# The Role of Type 2 Diabetes Mellitus on the Clinical Manifestation of Pulmonary Tuberculosis: A Study from Nepal

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# ABSTRACT

Public Health Section

**Introduction:** Tuberculosis (TB) ranks as the seventh leading cause of death in Nepal. Similarly, the prevalence of Diabetes Mellitus (DM) has also shown an increasing trend in the country and it has been observed that diabetes is strongly associated with falling treatment outcome of tuberculosis. Hence, the association of tuberculosis with Type 2 Diabetes Mellitus (T2DM) might be higher than the assumption and it needs more attention as well as appropriate measures to improve treatment outcomes of both diseases.

**Aim:** To determine the risk factors of T2DM comorbidity among TB patients in the Central Development Region of Nepal.

**Materials and Methods:** A case-control study was conducted by administration of structured questionnaire interview among all forms of pulmonary tuberculosis patients. A total of 102 tuberculosis patients with T2DM who met the inclusion criteria were considered as cases and 306 non-diabetes tuberculosis cases were considered as controls. The study was conducted among the patients attending the tuberculosis treatment centres of all 19 districts of central Nepal. The risk factors of diabetes among tuberculosis patients was estimated by using unconditional multiple logistic regression, adjusted odds ratio and their 95% CI were measured.

**Results:** This present study found that the risk factors of type 2 DM comorbidity among tuberculosis patients were; age  $\geq$ 45 years (adj. OR=8.00, 95% CI: 4.21-15.21, p-value <0.001), formal education (adj. OR=2.12, 95% CI: 1.08-4.15, p-value is 0.027), being underweight {Body Mass Index (BMI) <18.5 Kg/m<sup>2</sup>} (adj. OR=2.61, 95% CI: 1.49-4.59, p-value <0.001) and with diastolic blood pressure  $\geq$ 80 (adj. OR=3.05, 95% CI: 1.72-5.43, p-value <0.001). In addition, tuberculosis patients who visited more than two health facilities for diagnosis and treatments (adj. OR=2.06, 95% CI: 1.10-3.85, p-value is 0.024) and had medium level of knowledge (60-80%) on tuberculosis and diabetes (adj. OR=2.19, 95% CI: 1.09-4.39, p-value is 0.027) were more prone to having tuberculosis and diabetes.

**Conclusion:** Tuberculosis with diabetes is strongly associated with age, education, hypertension comorbidity as well as delayed diagnosis. Therefore, regular DM screening program as well as timely health monitoring system of tuberculosis patients will enhance the tuberculosis control program in reducing TB burden from delayed cure in Nepal.

Keywords: Central Nepal, Observational study, Tuberculosis with diabetes

## INTRODUCTION

The double burden of TB with DM is a well-known scenario in the world. Since prehistoric time to the earlier 20th century, diabetes was accounted as co-morbidity among tuberculosis patients [1]. Globally, 15-25% TB patients suffer from DM [2,3]. Moreover, diabetes is a well-known risk factor for tuberculosis and is significantly associated with worse tuberculosis consequences [4-6]. Similarly, TB is associated with worsening of glycaemic control [1,7-10]. A number of studies from America, Europe and Asia have described firm association between TB and DM [1,11-17]. In general, the expected threat of active TB is three-fold among diabetic people [5]. Simultaneously, a study in Tanzania revealed that DM in urban population raised the consequences of active TB four-fold [8]. In addition, a systematic review observed that diabetes is strongly associated with high risk of failure and death during treatment of TB. Patients with diabetes have a Risk Ratio (RR) for the collective outcome of treatment failure and death of 1.69 (95% CI, 1.36 to 2.12) [5].

Tuberculosis (TB) remains a major public health burden in the South-East Asian Region (SEAR). The region possesses 38% of the global burden of TB in terms of new cases, whereas Nepal accounts for 1.3% [18]. TB remains the 7<sup>th</sup> common cause of life loss in Nepal [19]. In the fiscal year 2017 /2018, National Tuberculosis Program (NTP) enumerated 32,474 TB cases. Of which, bacteriologically confirmed TB cases were 57% (18,000), pulmonary clinically diagnosed cases were 14% (4,411) and 29% (9,312) were extra-pulmonary TB cases [19]. In addition, tuberculosis deaths in Nepal reached 5,506 as

per WHO which is 3.5% of total death [20]. Accordingly, the global estimate of the prevalence of diabetes for 2010-2030 shows that, the prevalence of DM was 3.3% in Nepal and it will be reached to 4.2% with 28/1000 average annual increment in 2030 [21].

