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RESEARCH ARTICLE

Prevalence, Predictors and Treatment Outcome of Type 2 Diabetes among Newly Diagnosed Sputum Positive Pulmonary Tuberculosis Patients in Western Cameroon

Leonard Sama Fonkeng[1], Innocent Mbulli Ali[1,2], Michel Noubom[3,4,5], Roland Bamou[6], Assoua HSR Sterve[7], Ayuk Leo[8], JR Kuiate[1] and Christopher B Tume[1*]

[1]*Laboratory of Microbiology and Antimicrobial Substances, Department of Biochemistry, University of Dschang, Dschang, Cameroon*

[2]*Laboratory for Public Health Research Biotechnologies, The Biotechnology Centre, University of Yaoundé I, Yaoundé, Cameroon*

[3]*Department of Biomedical Science, University of Dschang, Cameroon*

[4]*Centre Médical d'Arrondissement [CMA] de Baleng, Bafoussam*

[5]*Centre de Diagnostic et de Traitement de la Tuberculose, Bafoussam*

[6]*Laboratory of Applied biology and Ecology, Department of Animal Biology, University of Dschang, Dschang, Cameroon*

[7]*Ministry of Public Health, Far North Regional Delegation, Maroua, Cameroon*

[8]*Regional Tuberculosis Control Program, North West Region of Cameroon*

***Corresponding author:** *Prof. Tume B Christopher, Faculty of Science, Laboratory of Microbiology and Antimicrobial Substances, Department of Biochemistry, University of Dschang, P.O Box 96, Dschang, West Region, Cameroon, E-mail: tumechrist@yahoo.com*

Abstract

There is a growing awareness on a global scale on the possible relationship between tuberculosis (TB) and diabetes mellitus (DM). We conducted a prospective study in sputum positive pulmonary TB patients in two TB management clinics in Bamenda and Bafoussam in the North West and West regions of Cameroon respectively to determine the prevalence of type 2 diabetes, associated risk factors and the impact of diabetes in the treatment outcome. Of the 222 patients who participated in the study, 9.4% [21/222] were diabetic with age 21-70 years, 15.32% [34/222] had impaired glucose tolerance whereas 32.43% [72/222] had a family history of diabetes. Among the 21 patients who had diabetes, 20 had T2D (17 where newly diagnose whereas 3 were known T2D) and one had type 1 diabetes and was also newly diagnose. We noted a threefold increase in the risk of diabetes among unmarried TB patients and a 32% increase in the risk of diabetes for every unit increase in the body mass index (BMI). HIV Patients had a four-fold risk of being diabetic in our analysis. In conclusion the prevalence of DM among TB patients was found to be 9.4%. The principal risk factors associated with the DM among TB patients were BMI, unmarried and HIV infected. We observe no significant difference in sputum conversion at two month of treatment with 28.8% [6/21] TB with DM and 70.4% [95/136] TB without DM that are still positive after 2 months of treatment versus 57.1% [12/21] of TB with DM and 21.5% [29/136] TB without DM that pass from positive to negative after 2 months of treatment (P = 0.442). Whereas in the treatment outcome, there was a significant difference when comparing cured TB with DM (90%) and TB without DM (96.0%) (*P = 0.04*). Likewise we also noted a significant difference in treatment outcome when comparing treatment completion between TB patients with DM (90.0%) and TB patients without (97.6%) (P = 0.002).

Keywords: Diabetes mellitus, Oral glucose tolerant test, Risk factors, Pulmonary tuberculosis, Treatment outcome

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List of Abbreviations

ADA: American Diabetes Association; AFB: Acid Fast Bacilli; BMI: Body Mass Index; CMA: Medicalised Health Centre; DM: Diabetes Mellitus; OGTT: Oral Glucose Tolerance Test; RBS: Random Blood Sugar; RHB: Regional Hospital Bamenda; SSA: Sub-Saharan Africa; TB: Tuberculosis; T2D: Type 2 Diabetes; W.H.O: World Health Organisation

Background

Tuberculosis (TB) continues to be the leading killer among bacterial diseases worldwide [1,2]. It is estimated that one-third of the world's population have TB infection, and there are 9.4 million new cases of TB per year [3]. The World Health Organization [WHO] suspects that TB control is being undermined by the growing number of patients with diabetes mellitus (DM) in the world. In 2011, the International Diabetes Federation [IDF] estimated that about 366 million people worldwide have diabetes mellitus (DM) [4]. 80% of these people live in the low and middle income countries where tuberculosis (TB) is highly prevalent [5]. Diabetic patients have impaired cell mediated immunity, renal failure, micronutrient deficiency and pulmonary microangiopathy, all of which increase their propensity to develop TB [6]. DM is also known to alter the clinical presentation of TB and its outcomes in terms of delayed sputum/culture conversion, case fatality and treatment failure [7].

Currently, both TB and DM are of great public health importance globally, especially in Sub Saharan Africa (SSA) due to the converging epidemics of both communicable and non-communicable diseases. As recently reviewed, little is known about the prevalence of diabetes in TB burden countries [8] and none or little studies on the role of diabetes for TB have been carried out in Africa. In addition, a recent study in Taiwan, showed that diabetes was the most common underlying co-morbidity in patients with culture-confirmed TB, present in 21.5% of patients [9] and among patients afflicted with both TB and DM, diabetes was reported to be associated with poor TB treatment outcomes [10-12]. However, a systematic analysis to both clarify and quantify the association between DM and TB outcomes; especially in those with poor glycaemic control, including persistence of sputum conversion positive (2-month, 4-month and 6-month culture conversion rates), death and relapse, are poorly documented in low income countries precisely in Sub-Saharan area with high rates of infection with human immuno-deficiency virus (HIV) as a strong competing risk factor. Cameroon is one of the countries where the prevalence of TB is still high with no prevalence since 2012. The W.H.O estimated in 2012 that the rate of mortality due to TB in Cameroon was 29/100,000 excluding HIV and the prevalence of all forms including HIV positive was 319/100,000 and the rate of incidence including HIV positive was 338/100,000 inhabitants [13]. In Cameroon, the prevalence of diabetes is 6.82% [14]. There is no difference in sputum conversion at 2 month but significant in the treatment outcome and treatment failure.

