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Vitamin D Deficiency among Patients with Newly Diagnosed Tuberculosis

Bassam Salih Rawe [1]; Lara Abbas Mohammed [2]

[1]M.B.Ch.B, Higher Diploma student in Family Medicine/College of medicine-Hawler Medical University-Erbil-Kurdistan region/Iraq
[2]M.B.Ch. B, FKHCMS/FM, Family Medicine Specialist at College of Medicine-Hawler Medical University-Erbil city-Kurdistan region/Iraq

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Corresponding Email:
drbassam7786@yahoo.com

ABSTRACT

Background: Tuberculosis is a common public health problem in Kurdistan region and Iraq.

Objective: To determine the prevalence of vitamin D deficiency among newly diagnosed individuals with tuberculosis.

Methods: Present study was an observational cross-sectional carried out in Erbil Tuberculosis center at Erbil city-Kurdistan region/Iraq through the period of eight months from 1st of October, 2024 to 30th of April, 2025 on sample of sample of one hundred patients with newly diagnosed tuberculosis and sample of one hundred healthy individuals as controls.

Results: The vitamin D deficiency was recorded in 74% of newly diagnosed tuberculosis cases. Our study showed a statistically significant relationship was observed between severe vitamin D level deficiency and TB cases ($p<0.001$). Risk factors related to vitamin D deficiency among newly diagnosed tuberculosis cases are increased age, illiteracy, unemployment, widow relationship, positive menopause for females, low family income, high crowding index, current smoking, shorter exposure duration to sunshine, no vitamin D supplement and rare frequency of food rich in vitamin D.

Conclusion: The prevalence of vitamin D deficiency in newly diagnosed tuberculosis cases in Erbil city-Kurdistan region/Iraq is high. The vitamin D deficiency may play a significant role in development of tuberculosis.

INTRODUCTION

Tuberculosis (TB) is an ancient highly infectious airborne disease spreading all over the world with about two billion people with latent TB infection, and it is one of ten causes of mortality globally.[1] TB causative agent is known as *mycobacterium tuberculosis* identified firstly by Robert Koch at 1882.[2] The TB is highly endemic in South-East Asian, African and Western-Pacific countries with about 1.3 million deaths every year.[3] It is shown that approximately ten million people had active TB in the world, more than half of them are males, one third are females and 13% of them are children.[4] In Iraq, the incidence rate of TB showed a gradual decline from 45 cases per 100,000 populations at 2013 to 23 cases per 100,000 populations at 2023.[5] However, the incidence rate of TB was increasing in Erbil city-Kurdistan region/Iraq from 16 per 100,000 populations at 2012 to 21.7 per 100,000 populations at 2016.[6]

The causative agent of tuberculosis is exposure to infectious respiratory pathogen (*mycobacterium tuberculosis*) which is attacked by body immune system in order to prevent their growth. However, these pathogens could by multiplied and activated especially with weaning of immunity and other co-morbidities.[7] Most of cases contacted directly to pathogens developed latent infection, about 5% of cases developed active infection within first two years and 5% of cases developed active infection later.[8] Tuberculosis resulted from complicated interaction between host, bacteria and risk factors. At population level, common risk factors of TB are poverty, illiteracy, crowed living and poor hygiene, while at individual level; the main risk factors are male gender, human acquired immunodeficiency disease, immune disorders, smoking, alcohol consumption, immunosuppressive medications, diabetes mellitus, renal transplant, malnutrition and family history of TB.[9]

The vitamin D (calciferol) plays an important function in calcium distribution and bone development. Source of vitamin D is either from skin or food and the metabolism of this vitamin is implemented the liver that converts it to 25-hydroxyvitamin D, then activated in kidneys to 1,25-dihydroxy vitamin D.[10] Vitamin D deficiency is commonly related to low cutaneous secretion, poor food intake, mal-absorption, gastric surgeries, higher vitamin D metabolism, blocked enterohepatic circulation, nephrotic syndrome, defective activation of vitamin D, renal dysfunction and obesity.[11] The deficiency of vitamin D is spreading all over the world and leads to many adverse outcomes such as osteomalacia, hypertension, diabetes mellitus, heart diseases, tumors, etc.[12]

