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Prevalence of Diabetes Mellitus Among Tuberculosis Patients in the Pulmonary TB Ward, Mahosot Hospital, Lao PDR

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Abstract

Background: Diabetes mellitus (DM) is documented as an important risk factor to tuberculosis (TB). Lao PDR has high TB burden, along with increasing DM prevalence. There are inadequate data on prevalence of DM among TB cases in Lao PDR and lack of data about the effect of DM on treatment outcomes of TB.

Objective: To determine prevalence of DM among TB patients admitted to the Pulmonary Department, Mahosot hospital, Lao PDR, to describe the socio-demographics and others factor associated with TB-DM co-occurrence and to compare the clinical features and treatment outcomes between TB with and without DM patients.

Methods: Using a retrospective design, 199 active TB diagnosed at the Pulmonary-Tuberculoisis Ward, Mahosot Hospital, Lao PDR between February 2015 to August 2016 that met the study criteria were selected. Data regarding socio-demographic characteristics, factors associated with TB-DM co-occurrence, clinical and laboratory parameters, drug susceptibility and treatment outcomes were compared between TB patients with DM and those without DM.

Results: Of the 199 patients, 48 (24.12%) had DM, of which 33 (68.75%) previously diagnosed, 15 (31.25%) new diagnosis at TB diagnosis. On baseline characteristics found that mean age of participating was 52.56 (SD=18.88) years, TB with DM were significantly older than TB without DM with p=0.007, male patients were more than female (69% *vs*. 31%), Government staff with TB-DM was higher proportion than those without DM (41.67% *vs*. 23.84%, p=0.05), patients with family history of DM shown diagnosed DM higher than those without family history of DM (25.00%) *vs.* 11.26%, p=0.005). While, alcohol consumption and smoking was not significant differed between both groups, weight loss >5% of TB patients with DM was significantly lower than those without DM (25.00% *vs* 41.06%, p=0.04). TB with DM patients presented cavity on chest radiograph significantly higher than those without DM (91.67% *vs* 78.15%, p=0.03), sputum AFB conversion at month 2 after treatment shown TB with DM significantly lower than those without DM (43.75% *vs*. 61.59%, p=0.03). Cured rate of TB with DM patient was significantly lower than TB-non DM (58.33% *vs*. 74.17%, p=0.036).

Conclusion: Screening for DM in TB patients would help for its early detection and a good control plasma glucose levels to improve the treatment outcomes of TB patients.

Keywords: Diabetes mellitus; Tuberculosis; Diabetes; Prevalence factors associated; Treatment outcomes; Risk factors

Introduction

The global burden of diabetes mellitus (DM) and tuberculosis (TB) is huge. TB continues to be the leading killer among bacterial diseases worldwide. Nearly one-third of world's population is infected with *Mycobacterium tuberculosis*, approximately nine million people develop the disease each year, and almost two million die annually from the disease, in 2015 was one of the top 10 causes of death worldwide [1].

The global burden of DM is rising; Diabetes is one of the most important diseases of the 21st century. World Health Organization illustrated that the prevalence is estimated to reach 438 million by 2030, and more than 80% of the adult cases will be in newly developed or developing countries (IDF Diabetes Atlas, 2009). Available reports suggested that 95% of patients with TB live in the low-and middle-income countries and at the same time there was more than 70% of patients with DM also live in the same countries, especially in South East Asia is home to >72 million adults with diabetes in 2013 and is expected to exceed 123 million in 2035. Every 6 seconds a person dies because of diabetes. In 2015, five million deaths were recorded from this cause. Diabetes represents 14.5% of all-cause mortality, almost half of these in subjects under the age of 60 [2].

According to a systematic review and meta-analysis to quantitatively summarize evidence for the impact of diabetes on TB outcomes. The result showed that Diabetes increases the risk of failure and death combined, death, and relapse among patients with TB. This study highlights a need for increased attention to treatment of TB in people with diabetes, which may include testing for suspected diabetes, improved glucose control, and increased clinical and therapeutic monitoring [3]. This is despite the fact that with a timely diagnosis and correct treatment, most people with DM who develop TB disease can be cured. Workneh et al. illustrated that DM increases the risk of active TB as it is hard to treat an infection in the face of poor glycemic control [4].