The aim of this study was to determine the prevalence of type 2 diabetes among all TB patient (Bafoussam and Bamenda), the associated risk factors of T2D and to determine and compare treatment outcomes among TB patients with versus without DM.

Methods

Study site description and population

The study was carried out at the TB unit of the Regional Hospital Bamenda [RHB] situated in the North-West Region of Cameroon and at the TB unit of the "Centre Médical d'Arrondissement (CMA) de Baleng Bafoussam" located in the West Region of Cameroon. The two hospitals have dedicated adult pulmonology wards primarily for admission of TB patients during the intensive phase of treatment.

Patients enrolled into the study were admitted on the pulmonology wards during the study period and had a confirmed microscopic diagnosis of pulmonary TB. All the patients who refused informed consent and minors who provided assent but whose guardians/legal representatives refused to consent were excluded from the study.

Type of study

This was a cross sectional study in which patients with a microscopically confirmed diagnosis of pulmonary TB admitted on the TB wards of the regional hospital Bamenda [RHB] and CMA Baleng Bafoussam were consecutively recruited during the study period from November 2014 to July 2015. Collectively, these two study centres include more than 80% of the state's incident TB cases and have dedicated adult pulmonology wards primarily for admission of TB patients during the intensive phase of treatment. The treatment outcome at six months was evaluated in a nested cohort of patients with or without diabetes in the study population.

Patients were excluded from the study if they died during the TB diagnosis, initiated TB treatment or died before information regarding diabetes status could be obtained. Analyses of time to sputum culture conversion included only those patients with a baseline diagnostic sputum culture positive for *Mycobacterium tuberculosis*. Sputum cultures were collected under programmed conditions, and frequency of sampling varied but was at least monthly. For each TB case, information about demographics, medical history, cavitary disease status where recorded while admitting him to the war.

Sample size and sampling technique

In the present study, a convenient sample of 222 sputum positive pulmonary TB patients who visited

the health facilities and who provided consent prior to the onset of any study procedure were included. These sample size was designed according to the prevalence of the co-infection between these two diseases which is 15% to 25% [2]. Enrolment of participants was consecutive and based on three sputum smear positivity with *M. tuberculosis* during diagnosis and prior to treatment.

Data Collection Tools

Questionnaire administration

A structured questionnaire was administered to all participants to obtain data on socio-demographic characteristics, family history of diabetes, smoking, alcohol consumption, educational level, outdoor activity, and marital status. Those who could not read were assisted to fill the questionnaires. Anthropometric parameters including height and weight were measured by trained nurses following standard procedures. The body mass index (BMI, kg/m^2) was calculated by using the formula: BMI = Weight (kg)/Height^2 (m^2). Underweight, normal weight, overweight, and obesity were defined using the method describe by Wikner, et al. 2012. The BMI cut-off value for underweight (severe underweight, moderate underweight, and mild underweight), normal weight, overweight, and obesity were < 18.5 kg/m^2 (< 16 kg/m^2, 16-16.9 kg/m^2 and 17 to 18.4 kg/m^2), 18.5 to 25 kg/m^2 respectively.

Laboratory investigation and specimen collection

Diagnosis of smear positive pulmonary TB was performed for all patients following the national TB diagnosis guidelines [15]. Briefly, two consecutive sputum samples [first spot and morning-spot] were collected, smeared, and stained with the auramine staining technique. The stained smears were then examined under the oil immersion objective for acid-fast bacilli using the light microscope. Pulmonary TB was confirmed when at least two consecutive smear results are positive for acid fast bacilli assay (AFB) or one sputum specimen is positive with additional x-ray abnormality, as required by the consultant physician. If the smear result were negative with positive clinical symptoms, culture was done using Löwenstein-Jensen media. After admission to the ward, culture was then performed for those who accepted to participate to the study. For those who were TB confirm, fasting blood glucose was performed on capillary blood after an overnight fasting (at least 10 hours without eating or smoking but can drink water during this period). Random blood sugar (RBS) level was measured using the OneTouch Ultra W glucometer from Johnson and Johnson Company, United Kingdom.

The diagnosis of DM was based on the recent American Diabetes Association [ADA] guidelines of fasting blood sugar ≥ 126 mg/dl or a random or casual blood sugar level ≥ 200 mg/dl in the presence of the classical symptoms of diabetes [16,17] and the hyperglycaemia was noted when the fasting blood glucose was found between 70 to 130 mg/dL or the postprandial (1-2 hours after eating) blood glucose level above 180 mg/dL.

The Oral Glucose Tolerance Test [OGTT] was also perform by giving 75 g anhydrous glucose dissolved in 200 ml-300 mls of water to patients to be consumed within 5 minutes, followed by a further 100 ml of water; and capillary plasma glucose was measured after 2 hours as describe in the W.H.O and ADA guidelines [16,17]. Only those with apparently normal (fasting blood glucoce level less than 99 mg/dL) glucose levels were subjected to the oral glucose tolerance test and patient were consider diabetic if two successive week's measurement of fasting blood glucose ≥ 126 mg/dl or 2h-OGTT ≥ 200 mg/dl. In a patient with classic symptoms of hyperglycaemia or hyperglycaemic crisis, only a random plasma glucose was performed and the patient was considered diabetic if two successive weeks random plasma glucose ≥ 200 mg/dl [15,17].

Tuberculosis treatment was initiated in all patients in accordance with current guidelines [18]. Human immunodeficiency virus status was determined using chart documentation of serologic testing.

Availability of Dataset

The full dataset can be consulted from the University of Dschang, through institutional guidelines.

Ethical Considerations

Ethical clearance for this study was obtained from the Ethics Review and Consultancy Committee of the Cameroon Bioethics Initiative [CAMBIN] under the reference number **CBI/294/ERCC/CAMBIN** on the 16 September 2014. An authorisation to collect and analyse blood samples was also obtained from the regional delegation of public health Bamenda and the Baleng Medicalised Centre in Bafoussam. All participants were fully informed of the study goals, procedures, potential harm and benefits, cost as well as the finality of the study. They willingly provided informed consent either by signing or placing their thumbprint on the consent form after being satisfied with responses to all questions asked the investigator. Information was provided in English, French or interpreted in the local dialect by a hospital volunteer independent of the study team.

