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Diabetes Mellitus and Its Associated Factors among Tuberculosis Patients Attending Directly Observed Treatment Centres in Oyo State, Nigeria: A cross sectional evaluation

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Abstract

Objective

Diabetes mellitus (DM) and Tuberculosis (TB) co morbidity is evolving into an emerging epidemic globally. In Nigeria, a high burden of both diseases respectively exists with limited information on Tuberculosis-Diabetes mellitus (TB-DM) comorbidity. We determined the fasting blood glucose (FBG) level among patients with TB and factors associated with TB-DM comorbidity in Oyo State, South-west Nigeria.

Methods

A cross-sectional study was conducted among TB patients aged 15 years and above, who were selected using a multistage sampling. Data were collected on patients' bio data, anthropometric measurements and FBG levels using a pretested semi-structured questionnaire. The FBG test was conducted on confirmed Pulmonary TB patients (old and newly diagnosed TB patients) at any stage of anti-tuberculosis treatment. Background characteristics and FBG level were summarized using descriptive statistics and factors associated with TB-DM comorbidity were presented using odds ratios (OR) at 95% Confidence Interval.

Results

Of the 404 TB patients, 30 (7.4%) had Impaired Fasting Glucose and 32(7.9%) diagnosed with diabetes. The TB-DM patients' mean age was 49.5 (±15.91) years. There was a female preponderance (10.6%) for TB-DM. Median FBG level for the patients was 88 (Interquartile range: Q1: 99, Q3:79) mg/dl. Being at least 40 years [(OR 3.93; 95% CI: 1.72-8.98)], marital status [(OR= 11.18; 95% CI: 1.68-74.51)] and middle socioeconomic status [(OR=0.4; 95% CI: 0.14-0.98)] were associated with comorbidity individually. The results of the adjusted odds ratio show that only age was marginally associated, P=0.06 and [(OR=2.46; 95% CI: 0.97-6.21)].

Conclusion

Tuberculosis-Diabetes mellitus was prevalent among studied population in South-west Nigeria. We recommend the integration of DM screening within the continuum of care for TB management.

Key words: Tuberculosis-Diabetes mellitus comorbidity, Hyperglycaemia, Nigeria.

Article summary:

Strengths and limitations of the study

- This is one of the few studies documenting TB-DM comorbidity in Nigeria.
- It suggests the need for integration of DM screening in the management of TB patients to reduce the burden of these two diseases.
- This study adds to the volume of documented evidence that more studies should be conducted and documented, especially in low-to-middle-Income countries that have and are experiencing an increase in DM prevalence, coupled with a high burden of TB globally.
- Tendency for social desirability bias with reporting lifestyle habits such as alcohol consumption and drug use might have occurred is a limitation of this study.
- The outcomes of TB management in TB-DM comorbid individuals such as cure rate, treatment success rate or death could not be ascertained being a cross-sectional study.

Introduction

Tuberculosis remains a major global infectious disease that causes morbidity and death. The low- and middle-income countries harbor about 95% and 75% of tuberculosis (TB) and diabetes mellitus (DM) patients respectively.[1 2] Incident cases of TB were reported to be the highest among people with impaired immunity, human immunodeficiency virus (HIV) infection, or DM.[2] In 2018, an estimated 10.0 million individuals were newly diagnosed with TB, 1.2 million and 250,000 people died among HIV-negative and HIV- positive people respectively, of which Africa region accounted for 24%.[3] Nigeria belongs to one of the 30 high-burden TB countries worldwide.[3] In 2018, Nigeria was among the top 8 high TB burden countries, with an estimated 429,000 incident TB cases (219 per 100,000 population); and mortality of 123,000 (64 per 100,000 population) those due to excluding TB-HIV.[3] Nigeria, with a population of more than 190 million,[4] has the highest burden of the disease in the with a total TB incidence of 418,000 (219 per 100,000).[5]