Recent studies have shown an increased prevalence of diabetes in

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people with TB. Unpublished data from the South Pacific shows the facts that between 40%-45% of the subjects with TB have DM. The prevalence of DM in patients with TB is also high in other regions: Kerala, India 44%, Karnataka, India 32%, Texas 39%, Mexico 36%, Tanzania 16.7%, Pakistan 16% and Indonesia 14.8%, Thailand 16.3%, Vietnam 9% [5]. Screening for DM in TB patients could improve DM case detection and early treatment and indirectly lead to better TB specific treatment outcomes [6]. Many research questions regarding association between diabetes and TB remain unanswered because of lack of well-designed studies.

Laos is located in Southeast Asia, the region of high prevalence of TB and DM. Moreover that the socio-economic condition is still low, lacking the report of DM-TB, DM is a known risk factor for TB, and with the increasing prevalence of type 2 DM in less developed regions, many patients with TB will have concomitant DM. Presently, lack of known about the effect of DM on the clinical presentation and treatment outcome of TB. Therefore, this study was planned to assess the prevalence of DM and associated risk factors such as smoking and alcohol consumption amongst active TB patients, Treatment outcome between TB with and without DM patients admitted to the Pulmonary Department, Mahosot Hospital, Lao PDR.

Material and Methods

This was a retrospective study that included adult participants diagnosed with TB at Pulmonary department at Mahosot hospital, Lao PDR, during 1st February 2015 to 31st August 2016, with inclusion criteria: Lao nation age ≥ 15 years old and complete perform baseline evaluation at first visit in SSc patients including plasma glucose. We excluded patients if they were age <15, foreigner.

A diagnosis of TB was based on the World Health Organizaiton (WHO) criteria [7] base on clinical symptoms of the patients suspected. More than 80% of TB patients infected with the lung. Therefore, patients with both Pulmonary and Extrapulmonary TB also counts in groups of Pulmonary TB patients such as (i) Sputum Microscopy (Acid Fast Bacilli Technique): Positive called (Ps+), (ii) Sputum Microscopy (AFB): Negative, but Gene x-pert: Positive called (Ps-b+), (iii) Sputum Microscopy (AFB): Negative, Gene x-pert: Negative, but CXR suspected TB by Radiologist after rule out other causes called (Ps-b-).

DM was diagnosed by American Diabetes Association (ADA) 2016 guideline by: (i) Fasting Plasma Glucose ≥ 126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.* or (ii) 2-h PG ≥ 200 mg/dL (11.1 mmol/L) during an OGTT. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.* or (iii) A1C ≥ 6.5% (48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.* or (iv) In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥ 200 mg/dL (11.1 mmol/L).*In the absence of unequivocal hyperglycemia, results should be confirmed by repeat testing [8].

Statistical analysis

Data was entered into Excel and exported to software STATA version 14 for analysis, calculated including Mean (Standard Deviation), frequency, two way table with measures of association Chi-square test, fisher's exact test, p-value. The data was summarized and organized using graphs, tables and texts. The study flowchart was summarized in Figure 1.