Consent to Publish

No identifiable information was included either in the dataset analysed or results being published. Therefore, consent to publish was not applicable. During the informed consent process, patients were informed the principal results will be published in peer review journals in an anonymised and unlinked manner.

Data Processing and Analysis

Data was entered into Microsoft Excel sheets and exported to Statistical Package for Social Science (SPSS) software Version 18 for analysis. The data was summarized and organized using graphs, tables and texts. The Chi square test was used for association analyses. The level of association presented as odds ratios [OR] was estimated using a binary logistic regression model to identify possible predictors of occurrence of DM among the newly diagnosed sputum positive TB patients. This model determines the probability of not being diabetic given the determinant fitted in the model through backward elimination. Therefore, the reference condition was being diabetic. Univariate statistic was used to compare mortality between the two groups. Covariates in mortality analyses included factors known to be risk factors for death from TB, including HIV status, weight, and age, as well the predictor shown in our data to be strongly associated with improved outcomes. To compare proportions of patients with and without DM with sputum culture conversion by 2, 4 and 6 months of treatment, multiple logistic regressions was used. To compare time to culture conversion, log-rank and stratified log-rank tests were performed. For those individuals who had negative sputum conversion, their data was right-censored and included in the survival analysis. A p-value < 0.05 was considered as statistically significant in all the analyses. The dataset for this analysis was anonymous and unlinked.

Results

Socio-demographic characteristics of study participants

Out of the 222 participants that were recruited in this study, 64.41% [143/222] were males while 35.58% [79/222] were females. The mean age of the participants was 39.05 ± 14.305 years with minimal being 12 years and the maximal 82 years. Also, 73.42% [163/222] of the participants were alcoholic against 26.57% [59/222] who were not alcoholic consumers. 35.13% [78/222] were smokers against 65.86% [144/222] non-smokers. 57.65% [128/222] had a settled way of life against 42.34% [94/222].

Amongst all the participants, 54.95% [122/222], 40.99% [91/222] and 4.05% [9/222] had primary, secondary and higher level of education, whereas 55.6% were married and 44.4% unmarried. Furthermore, 38.74% [86/222] of the total population were HIV positive with higher prevalence found in patients from Bamenda 29.74% [66/222] compared to those from Bafoussam 9% [20/222] and almost all HIV positive patients were on Anti-Retro-Viral (ARV) treatment. Among these HIV patients, 2.3% [2/87] were diabetic, and 19.76 % [17/86] had impaired glucose control (Table 1).

Prevalence of T2D among newly diagnosed TB patients

The combined blood glucose levels on random blood glucose testing of all registered tuberculosis patients and oral glucose tolerance test (This variable contained five modalities as proposed by WHO and ADA [16,17] on subjects showing blood glucose levels in borderline range from 6.0128 ± 0.87928 for impaired oral glucose tolerant test and 6.4132 ± 0.23636 for impaired fasting blood glucose), showed that, 9.4% [21/222] in total were diabetic with age range between 21 and 70 year and high cumulative found between 31 to 60 years, 14.42% [32/222] had impaired oral glucose tolerance, 12.61% [28/222] had impair fasting blood glucose. The

Table 1: Socio-demographic and anthropometric characteristics of the study population.

Host characteristic	Bafoussam (n = 110)	Bamenda (n = 112)	*P*-value
Age in years, mean (± SD)	40.21 ± 15.26	37.87 ± 13.32	0.226
Males	40.59 ± 15.48	38.89 ± 11.82	0.483
Female	38.83 ± 14.69	36.82 ± 14.76	0.578
Age stratification (years)			
21-30	31 (29.2%)	25 (24.0%)	
31-40	31 (29.2%)	42 (40.4%)	
41-50	16 (15.1%)	20 (19.2%)	
51-60	13 (12.3%)	10 (9.6%)	0.845
61-70	10 (9.4%)	5 (4.8%)	
> 70	5 (4.7%)	2 (1.9%)	
Number of diabetics			
21-30	1 (3.2%)	3 (12.0%)	
31-40	2 (6.5%)	3 (7.1%)	
41-50	1 (6.2%)	3 (15.0%)	
51-60	3 (23.1%)	2 (20.0%)	
61-70	2 (20.0%)	0 (0.0%)	
> 70	0 (0.0%)	0 (0.0%)	
p-value	0.070	0.829	
Marital status			
Married	65 (59.1%)	58 (51.8%)	
Unmarried	45 (40.9%)	54 (48.2%)	0.274

Level of education			
Primary	62 (56.4%)	60 (53.6%)	
Secondary	44 (40.0%)	47 (42.0%)	0.894
Tertiary	4 (3.6%)	5 (4.5%)	
Settled way of life			
Yes	60 (54.5%)	68 (60.7%)	0.352
No	50 (45.5%)	44 (39.3%)	
Smoking status			
Smoker	48 (43.6%)	30 (26.8%)	0.009
Non smoker	62 (56.4%)	82 (73.2%)	
Alcohol intake			
Yes	86 (78.2%)	77 (68.8%)	0.112
No	24 (21.8%)	35 (31.2%)	
BMI			
Normal *18.5 ≤ BMI < 25* *Male* *Female*	 65 (59.1%) 15 (13.6%)	 51 (45.5%) 32 (28.6%)	
Overweight *25 ≤ BMI < 30* *Male* *Female*	 3 (2.7%) 2 (1.8%)	 1 (0.9%) 6 (5.4%)	
Obese *BMI ≥ 30* *Male* *Female*	 0 (0.0%) 2 (1.8%)	 0 (0.0%) 2 (1.8%)	
Underweight *BMI < 18.5* *Male* *Female* *P-value*	 18 (16.4%) 5 (4.5%) 0.035	 5 (4.5%) 15 (13.4%) 0.002	
Waist circumference			
> 90 cm (Male)	3 (3.5%)	5 (5.3%)	0.604
< 90 cm	83 (96.5%)	54 (94.7%)	
> 80 cm (Female)	10 (41.7%)	25 (45.5%)	
< 80 cm	14 (58.3%)	30 (54.5%)	0.755
Family history of diabetes			
Yes	32 (29.1%)	38 (33.9%)	
No	74 (67.3%)	73 (65.2%)	0.316
Unknown	4 (3.6%)	1 (0.9%)	
Serological status			
HIV+ *Male* *Female*	 14 (12.7%) 6 (5.5%)	 32 (30.4%) 34 (30.4%)	
HIV- *Male* *Female* *P-value*	 72 (65.5%) 18 (16.4%) 0.000	 25 (22.3%) 21 (18.8%) 0.000	0.0001
Non diabetic	73 (68.9%)	63 (56.8%)	
Impair fasting blood glucose	11 (10.4%)	17 (15.3%)	
Impaired OGTT	13 (40.6%)	19 (59.4%)	0.326
Diabetes patients	9 (8.5%)	12 (10.8%)	

rest [136/222 (61.26%)] had a normal blood glucose levels. Among all the TB patients 31.53% [70/222] had a family history of diabetes and 57.66% [128/222] had settled way of life (Table 2 and Table 3).

