normal nutritional status, 14 (22.58%) had mild malnutrition, 22 (35.48%) had moderate malnutrition and 10 (16.13%) had severe acute malnutrition. Among the 16 patients with normal nutritional status, 2 (12.5%) had deficient (<20) vitamin D level, 8 (50.00%) had insufficient (20-30 ng/ml) vitamin D level and 6 (37.5%) had sufficient vitamin D level. Among the 14 patients with mild malnutrition, 8 (57.1%) had deficient (<20 ng/ml) vitamin D level, 4 (28.6%) had insufficient (20-30 ng/ml) vitamin D level and 2 (14.3%) had sufficient (>30 ng/ml) vitamin D level. Among the 22 patients with moderate malnutrition, 17 (77.3%) had deficient (<20 ng/ml) vitamin D level, 5 (22.7%) had insufficient (20-30 ng/ml) vitamin D level and none had sufficient (>30 ng/ml) vitamin D level.Among the 10 patients with severe acute malnutrition, 4 (40%) had deficient (<20ng/ml) vitamin D level, 6 (60%) had insufficient (20-30 ng/ml) vitamin D level and none had sufficient (>30 ng/ml) vitamin D level (Table 6). Patient nutrition status and vitamin D level were significantly associated p<0.05 (0.001).

Out of total 62 patients, 31 (50.00%) had deficient (<20ng/ml) vitamin D level, 23 (37.10%) had insufficient (20-30ng/ml) vitamin D level, 8 (12.90%) had sufficient (>30ng/ml) vitamin D level. level of vitamin D were not significantly associated p=0.695 with diagnosis. Among the 39 patients of pulmonary TB 20 (51.3%) had deficient (<20ng/ml) vitamin D level, 12 (30.8% had insufficient (20-30ng/ml) vitamin D level and 7 (17.9 %) had sufficient(>30ng/ml) vitamin D level. Among the 6 patients of TB lymphadenitis 2 (33.3%) had deficient (<20ng/ml) vitamin D level,3 (50%) had insufficient (20-30ng/ml) vitamin D level and 1 (16.7 %) had sufficient(>30ng/ml) vitamin D level. Among the 2 patients of abdominal TB 1(50%) had deficient (<20ng/ml) vitamin D level,1 (50%) had insufficient (20-30ng/ml) vitamin D level and no one had sufficient(>30ng/ml) vitamin D level Among the 39 patients of pleural TB 1 (20.0%) had deficient (<20ng/ml) vitamin D level, 4 (80%) had insufficient (20-30ng/ml) vitamin D level and no one had sufficient (>30ng/ml) vitamin D levelAmong the 5 patients of TB meningitis 4 (80%) had deficient (<20ng/ml) vitamin D level, 1 (20.0%) had insufficient (20-30ng/ml) vitamin D level and no one had sufficient (>30ng/ml) vitamin D level. Among the 3 patients of military TB 2 (66.7%) had deficient (<20ng/ml) vitamin D level,1 (33.3%) had insufficient (20-30ng/ml) vitamin D level and no one had sufficient (>30ng/ml) vitamin D level. Among the 2 patients of disseminated TB 1(50%) had deficient (<20ng/ml) vitamin D level,1 (50%) had insufficient (20-30ng/ml) vitamin D level and no one had sufficient

(>30ng/ml) vitamin D level. Level of vitamin D were not significantly associated p=0.695 with diagnosis (Table 7).

Table 7: Distribution of the patients according to vitamin D level and diagnosis.

Diagnosis		Vitamin D Level			Total
		Deficient (<20)	Insufficient (20-30)	Sufficient (>30)	
Pulmonary TB	Count	20	12	7	39
	% within Diagnosis	51.3%	30.8%	17.9%	100.0%
TB lymphadenitis	Count	2	3	1	6
	% within Diagnosis	33.3%	50.0%	16.7%	100.0%
Abdominal TB	Count	1	1	0	2
	% within Diagnosis	50.0%	50.0%	.0%	100.0%
Pleural TB	Count	1	4	0	5
	% within Diagnosis	20.0%	80.0%	.0%	100.0%
TB Meningitis	Count	4	1	0	5
	% within Diagnosis	80.0%	20.0%	.0%	100.0%
Miliary TB	Count	2	1	0	3
	% within Diagnosis	66.7%	33.3%	.0%	100.0%
Disseminated TB	Count	1	1	0	2
	% within Diagnosis	50.0%	50.0%	.0%	100.0%
Total	Count	31	23	8	62
	% within Diagnosis	50.0%	37.1%	12.9%	100.0%

Chi square- 9.098; Degree of freedom-12; p= 0.695

Table 8: Distribution of the patients according to vitamin D level and severity of TB.