Despite the success of the TB control strategies, TB persists in several parts of the world.[5] This signifies the need to intensify control efforts that identify and address the individual and social determinants of the disease. Structural factors, such as suboptimal case detection and non-adherence to therapy, as well as host-level factors, such as HIV and diabetes mellitus (DM) that increase vulnerability to active TB are major challenges to TB control.[6 7] In 2019, according to International Diabetes Federation (IDF),[8] there were an estimated 463.0 million and 19.4 million people with DM globally and in Africa respectively. By 2030, it is projected that 28.6 million adults in the Africa region will have DM.[8] In 2019, an estimated 4.2 million (20-79 years) and more than 366,200 deaths globally and in Africa respectively, could be attributed to DM.[8] In Nigeria, the prevalence of DM in the general population was 4.3% and 2% of total death in all ages was caused by the disease.[9]

Many studies conducted in different parts of the globe have revealed bidirectional association between TB and DM.[10] This close link is striking in developing countries, where TB is endemic and the burden of DM is high and increasing,[10] including Nigeria.

DM directly impairs innate and adaptive immune responses that are necessary to combat the progression from infection to clinical diseases.[11] Diabetes mellitus is a known risk factor for tuberculosis,[12] and is associated with poorer tuberculosis outcomes, while tuberculosis is associated with regressing glycaemic control.[13] Hence, it is advantageous to screen and identify undiagnosed DM among TB patients and then, offer glycaemic control, to prevent or delay diabetes-related complications and improve TB treatment outcome accordingly.

Despite the evidence which support DM as a risk factor for TB, few studies have been documented in Nigeria. No study has been conducted and reported in Oyo State to the best of our knowledge. This study aimed at determining the prevalence of DM and its associated

factors among patients attending Directly Observed Treatment Centres (DOTS) in Oyo State, South-west, Nigeria.

Methods

Study setting

Oyo State is in South-west Nigeria, the most populous country in sub-Saharan Africa. It has

33 Local Government Areas (LGAs) distributed over its three (3) senatorial districts. The State has 244 Directly Observed Treatment Centre-Short course (DOTS) centres across the

33 LGAs in Oyo State; comprising 200 public and 44 private DOTS centres. All the LGAs have several DOTS centres and are supported by Damien Foundation, Belgium, a leading Non-Governmental Organization (NGO) with focus on effective TB management and

control. Overall, there were 1,743 TB patients on treatment in all the DOTS clinics in Oyo State as at the time of the study.

Sputum smear microscopy was the prevailing primary test for the diagnosis of pulmonary tuberculosis (PTB) in Nigeria. Smears may be prepared directly from clinical specimens or from concentrated preparations using Ziehl-Nielsen staining or Fluorescent Auramine

staining) to observe acid-fast bacilli. A sputum result is positive if at least one tubercle bacillus (acid-fast/fluorescent) is detected on one or more sputum smears. The glycated haemoglobin test is used to both diagnose DM and assess control in DM.

Study design

A cross-sectional facility-based study was conducted among consenting TB patients aged ≥15years attending DOTS centres in Oyo State. Participants were systematically selected in each DOTS centre and respondents aged 15 were part of the selected lot. However,

parents/guardians gave consent for participants who were between the ages of 15 and 17 years old. Pregnant TB patients and extra-pulmonary TB cases were excluded from the study. The fasting blood glucose level was ascertained for confirmed old and newly diagnosed pulmonary TB (PTB) patients both at any stage of anti-tuberculosis treatment.

Sampling technique

A stratified sampling approach was used to select the study participants in the first stage. The LGAs were proportionally allocated to the 3 senatorial zones of the State. 11 of the 33 LGAs in Oyo State, Nigeria was selected for the study, using simple random sampling by balloting in each of the 3 senatorial zones, namely, Oyo central (4 out of 11 LGAs were selected), Oyo north (3 out of 13 LGAs were selected) and Oyo south (4 out of 9 LGAs were selected) of the

State. In the second stage, one DOTS centre was selected using simple random sampling in each of the 11 LGAs selected, and 404 patients were systematically selected, proportional to size in each of the 11 DOTS centres selected. (Figure). It is worth mentioning that patients who refused to participate in the study were replaced immediately.

Data collection

The study instrument was adapted from an earlier study. Trained data collectors administered the pre-tested interviewer-administered semi-structured questionnaire to the selected TB

patients to collect information on respondents' socio-demographic characteristics, lifestyle factors, clinical characteristics, and socio-economic status.