Among the 21 (9.4%) patients who had diabetes, 20 (9.0%) had T2D (17 where newly diagnose whereas 3 were known T2D) and one had type 1 diabetes and was also newly diagnose. The 3 cases that were known T2D had a poor glycaemic control [defined as RBS level > 200 mg/dl] despite being on glucose lowering therapy. The most frequent symptoms among the study participants with DM-TB co-infection were polyuria, polydipsia and progressive weight loss.

TB patients with a diagnosis of DM were slightly older but not significantly different from others (mean age 41.38 ± 14.36 VS. 37.86 ± 14,74; 39.50 ± 12.76;

Table 2: Prevalence of diabetes among the study population.

Characteristic	Diabetes	Non diabetes	*P-value*
Study site			
Bafoussam	9	73	
Bamenda	12	63	
Mean age	41.38 ± 14.36	37.86 ± 14.74	0.356
Male	41.55 ± 18.65	38.15 ± 13.39	0.483
Female	41.25 ± 11.05	37.13 ± 17.81	0.454
Level of education			
Primary	10 (47.6%)	72 (52.9%)	
Secondary	11 (52.4%)	57 (41.9%)	0.440
Tertiary	0 (0.0%)	7 (5.1%)	
Alcohol intake			
Yes	14 (66.7%)	102 (75.0%)	
No	7 (33.3%)	34 (25.0%)	0.418
Smoker status			
Yes	4 (19.0%)	53 (39.0%)	
No	17 (81.0%)	83 (61.0%)	0.077
Basal metabolic index			
Obese			
Male	0 (0.0%)	0 (0.0%)	
Female	1 (4.8%)	3 (1.9%)	
Overweight			
Male	0 (0.0%)	4 (2.5%)	
Female	1 (4.8%)	5 (3.2%)	
Normal			
Male	6 (28.6%)	84 (53.5%)	
Female	7 (33.3%)	32 (20.4%)	0.641
Underweight			
Male	3 (14.3%)	15 (11.0%)	
Female	3 (14.3%)	8 (5.9%)	
Waist circumference			
Male			
> 90 cm	3 (14.3%)	10 (7.4%)	
< 90 cm	18 (85.7%)	126 (92.6%)	0.283
Female			
> 80 cm	9 (42.9%)	60 (44.1%)	0.914
< 80 cm	12 (57.1%)	76 (55.9%)	
Family history of diabetes			
Yes	9 (42.9%)	32 (24.4%)	
No	12 (57.1%)	99 (75.6%)	0.077
Settled way of life			
Yes	13 (61.9%)	70 (51.5%)	0.054
No	8 (38.1%)	66 (48.5%)	
Serological status			
HIV+	12 (9.0%)	45 (91.0%)	
HIV-	9 (57.1%)	91 (33.1%)	0.033

40.3214 ± 14.14 respectively for TB patients without DM, Impaired oral glucose tolerant test and impaired fasting blood glucose *P = 0.648*). They were more female diabetic patients (57.1% VS. 42.9% whereas in the others groups, there were more males compared to females 71.3% VS. 28.7% for patient without DM; 53.1% VS. 46.9% for patient with Impaired Oral glucose tolerant test and 57.1 VS. 42.9% for impaired fasting blood glucose *P = 0.024*). There were more HIV positive patients that had DM compared to HIV negatives (57.1% VS. 42.9%), whereas in the patients without DM, there were more HIV negatives compared to positive 66.9% VS. 33.1%, 56.2% VS. 43.8% for patients with impaired Oral glucose tolerant test and 50% VS. 50% for patient with impaired fasting blood glucose *P = 0.085*) (Table 3).

Factors associated with the risk of developing type II diabetes among TB patients

Among the determinants that were analysed for association with susceptibility to type 2 diabetes among sputum positive TB patients, the marital status, HIV and increased BMI were found to be associated with occurrence of diabetes among TB patients in varying proportions. Indeed, TB patients who were unmarried had 24% less chance of being diabetic compared to patients who were married [Wald statistic: 5.4; *P* = 0.02,

Table 3: Demographic and clinical characteristics of TB patients with and without DM.

Host characteristic	TB patients with DM (n = 21) N (%)	TB patients without DM (n = 136) N (%)	Impair oral glucose tolerant test (n = 32) N (%)	Impair fasting blood glucose (n = 28) N (%)	*P*-value
Age group (years)					
< 21	1 (4.8%)	10 (7.4%)	1 (3.1%)	2 (7.1%)	
21-30	4 (19.0%)	37 (27.2%)	8 (25.0%)	5 (17.9%)	
31-40	5 (23.8%)	47 (34.6%)	11 (34.4%)	9 (32.1%)	
41-50	4 (19.0%)	19 (14.0%)	7 (21.9%)	4 (14.3%)	
51-60	5 (23.8%)	10 (7.4%)	3 (9.4%)	5 (17.9%)	
61-70	2 (9.5%)	7 (5.1%)	1 (3.1%)	3 (10.7%)	0.845
71-80	0 (0.0%)	5 (3.7%)	1 (3.1%)	0 (0.0%)	
> 81	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	
Mean age (± SD)	41.38 ± 14.36	37.86 ± 14.74	39.50 ± 12.76	40.3214 ± 14.14	0.648
Sex					
Male	9 (42.9%)	97 (71.3%)	17 (53.1%)	16 (57.1%)	0.024
Female	12 (57.1%)	39 (28.7%)	15 (46.9%)	12 (42.9%)	
Diagnostic method					
Culture	3 (14.3%)	9 (6.6%)	2 (6.2%)	1 (3.6%)	0.512
Smear	18 (85.7%)	127 (93.4%)	30 (93.8%)	27 (96.4%)	
X-ray					
HIV status					
HIV+	12 (57.1%)	45 (33.1%)	14 (43.8%)	14 (50.0%)	
HIV-	9 (42.9%)	91 (66.9%)	18 (56.2%)	14 (50.0%)	0.085
Unknown					
BMI ± SD	20.82 ± 4.31	20.87 ± 3.41	20.10 ± 4.74	21.05 ± 2.06	0.572