Results

Description of socio-demographic characteristics of patients

A total of 199 TB patients were diagnosed and subsequently managed at the Pulmonary Department, Mahosot hospital between February 2015 to August 2016. Mean age of participating in the study was 52.56 (SD=18.88) years, patients with TB who had DM were significantly older than TB without DM with p=0.007, the male patients were more than female (69% *vs*. 31%), Gov/pvt.employed 28.14% Government staff with TB-DM is higher proportion than without DM (20 (41.67%) *vs*. 36 (23.84%), 38.69% was farmer/ worker, unemployed 26.13%, student 7.04%. In this study found that the patients in Vientiane Capital is more than others (69.35% *vs*. 30.65%) but not significant differed between TB with and without DM, patient who has family history of DM was 29 (14.57%) and found TB-DM was significantly higher than without DM [12 (25.00%) *vs*. 17 (11.26%), p=0.005]. Of these 199 patients, underlying medical illness was found including DM 33 (16.58%), previous TB 20 (10.05%), hypertension 22 (11.06%) and occuring higher in TB with DM than without [11 (22.92%) *vs*. 11 (7.28%), p=0.003], chronic heart failure 10 (5.03%), liver disease 9 (4.52%), renal disease 8 (4.02%), gout 8 (4.02%), pneumopathy 7 (3.52%), stroke 4 (2.01%). Smoking 94 (47.14%), alcohol consumption 132 (66.33%) but were not significantly differed between TB patient with and without DM (Table 1).

Based on the review of the data collected thus far, of these 199 new patients, 48 (24.12%) were also diagnosed with DM and 151 (75.88%) were not diagnosed with DM (Figure 2). Among the 48 TB patients with DM, 33 (68.75%) had been previously diagnosed with the disease, 15 (31.25%) patients were diagnosed during this study

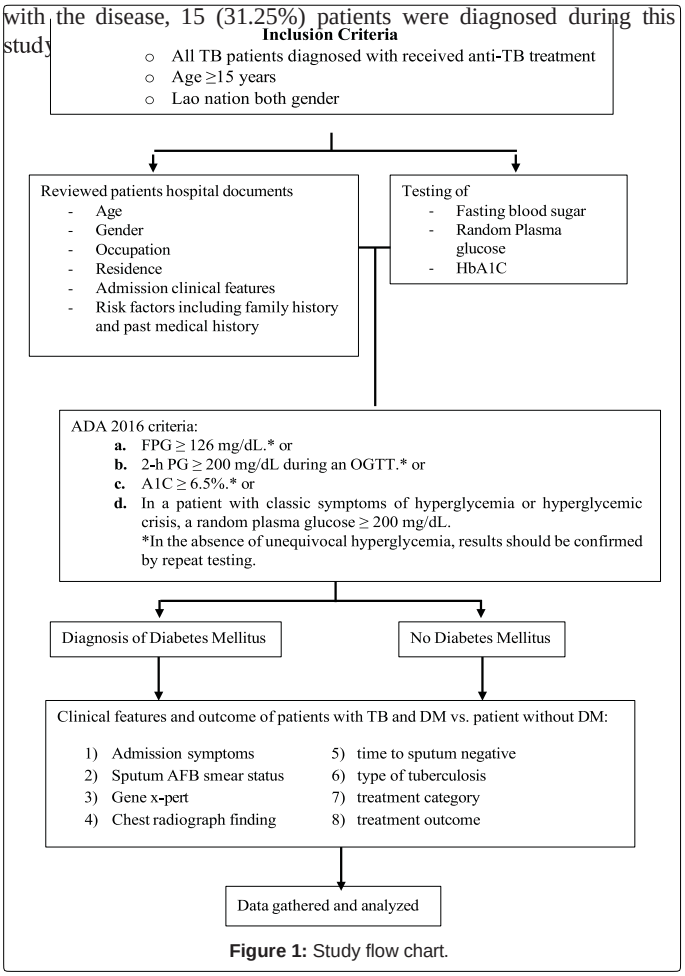

Figure 1: Study flow chart.