Data on past medical history and duration of their treatment on anti-TB drugs were extracted from patients' clinical records.

Anthropometric measures: height, weight and waist circumference using standard procedures. Body Mass index (BMI, kg/m^2) were obtained using standard procedures: BMI (kg/m^2) was calculated as Weight (kg)/Height (m^2). Blood pressure was measured in millimeters of

mercury (mm Hg) using a digital BP measurement device.

All participants were tested for DM, irrespective of prior diabetes status. Screening for DM among the respondents was done by Fasting Blood Sugar (FBS) test, using an electronic

glucometer and test strips (ACCU-CHEK Active by Roche), in the morning at the respective DOTS centres, in respondents who have fasted for at least 8 hours overnight. The DM status was assessed in line with the WHO recommendation for the diagnostic criteria for diabetes and intermediate hyperglycaemia.[9] (110mg/dl to 125mg/dl - prediabetic/impaired fasting

glucose; (≥126mg/dl - diabetic/fasting plasma glucose).

TB patients who were diagnosed with DM were referred to DM clinics situated in Oyo State of Nigeria for prompt and appropriate management.

Data processing and analysis

The dependent variable is diabetes status (Fasting Blood Glucose level). The independent variables include age, sex, residence, education, marital status, occupation, status of HIV, smoking, BMI, drinking of alcohol, family history of diabetes, habit of physical exercise and socio-economic status. The main outcome variables were proportions of patients with a

diagnosis of TB-DM and TB without DM (TB-DM co-infection status). Variables were summarized with descriptive statistics. Bivariate analysis using Pearson's chi-squared test or Fisher's Exact Test appropriately was conducted to determine the relationship between dependent variable and other independent variables. Predictors of the outcome variable (DM) was identified with a multiple binary logistic regression analysis. Covariates selected for the adjusted model was predictive, hence all significant variables at 10% level of significance were carried over to the adjusted model. The SES definitions was computed through principal component analysis which aggregates possession of economic household items and divides it into quintiles. In this case, the SES was categorized in 3 quintiles. Results were presented at 5% alpha significant level. Analysis was performed using Epi info version 7 and SPSS Statistical Software.

Ethical consideration

Ethical clearance was obtained from the Ethics Committee of the Oyo State Ministry of Health (reference number: AD 13/479/277, date: 15 November 2016). Informed consent was obtained from the study participants and guardians- for participants below the age of 18 years. Confidentiality of information obtained was maintained. Data were de-identified.

Patient and Public Involvement

Patients and public were not involved in the design of this study. However, patients served as study participants and were recruited after obtaining an informed consent.

Results

The overall prevalence of TB-DM co morbidity was 7.9% (32/404) [95% CI: 5.7- 10.9]. The proportion of IFG TB patients was 7.4% (30/404). The mean age of the male and female respondents were 41 (±14.2) and 36.8 (±15.0) respectively. There was a female preponderance for TB-DM co- morbidity (Table 1). The median FBG level of male and female patients with TB-DM co-morbidity was 89 (Interquartile range:148) and 88 (Interquartile range:319) respectively (Table 2). TB-DM co-morbidity among poor (10.1%) and average (6.1%) socio-economic status (SES) was lower and 9 (22%) had no formal education, and 9 (22%) had no formal education (Table 1).

There was statistically significant association (OR=134.46, CI:40.02-451.73) between respondents who have been previously diagnosed with DM compared to newly diagnosed respondents (Table 2). Other associated factors of TB such as smoking (OR=1.11, CI: 0.49 - 2.48), alcohol intake (OR=0.83, CI: 0.37 - 1.85), close contact with TB patients (OR=0.42, CI:0.09 - 1.81), family history of DM (OR=14.40, CI: 0.75-204.24), duration of TB treatment (OR=0.79, CI: 0.32 - 1.98), intake of other stimulants (OR=0.86, CI:0.25 - 2.95), habit of exercise (OR: 0.61, CI:0.21 - 1.78) and BMI (OR=2.29, CI:0.99 - 5.28) did not show any statistical association with the prevalence of DM among TB patients (Table 2). Respondents 40 years and above were found to be 0.43 times (1/2.33) less likely to have TB-DM comorbidity compared to those <40 years. Married respondents were 0.43 times (1/2.32) less likely to have TB with DM co-morbidity than unmarried ones. Respondents who were not living with a spouse were 0.26 times (1/3.79) less likely to have TB-DM comorbidity than respondents who were single (Table 3).