OR: 24.3]. In addition, the body mass index was found to only have a marginal association with type 2 diabetes among TB patients. Indeed, for every unit increase in BMI, the probability of not being diabetic was found to reduce by 32.5% [Wald statistic: 3.7, *P* = 0.05, OR: 0.75]. Similarly, HIV infected TB patients seemed to have 87% less chance of not being diabetic compared to HIV negative TB patients [Wald statistic: 3.87, *P* = 0.04, OR: 0.13]. Also the settled way of life was found to be an associated risk factor (*P* = 0.054, 95% CI). The general mean waist circumference was 79.18 ± 8.090 with that in females slightly higher than that in males. It was 80.00 ± 10.371 in females and 79.18 ± 8.090 in males though not significantly different. The analysis of multiple logistic regression of selected variables risk factors associated with diabetes among TB is found in Table 4.

Treatment outcomes among newly diagnosed TB patients with and without T2D

There was no difference in culture conversion status at 2 months among TB patients with DM compared to TB patient without DM (*P = 0.442*) (Table 5). Whereas in the treatment outcome, there was a significant differences in treatment outcome when comparing cured patients with DM (90%) and patients without DM (96.0%) (*P = 0.04*). Likewise we also noted a significant difference in treatment outcome when comparing treatment completion between TB patients with DM (90.0%) and TB patients without (97.6%) (*P* = 0.002). A significant difference was also observed in TB patients with DM compared to TB patient without DM. When comparing lost to follow-up between these two patients (0.0% for TB patient with DM and 1.0% for TB patient without DM (*P = 0.002*) (Table 6) however, overall numbers were small. The general follow up comparing TB with DM VS TB without DM patient is reprented by the Kaplan-Meier curves (Figure 1).

Table 4: Multiple logistic regression of selected variables risk factors associated with diabetes.

Variable	Odd ratio (95% CI)	*P value*
Weight		
Obese		0.223
Overweight		0.029
Normal		0.035
Underweight		0.505
Age (years)		
21-30		0.634
31-40		0.105
41-50		0.017
51-60		0.116
> 60		0.845
Gender		
Male		
Female	3.316 (1.294-8.496)	0.454
Immunological status (HIV)	0.371 (0.146-0.945)	0.033
Alcohol intake	1.50 (0.559-4.024)	0.418
Overweight		
Male	2.1 (0.528-8.360)	
Female	0.950 (0.376-2.403)	0.641

Table 5: Culture status of sputum culture-positive pulmonary TB patients with and without DM at 2 months.

Sputum status at 2 months	TB Patient with DM N = 21 n (%)	TB Patient without DM N = 136	*P value*
Culture-positive	6 (28.6%)	95 (70.4%)	
Culture-negative	12 (57.1%)	29 (21.5%)	
Culture not registered	3 (14.3%)	11 (8.1%)	0.442

In terms of mortality, 25% of TB patients with DM

Table 6: Treatment outcomes for TB patients with and without DM.

Treatment outcome	TB and diabetes N = 21 n (%)	TB and non-diabetic N = 136	*P value*
Cured	18 (90.0%)	120 (96.8%)	0.04
Completed	18 (90.0%)	121 (97.6%)	
Treatment failure	0 (0.0%)	3 (2.4%)	0.002
Loss to follow-up	0 (0.0%)	2 (1.0%)	

Table 7: Comparison of proportion of patients who died during tuberculosis (TB) therapy by demographic or clinical characteristics.

Characteristic	Number of deaths (%)
TB patients with DM	6 (25%)
TB patients without DM	11 (8.08%)
Number of death/Gender	
Male	9 (8.49%)
Female	5 (9.8%)

died compared to 8.08% of TB without DM, with more females compared to males (9.8% VS. 8.49%) (Table 7).

