ORIGINAL ARTICLE

Vitamin D Deficiency in Children with Tuberculosis: A Cross Sectional Study

SIDRA TUL MUN THA¹, SAIMA RASHEED², AYESHA MUKHTAR³, MADIHA RASHEED⁴, SEHRISH NAZ⁵, MUHAMMAD FAISAL JAVAID⁶ ¹Consultant, Child Life Foundation Civil Hospital Karachi

²Associate Professor, Niazi Medical and Dental College, Sargodha

³Consultant Pediatrician, Mian Muhammad Trust Hospital, Faisalabad

⁴Associate professor, WATIM Dental College Rawat

⁵Assistant professor Pathology, Watim medical and dental college, Rawat

⁶Assistant professor of Biochemistry, Niazi medical and dental college Sargodha

Correspondence to: Sidra Tul Mun Tha, Email: dr.sidrasheikh@yahoo.com

ABSTRACT

The purpose of this study was to determine how common vitamin D insufficiency is among TB patients between the ages of 2 and 12. Specifically, a descriptive and cross-sectional research strategy was used for this investigation. The research was conducted in the Faisalabad, Pakistan location of the DHQ Hospital's Pediatric Medicine Division.

Material and Methods: In this study, total 93 patients presented to the out-patient department of Pediatrics Medicine, DHQ Hospital, Faisalabad were selected from: December, 2021 to May, 2022 and informed written consent was taken. Blood sample 3 ml of each patient was sent vitamin D levels for presence or absence of vitamin D deficiency.

Results: Among the 93 cases, 44.09% (n=41) were between 2-6 years of age whereas 55.91% (n=52) were between 7-12 years of age, mean+sd was calculated as 7.14+2.22 years, 54.84% (n=51) were male whereas 45.16% (n=42) were females. Frequency of Vitamin D deficiency among children suffering tuberculosis age 2-12 years shows that 49.46% (n=46) had vitamin D deficiency.

Conclusion: We concluded that the frequency of vitamin D deficiency is higher among children suffering with tuberculosis age 2-12 years; however, further multicenter studies are required to validate our results.

Keywords: Children, tuberculosis, vitamin D deficiency, TB,

INTRODUCTION

As tuberculosis (TB) is a major public health problem, especially in the under-developed and developing nations like our South East Asia,¹ early diagnosis and prompt treatment is the main stay of the prognosis. To treat tuberculosis in children, the same medications that are used in adults must be administered for an extended period of time. Treatment for children with tuberculosis comprises of an intensive phase followed by a follow-up period.² This phase uses more TB medications than the continuation phase, whose goal is to destroy any dormant bacteria that remains after the intensive phase has been completed.3 There is evidence to suggest that the biologically active version of vitamin D affects the development of innate immunity by altering macrophage function, which could help in prevention of TB.⁴ The increased destruction of intracellular M. tuberculosis antigen by vitamin D also leads in reduced synthesis of the antibacterial peptide cathelicidin.⁵ Several other studies have previously reported the incidence of hypovitaminosis D among the patients of TB,6,7 Studied have reported that tuberculosis was associated with decreased serum level of vitamin D [25-hydroxycholecalciferol] compared to healthy controls.8,9 A low level of vitamin D was discovered in 40.9% of tuberculosis patients in a research investigation.¹⁰ Epidemiological data reported an higher incidence of rickets after vitamin D deficiency among the patient of tuberculosis. It is highest among residents near the poles and decreased in the tropical latitudes. On searching the literature, I have found only international literature, so I have decided to determine the frequency of vitamin D deficiency in tuberculosis patients taking anti tuberculosis therapy. This study will not only provide the local magnitude of the problem but will also be a useful addition in the existing literature. Moreover, the results of my study will help the clinicians to design a protocol for screening and managing vitamin D deficiency in these particular patients which help to improve the results and thus reducing the morbidity of our population.

