Prevalence and Determinants of Type 2 Diabetes among the Pulmonary Tuberculosis Cases in Nepal: A Cross Sectional Study

Mahato RK,[1] Laohasiriwong W,[1] Koju RP[2]

[1]Faculty of Public Health,
Khon Kaen University,
Khon Kaen, Thailand.
[2]Departments of Internal Medicine/Cardiology,
Dhulikhel Hospital, Kathmandu University Hospital,
Kathmandu University School of Medical Sciences,
Dhulikhel, Kavre, Nepal.

Corresponding Author
Wongsa Laohasiriwong
Faculty of Public Health,
Khon Kaen University,
Khon Kaen, Thailand.
E-mail: drwongsa@gmail.com

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ABSTRACT

Background

Since prehistoric time to the earlier 20th century, diabetes was accounted as co-morbidity among tuberculosis patients, which is reducing the treatment efficiency.

Objective

To investigate the prevalence and determinants of type 2 diabetes mellitus among tuberculosis patients in central development region of Nepal.

Method

An analytical cross-sectional study was conducted by using structured questionnaire. Face to face interview as well as reviewing of the medical records of the tuberculosis cases has been performed during September 2018 - February 2019. The systematic random sampling was applied to select 306 tuberculosis cases. Then the respondents were examined for blood glucose level as well as Glycated haemoglobin (HbA1c) level to identify TB with Diabetes Mellitus. The proportion of respondents with fasting blood glucose level ≥ 126 mg/dl or a random blood glucose ≥ 200 mg/dl was considered as Tuberculosis with Diabetes Mellitus cases. Similarly, haemoglobin A1C ≥ 7% was accessed as amplified risk for tuberculosis. Multiple logistic regression was performed to analyse the factors associated with Tuberculosis with Diabetes Mellitus by using STATA. P value < 0.05 was taken as statistically significant.

Result

A total of 306 tuberculosis patients were included in the study. The mean ± standard deviation of age of participants was 36.82±15.94 years. The proportion of male slightly exceeded than that of female with a ratio of 1.73:1. The prevalence of TBDM was 17.32% (95% CI: 13.05-21.58) of all diagnosed tuberculosis cases. Our multivariable analysis identified the factors those were associated with TBDM were age ≥ 45 years (adj.OR=3.97, 95% CI 1.81-8.71, p value 0.001), patients residing in the urban areas (adj.OR=9.75, 95% CI 1.99-47.6, p value 0.005), had Body Mass Index (BMI) <18.5 Kg/m^2 (adj.OR=3.20, 95% CI 1.58-6.51, p value 0.001), had diastolic blood pressure ≥ 80 mmHg (adj.OR=2.34, 95% CI 1.17-4.66, p value 0.015) and patients who were treated with Cat II and Cat III tuberculosis treatment regimens (adj.OR=2.65, 95% CI 1.22-5.73, p value 0.013).

Conclusion

The prevalence of type 2 diabetes mellitus among tuberculosis patients was higher than prevalence of diabetes in general population of Nepal and it was higher among male, urban residents, patients with low BMI and the older aged tuberculosis patients.

KEY WORDS

Diabetes mellitus, HbA1c, Multiple logistic regression, Tuberculosis

INTRODUCTION

Tuberculosis (TB) is a contagious airborne disease caused by the bacillus Mycobacterium tuberculosis existed for millennial and still leftovers a major global health problem.[1,2] TB was one of the 10 causes of demise worldwide in 2015.[1,3] There were a projection of 10.4 million new TB cases globally, of which 5.9 million (56%) were among men, 3.5 million (34%) among women and 1.0 million (10%) among children.[1]

Simultaneously, Diabetes Mellitus is a multifaceted metabolic illness that is categorized by high level of blood sugar either due to body does not yield enough insulin or cells don't react to insulin.[4,5] WHO has identified diabetes mellitus as a global epidemic which is commonly affecting low and middle income countries where 80% of all deaths are from DM.[6-8] In addition, in 2014, an approximated 422 million adults were diabetic whereas in 1980 it was only 108 million and the prevalence is estimated to reach 438 million by 2030, globally.[7] Furthermore, the worldwide age-standardized prevalence of diabetes has approximately twofold since 1980 (4.7% to 8.5%) among the adult population.[4,9] Although the DM epidemic was first and fore mostly documented in high-income countries, the numbers of diabetic people, currently and in the years ahead, will live in low and middle income countries, with health systems already troubled by low budgets and other, similarly vital, diseases.[10] Which clearly signifies that Nepal is already under the risk of double burden of diseases. So, there are many factors that need to be addressed towards the goal of reducing TB burden. There is need to carry out a broad attempt to overcome the burden of tuberculosis by well-organized planning and implementation of preventive, therapeutic and rehabilitative aspects. Therefore, this study aimed to investigate the prevalence and determinants of type 2 diabetes mellitus (T2DM) among tuberculosis patients in central development region of Nepal.