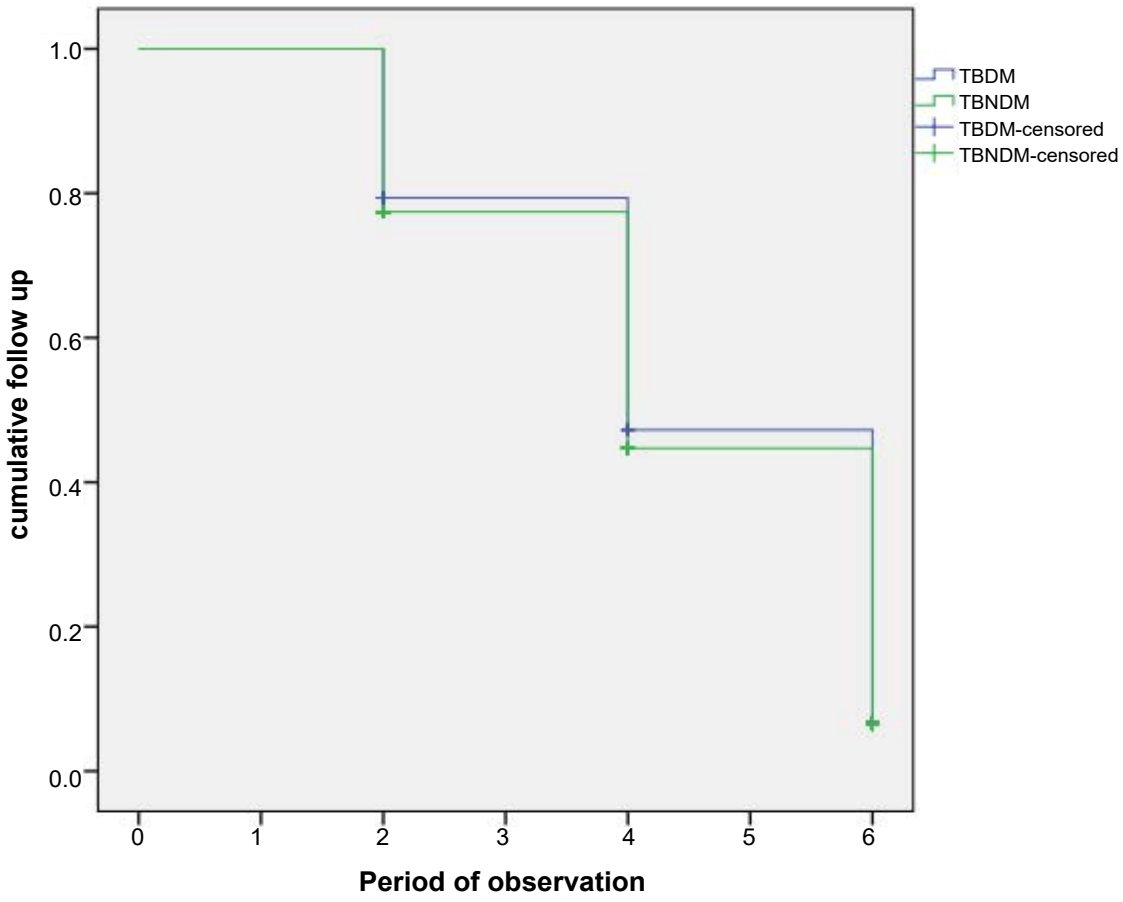
Discussion

The aim of this study was to determine the prevalence of type 2 diabetes, the associated risk factors and to determine and compare treatment outcomes among TB patients with versus without DM. This study observed a total diabetes prevalence of 9.4% with T2D prevalence being 9.0%. To our knowledge, this is the first study to examine this association in Cameroon, one of the high burden TB countries in sub-Saharan Africa. The reported prevalence of DM among the TB patients of 9.0% is higher than the estimated prevalence of DM among the general population in Cameroon (6.82%) [14]. The background prevalence of DM in the medical units in the hospitals during the study period was 7.3%. The documented prevalence of DM among TB patients in the African studies published between 1980 and 2016 varies between 2.1%-38% [4,19]. The observed prevalence of DM among TB patients in our study is comparable to that reported in Uganda where the prevalence of DM among the TB patients was found higher (8.5%) than DM prevalence reported in the general population 2.2% [4], higher than that reported in Nigeria [20]. Similar results have also been obtained in Ethiopia [19] where they found DM prevalence among newly diagnosed TB patients (8.3%) higher than the DM prevalence reported in the general population (4.84%). Such result was also reported in Nigeria [21] where they found higher prevalence of DM among TB patient (38%) compared to the national DM prevalence 4.64% and in India [22] but much lower than the findings of Restrepo, et al. [23], in the United States where the epidemic of DM prompted them to explore associations between DM and TB on the South Texas Mexico border. In that study they found a self-reported DM prevalence of 27.8% among Texans with TB and 17.8% in Mexicans with TB which significantly exceeded the national self-reported rates for both countries [23]. In Indonesia, DM was found to be strongly associated with TB with 60 out of 454 patients with TB reportedly diabetic compared with 3.2% of control subjects [24]. The higher prevalence we obtained compared to the prevalence obtained in Nigeria [25] could be due to their lower DM prevalence at the period of study 2.2% [25] and also the effects of co-morbidities like HIV. Although this study did not look at TB risks among diabetes patients, and the present design could not answer the question on whether diabetes predisposed patients to increased TB risk or vice versa, it however indicates that the former may be a plausible hypothesis, given that about one third (Table 1) of the patients in the two study areas presented with a family history of diabetes. Despite this, more than 90% of those diagnosed with diabetes occurred during the study and could have been missed emphasising the importance of routine screening for DM in all patients with TB. The already fairly well established TB infrastructure and health personnel could also serve to improve early detection and management of DM.

The higher prevalence of DM among patients with TB was associated with marital status, body weight. Settle way of live which was higher among Diabetic patients [13/21] (61,9%). Furthermore, it has been shown that the population of the study area have the higher overweight (33.63%) and the higher obesity (23.33%) population compared to the national population [26].

The HIV burden, and Body Mass Index [BMI] < 18.5 kg/m^2 which combined together could triple or quadruple the risk of development of DM among TB patients. This could be due to the fact that, initiation of ART is associated with rapid weight gain which correlates with increased insulin resistance [27,28]. The higher level of HIV patients from Bamenda compared to patients from Bafoussam is related to the higher prevalence of HIV in this region which has the second higher prevalence of HIV infection after the South region in Cameroon [29]. Observations of increased diabetes risk with factors seen in this study were also reported by Petra, et al. [30].