Varient		Vitamin D level			Total
		Deficient (<20)	**Insufficient (20-30)**	**Sufficient (>30)**	
Non severe variant	Count	24	20	8	52
	% within varient	46.2%	38.5%	15.4%	100.0%
Severe variant	Count	7	3	0	10
	% within varient	70.0%	30.0%	.0%	100.0%
Total	Count	31	23	8	62
	% within varient	50.0%	37.1%	12.9%	100.0%

Chi square- 2.654; Degree of freedom-2; p= 0.265

Out of 62 total patients, 10 (62.13%) had severe variety of TB and 52 (83.87%) had non-severe TB. Among the 52 patients, 24 (46.2%) had deficient (<20ng/ml) vitamin D level, 20 (38.5%) had insufficient (20-30ng/ml) vitamin D level and 8 (15.4%) had sufficient (>30ng/ml) vitamin D level. Among the 10 patients with severe TB, 7 (70.00%) had deficient (<20ng/ml) vitamin D level, 3 (30.00%) had insufficient (20-30ng/ml) vitamin D level and none had sufficient (>30ng/ml) vitamin D level (Table 8). Vitamin D level were significantly not associated with severity of TB p=0.265.

DISCUSSION

In this study out of 62 patients, 31 (50.00%) had deficient (<20 ng/ml) vitamin D level, 23 (37.10%) patients had insufficient (20-30ng/ml) vitamin D level and only 8 (12.90%) patients had sufficient (>30 ng/ml) vitamin D level(Table 1). Similar study was done by Khandelwal D, Gupta N, Mukherjee A, et al. in which Majority of Indian children with newly diagnosed intrathoracic tuberculosis were deficient in vitamin D. This study included 266 children, out of which 186 (69.9%) children were vitamin D deficient, 55 (20.7%) were insufficient and only 25 (9.4%) were vitamin D sufficient.[9] In this study hypovitaminosis vitamin D was seen in most of the patients.

In this study among 29 female patients, 13 (44.83%) had deficient (<20 ng/ml) vitamin D level, 11 (37.93%) had insufficient (20-30 ng/ml) vitamin D level and 5 (17.24 %) had sufficient (>30 ng/dl) vitamin D level. Out of 33 male patients, 18 (54.55%) had deficient (<20 ng/ml) vitamin D level, 12 (36.36%) patients had insufficient (20-30 ng/ml) vitamin D level and only 3 had sufficient (>30 ng/ml) vitamin D level(Table 2). Similar study done by Gordon CM et al. there was no significant difference in prevalence between adolescent girls and boys (26.0% vs 20.6%, p = 0.33) done among 307 adolescent age between 11-18 years.[10] In our study prevalence of vitamin D insufficiency were same in both male and female.

Out of total 62 patients, 8 (12.90%) were in the age group 0-5 years, 11 (17.74%) were in the age group 6-10 years and 43 (69.35%) were of age >10 years. Among the 8 patients in 0-5 years of age group, 4 (50.00%) of them had deficient (<20 ng/ml) vitamin D level, 2 (25.00%) had insufficient (20-30 ng/ml) vitamin D level and 2 (25.00%) had sufficient (>30 ng/ml) vitamin D level. Among the 11 patients in 6-10 years age group, 7(63.6%) had deficient (<20 ng/ml) vitamin D level, 4(36.4%) had insufficient (20-30 ng/ml) vitamin D level and none of them had sufficient (>30 ng/ml) vitamin D level. Among the 43 patients of >10 years, 20 (46.5%) had deficient (<20 ng/ml) vitamin D level, 17 (39.5%) had insufficient (20-30ng/ml) vitamin D level and 6 (14%) had sufficient (>30 ng/ml) vitamin D level(Table 3). Another study done by Isa HMA et al in which total of 593 healthy children were tested for serum 25(OH)D level. significantly greater proportion of primary-school children and adolescents had low vitamin D than preschool children Children's average vitamin D level decreased by–2.164 nmol/L for each year of age.[11] It has observed in our study school going age groups were more deficient in vitamin D levels ,out of 11 patient between 5-10 years all patients(100%) had hypovitaminosis and in >10 year age group out of 43 patient 37 (86%)patient had subnormal vitamin D level, this was because of increase in indoor activity and decrease in exposure to sunlight, diet modifications due to change in life style in modern society