Variable	Total (n=199) No. (%)	TB patients with DM (n=48) No. (%)	TB patients without DM (n=151) No. (%)	p-value
Baseline characteristic				
Age (Mean (SD))	52.56 (18.88)	58.85 (14.06)	50.56 (19.80)	0.00*
Male	137 (69)	36 (75.00)	101 (66.89)	0.29
Female	62 (31)	12 (25.00)	50 (33.11)	
Occupation				
Farmer/worker	77 (38.69)	14 (29.17)	63 (41.72)	0.05
Gov/pvt Employed	56 (28.14)	20 (41.67)	36 (23.84)	
Student	14 (7.04)	1 (2.08)	13 (8.61)	
Unemployed	52 (26.13)	13 (27.08)	39 (25.83)	
Residence				
Vientiane Capital	138 (69.35)	34 (70.83)	104 (68.87)	0.79
Others	61 (30.65)	14 (29.17)	47 (31.13)	0.79
Family history				
DM family hx	29 (14.57)	12 (25.00)	17 (11.26)	0.01*
TB family hx	26 (13.07)	4 (8.33)	22 (14.57)	0.26
Past Medical history				
Previous TB	20 (10.05)	3 (6.25)	17 (11.26)	0.31
HTN	22 (11.06)	11 (22.92)	11 (7.28)	0.00*
CHF	10 (5.03)	3 (6.25)	7 (4.64)	0.65
Liver disease	9 (4.52)	2 (4.17)	7 (4.64)	0.89
Renal disease	8 (4.02)	3 (6.25)	5 (3.31)	0.36
Gout	8 (4.02)	1 (2.08)	7 (4.64)	0.43
Pneumopathy	7 (3.52)	0 (0.00)	7 (4.64)	0.12
Stroke	4 (2.01)	1 (2.08)	3 (1.99)	0.96
Smoking	94 (47.14)	21 (43.75)	73 (48.34)	0.57
Alcohol consumption	132 (66.33)	32 (66.67)	100 (66.23)	0.95
* p<0.05				

Table 1: The socio-demographics and factors associated of new case of TB with and without DM.

referred to the physician for further treatment.

Clinical features and laboratory parameters of TB patients with and without DM

Regarding Admission Clinical Presentation, weight loss >5% was 74 (37.19%) and was significantly lower in TB patients with DM than those without DM (25.00% *vs* 41.06%), p=0.04. But the others presenting symptoms and signs, including cough 167 (83.92%), fever 114 (57.29%), dyspnea 83 (41.71%), hemoptysis 79 (39.70%), night sweat 39 (19.70%), chest pain 27 (13.57%), myalgia 21 (10.55%), fatigue 22 (11.06%), anorexia 9 (4.52%), Etra-PTB form 12 (6.03%), Mean(SD) systolic blood pressure 109.73 (25.53), diastolic blood pressure 68.68 (13.35), Mean (SD) temperature (°C) 37.26 (0.83), mean peripheral saturation of oxygen is 94.09 (4.71), Respiratory Rate (bpm) Mean (SD) 23.28 (2.97), Pulse (bpm) Mean (SD) 98.56 (19.45) from baseline were similar in both groups (Table 2).

Regarding laboratory parameters, the only parameter that significantly differed between the two groups was the proportion of patients with presented cavity on chest radiograph, which was significantly higher in TB patients with DM than those without

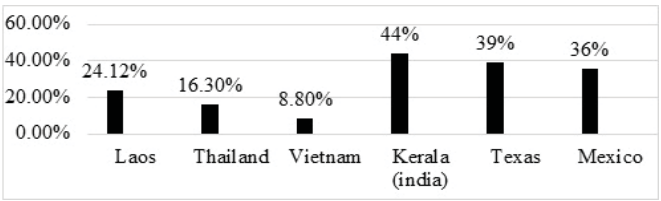

Figure 2: Prevalence of DM among TB patients in Laos *vs*. others countries.