It was shown that vitamin D has a defensive role against *Mycobacterium tuberculosis*. The vitamin D stimulates an antimicrobial peptide cathelicidin that impaired the multiplication of bacteria in macrophages.[13] Historically, some authors reported role of cod liver oil (vitamin D rich content) in management of TB patients with good outcomes.[14] Additional, others reported role of sun exposure, nutrition and high attitudes in treatment of TB.[15] Exposing to sun was regarded as the first-line treatment of TB for several years, which induces vitamin D production from the skin.[16] Some authors reported the role of short-wave UV light in treating cutaneous TB.[17] Despite these facts, some literature revealed that elevated serum vitamin D and calcium levels are

recognised in TB patients and explained this elevation as activated macrophages in granulomas.[18] However, most of the literature suggested the role of vitamin D deficiency in the development of pulmonary tuberculosis.[19, 20]

The aim of present study was to determine the prevalence of vitamin D deficiency among newly diagnosed individuals with tuberculosis and identifying risk factors related to vitamin D deficiency.

PATIENTS AND METHODS

The design of this study was an observational cross-sectional carried out in Erbil Tuberculosis center at Erbil city-Kurdistan region/Iraq through the period of eight months from 1st of October, 2024 to 30th of April, 2025. The studied population was newly diagnosed patients with tuberculosis. Inclusion criteria were newly diagnosed patients with tuberculosis (either pulmonary or extra-pulmonary) with different age groups and gender. History of TB treatment, use of vitamin D supplements or medications affecting vitamin D metabolism within the last 6 months, Human immunodeficiency viral infection, pregnancy and patients refused to participate in the study were the exclusion criteria. The study ethics were implemented in regard to guidelines of Ethical Committee of School of Medicine-Hawler Medical University and Hospital authority, informed consent of patients and management of complications accordingly. A sample of one hundred patients with newly diagnosed tuberculosis was selected after eligibility to inclusion and exclusion criteria. Another sample of one hundred healthy individuals was selected with comparable age and gender as controls.

Information of patients was collected directly and filled in a prepared questionnaire designed by researchers. The questionnaire included demographic characteristics of patients (age and gender), socioeconomic characteristics of patients (marital status, residence, educational level, occupation, house ownership, family income, number of rooms, number of households and car ownership), parity and menopause history for women, smoking history, exposure to sunshine and duration of this exposure, history of vitamin D supplement and results of vitamin D test. The cases were diagnosed by the identification of acid-fast bacilli in sputum smears, isolation of Mycobacterium tuberculosis on culture or demonstration of chronic caseating granulomatous inflammation in tissue specimens, ESR test and chest x-ray for pulmonary tuberculosis.

The patient's information were entered and interpreted statistically by Statistical Package of Social Sciences program-26. Suitable tests like chi square and fishers' exact tests were implemented accordingly. Significance level was ≤ 0.05.

RESULTS

Current study included 100 patients with early diagnosed TB and 100 healthy controls. No statistically significant differences between both study groups in regard to age, gender and residence. There was a highly significant association between TB cases and each of illiteracy, unemployment and widows ($p<0.001$), (Table 1).

There was a highly significant association between TB cases and obesity ($p<0.001$). No statistically significant differences between both study groups in regard to

menopause of females. However, grand-multiparity of females was significantly associated to TB cases (p<0.001). Rented home, not enough family income, high crowding index, no car ownership and current smoking were significantly related to TB cases (p<0.001) (Table 2).

There was a highly significant association between TB cases and low sunshine (p<0.001). Low sun exposure duration was significantly associated to TB cases (p<0.001). Low vitamin D supplements, not consuming food rich in vitamin D and rare consumption food rich in vitamin D were significantly related to TB cases (p<0.001). A statistically significant relationship was observed between severe vitamin D level deficiency and TB cases (p<0.001), mean vitamin D level was significantly lower among TB cases (p<0.001), (Table 3 and Figure 1).

There was a highly significant association between TB cases and positive family history of TB (p<0.001). Lack of BCG vaccination history was significantly associated to TB cases (p<0.001). Lack of BCG scar left was significantly related to TB cases (p<0.001), (Table 4). There was a significant association between older age TB cases and vitamin D deficiency (p=0.007). No statistically significant differences between TB cases with different vitamin D level in regard to gender and residence. There was a significant association between each of illiteracy, unemployment and widow relationship with vitamin D deficiency of TB cases (p<0.05). (Table 5)

There was a highly significant association between positive menopause for female TB cases and vitamin D deficiency (p<0.001). No statistically significant differences between TB cases with different vitamin D level in regard to body mass index, parity, home ownership and car ownership. There was a significant association between each of low family income, high crowding index and current smoking with vitamin D deficiency of TB cases (p<0.05). (Table 6)

There was a significant association between shorter exposure duration to sunshine and vitamin D deficiency (p=0.04). There was a significant association between each of no vitamin D supplement and rare frequency of food rich in vitamin D with vitamin D deficiency of TB cases (p<0.05). No statistically significant differences between TB cases with different vitamin D level in regard to sunshine and food rich in vitamin D. (Table 7). No statistically significant differences between TB cases with different vitamin D level in regard to family history of TB, duration since TB diagnosis and BCG vaccination in childhood (Table 8).