Therefore, understanding real causes of the both diseases will prove to be productive for the controlling of TB and DM. This present study focused on identifying the role of T2DM on the clinical manifestation of pulmonary TB when controlling others covariates in the Central Development Region of Nepal (CDR).

# MATERIALS AND METHODS

#### Study Design

A case control study was conducted by administrating a structured questionnaire interview among the TB with DM (Cases) and TB without DM (Control) to determine the risk factors of DM TB patients. This study recruited all forms of tuberculosis patients from the TB treatment centres of all 19 districts of central Nepal, during September 2018 to February 2019. This study area also covered the National Tuberculosis Centre (NTC) which is the main point of the NTP. NTC is accountable for formation of programme policies, strategy and planning.

#### **Ethical Considerations**

This present study has been approved by the Ethics Committee in Human Research of Khon Kaen University, Khon Kaen, Thailand (HE612209), the Nepal Health Research Council (2640) and the Nepal and Institutional Review Committee (Protocol approved number 01/18), Kathmandu University School of Medical Sciences, Dhulikhel, Nepal.

#### Sample Size and Sampling Procedure

The sample size of 408 was calculated by applying the formula of case-control study sample size estimation [22]. Among the total of 408 samples, 102 cases and 306 controls were selected respectively. As per the result of the previous study which observed that the Odds Ratio (OR) of DM have risk of treatment failure was 2.14, AFB positivity after two months of treatment of TB was taken as reference OR for the calculation of sample size [23]. All forms of diagnosed TB patients of both sex, aged 18 years and old as well as those willing to participate in this study were screened for DM, by plasma glucose examination. Then after, TB patients with DM were included as cases and patients without DM were considered as controls. Among the eligible controls, the systematic random sampling was used to select control with reference to case. However, the critically ill patients as well as those who were not willing to participate in any stage of study period were excluded.

#### **Data Collection**

A structured guestionnaire was prepared based on the objective and relevant literature to identify the factors associated with TB and DM comorbidity [2]. The questionnaire was tested by five experts for the content validity. The reliability test was conducted among 30 T2DM patients in other regions. The Cronbach's alpha coefficient of this questionnaire was 0.874. Regarding the scoring technique we adopted for this study to identify knowledge and attitude, the first and foremost step that we took was to reverse the scores before adding them to their domains. It was done to reflect the increment in the variables that we studied. Moving beyond, the present authors calculated the percentage score for level of knowledge, attitude using the following technique: (Sum of scores obtained/maximum possible score that could be obtained)×100. Percentiles scores were computed following the previous step and the studied variables were expressed as laying between a ranges of 0 to 100 percentage, the highest percentage reflected the increase in the characteristic/variable. In addition, scores exceeding 80% was considered as the high level of knowledge and good attitude on diseases, similarly score between 60-80 percentage was considered as medium level and below 60 percentage has been considered as low level of knowledge and poor attitude respectively [24].

The study required two additional data enumerators apart from the investigator to collect the data. The enumerators were the paramedics (health assistants and laboratory technician) who had basic understanding on medicine surgery and laboratory technology for three years after finishing ten years of schooling. They were received formal training before the start of the investigation. The data were collected from each TB treatment centres of central Nepal. In addition, medical records of the study participants were reviewed to assure the quality of the data. Furthermore, the laboratory tests have been conducted in the certified laboratory and all tools were cross checked properly.