Out of total 62 patients, 11(17.74%) were pre-term and 51 82.26%) were full term deliveries. Among the 11 patients with pre-term delivery, 5 (45.5%) had deficient (<20ng/ml) vitamin D level, 5(45.5%) had insufficient (20-30ng/ml) vitamin D level and 1(9.1%) had sufficient (>30ng/ml) vitamin D level. Among the 51 patients with full term delivery, 26 (51%) had deficient (<20ng/ml) vitamin D level, 18 (35.3%) had insufficient (20-30ng/ml) vitamin D level and 7 (13.7%) had sufficient (>30ng/ml) vitamin D level(Table 4). in study done by Gurmeet Singh et al.in which total 300 neonates were enrolled out of which 150 were term and 150 preterm. Overall 85.67% neonates were found to be deficient in vitamin D. Mean 25 (OH) levels in <32, 32≤37, ≥37 weeks gestation was 12.46, 17.96, 19.36 ng/dl respectively. Deficiency was present in 94.74%, 87.78%, 82.67% and neonates born <32 weeks, 32≤37 weeks, ≥37 weeks gestation respectively. No significant relationship was found between vitamin D and gestational age.

Out of 62 patients, 40 (64.52%) were of low birth weight <2.5 kg and 22 (35.48%) were of birth weight >= 2.5kg. Among the 40 patients with low birth weight <2.5kg, 23 (57.50%) had deficient (<20ng/ml) vitamin D level, 12 (30.00%) had insufficient (20-30ng/ml) vitamin D level and 5 (12.50%) had sufficient (>30ng/ml) vitamin D level. Among the 22 patients with >=2.5kg birth weight, 8 (36.4%) had deficient (<20ng/ml) vitamin D level, 11 (50.00%) had insufficient (20-30ng/ml) vitamin D level and 3 (13.6%) had sufficient (>30ng/ml) vitamin D level(Table 5). Birth weight and level of vitamin D were not significantly associated p=0.245. however 57.5 % of low birth weight babies were vitamin D deficient in our study like another study done by Saloni Arora et al stated that a very high prevalence of hypovitaminosis D (86% had vitamin D deficiency, and 9.5% had vitamin D insufficiency) among pregnant women in a tertiary care hospital of northern India and excellent correlation between maternal and fetal 25(OH) D levels. Hypovitaminosis D in mother was an independent risk factor associated with low birth weight babies.[13]

Out of total 62 patients, 16 (25.81%) had normal nutritional status, 14 (22.58%) had mild malnutrition, 22 (35.48%) had moderate malnutrition and 10 (16.13%) had severe acute malnutrition. Among the 16 patients with normal nutritional status, 2 (12.5%) had deficient (<20) vitamin D level, 8 (50.00%) had insufficient (20-30 ng/ml) vitamin D level and 6 (37.5%) had sufficient vitamin D level.Among the 14 patients with mild malnutrition, 8 (57.1%) had deficient (<20 ng/ml) vitamin D level, 4 (28.6%) had insufficient (20-30 ng/ml) vitamin D level and 2 (14.3%) had sufficient (>30 ng/ml) vitamin D level.Among the 22 patients with moderate malnutrition, 17 (77.3%) had deficient (<20 ng/ml) vitamin D level, 5 (22.7%) had insufficient (20-30 ng/ml) vitamin D level and none had sufficient (>30 ng/ml) vitamin D level.Among the 10 patients with severe acute malnutrition, 4 (40%) had deficient (<20ng/ml) vitamin D level, 6 (60%) had insufficient (20-30 ng/ml) vitamin D level and none had sufficient (>30 ng/ml) vitamin D level(Table 6).. Patient nutrition status and vitamin D level were significantly associated p<0.05 (0.001). Similar observation was noticed by Walli NZ et al was that VDD was found in 41 of 134 children (30.6%). The mean vitamin D level was 74.8 nmol/l. Sixty-four (48%) children were found to have severe stunting, of whom 20 (31.2%) were vitamin D deficient. Marasmic children had higher odds of VDD compared with other forms of malnutrition. The high prevalence of VDD in malnourished children underlines the need for active surveillance and aggressive management.[14]

Out of total 62 patients, 31 (50.00%) had deficient (<20ng/ml) vitamin D level, 23 (37.10%) had insufficient (20-30ng/ml) vitamin D level, 8 (12.90%) had sufficient (>30ng/ml) vitamin D level, level of vitamin D were not significantly associated p=0.695 with diagnosis. Among the 39 patients of pulmonary TB 20 (51.3%) had deficient (<20ng/ml) vitamin D level, 12 (30.8% had insufficient (20-30ng/ml) vitamin D level and 7 (17.9 %) had sufficient(>30ng/ml) vitamin D level. Among the 6 patients of TB lymphadenitis 2 (33.3%) had deficient (<20ng/ml) vitamin D level, 3 (50%) had insufficient (20-30ng/ml) vitamin D level and 1 (16.7 %) had sufficient(>30ng/ml) vitamin D level. Among the 2 patients of abdominal TB 1(50%) had deficient (<20ng/ml) vitamin D level,1 (50%) had insufficient (20-30ng/ml) vitamin D level and no one had sufficient(>30ng/ml) vitamin D level. Among the 39