We observed a difference in sputum conversion at two month of treatment between TB with DM (28.8%) and TB without DM (70.4%) that are positive versus 57.1% of TB with DM and 21.5% of TB without DM that are negative even though the difference was not significant (P = 0.442). This result is comparable to the result reported in Fiji [31], in Ethiopia [32] and those reported by Kelly Dooley in 2009 [33] but different from the reported study in China [34] in Texas-Mexico [35], Taiwan [36], Maharashtra-India [37], Saudi Arabia [38], and Turkey [39] where sputum conversion among TBDM patient groups were lower. The good sputum conversions observed in both patient groups in our study may be related to good treatment adherence among patients. Poor adherence to anti-TB treatment is associated with sub-therapeutic levels of anti-TB drugs and often results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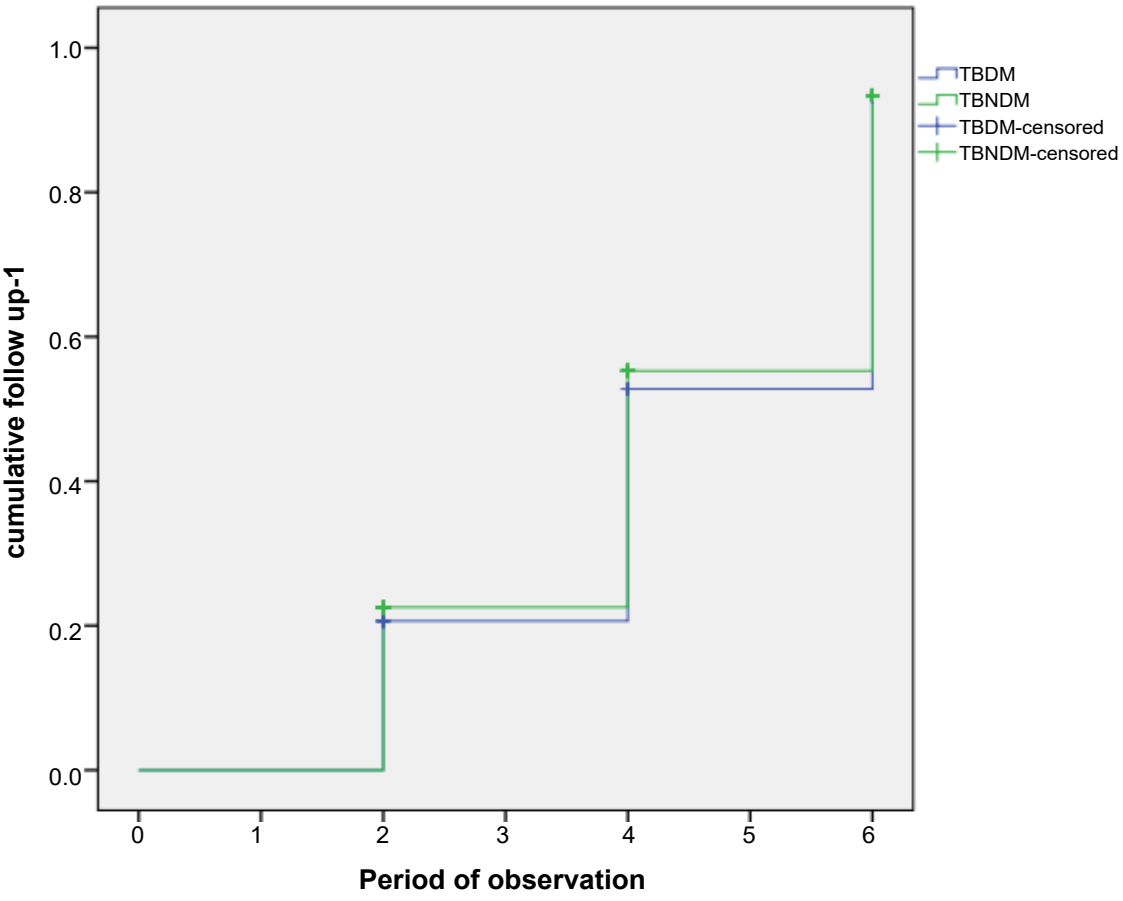
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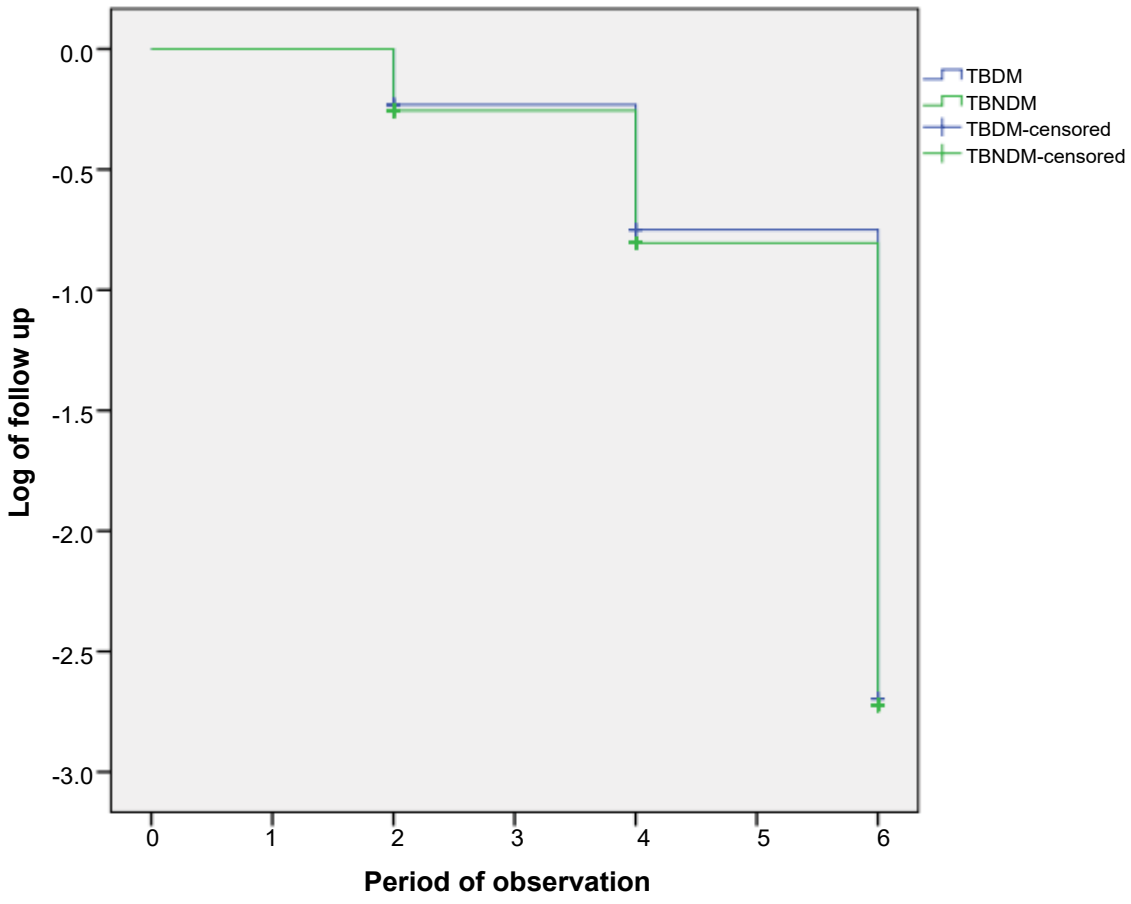