Table 1: Socio-demographic characteristics of diabetic and non-diabetic Tuberculosis patients

	Diabetics n (%)	Non- diabetics n (%)	Total n (%)	P-value
Sex				
Male	16(6.3)	237(93.7)	253(62.6%)	0.124
Female	16(10.6)	135(89.4)	151(37.4%)	
Age				
15-24	1(1.7)	57(98.3)	58(14.4)	
25-44	11(5.1)	203(94.9)	214(53.0)	0.000
45-64	12(12.2)	86(87.8)	98(24.3)	
≥65	8(23.5)	26(76.5)	34(8.4)	
Religion				
Christian	9(8.3)	99(91.7)	108(26.7)	0.853
Muslim	23(7.8)	273(92.2)	296(73.3)	
Educational level				
No formal Education	9(22.0)	32(78.0)	41(10.1)	
Primary school	11(9.7)	102(90.3)	113(28.0)	0.02
Secondary school	10(4.5)	205(95.3)	215(53.2)	
University/ Higher education	2(5.7)	32(94.3)	35(8.7)	
Marital status				
Single	2(2.4)	82(97.6)	84(21.0)	
Married	27(8.8)	279(91.2)	306(75.4)	0.025
Divorced/Separated/Widowed	3(21.4)	11(78.6)	14(3.5)	
Place of residence				
Urban	24(8.2)	269(91.8)	293(72.5)	0.744
Rural	8(7.2)	103(92.8)	111(24.5)	
Occupation				
Govt/Privately employed	2(5.9)	32(94.1)	34(8.4)	
Self-employed	25(8.3)	277(91.7)	302(74.8)	0.296
Student	1(2.4)	40(97.6)	41(10.1)	
Unemployed	4(14.8)	23(85.2)	27(6.7)	
Average monthly income (Naira)				
< 18,000	15(6.6)	211(93.4)	226(55.9)	
18,000-50,000	9(7.6)	109(92.4)	118(29.2)	0.202
> 51,000	8(13.3)	52(82.6)	60(14.9)	
Ethnicity				
Yoruba	31(7.7)	360(92.1)	391(96.8)	0.975
Others (Hausa, Ibo, etc)	1(0.2)	12(92.3)	13(3.2)	
Socio Economic Status				
Poor	7(10.1)	62(89.9)	69(17.0)	
Average	19(6.4)	278(93.6)	297(73.5)	0.098
Rich	6(15.8)	32(84.2)	38(9.4)	

Table 2: Factors associated with diabetes status among TB patients

Characteristics	Diabetics n (%)	Total	DM among TB patients OR (95% C.I)
Age group			
<40	8 (3.7)	219	1.00
40+	24 (12.9)	185	3.93(1.72 - 8.98)
Marital Status			
Single	2 (2.4)	84	1.00
Married	27 (8.8)	306	3.97 (0.92-17.04)
Divorced/Separated/Widowed	3 (21.4)	14	11.18 (1.68 -74.51)
Socio Economic Status			
Poor	7 (10.1)	69	0.60 (0.19-1.94)
Average	19 (6.4)	297	0.37 (0.14-0.98)
Rich	6 (15.8)	38	1.00
Educational Level			
No formal education	9 (22.0)	41	4.64 (0.93 -23.16)
Primary school	11(9.7)	113	1.78 (0.38-8.44)
Secondary school	10 (4.7)	215	0.81 (0.17-3.84)
University/higher education	2 (5.7)	35	1.00
Told in the past that you have DM?	19(82.6)	23	134.46 (40.02 – 451.73)
Yes	13(3.4)	381	1.00
No			
Smoking			
Yes	9(8.5)	106	1.11 (0.49 – 2.48)
No	23(7.7)	298	1.00
Drinking Alcohol			
Yes	9(7.0)	128	0.83 (0.37 – 1.85)
No	23(8.3)	276	1.00
Duration of TB treatment			
< 1 month	26(8.3)	314	0.79 (0.32 – 1.98)
> 1 month	6(7.5)	90	1.00
Do you take any other stimulant?			
Yes	3(7.0)	43	0.86 (0.25 – 2.95)
No	29(8.0)	361	1.00
Habit of exercise			
Yes	4(5.3)	75	0.61 (0.21 – 1.78)
No	28(8.5)	329	1.00
BMI (Kg/m^2)			
Underweight	8(4.8)	167	1.00
Normal	22(10.3)	213	2.29 (0.99 – 5.28)
Overweight/Obese	2(8.3)	24	1.81 (0.36 – 9.06)
Family History of Diabetes Mellitus			
Yes	1(50.0)	2	12.00 (0.73 – 196.00)
No	31(7.7)	402	1.00
Close contact with TB patient			
Yes	2(3.8)	53	0.42 (0.10 – 1.81)
No	30(8.6)	351	1.00