#### STATISTICAL ANALYSIS

In reference with a previous study, fasting blood glucose level glucose ≥126 mg/dL or a random blood glucose ≥200 mg/dL was estimated on the same day of data collection; has been considered as cut-off value to determine cases [25]. The categorical data were reported as number and percentage. Mean, standard deviation, median and range (minimum: maximum) was described for the continuous variable. Odds Ratio (OR) and their 95% Confidence Intervals (CI) was estimated by using unconditional logistic regression with DM as an outcome. Bivariate analysis was performed to

measure the effect of each independent variable or risk factors of DM. Multivariable analysis was performed by using multiple logistic regression including variables that showed a significant statistical effect in prediction of DM in bivariate analysis. Variables which had potential of association with DM in the bivariate analysis (p $\leq$ 0.25) were included in the multivariable analysis model, presenting adjusted odds ratio and 95% confidence interval for the magnitude of association. Statistical significance was considered as p<0.05. All the data were analysed by using STATA (Version 13, Stata Corporation, College Station TXUSA).

## RESULTS

Majority of the participants in both case and control groups were male (66.67%) and (60.46%) respectively [Table/Fig-1]. Majority of the TB with DM patients aged ≥45 years (69.61%) that was higher than that of control (25.49%). Most cases were married (85.29%) than controls (61.76%). However, more than 80% of the respondents from both groups were residing in urban areas of Nepal i.e. 88.24% among cases and 85.62% among control. In addition, less than half of the patients with diabetes earned USD ≥150 (47.44%) however, nearly two third of the control earned USD ≥150 (64.42%).

Furthermore, both systolic and diastolic blood pressure has been raised amongst the cases i.e. 59.80% than that of control 37.58 and 32.68 respectively. In relation with access to the services of both groups were considered more than 7 days to get diagnosis of disease. However, 78.43% of the TB with DM patients visited more than 2 health facilities for the diagnosis. In addition, majority of the patients with positive 3+ sputum grade were observed among the cases group (26.47%).

This study revealed that the 60.78% of the study participants were residing on their own houses however only half of the controls had their own houses (37.25%). In terms of the knowledge on the diseases, 30.39% of the cases has medium level of knowledge however only 15.03% of the control were aware on it. The attitude score was observed well on both groups i.e. 58.82% and 43.46% respectively. The demographic details with treatment and other important information are given in [Table/Fig-1].

#### Factors Associated with TB with DM: Bivariate Analysis

The bivariate analysis revealed a crude association of each independent factor with developing TB with DM. Our study observed that the patients who were aged  $\geq$ 45 years (OR=6.69, 95% CI 4.08-10.97, p-value <0.001) and got married (OR=3.58, 95% CI 1.98-6.50, p-value <0.001) had higher risk of having TB with DM. Similarly, health status factors such as BMI <18.5 Kg/m<sup>2</sup> (OR=2.73, 95% CI 1.72-4.33, p-value <0.001), systolic blood pressure  $\geq$ 120 (OR=2.47, 95% CI 1.56-3.91, p-value <0.001), diastolic blood pressure  $\geq$ 80 (OR=3.06, 95% CI 1.93-4.87, p-value <0.001), and health seeking behaviour of visited  $\geq$ 2 health facilities for the diagnosis (OR=2.06, 95% CI 1.22-3.50, p-value 0.005) and had positive three + Sputum grade (OR=2.00, 95% CI 1.14-3.50, p-value is 0.005) were more likely to be TB with DM comorbidity. However, those who lived in rental houses (OR=0.38, 95% CI 0.24-0.61, p-value <0.001) were less likely to have TB with DM.

Moreover, the study population who had medium level of knowledge (60-80%) on diseases (OR=2.47, 95% Cl 1.46-4.17, p-value <0.001) and had good attitude (>80%) to overcome the disease (OR=2.26, 95% Cl 1.10-4.61, p-value is 0.021) were associated to getting TB with DM [Table/Fig-2].

Factor associated with TB DM patients: multivariable analysis, Age, Educational attainment, Body mass index, Diastolic blood pressure, Numbers of health facilities visited, Knowledge on TB and DM are shown in [Table/Fig-3]. Roshan Kumar Mahato et al., The Role of Type 2 DM on the Clinical Manifestation of Pulmonary Tuberculosis