Variable	Total (n=199) No. (%)	TB patients with DM (n=48) No. (%)	TB patients without DM (n=151) No. (%)	p-value
Admission Clinical Presentation				
Fever	114 (57.29)	27 (56.25)	87 (57.62)	0.86
Cough	167 (83.92)	44 (91.67)	123 (81.46)	0.09
Hemoptysis	79 (39.70)	16 (33.33)	63 (41.72)	0.3
Night sweat	39 (19.60)	12 (25.00)	27 (17.88)	0.27
Dyspnea	83 (41.71)	21 (43.75)	62 (41.06)	0.74
Weight loss >5%	74 (37.19)	12 (25.00)	62 (41.06)	0.04*
Chest pain	27 (13.57)	10 (20.83)	17 (11.26)	0.09
Myalgia	21 (10.55)	7 (14.58)	14 (9.27)	0.29
Fatigue	22 (11.06)	5 (10.42)	17 (11.26)	0.87
Anorexia	9 (4.52)	2 (4.17)	7 (4.64)	0.89
Extra-Pulmonary TB	12 (6.03)	0 (0.00)	12 (7.95)	0.17
Systolic BP (mmHg) Mean (SD)	109.7 (25.53)	115.70 (30.21)	107.8 (23.65)	0.06
Diastolic BP (mmHg) Mean (SD)	68.68 (13.35)	71.35 (14.86)	67.83 (12.7)	0.11
Pulse (bpm) Mean (SD)	98.56 (19.45)	99.56 (20.01)	95.43 (17.37)	0.2
Temperature (C) Mean (SD)	37.26 (0.83)	37.23 (0.11)	37.27 (0.06)	0.77
SpO_2 (%) Mean (SD)	94.09 (4.71)	95.14 (3.67)	93.76 (4.96)	0.07
Resp. Rate (bpm) Mean (SD)	23.28 (2.97)	22.58 (2.48)	23.50 (3.08)	0.06
Laboratory Parameter				
Hemoglobin level <12 g/dL, (n=82)	54 (65.85)	18 (72.00)	36 (63.16)	0.43
WBC count >10 x 10^3/mm^3, (n=82)	30 (36.59)	10 (40.00)	20 (35.09)	0.67
Creatinine level >1.2 mg/dL, (n=53)	21 (39.62)	8 (47.06)	13 (36.11)	0.44
AST level >37 U/l, (n=56)	34 (60.71)	12 (70.59)	22 (56.41)	0.31
ALT level >45 U/l, (n=56)	15 (26.79)	6 (35.29)	9 (23.08)	0.34
Cavity on chest radiograph	162 (81.41)	44 (91.67)	118 (78.15)	0.03*
Sputum AFB positive	126 (63.32)	33 (68.75)	93 (61.59)	0.37
Gene x-pert				
T	170 (85.43)	44 (91.67)	126 (83.44)	0.17
N	27 (13.57)	3 (6.25)	24 (15.89)	
RR	2 (1.01)	1 (2.08)	1 (0.66)	
HIV positive	22 (11.06)	4 (8.33)	18 (11.92)	0.49
* p<0.05				

Table 2: Clinical features and laboratory parameters of TB patients with and without DM.

Variable	Total (N=199)	TB patients with DM (n=48)	TB patients without DM (n=151)	p-value
Treatment outcome				
Category				
Cat 1	185 (92.96)	46 (95.83)	139 (92.05)	0.29
Cat 2	12 (6.03)	1 (2.08)	11 (7.28)	
Cat MDR	2 (1.01)	1 (2.08)	1 (0.66)	
Sputum AFB conversion				
At month 2	114 (57.29)	21 (43.75)	93 (61.59)	0.03*
At month 3	26 (17.57)	6 (12.50)	20 (13.25)	0.89
At month 5	8 (5.41)	4 (8.33)	4 (2.56)	0.09
Treatment Complete				
Cured	140 (70.35)	28 (58.33)	112 (74.17)	0.03*
Treatment Failure	6 (3.02)	3 (6.25)	3 (1.99)	0.15
Treatment not complete				
Lost to follow up	29 (14.57)	10 (20.83)	19 (12.58)	0.15
Death	24 (12.06)	7 (14.57)	17 (11.26)	0.53
* p<0.05				

Table 3: Management and treatment outcome of Pulmonary TB with and without DM.

DM (91.67% *vs* 78.15%, p=0.03). The proportions of patients within each group for which specific laboratory parameter results had been obtained, including hemoglobin level <12 g/dL, white blood cell count >10 x 10^3 /mm^3, serum creatinine level >1.2 mg/dL, aspartate aminotransferase level >37 U/l, alanine aminotransferase level >45 U/l, sputum AFB positive, Gene x-pert form (T, N, RR), HIV positive were similar (Table 2).