MATERIAL AND METHODS

In this descriptive and cross-sectional study, prevalence of vitamin D deficiency in children with tuberculosis aged 2 to 12 years was determined, at the Department of Pediatric Medicine, DHQ Hospital, Faisalabad in Six months from the date of acceptance of synopsis from: December, 2021 to May, 2022. Diagnosed

tuberculosis cases who had been on anti-tuberculosis therapy for the previous two months were included in the study. Microscopy or molecular approaches can detect the presence of Mycobacterium tuberculosis, which causes tuberculosis. .Vitamin D deficiency: serum vitamin D levels <25 ng/ml was taken as positive.

The calculated sample size was 93 by taking 95% confidence level, 10% margin of error, taking percentage of vitamin D deficiency as 40.9%¹⁰ in tuberculosis cases. Testing involves the use of sampling technique, which is a Consecutive method without probability. All outdoor patients Males and females between the ages of two and twelve who had been diagnosed with tuberculosis and had been receiving anti-tuberculosis treatment for the previous two months were all eligible and selected in the sample criteria. These individuals were ruled out because they had diabetes mellitus, chronic renal failure, or had two consecutive readings of Sr. Creatinine >1.1 mg/dl, all of which were based on history and medical records, and patients with congenital anomalies were also ruled out (assessed on medical record)

After obtaining their written agreement, a total of 93 patients who sought treatment in the outpatient paediatric medicine clinic at DHQ Hospital in Faisalabad were included in the study. The committee conducting the ethical assessment at the institution gave their permission. It was determined whether or not patients had vitamin D insufficiency by sending blood samples to be tested. Specifically, version 26.0 of the statistical package SPSS was used to input and evaluate the data. The average and standard deviation for patient age, illness duration, height, weight, and body mass index were provided. Variables were gender, location (rural/urban), sun exposure (low/moderate/high), wealth (low/middle/high), TB risk (yes/no), and vitamin D insufficiency. Effect modifiers such as age, gender, illness duration, body mass index, rural/urban residence, presence/absence of a TB family history, sun exposure (low/moderate/high), and socioeconomic position (poor/middle/upper) were accounted for using stratification and the chi-square test. After stratification, a p-value of 0.05 was regarded to indicate statistical significance.

RESULTS

Children with TB between the ages of 2 and 12 were evaluated, and a total of 93 patients meeting the selection criteria were enrolled. The patients' ages ranged from 2 to 12, with 44.09% (n=41) falling in that range and 55.91% (n=52) falling in the 7-12

age range (mean+sd = 7.14+2.22 years).Gender distribution shows that 54.84%(n=51) were male whereas 45.16%(n=42) were females. Mean duration of disease was calculated as 1.78+0.70 years. Mean BMI was calculated as 25.47+1.52. Place of living shows that 49.46%(n=46) were living in urban areas and 50.54%(n=47) belong to rural area. Sun exposure was recorded, it shows that 65.59%(n=61) cases had low exposure and 34.41%(n=32) had medium sun exposure. Socioeconomic status of the patients shows that 64.52 %(n=60) had poor socioeconomic status and 35.48%(n=33) had middle socioeconomic status. Family history of the patients shows that 20.43%(n=19) had family history of tuberculosis and 79.57%(n=74) had no family history. Frequency of Vitamin D deficiency among children suffering tuberculosis age 2-12 years shows that 49.46%(n=46) had vitamin D deficiency whereas 50.54%(n=47) had no vitamin D deficiency. (Table No. 1)

Using a chi-square test, we adjusted for impact modifiers such as age, gender, illness duration, body mass index, rural/urban residence, TB in the family (yes/no), sun exposure (low/moderate/high), and socioeconomic position (poor/middle/upper). After stratification, a p-value of 0.05 was regarded to indicate statistical significance. As seen in (Table No. 2)

Table 1: showing various	demographic and other variables of the patients

Place of living (n=93)	Urban	46	49.46
Flace of living (II=95)	Rural	47	50.54
Sup overcours of the notion to	Low	61	65.59
Sun exposure of the patients (n=93)	Medium	32	34.41
(1=93)	High	0	0
Socio economic status of the	Poor	60	64.52
patients (n=93)	Middle	33	35.48
patients (n=93)	High	0	0
Family history of tuberculosis of the	Yes	19	20.43%
patients (n=93)	No	74	79.57%
Vitamin D Deficiency Among	Yes	46	49.46
Children Suffering Tuberculosis	No	47	50.54

Table 2: showing stratification of data with respect to various effect modifiers.