Sputum grade

Characteristics	Case (n=102)	Control (n=306)
Gender	1	
Male	68 (66.67)	185 (60.46)
Female	34 (33.33)	121 (39.54)
Age (years)	1	1
18-29	19 (18.63)	153 (50.00)
30-44	12 (11.76)	75 (24.51)
≥45	71 (69.61)	78 (25.49)
Family size (person)		
<5	45 (44.12)	168 (54.90)
≥5	57 (55.88)	138 (45.10)
Marital status		100 (10110)
Single	15 (14.71)	117 (38.24)
Married	87 (85.29)	189 (61.76)
	07 (03.29)	189 (01.70)
Place of residence	00 (80 04)	060 (05 60)
	90 (88.24)	262 (85.62)
Rural	12 (11.76)	44 (14.38)
Educational attainment		74/04/10
No formal education	33 (32.35)	74 (24.18)
Formal education	69 (67.65)	232 (75.82)
Employment status	1	
Unemployed	23 (22.55)	75 (24.51)
Employed	79 (77.45)	231 (75.49)
Average family monthly	income (USD)	1
<150	9 (8.82)	39 (12.75)
≥150	93 (91.18)	267 (87.25)
Average monthly expen	se (USD)	γ
<150	60 (58.82)	196 (64.05)
≥150	42 (41.18)	110 (35.95)
Financial status	1	1
Inadequate	24 (23.53)	98 (32.03)
Adequate	78 (76.47)	208 (67.97)
Body mass index (Kg/m	2)	
<18.5	60 (58.82)	105 (34.31)
18.5-24.9	40 (39.22)	175 (57.19)
≥25	2 (1.96)	26 (8.50)
Systolic blood pressure	(mmHg)	
<120	41 (40.20)	191 (62.42)
≥120	61 (59.80)	115 (37.58)
Diastolic blood pressure	e (mmHg)	
<80	41 (40.20)	206 (67.32)
≥80	61 (59.80)	100 (32.68)
History of prior TB		
No	82 (80.39)	236 (77.12)
Yes	20 (19.61)	70 (22.88)
Family history of TB		1
No	90 (88.24)	255 (83.33)
Yes	12 (11.76)	51 (16.67)
Time taken for diagnosi	s	
<7 Days	21 (20.59)	71 (23.20)
≥7 Days	81 (79.41)	235 (76.80)
Numbers of health facili	ties visited	
<2	22 (21.57)	111 (36.27)
	80 (78.43)	195 (63.73)

Sputum grade							
Positive+		50 (49.02)			7)		
Positive++		25 (24.51)		61 (19.93)			
Positive+++		27 (26.47)		52 (16.99)			
Treatment of categ	ory						
Cat I		81 (79.41)		252 (82.3	5)		
Cat II & Cat III		21 (20.59)		54 (17.65	5)		
Treatment period							
Intensive		68 (66.67)		170 (55.5	6)		
Continuous		34 (33.33)		136 (44.4	4)		
Ownership of hous	e						
Rented house		40 (39.22)		192 (62.7	5)		
Own house		62 (60.78)		114 (37.2	5)		
Type of house							
Cement		86 (84.31)		245 (80.0			
Mud/Brick		16 (15.69)		61 (19.93	3)		
Type of the floor							
Cement		87 (85.29)		262 (85.6			
Mud/Brick		15 (14.71)		44 (14.38	3)		
Type of wall					-		
Cement		79 (77.45)		251 (82.03)			
Mud/Brick		23 (22.55)		55 (17.97	7)		
Provision of ventila	tion at home	85 (83.33)					
Satisfactory		243 (79.41)					
Unsatisfactory		17 (16.67)		63 (20.59	9)		
Means of Transpor			es				
Traveling using vehic	le	63 (61.76)		166 (54.2			
Walking		39 (38.24)		140 (45.7	5)		
Time of travel to DO	OTs centres b	-					
<30 Minutes		60 (58.82)		193 (63.0			
≥30 Minutes		42 (41.18)		113 (36.9	3)		
Knowledge on TB		74 (00 5 1)		0.000			
Low (<60%)		71 (69.61)		260 (84.9	,		
Medium (60-80%)		31 (30.39)		46 (15.03	3)		
Attitude on disease	•				_,		
Poor (<60%)		11(10.78)		55 (17.97)			
Medium (60-80%)		31 (30.39)		118 (38.56)			
Good (>80%)		60 (58.82)		133 (43.4			
[Table/Fig-1]: Char	acterises of TI	3 DM patients (	case) and	d TB patients (co	ontrol).		
Factors	Case (n=102)	Control (n=306)	OR	95% CI	p-value		
Gender	(	(					
Male	68 (66.67)	185 (60.46)	1	1			
	. ,				0.260		
Female	34 (33.33)	121 (39.54)	0.76	0.477-1.22			
Age (years)	0.1 (0.5 - 5-)	000 (= · = · :	1				
<45	31 (30.39)	(30.39) 228 (74.51)		1	<0.001		
≥45	71 (69.61)	78 (25.49)	6.69	4.08 -10.97			