METHODS

The study was conducted in the Central Development Region of Nepal from September 2018 to February 2019. An analytical cross-sectional study was conducted by using structured questionnaire. An interview was taken to all forms of TB patients.

The sample size of 306 was calculated by using the sample size estimation formula for multivariable logistic regression formula ($n=[P(1-P)(Z1-\alpha+Z1-\beta)^2/B(1-B)(P0-P1)^2X1/(1-P)2]$) to detect the DM among tuberculosis cases.[11] The required proportions for the sample size calculation were obtained from a previous study conducted in Nepal.[12] TB patients aged 18 years old or more, who had been diagnosed and registered for treatment at TB treatment centres were included. However, non-ambulatory and critically ill patients were excluded from the study. The systematic random sampling procedure was applied to select respondents from each treatment centres of Central Nepal.

A structured questionnaire interview was used to collect the study data. The questionnaire assessed socio-demographic details, major presenting symptoms of TB, duration of major presenting symptoms and BMI. After that, all patients with diagnosed TB were screened for DM by measurement of fasting as well as random blood glucose level. In addition, haemoglobin A1C ≥ 7% was assessed as amplified risk for TB. The questionnaire were prepared in English and subsequently translated to the national language, Nepali by Nepal Notary Public Council (2916). In addition, medical records were also reviewed to assure the quality of the data.

Data were entered in Epi-Data (Version 3.1) and transferred to STATA (Version 13, Stata Corporation, College Station TXUSA) for analysis. The categorical data were reported as number and percentage. Mean, standard deviation, median and range (minimum: maximum) were described for the continuous variable. The proportion of subjects with fasting blood glucose level ≥ 126 mg/dl or a random blood glucose ≥ 200 mg/dl was estimated on the same day of data collection.[13] Multivariable analysis was performed by multiple logistic regression including variables that showed a significant statistical effect in prediction of TBDM in bivariate analysis. Variables associated with TBDM in the bivariate analysis ($p \leq 0.25$) were included in the model. Statistical significance was taken as p value < 0.05.

Human Ethical permission for the study was obtained from the Ethics Committee in Human Research of Khon Kaen University, Khon Kaen, Thailand (HE612209), Nepal Health Research Council (2640), Nepal and Institutional Review Committee (Protocol approved number 01/18), Kathmandu University School of Medical Sciences, Dhulikhel, Nepal.

RESULTS

A total of 306 TB patients were randomly enrolled from 19 districts of CDR of Nepal. Less than a quarter (24.18%) of the respondents were previously affected by tuberculosis. In addition, 17.32% of the study participants had family history of TB. Furthermore, 75.82 % of the respondents waited for ≥ 7 days to get TB diagnosis and 64.71% of them visited ≥ 2 health facilities for it. More than three quarters (79.08%) of the participants were treated with Cat I treatment therapy and 87.91% didn't have any type of drug resistant. Our study revealed that still nearly half (44.12%) of the tuberculosis patients had to walk to reach DOTS centre and more than one third (38.89%) of them had to expend ≥ 30 minutes to reach there (Table 1).

Factors associated with TB with DM

Bivariate analysis of this study observed that the factors that were associated with prevalence of DM among tuberculosis patients were; aged ≥ 45 years (OR=3.59, 95% CI 1.78-7.29, p value < 0.001), married (OR=2.46, 95% CI 1.18-5.12, p