DISCUSSION

Tuberculosis has a higher incidence in Erbil city and Iraq.[6, 21] Identifying risk factors and complications of tuberculosis is important in prevention strategies and plans of management.[22]

In current study, the vitamin D deficiency was recorded in 74% of newly diagnosed TB cases. A recent study conducted in Iraq on newly diagnosed TB cases found that vitamin D deficiency was found in 87.5% of them.[23] Another recent prospective case control study carried out in India revealed that prevalence of vitamin D deficiency among newly diagnosed TB patients was (68.96%).[14] Variances in vitamin D deficiency in TB cases might be related to differences in risk factors between

different communities. Our study showed a statistically significant relationship was observed between severe vitamin D level deficiency and TB cases (p<0.001). Recent prospective cross sectional study implemented in Erbil city-Kurdistan region/Iraq found that 51.9% of TB cases had vitamin D level deficiency.[24] Mean vitamin D level in our study was significantly lower among TB cases (p<0.001). This finding is consistent with results of previous literatures.[19, 20] Additionally, recent Indian study reported that mean vitamin D level was lower in children with newly diagnosed TB cases.[25] Vitamin D deficiency in newly diagnosed tuberculosis patients may be related to low sun exposure, poverty, poor diet and may be effects of TB disease or its treatment.[26] In our study, all parameters of vitamin D like sun exposure, vitamin D supplements, food rich in vitamin D and frequency of food rich in vitamin D are significantly lower among newly diagnosed TB cases as compared to controls (p<0.001). These findings are parallel to results of previous Georgian study.[27]

In present study, newly diagnosed TB cases were significantly related to illiteracy, unemployment and widows (p<0.001). These findings are in agreement with results of recent systematic review study in South Korea.[28] Our study showed a highly significant association between newly diagnosed TB cases and obesity (p<0.001). This finding coincides with results of Chinese study.[29] In our study, grand-multiparity of females was significantly associated to TB cases (p<0.001). Similarly, previous retrospective study implemented in Nigeria revealed that both tuberculosis and grand-multiparity are related to poverty and illiteracy.[30] Our study showed that rented home, not enough family income, high crowding index, no car ownership and current smoking were significantly related to newly diagnosed TB cases (p<0.001). These findings are similar to results of different literatures.[31, 32]

This study found a significant association between older age TB cases and vitamin D deficiency (p=0.007). Consistently, previous case control study conducted in Ethiopia revealed that older age population had higher risk chance of vitamin D deficiency which increased with infection by tuberculosis.[33] In our study, there was a significant association between each of illiteracy, unemployment and widow relationship with vitamin D deficiency of TB cases (p<0.05). Our study also revealed a significant association between each of positive menopause for females, low family income, high crowding index and current smoking with vitamin D deficiency of TB cases (p<0.05). The tuberculosis shared many risk factors of vitamin D deficiency like illiteracy, smoking and low socioeconomic status.[34] In our study, there was a significant association between each of shorter exposure duration to sunshine, no vitamin D supplement and rare frequency of food rich in vitamin D with vitamin D deficiency of TB cases (p<0.05). These findings are coincide with results of many literatures which reported that vitamin D deficiency in TB cases might be attributed to infection itself or due to risk factors of both TB and vitamin D deficiency.[26, 35]

CONCLUSION

In conclusion, the prevalence of vitamin D deficiency in newly diagnosed tuberculosis cases in Erbil city-Kurdistan region/Iraq is high. Risk factors related to vitamin D deficiency among newly diagnosed

tuberculosis cases are increased age, illiteracy, unemployment, widow relationship, positive menopause for females, low family income, high crowding index, current smoking, shorter exposure duration to sunshine, no vitamin D supplement and rare frequency of food rich in vitamin D. This study recommended adjunctive vitamin D supplementation with standard anti-TB treatment and further national literatures on role of vitamin D in newly diagnosed TB cases.