Table 3: Multivariate analysis of significant predictors of DM

Characteristics	Adjusted Odds Ratio (95% CI)	p-value
Age group		
<40 **(ref)**	1.00	
40+	2.33 (0.92-5.89)	0.073
Educational level		
No formal education	2.54 (0.43-14.81)	0.300
Primary school	1.13 (0.22-5.87)	0.884
Secondary school	0.65 (0.13-3.32)	0.604
University/higher education **(ref)**	1.00	
Marital Status		
Single **(ref)**	1.00	
Married	2.32 (0.47-11.49)	0.301
Divorced/Separated/Widowed	3.79 (0.47-30.36)	0.210
Socio Economic Status		
Poor	0.76 (0.21-2.78)	0.680
Average	0.46 (0.16-1.39)	0.170
Rich **(ref)**		
BMI (Kg/m^2)		
Underweight **(ref)**	1.00	
Normal	2.82 (1.15-6.94)	0.024
Overweight/Obese	1.67 (0.31-9.03)	0.552

*=statistically significant at ≤5%

Discussion

Our study revealed that the prevalence of DM among diagnosed TB patients was 7.9%. Factors associated with TB-DM co-morbidity were age (being at least 40 years of age), marital status and poverty. Although, the above-mentioned factors were not shown to be significant risk at the multivariate level. Screening for DM in TB patients could improve DM case detection and early initiation of treatment, education of patients and correction of hyperglycaemia, which potentially could have positive effects on the outcome of TB treatment.

The prevalence of DM in this study is quite alarming, recalling that in Nigeria, the most recent prevalence of DM in the general population was 4.3%. This is similar to 4.6% as reported by Shittu et al in a similar population in the Oke-Ogun geo-political zone of Oyo State, Nigeria.[14]

The prevalence of 7.9% in our study is comparable with the studies conducted in Uganda (8.5%),[15] and Ethiopia (8.3%).[16] However, the current findings were lower than what were reported from Taiwan (29.5%),[17] Southern-Mexico (29.3%),[18] Kerala-India (44%),[19] Lagos, Nigeria (12.3%).[20] The reported finding in Tanzania was lower (4%).[21] Reasons for the observed variation in prevalence might be related to differences in background between populations (rural and urban settings) and screening methods (RBS, FBS and Oral Glucose Tolerance Test etc.) used in DM diagnosis.

The prevalence of IFG in this study was 7.4%. This finding is similar to the study done in Taian, Dingxi, Jinan, Shijiazhuang, Guiyang- China (7.8%),[22] Gujarat-India (7%),[23] higher than Kolar-India (3.1%),[24] but lower than the study findings from Gondar-Ethiopia (29.6%), Addis Ababa-Ethiopia (26.7%) and Tamil Nadu-India (24.5%),[25-27] respectively. Individuals with Impaired Fasting Glucose are at high risk of progressing to type 2 DM, although this is not inevitable,[9] and this may go further to indicate an increased risk of DM in the future in Nigeria. The observed DM and IFG prevalence in our study poses threats to gains made in TB control; hence, necessitates integrated health services approach to effectively address the burden of the two diseases.