Table 1. Characteristics of the study population

Characteristics	Number
Gender	
Male	194
Female	112
Age (years)	
18–29	132
30–44	77
≥ 45	97
Mean (SD)	36.82 (15.95)
Median (Min: Max)	32 (18: 78)
Family size (person)	
< 5	169
≥ 5	137
Mean (SD)	4.53 (2.28)
Median (Min: Max)	4 (1: 21)
Marital status	
Single	102
Married	204
Place of residence	
Urban	267
Rural	39
Educational attainment	
No formal education	77
Formal education	229
Employment Status	
Unemployed	79
Employed	227
Average family monthly income (USD)	
< 150	41
≥ 150	265
Mean (SD)	355.56 (235.82)
Median (Min: Max)	300 (10: 990)
Financial Status	
Inadequate	102
Adequate	204
Body Mass Index (Kg/m²)	
< 18.5	106
≥ 18.5	200
Mean (SD)	20.18 (4.25)
Median (Min: Max)	19.49 (10.38: 40.83)
Systolic Blood Pressure (mmHg)	
< 120	174
≥ 120	132
Mean (SD)	113.70 (14.96)
Median (Min: Max)	110 (80: 170)
Diastolic Blood Pressure (mmHg)	
< 80	193
≥ 80	113
Mean (SD)	76.42 (47.68)
Median (Min: Max)	70 (50: 88.8)
History of Prior TB	
No	232
Yes	74
Diagnosed Initial TB	
Paramedic's	10
Medical Officer	31
Chest specialist	251
Other	14
Family history of TB	
No	253
Yes	53
Time Taken for diagnosis	
< 7 Days	74
≥ 7 Days	232
Number of Health Facilities visited	
< 2	108
≥ 2	198
Sputum grade	
Positive +	193
Positive ++	60
Positive +++	53
Treatment of category	
Cat I	242
Cat II and Cat III	64
Treatment Period	
Intensive	167
Continuous	139
Drug resistant	
None	269
Any drug resistance	29
Multi drug resistance	8
History of smoking	
Never	153
Currently	15
Ever smoke but now quitted	138
History of alcohol consumption	
Never	170
Currently	7
Ever drunk but now quitted	129
Ownership of house	
Own house	113
Rented house	193
Type of house	
Cement	246
Mud/Brick	60
Type of the floor	
Cement	265
Mud/Brick	41
Type of wall	
Cement	247
Mud/Brick	59

Provision of Ventilations	
Satisfactory	242
Unsatisfactory	64
Means of Transportation to DOTS Centre	
Traveling using vehicle	171
Walking	135
Time of travel to reach DOTs Centre by Foot	
<30 Minutes	187
≥30 Minutes	119
Mean (SD)	33.43 (55.75)
Median (Min: Max)	20 (2: 560)

value <0.011) and residing in urban areas (OR=2.46, 95% CI 1.18-5.12, p value < 0.015). In addition, the health service factors such as BMI < 18.5 (OR=2.51, 95% CI 1.38-4.58, p value < 0.003), systolic blood pressure ≥ 120 (OR=1.93, 95% CI 1.06-3.51, p value < 0.031) and diastolic blood pressure ≥ 80 (OR=2.02, 95% CI 1.11-3.67, p value < 0.022) were significantly likely to be associated with TBDM patients. Furthermore, patients who visited ≥ 2 health facilities for the diagnosis of tuberculosis were equally likely to be associated with TBDM (OR=2.37, 95% CI 1.17-4.83, p value < 0.017). Moreover, those who were treating tuberculosis by Cat II and Cat III treatment regimens (OR=2.31, 95% CI 1.21-4.44, p value < 0.014) and had history of alcoholism (OR=2.27, 95% CI 1.22-4.22, p value < 0.008) had higher risk of having TB with DM (Table2).