Family size (persons)								
<5	45 (44.12)	168 (54.90)	1	1	0.050			
≥5	57 (55.88)	138 (45.10)	1.542	0.98-2.42	0.059			
Marital status								
Single	15 (14.71)	117 (38.24)	1	1	<0.001			
Married	87 (85.29)	189 (61.76)	3.58	1.98-6.50	<0.001			
Place of residence								
Urban	90 (88.24)	262 (85.62)	1	1	0.500			
Rural	12 (11.76)	44 (14.38)	0.79	0.40-1.57	0.000			

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No formal education	33 (32.35)	74 (24.18)	1	1	
	. ,	. ,			0.11
Formal education	69 (67.65)	232 (75.82)	0.66	0.41-1.09	
Employment status	23 (22.55)	75 (01 54)	1	1	
Unemployed	. ,	75 (24.51)			0.69
Employed	79 (77.45)	231 (75.49)	1.12	0.65-1.89	
Average family mo	, , , , , , , , , , , , , , , , , , ,				
<150	9 (8.82)	39 (12.75)	1	1	0.27
≥150	93 (91.18)	267 (87.25)	1.51	0.70-3.23	
Average monthly e					
<150	60 (58.82)	196 (64.05)	1	1	0.34
≥150	42 (41.18)	110 (35.95)	1.247	0.79-1.97	
Financial status	1	1			
Inadequate	24 (23.53)	98 (32.03)	1	1	0.09
Adequate	78 (76.47)	208 (67.97)	1.53	0.91-2.57	
Body mass index (I	Kg/m²)	1			
≥18.5	42 (41.18)	201 (65.69)	1	1	<0.001
<18.5	60 (58.82)	105 (34.31)	2.73	1.72-4.33	2.001
Systolic blood pres	sure (mmHg)	)			
<120	41 (40.20)	191 (62.42)	1	1	< 0.001
≥120	61 (59.80)	115 (37.58)	2.47	1.56-3.91	.0.001
Diastolic blood pre	ssure (mmHg	3)			
<80	41 (40.20)	206 (67.32)	1	1	<0.001
≥80	61 (59.80)	100 (32.68)	3.06	1.93-4.87	<0.001
History of prior TB					
No	82 (80.39)	236 (77.12)	1	1	0.400
Yes	20 (19.61)	70 (22.88)	0.82	0.47-1.44	0.486
Family history of T	В	·			
No	90 (88.24)	255 (83.33)	1	1	0.004
Yes	12 (11.76)	51 (16.67)	0.67	0.34-1.31	0.224
Time taken for diag	jnosis				
<7 Days	21 (20.59)	71 (23.20)	1	1	
≥7 Days	81 (79.41)	235 (76.80)	1.16	0.67-2.02	0.58
Numbers of health	facilities visit	ted	LI		
<2	22 (21.57)	111 (36.27)	1	1	
≥2	80 (78.43)	195 (63.73)	2.06	1.22-3.50	0.005
Sputum grade	1 (	(/			1
Positive+	50 (49.02)	193 (63.07)	1	1	
Positive++	25 (24.51)	61 (19.93)	1.58	0.90-2.77	0.035
Positive+++	27 (26.47)	52 (16.99)	2.00	1.14-3.50	-
Treatment of categ	. ,	(			1
Cat I	81 (79.41)	252 (82.35)	1	1	
Cat II & Cat III	21 (20.59)	54 (17.65)	1.21	0.69-2.12	0.511
Treatment period					1
Intensive	68 (66.67)	170 (55.56)	1	1	
Continuous	34 (33.33)	136 (44.44)	0.63	0.39-0.99	0.047
Ownership of hous	. ,	. , , ,			1
Own house	62 (60.78)	114 (37.25)	1	1	
Rental house	40 (39.22)	192 (62.75)	0.38	0.24-0.61	<0.001
		102 (02.10)	0.00	0.24-0.01	<u> </u>
Type of house	86 (94 21)	215 100 07	4	-1	
Cement	86 (84.31)	245 (80.07)	1	1	0.335
Mud/Briek	16 /15 00)				
	16 (15.69)	61 (19.93)	0.75	0.41-1.37	
Mud/Brick Type of the floor					<u> </u>
	16 (15.69) 87 (85.29) 15 (14.71)	262 (85.62) 44 (14.38)	1	1 0.54-1.94	0.935