Vitamin D Deficiency With Regards	-	Age (in	Vitamir	n D	Р	
	To age	years)	Deficiency		value	
	To condor	Male	24	27	0.61	
	To gender	Female	22	20		
	To duration of disease	1-2	39	38	0.62	
		>2	7	9		
	To bmi	Upto 27	40	38	0.42	
		> 27	6	9		
	To place of living	Rural	21	25	0.47	
		Urban	25	22		
	To family history of Tuberculosis	Yes	11	8	0.41	
		No	35	39		
		Low (n=61)	25	36	0.02	
	To sun exposure		21	11	0.02	
		Middle(n=32)	21	11	0.02	
			25	36		
	To socioeconomic	Poor(n=60)	32	28	0.31	
			14	19		
	status	Middle(n=33)	14	19	0.31	

DISCUSSION

The spread of tuberculosis (TB) is still a big issue in terms of public health. Around 1.4 million people lost their lives to TB, and it was believed that 8.7 million people were infected. An insufficiency in vitamin D is one of the variables associated with an upped chance of contracting TB (VDD). Humans get their vitamin D mostly through sun exposure, which triggers the skin to produce vitamin D3 from 7-dehydrocholesterol (a pre-vitamin D3). The liver then converts 25(OH)-D to the bioactive form of vitamin D, 1,25(OH)2D3, and the kidneys finish the process.

Epidemiological evidence suggests a link between vitamin D deficiency and rickets and TB. The prevalence of vitamin D deficiency in TB patients varies with geographic location. People living at the poles have the highest rates, while those living in the tropics have the lowest. After doing a literature search, we realised that only foreign studies addressed the prevalence of vitamin D insufficiency in TB patients on anti-tuberculosis treatment; hence, we undertook the present study.

This study was to provide the local magnitude of the problem but also a useful addition in the existing literature. Moreover, the results of my study may help the clinicians to design a protocol for screening and managing vitamin D deficiency in these particular patients which help to improve the results and thus reducing the morbidity of our population.

In our study, out of 93 cases, 44.09%(n=41) were between 2-6 years of age whereas 55.91%(n=52) were between 7-12 years of age, mean+sd was calculated as 7.14+2.22 years, 54.84%(n=51) were male whereas 45.16%(n=42) were females. Frequency of Vitamin D deficiency among children suffering tuberculosis age 2-12 years shows that 49.46%(n=46) had vitamin D deficiency.

Vitamin D insufficiency has been linked to 40.9% of TB infections, according to a prior study. ¹⁰ Vitamin D and TB have been the subject of previous scientific investigation. In patients with tuberculosis (TB), vitamin D deficiency (VDD) was reported to increase risk; however, this link was not seen in the general African population or in the HIV-infected African population. Patients on antiretroviral therapy for HIV/TB who developed TBassociated immunological reconstitution inflammatory syndrome had significantly lower vitamin D levels compared to those who did not develop the syndrome. Treatment with anti-TB drugs had no effect on vitamin D levels in TB patients, lending support to this theory. Vitamin D, they found, is associated with a lower risk of tuberculosis (TB). ¹¹ There is more evidence that VDD is a cause of TB than that it is a result of the disease. More study is required to determine if vitamin D supplementation can help prevent and cure TB. 12

Nnoaham et al.¹³ found that similar outcomes were observed in the Asian population but not in the African population, even after removing trials in which patients and controls had HIV, diabetes, or LTBI. More research is needed to determine why vitamin D's effect on TB varies so greatly across different ethnic groups. Humans must get enough sun and/or make dietary changes to keep vitamin D levels at optimal levels, as these are the two primary sources of vitamin D in the human body. Since vitamin D deficiency is certainly a risk factor for tuberculosis, we question if vitamin D supplementation is useful in the prevention and treatment of TB. Although a 2012 meta-analysis by Xia et al.¹⁴ concluded that vitamin D supplementation had no effect on TB treatment, they did not investigate the supplement's potential role in TB prevention. More study is required to prove the potential benefits of vitamin D supplementation for specific individuals.