Table 2. Factors associated with Prevalence of Tuberculosis with Diabetes

Factors	Total Number	%TB DM	OR	95% CI	P value
Gender					0.453
Male	194	18.56	1	1	
Female	112	15.18	0.78	0.41-1.47	
Age (years)					<0.001
18–29	132	10.61	1	1	
30–44	77	12.99	1.26	0.52-2.99	
≥45	97	29.90	3.59	1.78-7.27	
Family size (person)					0.405
<5	169	18.93	1	1	
≥5	137	15.33	0.77	0.42-1.42	
Marital status					0.011
Single	102	9.80	1	1	
Married	204	21.08	2.46	1.18-5.12	
Place of residence					0.015
Rural	39	5.13	1	1	
Urban	267	19.10	4.37	1.02-18.72	
Educational attainment					0.211
No formal education	77	22.08	1	1	
Formal education	229	15.72	0.65	0.34-1.25	
Employment Status					0.652
Unemployed	79	18.99	1	1	
Employed	227	16.74	0.86	0.44-1.66	
Average family monthly income (USD)					0.618
<150	41	14.63	1	1	
≥150	265	17.74	1.26	0.50-3.16	
Financial Status					0.126
Inadequate	102	12.75	1	1	
Adequate	204	19.61	1.67	0.84-3.28	
Body Mass Index (Kg/m²)					0.003
≥18.5	200	12.50	1	1	
<18.5	106	26.42	2.51	1.38-4.58	
Systolic Blood Pressure (mmHg)				0.031	
<120	174	13.22	1	1	
≥120	132	22.73	1.93	1.06-3.51	
Diastolic Blood Pressure (mmHg)				0.022	
<80	193	13.47	1	1	
≥80	113	23.89	2.02	1.11-3.67	
History of Prior TB					0.150
No	232	15.52	1	1	
Yes	74	22.97	1.62	0.84-3.10	
Diagnosed Initial TB					0.882
Paramedic's	10	20.00	1	1	
Medical Officer	31	12.90	0.59	0.09-3.85	
Chest specialist	251	17.93	0.87	0.17-4.25	
Other	14	14.29	0.66	0.07-5.74	
Family history of TB					0.475
No	253	16.60	1	1	
Yes	53	20.75	1.32	0.62-2.76	
Time Taken for diagnosis					0.948
<7 Days	74	17.57	1	1	
≥7 Days	232	17.24	0.97	0.49-1.95	
Numbers of Health Facilities visited				0.017	
<2	108	10.19	1	1	
≥2	198	21.21	2.37	1.17-4.83	
Sputum grade					0.831
Positive+	193	16.58	1	1	
Positive++	60	20.00	1.25	0.60-2.62	
Positive+++	53	16.98	1.02	0.45-2.31	
Treatment of category					0.014
Cat I	242	14.46	1	1	
Cat II and Cat III	64	28.13	2.31	1.21-4.44	
Treatment Period					0.375
Intensive	167	15.57	1	1	
Continuous	139	19.42	1.31	0.72-2.36	
Drug resistant					0.114
None	269	15.99	1	1	
Any drug resistance	37	27.03	1.95	0.87-4.31	
History of smoking					0.141
Never	153	13.07	1	1	

Currently	15	20.00	1.66	0.43-6.41	
Ever smoke but now quitted	138	21.74	1.84	0.99-3.43	
History of alcohol consumption				0.008	
Never	170	11.76	1	1	
Currently	7	42.86	5.62	1.17-11.7	
Ever drunk but now quitted	129	23.26	2.27	1.22-4.22	
Ownership of house					0.857
Own house	113	16.81	1	1	
Rented house	193	17.62	1.05	0.57-1.95	
Type of house					0.591
Cement	246	17.89	1	1	
Mud/Brick	60	15.00	0.81	0.37-1.76	
Type of the floor					0.333
Cement	265	18.11	1	1	
Mud/Brick	41	12.20	0.62	0.23-1.68	
Type of wall					0.502
Cement	247	16.60	1	1	
Mud/Brick	59	20.34	1.28	0.62-2.63	
Provision of Ventilations					0.684
Satisfactory	242	17.77	1	1	
Unsatisfactory	64	15.63	0.85	0.40-1.81	
Means of Transportation to DOTS Centre					
Traveling using vehicle	171	18.71	1	1	
Walking	135	15.56	0.80	0.43-1.46	
Time of travel by Foot to DOTs Centre					0.296
<30 Minutes	187	15.51	1	1	
≥30 Minutes	119	20.17	1.37	0.75-2.50	

Our multivariable analysis found that the factors that were associated with DM were aged ≥ 45 years (adj.OR=3.97, 95% CI 1.81-8.71, p value 0.001), residing in the urban areas (adj.OR=9.75, 95% CI 1.99-47.6, p value 0.005), had BMI < 18.5 Kg/m^2 (adj.OR=3.20, 95% CI 1.58-6.51, p value 0.001), had diastolic blood pressure ≥ 80 mmHg (adj.OR=2.34, 95% CI 1.17-4.66, p value 0.015) and treated with Cat II and Cat III treatment regimens (adj.OR=2.65, 95% CI 1.22-5.73, p value 0.013) were significantly associated with TB with DM (Table 3).