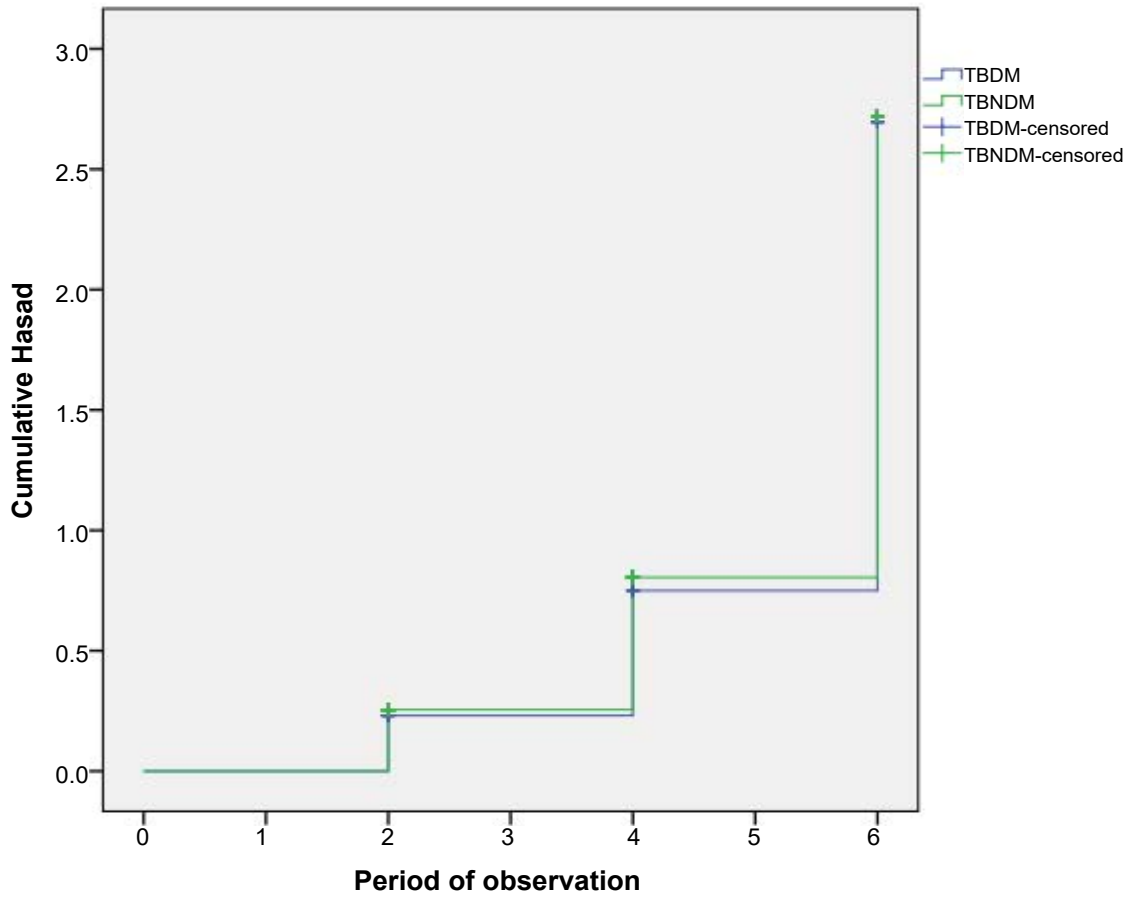

Figure 1: Kaplan-Meier curves for follow up comparing TB with DM Vs. TB without DM patient groups.

in treatment failure.

There was a significant difference in treatment outcome between TB with DM and TB without DM patient groups and this result is compare to result reported in Ethiopia [32]. However, we noted that an outcome of 'treatment completed and treatment failure' was more frequent among patients with DM. A systematic review has reported that TB patients with DM have a two-fold increased risk of anti-tuberculosis treatment failure and death (relative risk [RR] 1.69, 95% CI 1.36-2.12) and a four-fold increased risk of relapse (RR 3.89, 95% CI 2.43-6.23) [40] Higher treatment failure rates have also been observed in TB patients with DM in China (17% VS. 2%, $P < 0.01$), [35] Maryland, USA (OR 6.9, 95% CI 1.1-38.0, $P = 0.039$)[33] and in southern Mexico (adjusted OR 2.93, 95% CI 1.18-7.23) [41].

Our study may also be limited by the sample size which however flagged an important public health problem that may be developing among a patient population already burdened by tuberculosis.

Hence, our finding suggests a need for DM screening in TB patients. Screening TB patients for DM expedites early detection and treatment of patients with TBDM comorbidity. It may also enhance optimal glycaemic control as part of the TBDM patient management [33,12].

TB/HIV co-infected patients were more likely to die compared to HIV negative TB patients. HIV infection is a known risk factor for poor TB treatment outcome [42]. This finding suggests that there is a need to strengthen the existing TB/HIV collaborative activities in the study area.

Conclusion

We obtained a prevalence of 9.0%, 14.42%, and 12.61% of type 2 diabetes, impaired oral glucose tolerance and impair fasting blood glucose respectively among newly diagnosed TB patients. This was higher than the normal population prevalence. Among the TB patients, type 2 diabetes was found to be significantly associated with higher body mass index (BMI), and marginally associated with HIV infection and marital status. The result also demonstrated that there is no difference in sputum conversion at 2 month but significant in the treatment outcome and treatment failure.

Competing Interests

The authors declare that they have no conflicts of interest.

Authors' Contributions

CBT, IMA, and SFL conceived the study, SFL and IMA carried out sample analysis and data collection, AH, RB participated in analysis of the samples, data management and statistics, MN and AL supervised the field study, LSF, MN and IMA drafted the manuscript. All authors reviewed the manuscript and approved the final version prior to submission.

Authors' Information

1. LSF is a PhD student in the Department of Biochemistry of the University of Dschang, Cameroon.
2. JRK is a Professor of Biochemistry in the Department of Biochemistry of the University of Dschang in Cameroon.
3. CBT is an Associate Professor of Immunology and Molecular Biology in the Department of Biochemistry of the University of Dschang in Cameroon.
4. IMA is a Lecturer in the Department of Biochemistry of the University of Dschang and a Researcher in the Laboratory for Public Health Research Biotechnologies at the Biotechnology Centre, University of Yaounde 1 Cameroon.
5. RB is a PhD student in the Department of Animal Biology of the University of Dschang, Cameroon.
6. AHSRS is statistician statistical engineer National Malaria Control Program. In the Far North Cameroon.
7. NM medical doctor and lecturer in Department of Biomedical Sciencein the University of Dschang in Cameroon.
8. AL medical doctor and chief of regional unit for tuberculosis control in the North West Region of Cameroon.

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