Conflicts of interest

None

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TABLES

Table 1: Distribution of sociodemographic characteristics according to study groups.

Variable	Study groups				P-value
	TB cases		Controls		
	No.	%	No.	%	
Age					0.9 NS
<30 years	3	3.0	3	3.0	
30-39 years	9	9.0	9	9.0	
40-49 years	22	22.0	25	25.0	
50-59 years	31	31.0	32	32.0	
≥60 years	35	35.0	31	31.0	
Gender					1.0 NS
Male	38	38.0	38	38.0	
Female	62	62.0	62	62.0	
Residence					0.3 NS
Urban	59	59.0	65	65.0	
Rural	41	41.0	35	35.0	
Educational level					**<0.001** S
Illiterate	15	15.0	7	7.0	
Primary level	68	68.0	36	36.0	
Intermediate/secondary level	14	14.0	28	28.0	
High educational level	3	3.0	29	29.0	
Occupation					**<0.001** S
Employed	7	7.0	41	41.0	
Unemployed	93	93.0	59	59.0	
Marital status					**0.001** S
Single	1	1.0	0	-	
Married	82	82.0	98	98.0	
Divorced	0	-	1	1.0	
Widow	17	17.0	1	1.0	

S=Significant, NS=Not significant.

Table 2: Distribution of general characteristics according to study groups.

Variable	Study groups				P
	TB cases		Controls		
	No.	%	No.	%	
Body mass index					**<0.001** S
Normal	27	27.0	39	39.0	
Overweight	55	55.0	61	61.0	
Obese	18	18.0	0	-	
Menopause for female					0.8 NS
Yes	43	69.4	42	67.7	
No	19	30.6	20	32.3	
Parity					**<0.001** S
Para 1-2	1	1.6	0	-	
Para 3-4	1	1.6	16	25.8	
Para≥5	60	96.8	46	74.2	
Home ownership					**0.001** S
Owned	90	90.0	100	100.0	
Rented	10	10.0	0	-	
Family income					**<0.001** S
Enough	31	31.0	100	100.0	
Not enough	69	69.0	0	-	
Crowding index					**<0.001** S
≤2	7	7.0	68	68.0	
>2	93	93.0	32	32.0	
Car ownership					**<0.001** S
Yes	71	71.0	100	100.0	
No	29	29.0	0	-	
Smoking					**<0.001** S
Current smoking	60	60.0	15	15.0	
Non-smoking	40	40.0	85	85.0	

S=Significant, NS=Not significant.

Table 3: Distribution of vitamin D characteristics according to study groups.

Variable	Study groups				P
	TB cases		Controls		
	No.	%	No.	%	
Sunshine					**<0.001** S
Yes	71	71.0	100	100.0	
No	29	29.0	0	-	
Duration of exposure to sunshine					**<0.001** S
<15 minutes	73	73.0	44	44.0	
≥15 minutes	27	27.0	56	56.0	
Vitamin D supplement					**<0.001** S
Yes	27	27.0	74	74.0	
No	73	73.0	26	26.0	
Consumption of food rich in vitamin D					**<0.001** S
Yes	87	87.0	100	100.0	

No	13	13.0	0	-	
Frequency of food rich in vitamin D					**<0.001** S
Once week	9	9.1	27	27.0	
2-4	63	63.6	65	65.0	
Daily	21	21.2	8	8.0	
Rarely	6	6.1	0	-	
Vitamin D level					**<0.001** S
Normal	17	17.0	98	98.0	
Insufficiency	9	9.0	2	2.0	
Moderate deficiency	65	65.0	0	-	
Severe deficiency	9	9.0	0	-	
Mean±SD	19.54±10.8		40.54±7.8		**<0.001**

Table 4: Distribution of TB characteristics according to study groups.

Variable	**Study groups**				**P**
	TB cases		**Controls**		
	No.	**%**	**No.**	**%**	
Family history of TB					**<0.001** S
Yes	42	42.0	0	-	
No	58	58.0	100	100.0	
BCG vaccination in childhood					**<0.001** S
Yes	32	32.0	64	64.0	
No	68	68.0	36	36.0	
BCG scar left					**<0.001** S
Yes	0	-	27	42.2	
No	32	100.0	37	57.8	

Table 5: Distribution of sociodemographic characteristics according to vitamin D level of TB cases.