patients of pleural TB 1 (20.0%) had deficient (<20ng/ml) vitamin D level, 4 (80%) had insufficient (20-30ng/ml) vitamin D level and no one had sufficient (>30ng/ml) vitamin D level. Among the 5 patients of TB meningitis 4 (80%) had deficient (<20ng/ml) vitamin D level, 1 (20.0%) had insufficient (20-30ng/ml) vitamin D level and no one had sufficient (>30ng/ml) vitamin D level. Among the 3 patients of military TB 2 (66.7%) had deficient (<20ng/ml) vitamin D level,1 (33.3%) had insufficient (20-30ng/ml) vitamin D level and no one had sufficient (>30ng/ml) vitamin D level. Among the 2 patients of disseminated TB 1(50%) had deficient (<20ng/ml) vitamin D level,1 (50%) had insufficient (20-30ng/ml) vitamin D level and no one had sufficient (>30ng/ml) vitamin D level(Table 7). Level of vitamin D were not significantly associated p=0.695 with diagnosis. Similar type of study was done by Venturini, E et al in 2014 in which 996 children screened for TB, which have been tested for vitamin D. Forty-four children (4.4%) had active TB, 138 (13.9%) latent TB and 814 (81.7%) were controls. Hypovitaminosis D was found respectively in 354 (43.5%) of controls, 80 (58%) latent TB and 33 (75%) active TB.[15] Although our study was showing no significant results it could be due to small sample size, poor control of confounders, no controls in study, When we saw in term of percentage out of 62 TB cases in our study 31(50%) had vitamin D deficiency, 23 (37.1%) had vitamin D insufficiency and only 8 (12.9%) had sufficient vitamin D levels, so we can say that Hypovitaminosis D affected up to 87.1% children with active TB.

Out of 62 total patients, 10 (16.13%) had severe variety of TB and 52 (83.87%) had non-severe TB. Among the 52 patients, 24 (46.2%) had deficient (<20ng/ml) vitamin D level, 20 (38.5%) had insufficient (20-30ng/ml) vitamin D level and 8 (15.4%) had sufficient (>30ng/ml) vitamin D level. Among the 10 patients with severe TB, 7 (70.00%) had deficient (<20ng/ml) vitamin D level, 3 (30.00%) had insufficient (20-30ng/ml) vitamin D level and none had sufficient (>30ng/ml) vitamin D level (Table 8). Vitamin D level were significantly not associated with severity of TB p=0.265. In other study done by Rizvi I et al. included 130 subjects each in three arms (TBM, pulmonary tuberculosis and healthy control) showed that vitamin D deficiency was significantly more common in TBM compared to controls and pulmonary tuberculosis (TBM versus controls p <0.001; TBM versus pulmonary tuberculosis p <0.001).[16]

However in our study level of vitamin D is not significantly associated with severity of TB but out of 10 patient with severe form of disease 7 (70%) had vitamin D deficiency (<20ng/ml), remaining 3 (30%) patients had vitamin D insufficiency and none of them was vitamin D sufficient. Many studies have evaluated the association of tuberculosis with low serum vitamin D 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. The number of patient in our study with severe variant were very less so further studies with big sample size should be conducted for definite result.

CONCLUSION

The results of this study show that out of total 62 patients, 31 (50.00%) had deficient (<20ng/ml) vitamin D level, 23 (37.10%) had insufficient (20-30ng/ml) vitamin D level, 8 (12.90%) had sufficient (>30ng/ml) vitamin D level.

Out of 62 total patients, 10 (62.13%) had severe variety of TB and 52 (83.87%) had non-severe TB. Among the 52 patients, 24 (46.2%) had deficient (<20ng/ml) vitamin D level, 20 (38.5%) had insufficient (20-30ng/ml) vitamin D level and 8 (15.4%) had sufficient (>30ng/ml) vitamin D level. Among the 10 patients with severe TB, 7 (70.00%) had deficient (<20ng/ml) vitamin D level, 3 (30.00%) had insufficient (20-30ng/ml) vitamin D level and none had sufficient (>30ng/ml) vitamin D level.

Majority of the enrolled children with tuberculosis demonstrated low serum levels of 25-hydroxy vitamin D (deficient and insufficient levels) suggest that vitamin D deficiency is the risk factor of tuberculosis and very low serum levels of 25-hydroxy vitamin D were noted in severe variant of TB then non severe variant suggest that vitamin D levels were related to Tb severity and in severe form of tuberculosis vitamin D levels were less compared to non severe variant.

However statistical data of various clinical presentation of TB were not significantly associated with level of Vitamin D and severity of TB and vitamin D level were not significantly associated.

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