Type of wall									
Cement		79 (7	7.45)	251 (8	32.03)	1	1		
Mud/Brick		23 (2	2.55)	55 (1	7.97)	1.33	0.76-2.29	0.316	
Provision of v	/entila	tions							
Satisfactory		85 (8	3.33)	243 (	79.41)	1	1	0.05	
Unsatisfactory	,	17 (1	6.67)	63 (2	0.59)	0.77	0.43-1.39	0.381	
Means of trar	nsport	ation							
Traveling usino Vehicle	9	63 (6	1.76)	166 (	54.25)	1	1	0.183	
Walking		39 (3	8.24)	140 (4	45.75)	0.73	0.46-1.16		
Time of trave	l to DO	DTS							
<30 Minutes		60 (5	8.82)	193 (6	63.07)	1	1		
≥30 Minutes		42 (4	1.18)	113 (	36.93)	1.19	0.76-1.89	0.445	
Knowledge o	n TB								
Low (<60%)		71 (6	9.61)	260 (8	34.97)	1	1	0.001	
Medium (60-80%)		31 (3	0.39)	46 (1	5.03)	2.47	1.46-4.17	0.001	
Attitude on d	isease	s							
Poor (<60%)		11(1	0.78) 55 (1		7.97)	1	1		
Medium (60-8	0%)	31 (3	0.39)	118 (	38.56)	1.31	0.61-2.80	0.021	
Good (>80%)		60 (5	8.82)	133 (4	43.46)	2.26	1.10-4.61	1	
[Table/Fig-2]:	Facto	or asso	ciated	with DN	1 among	TB patie	ents: bivariate ar	nalysis.	
Factors		ise 102)	Control (n=306)		Crude (OR)	Adj. (OR)	95% CI	p- value	
Age (years)							· · · · · · · · · · · · · · · · · · ·		
<45	31 (3	0.39)	228 (	74.51)	1	1	1	.0.001	
≥45	71 (6	9.61)	78 (2	25.49)	6.69	8.00	4.21-15.21	<0.001	

<45	31 (30.39)	228 (74.51)	1	1	1	<0.001			
≥45	71 (69.61)	78 (25.49)	6.69	8.00	4.21-15.21	<0.001			
Educational	Educational attainment								
No formal education	33 (32.35)	74 (24.18)	1	1	1	0.027			
Formal education	69 (67.65)	232 (75.82)	0.66	2.12	1.08-4.15	0.027			
Body mass in	ndex (Kg/m²)								
≥18.5	42 (41.18)	201 (65.69)	1	1	1	0.001			
<18.5	60 (58.82)	105 (34.31)	2.73	2.61	1.49-4.59	0.001			
Diastolic blo	od pressure								
<80 mmHg	41 (40.20)	206 (67.32)	1	1	1	-0.001			
≥80 mmHg	61 (59.80)	100 (32.68)	3.06	3.05	1.72-5.43	<0.001			
Numbers of I	nealth facilitie	es visited							
<2	22 (21.57)	111 (36.27)	1	1	1	0.004			
≥2	80 (78.43)	195 (63.73)	2.06	2.06	1.10-3.85	0.024			
Knowledge on TB and DM									
Low (<60%)	71 (69.61)	260 (84.97)	1	1	1				
Medium (60-80%)	31 (30.39 )	46 (15.03)	2.47	2.19	1.09-4.39	0.027			
[Table/Fig-3]: Factor associated with TB DM patients: multivariable analysis.									