Variable	**Vitamin D deficiency**				**P**
	Yes		**No**		
	No.	**%**	**No.**	**%**	
Age					**0.007** S
<30 years	2	66.7	1	33.3	
30-39 years	4	44.4	5	55.6	
40-49 years	12	54.5	10	45.5	
50-59 years	24	77.4	7	22.6	
≥60 years	32	91.4	3	8.6	
Gender					0.59 NS
Male	27	71.1	11	28.9	
Female	47	75.8	15	24.2	
Residence					0.7 NS
Urban	43	72.9	16	27.1	
Rural	31	75.6	10	24.4	
Educational level					**0.01** S
Illiterate	15	100.0	0	-	
Primary level	50	73.5	18	26.5	
Intermediate/ secondary level	8	57.1	6	42.9	
High educational level	1	33.3	2	66.7	
Occupation					**0.004** S
Employed	2	28.6	5	71.4	
Unemployed	72	77.4	21	22.6	
Marital status					**0.02** S
Single	1	100.0	0	.0	
Married	56	68.3	26	31.7	
Divorced	0	-	0	-	
Widow	17	100.0	0	-	

Table 6: Distribution of general characteristics according to vitamin D level of TB cases.

Variable	**Vitamin D deficiency**				**P**
	Yes		**No**		
	No.	**%**	**No.**	**%**	
Body mass index					0.1 NS
Normal	17	63.0	10	37.0	
Overweight	45	81.8	10	18.2	
Obese	12	66.7	6	33.3	
Menopause for female					**<0.001** S
Yes	39	90.7	4	9.3	
No	8	42.1	11	57.9	
Parity					0.7 NS
Para 1-2	1	100.0	0	-	
Para 3-4	1	100.0	0	-	
Para≥5	45	75.0	15	25.0	
Home ownership					0.7 NS
Owned	67	74.4	23	25.6	
Rented	7	70.0	3	30.0	
Family income					**<0.001** S
Enough	12	38.7	19	61.3	

Not enough	62	89.9	7	10.1	
Crowding index					**0.05** S
≤2	3	42.9	4	57.1	
>2	71	76.3	22	23.7	
Car ownership					0.2 NS
Yes	50	70.4	21	29.6	
No	24	82.8	5	17.2	
Smoking					**0.03** S
Current smoking	49	81.7	11	18.3	
Non-smoking	25	62.5	15	37.5	

Table 7: Distribution of vitamin D characteristics according to vitamin D level of TB cases.

Variable	**Vitamin D deficiency**				**P**
	Yes		**No**		
	No.	**%**	**No.**	**%**	
Sunshine					0.4 NS
Yes	51	71.8	20	28.2	
No	23	79.3	6	20.7	
Duration of exposure to sunshine					**0.04** S
<15 minutes	58	79.5	15	20.5	
≥15 minutes	16	59.3	11	40.7	
Vitamin D supplement					**<0.001** S
Yes	1	3.7	26	96.3	
No	73	100.0	0	-	
Consumption of food rich in vitamin D					0.7 NS
Yes	64	73.6	23	26.4	
No	10	76.9	3	23.1	
Frequency of food rich in vitamin D					**0.004** S
Once week	8	88.9	1	11.1	
2-4 times/week	51	81.0	12	19.0	
Daily	9	42.9	12	57.1	
Rarely	5	83.3	1	16.7	

Table 8: Distribution of TB characteristics according to vitamin D level of TB cases.

Variable	**Vitamin D deficiency**				**P**
	Yes		**No**		
	No.	**%**	**No.**	**%**	
Family history of TB					0.6 NS
Yes	32	76.2	10	23.8	
No	42	72.4	16	27.6	
Duration since TB diagnosis					0.9 NS
≤1 month	26	74.3	9	25.7	
>1 month	48	73.8	17	26.2	
BCG vaccination in childhood					0.07 NS
Yes	20	62.5	12	37.5	
No	54	79.4	14	20.6	

FIGURES

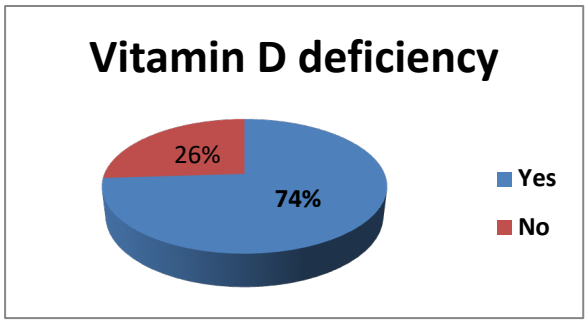

Figure 1: Vitamin D deficiency in TB patients.