Management and treatment outcome of TB with and without DM

The study showed category (Cat) 1: 185 (92.96%), Cat 2: 12 (6.03%), Cat MDR (multi-drugs resistant) 2 (1.01%). Of these TB patients sputum AFB conversion at month 2 was 114 (57.29%) with shown TB with DM significantly lower than those without DM (43.75% *vs*. 61.59%, p=0.030), but at month 3 was 26 (17.57%), and at month 5 was 8 (5.41%) were similar in both groups. The patients who completed treatment course showed cured was 140 (70.35%) and TB with DM was significantly lower than TB without DM (58.33% *vs.* 74.17%, p=0.036%. While failure 6 (3.02%), and the other group was not complete the course found loss of follow up 29 (14.57%), death during TB treatment 24 (12.06%) were found to be similar for TB patients with and without DM (Table 3).

Discussion

This present study included the accepted criteria to determine prevalence of DM among TB patients, to describe the socio-demographics and others factor associated with TB-DM co-occurrence, and to compare the clinical features and treatment outcome between TB with and without DM, admitted to the Pulmonary Department, Mahosot hospital, Lao PDR. This study, 199 patients with TB were included. The prevalence of TB-DM was 24.12%. Among the TB patients with DM, 68.75% had been previously diagnosed with the disease, 31.25% patients were diagnosed during this study. A percentage higher than found in other tropical countries such as Thailand, Vietnam shown 24.12% *vs*. 16.3%, 8.8% respectively [9,10]. But it was lower than Kerala (India) 44%, Karnataka (India) 32%, Texas 39%, Mexico 36%. It may related with higher endemic of type 2 DM prompted them to explore association between DM and TB of those country (Figure 2).

Regarding the majority of the baseline characteristics, TB-DM patients were older than those without DM and higher proportion of government employed, similarly with previous reports of advanced age and higher proportion of gov/pvt.employed as risk to prompt for DM [11], and we found a significantly higher proportion of underlying of hypertension in TB with DM patients similar the textbook of Harrison's Principle of Internal Medicine 19ed. The present study showed that smoking and alcohol consumption were not significantly differed between TB patients with and without DM, similar to previous study [11] while, other studies were illustrated that smoking and alcohol consumption were significant associated prompt the risk factor of DM [12].

In clinical and laboratory parameters of the patients we found a significantly higher proportion of TB patients without DM was found to have presented with the symptom of weight loss >5%, finding similar to those of previous reporting that the clinical presentation of TB differed little between patient with and without DM [9]. In this study also showed that the TB with DM patients has higher proportion of chest x-ray cavity lesion, it is similar to previous study that TB with DM patients may have more severe radiologic findings [10] may because of differences in duration and host immune status [13].

This study showed at 2 months after anti-TB therapy the TB patients with DM was found significantly lower proportion of number of sputum AFB conversion, similar to the study of Guler et al. that TB patients with DM are more infectious, due to greater sputum bacterial concentration [14], as well as longer sputum smear and culture conversion time. The end of treatment, the study showed TB patients without DM were found to be significantly higher proportion cured, while the end of treatment was found that TB patients with DM were found to be higher proportion of failure and loss of follow up, death during treatment but did not significant in statistics with P=0.05. similar to a systemic review and meta-analysis to quantitatively summarize evidence for the impact of DM on TB outcomes by the resulting showed that diabetes is associated with an increased risk of failure and death of 1.69 (95% CI, 1.36 to 2.12) during treatment [3].

Limitation of the study

It was a small was a retrospective study, prevalence of DM among TB patients might an obvious bias in some results, some result of laboratory such as CBC, LFT, Cr, BUN not found during the time data collection. Furthermore, sputum culture is the gold standard to detect M. tuberculosis but in this study was not performed. This study was conducted within a hospital setting; it may not truly represent the true prevalence of the conditions in the community.

Conclusion

We found the high prevalence of DM among TB patients (24.12%), based on clinical features, laboratory parameters and treatment outcomes, DM seems to have a negative effect out the outcome of TB treatment.

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Conflict of Interest

The authors declare there are no conflicts of interest.

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