The TB-DM co-morbidity demonstrated an association with older age. Occurrence of DM in older people is consistent with studies done in Addis Ababa-Ethiopia,[26] Ethiopia,[28] Kerala-India,[19] Tamil Nadu-India,[27] Brazil,[29] Southern-Mexico,[18] and China.[30] This may be due to the fact that DM is essentially an age-related illness that occur more in people older than 40 years. This is consistent with earlier studies conducted to determine the risk factors for TB.[31] Old age is related to immunosuppression and is one of the risk factors for both TB and DM.[8 2] In Nigeria, for example, the risk of developing DM increases 3-4 folds after the age of 44 years,[14] a consistent finding with this study, as age group > 44 years had a higher proportion of TB with DM co-morbidity. This goes to strongly suggest that health care system in Nigeria should improve its content and delivery of services with respect to older age.

A slightly higher preponderance TB-DM co-morbidity among females than males in this study is similar to those found in studies done in Ethiopia,[16] and Mexico.[32] The prevalence and complication of diabetes are more pronounced in females than males as a result of gender associated adiposity.[33] Unlike for men, increased androgen levels induce insulin resistance in women,[33] and increase the risk of type 2 Diabetes and cardiovascular diseases.[34] Women have a higher percentage of body fat and more often develop peripheral adiposity, where men accumulate fat centrally.[35] Women generally have poorer glycemic control.[36 37] The health system in Nigeria should be geared towards ensuring that concerned females are duly educated on preventive measures against DM and encouraged to utilise availability health services to halt the trend of DM among this female gender in Nigeria.

Positive family history is a known risk factor for DM.[38] However, there was no significant association with DM among TB patients who have a family history/genetic pre-disposition to DM. This finding is in contrast with the study done in Tamilu Nadu-India and China.[27 39]

Tuberculosis is a disease of poverty, and that is understandably consistent with the finding in this study, as quite a comparable proportion of the TB patients were poor and average in status as well as rich. This indicates a lack of adequate resources to a large proportion of the participants and therefore, a factor to be considered in the management of the disease. Thus, accessing healthcare is a challenge for people living with diabetes in Nigeria.

Majority of the respondents (78.0%) had no formal education. Many factors are shown to affect the health of individuals and communities, namely, low educational level, which relates to poor health, higher stress level and lower self-esteem.[40] Educational programmes that embody and emphasize awareness of DM and its preventative measures and complications, self-care management behaviour (adherence to diabetic medications, healthy diet, regular exercise and follow up should be effectively propagated across all levels. Death of a spouse currently ranks as the life-event needing the most intense social readjustment and poses health risks.[41]

Strengths and limitation

This is one of the few studies on TB-DM comorbidity to be conducted and further documented in Nigeria, as at the time of study. The findings are generalizable to similar settings in Nigeria and other low-and-middle- income countries. The outcomes of TB management in TB-DM comorbid individuals such as cure rate, treatment success rate or death could not be ascertained being a cross-sectional study.

Conclusion

There was a high prevalence of DM among TB patients. Age, educational level and marital status were associated with TB-DM co morbidity in this study. Although, not revealed to be significant risk factors at the multivariate level. Widowhood poses health risks. Hence, we recommend that physicians should also be aware of possible long-term health risks emerging after widowhood such as changes in lifestyle, diet and adiposity, which may be remedied by attention to healthy behaviour.

We hope that data obtained would be used to inform a new holistic national treatment guideline for TB, inclusive of routine screening for DM and an active management of the glycaemia in those found in TB-DM co-morbid individuals. These would result in improved treatment outcome and management in PTB patients.

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Authors' contributions

MOA, AK were involved in the conception, design and execution of the study. MOA, AK and NA were involved in the analysis and data interpretation. OA contributed to data

interpretation; drafting, formatting and final revision of the manuscript for intellectual content. MOA, OA, and AU reviewed the manuscript for intellectual content. All authors read and agreed to final version of the manuscript.

Data Availability Statement

All relevant data to the study are included in the article or uploaded as supplementary information.

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Competing interests

None declared.

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Figure: Sampling strategy flow chart

Oyo central senatorial zone: Akinyele, Egbeda, Ona-ara, Oyo East

Oyo north senatorial zone: Saki west, Kajola, Iseyin
Oyo south senatorial zones: Ibadan North East, Ibadan North West, Ibadan South East, Ibadan South West.