CONCLUSION

We found that vitamin D insufficiency was more common in children with TB, ages 2-12, but further multicenter studies are needed to confirm our findings.

REFERENCES

- Martineau AR, Timms PM, Bothamley GH, Hanifa Y, Islam K, Claxton AP, et al. High-dose vitamin D (3) during intensive-phase antimicrobial treatment of pulmonary tuberculosis: a double-blind randomized controlled trial. Lancet 2011;377:242-50.
- Campbell GR, Spector SA. Vitamin D inhibits human immunodeficiency virus type 1 and Mycobacterium tuberculosis infection in macrophages through the induction of autophagy. PLoS Pathog 2012;8:1523-5.
- Gray K, Wood N, Gunasekera H, Sheikh M, Hazelton B, Barzi F, et al. Vitamin D and tuberculosis status in refugee children. Pediatr Infect Dist J 2012;31:521-3.

- Khandelwal D, Gupta N, Mukherjee A, Lodha R, Singh V, Grewal HMS, et al. Vitamin D levels in Indian children with intrathoracic tuberculosis. Indian J Med Res 2014;140:531-7.
- Ganmaa D, Giovannucci E, Bloom BR, Fawzi W, Burr W, Batbaater D, et al. Vitamin D, tuberculin skin test conversion, and latent tuberculosis in Mongolian school-age children: a randomized, doubleblind, placebo-controlled feasibility trial. Am J Clin Nutr 2012;96:391-6.
- Ralph AP, Lucas RM, Norval M. Vitamin and solar ultraviolet radiation in the risk and treatment of tuberculosis. Lancet Infect Dis 2013;13:77-88.
- Koo HK, Lee JS< Jeong YJ, Choi SM, Kang HJ, Lim HJ et al. Vitamin D deficiency and changes in serum vitamin D levels with treatment among tuberculosis patients in South Korea. Respir 2012;17:808-13.
- Rathored J, Sharma SK, Singh B, Banavaliker JN, Sreenivas V, Srivastava AK. Risk and outcome of multidrug-resistant tuberculosis: vitamin D receptor polymorphisms and serum 25(OH)D. Int J Tuberc Lung Dis 2012;16:1522-8.

- Sato S, Tanino Y, Saito J, Nikaido T, Inokoshi Y, Fukuhara A, et al. The relationship between 25-hydroxyvitamin D levels and treatment course of pulmonary tuberculosis. Respir Investig 2012;50:40-5
- Venturini E, Facchini L, Martinez-Alier N, Novelli V, Galli L, de Martino M, et al. Vitamin D and tuberculosis: a multicenter study in children. BMC Infect Dis 2014;14:652.
- 11. Huang SJ, Wang XH, Liu ZD, et al. Vitamin D deficiency and the risk of tuberculosis: a meta-analysis. Drug Des Devel Ther. 2016;11:91–102.
- Kearns MD, Tangpricha V. The role of vitamin D in tuberculosis. J Clin Transl Endocrinol. 2014 Aug 23;1(4):167-169. doi: 10.1016/j.jcte.2014.08.002. PMID: 29159097; PMCID: PMC5684962.
- 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.
- Xia J, Shi L, Zhao L, Xu F. Impact of vitamin D supplementation on the outcome of tuberculosis treatment: a systematic review and metaanalysis of randomized controlled trials. Chin Med J (Engl) 2014;127(17):3127–34.