# DISCUSSION

In the present study, 102 cases and 306 controls from central Nepal were recruited. This study observed that diabetes is a strong risk factor for pulmonary tuberculosis. Although, this was an unmatched case-control study, more than 60% of male were recruited. This is because male population was equally high in both groups. This comparison has also been observed in the study conducted in Taiwan [10]. Majority of the respondents were married in case group. In addition, more than 85% of the respondents from both groups were residing in urban areas of central Nepal. However, the variations on socio-economic status have been observed among the both groups. Furthermore, the clinical factors such as systolic and diastolic blood pressure were increased among the cases than that of controls. This is because of renowned comorbidity of DM with hypertension.

This study performed a multivariable analysis to identify the risk factors of TB with DM. The present authors observed that six independent predictors were associated with TB DM, while controlling possible confounders. Rising age is one of the risk factor for having both diseases. This result is consistent with studies conducted in Bangladesh [2], Malaysia [26], China [27] and Taiwan [10]. This is because of the T2DM risk rises with age and poses a much greater threat at population level. In addition, the TB patients with DM were fundamentally older than TB patients without diabetes therefore more than 6 times higher risk has been observed [28,29]. Similarly, the TB patients who had taken formal education were found to be at an increasing risk of TB DM. It has also been revealed in the study conducted in Bangladesh. They found that the patients who had higher education (secondary level and above) were prone to develop TB-DM [2]. The possible reason for this could be that the DM cases were more observed in urban areas where majority of residence are educated.

Simultaneously, clinical factors such as reduced BMI doubled the burden of TB-DM. The possible explanation would be that TB has a well-known negative effect on patient's nutritional status by affecting dietary intake due to poor absorption of nutrients from the intestine, loss of appetite and increase uptake of nutrients by specific target tissue due to the increase of body metabolism. Therefore, severe malnutrition has a profound effect on cell-mediated immunity. A study conducted in Kuala Lumpur [26] and another review [30] had also observed similar findings. In addition, the study conducted in Mwanza, Tanzania reported that smear-positive TB was associated with a 10 kg weight loss, which was both reflected in large deficits in arm fat area and especially arm muscle area, suggesting that nutritional support to facilitate optimal recovery of lean body mass is needed during the TB treatment [31]. Moreover, rising diastolic blood pressure was also found to be associated with increasing risk of TB DM. A systematic review on TB and hypertension revealed that the association between TB and hypertension, all included hypertension as a potential confounder for TB cases [32]. Furthermore, the respondents who visited more than 2 health facilities for the diagnosis of diseases had more chances of having DM. This might be due to the delay in health system responses [33]. All TB treatment centres of Nepal are not well equipped to diagnose all forms of TB. Moreover, knowledge on the diseases were also responsible for the comorbidity which was similar with a study conducted in Ethiopia [34]. Therefore, the present authors advocate to screen patients with TB for DM, especially those aged >35 years and run public awareness programmes, mobile camps and other health related activities in the communities throughout the year.

## LIMITATION

This present study covered a significantly large population of Nepal. This study depended on responses of the patients as well as identifying blood glucose level to find out DM, therefore honest responses and validity of instrument was very critical. However, the questionnaire was pre-tested to confirm that all questions are clear and standard instruments were used so as to obtain valid tests results.

## CONCLUSION

Tuberculosis with diabetes is strongly associated with patients aged ≥45 years, those with formal education, low BMI, and raised diastolic blood pressure as well as face trouble to get an early diagnosis. In addition, level of knowledge is also identified as a strong determinant for having TB-DM. Therefore, priority needs to be given on making the screening practices uniform, universal and mandatory for all the patients diagnosed with TB and on treatment. In addition, awareness should be created for patients who complain of cough for more than two weeks, night sweating, chest pain and unusual weight loss, more so when DM is present as an associated comorbidity. They should be made to visit physicians as early as possible.

## ACKNOWLEDGEMENTS

The authors wishes to thank the research group on Prevention and Control of Diabetes Mellitus in the Northeast of Thailand of the Faculty of Public Health, Khon Kaen University.

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FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: Jul 01, 2019 Date of Peer Review: Jul 16, 2019 Date of Acceptance: Jul 31, 2019 Date of Publishing: Sep 01, 2019