Table 3. Factors associated with Tuberculosis with Diabetes: Multivariable Analysis

Factors	n	(% TBDM)	Crude (OR)	Adj. (OR)	95% CI	P-Value
Age (years)						0.001
18–29	132	10.61	1	1	1	
30–44	77	12.99	1.26	1.49	0.59-3.76	
≥ 45	97	29.90	3.59	3.97	1.81-8.71	
Place of residence						0.005
Rural	39	5.13	1	1	1	
Urban	267	19.10	4.37	9.75	1.99-47.6	
Body Mass Index						0.001
≥ 18.5	200	12.50	1	1	1	
< 18.5	106	26.42	2.51	3.20	1.58-6.51	
Diastolic Blood Pressure (mmHg)						0.015
< 80	193	13.47	1	1	1	
≥ 80	113	23.89	2.02	2.34	1.17-4.66	
Treatment of category						0.013
Cat I	242	14.46	1	1	1	
Cat II and Cat III	64	28.13	2.31	2.65	1.22-5.73	

DISCUSSION

This is the first study in central Nepal that assessed the prevalence and determinants of type 2 diabetes among the pulmonary tuberculosis cases. In our setting, the prevalence of TB with DM was 17.32% (95% CI: 13.05-21.58). This is more than the prevalence among general Nepalese population. However, this finding was less than the previous study conducted in Nepal.[14] This might be due to the study was only focused on all 19 districts of the central Nepal. The finding is similar with the several other studies in China and Bangladesh.[15,16] Although the prevalence was tremendously low in the studies conducted in few countries such as Saudi Arabia and Ethiopia.[17,18] The major causes for this variation in prevalence might be due to Nepal doesn't have proper screening program for DM and the prevalence of TB is also significantly high. Therefore, TBDM is raising day by day. The proportion of male slightly exceeded than that of female with a ratio of 1.73:1. This might be due to the exposure of male is higher than that of female. The respondents from the productive age group (18-29 years) found to be associated with TBDM and 87.25% of the respondents were from urban areas of central Nepal. Which indicated that the lifestyle factors are mostly enhancing the TBDM cases.

The factors associated with the TBDM were identified by performing multiple logistic regression analysis. This study observed that the patients aged ≥ 45 years had three times risk of having TBDM. This was similar with studies conducted in China and Mexico.[6,12,15] The consistent linkage could be illustrated with the fact that this study focused on type 2 DM patients only. In addition, this study also revealed that TB patients living in the urban areas had more than 9 times chances of getting DM. This might be due to increasing of sedentary life style among urban population in Nepal. A systematic review on adult sedentary behaviours revealed that the people living in the urban areas were more likely to spend ample amount of time in sedentary activities.[19] However, a study conducted in Bangladesh found that the TBDM was most common in rural areas than urban.[16] Therefore, TB as well as TBDM are affecting both rural and urban populations.

In addition, our study found that more TB patients with low BMI had DM. This might be due to the tuberculosis disease results in weight deficit in comparison to those without tuberculosis, which affects both lean and fat mass. When the body mass improves during tuberculosis treatment, it is therefore important that the regain also affects slim body mass, since sole build-up of fat may cause insulin resistance and predispose to weaken glucose metabolism.[20] Furthermore, factors such as increasing diastolic blood pressure and failure of Cat I TB treatment regimen were equally leading to the co-infection with DM. The one possible answer for the failure of Cat I TB treatment regimen could be TB patients with DM reduce the isoniazid concentration than pyrazinamide.[21]

This study covers all 19 districts of central Nepal which has more than one third of TB patients therefore we can generalize the study outcome to the central Nepal. However, this study has also some limitations such as the study was dependent on responses of the patients as well as identifying blood glucose level to diagnose DM, so there might be the recall bias. In addition, the study was also based on laboratory findings therefore instrument validity might be also one of the limitation. To overcome those limitations, the recruited data enumerators were trained prior to the conduction of the study and validity of instruments was tested in a regular basis.

CONCLUSION

The prevalence of T2DM among tuberculosis patients was higher than the prevalence of diabetes in general population of Nepal and it was higher among male and the older aged TB patients. In addition, social factors as well as health service factors were seemed as strong predictors for having TBDM. Therefore, early screening of DM among the TB patients will be a novel initiation on the way to reduce TB burden in Nepal.

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