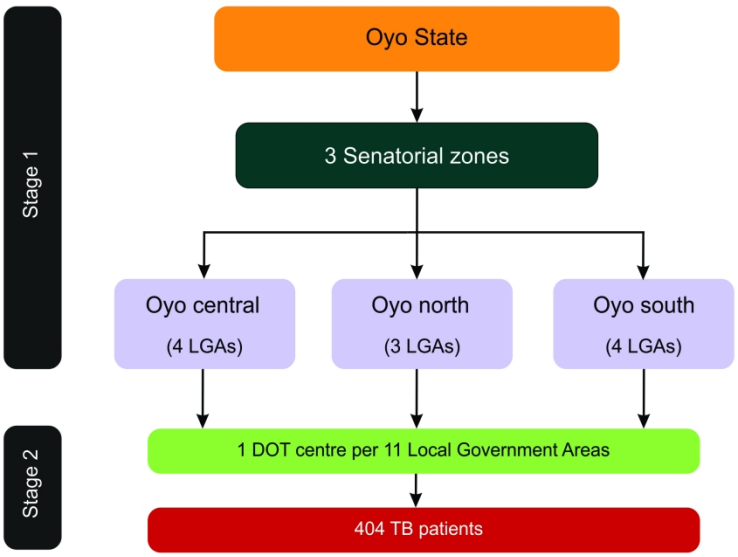

Figure
Sampling strategy flow chart

210x297mm (300 x 300 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*6*
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	6
		(*c*) Explain how missing data were addressed	Not Applicable (N/A)
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	6
		(*e*) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—e.g. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	(uploaded)
Descriptive data	14*	(a) Give characteristics of study participants (e.g. demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	N/A
Outcome data	15*	Report numbers of outcome events or summary measures	9-11

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10
		(*b*) Report category boundaries when continuous variables were categorized	9
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—e.g. analyses of subgroups and interactions, and sensitivity analyses	10
Discussion			
Key results	18	Summarise key results with reference to study objectives	11-12
Limitations	19	Discuss limitations of the study, considering sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12-13
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	13

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Diabetes Mellitus and Its Associated Factors among Tuberculosis Patients Attending Directly Observed Treatment Centres in Oyo State, Nigeria: A cross sectional evaluation

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Abstract

Objective

Diabetes mellitus (DM) and Tuberculosis (TB) co-morbidity is evolving into an emerging epidemic globally. In Nigeria, a high burden of both diseases respectively exists with limited information on Tuberculosis-Diabetes Mellitus (TB-DM) comorbidity. We determined the fasting blood glucose (FBG) level among patients with TB and factors associated with TB-DM comorbidity in Oyo State, South-west Nigeria.

Methods

A cross-sectional study was conducted among TB patients aged 15 years and above, who were selected using multistage sampling. Data were collected on patients' biodata, anthropometric measurements and FBG levels using a pretested semi-structured questionnaire. The FBG test was conducted on confirmed Pulmonary TB patients (old and newly diagnosed TB patients) at any stage of anti-tuberculosis treatment. Background characteristics and FBG level were summarized using descriptive statistics and factors associated with TB-DM comorbidity were presented using odds ratios (OR) at 95% Confidence Interval.

Results

Of the 404 TB patients, 30 (7.4%) had Impaired Fasting Glucose and 32 (7.9%) were diagnosed with diabetes. The TB-DM patients' mean age was 49.5 (SD:15.9) years. Females were more likely than males to have diabetes (10.6% vs. 6.3%). Median FBG level for the patients was 88 (Interquartile range: Q1: 99, Q3:79) mg/dl. Being at least 40 years [(OR 3.93; 95% CI: 1.72-8.98)], marital status [(OR= 11.18; 95% CI: 1.68-74.51)] and middle socioeconomic status [(OR=0.4; 95% CI: 0.14-0.98)] were associated with comorbidity individually. In the multivariable model, only body mass index was independently and significantly associated with diabetes.

Conclusion

Tuberculosis-Diabetes Mellitus was prevalent among the studied population in South-west Nigeria. We recommend the integration of DM screening within the continuum of care for TB management.

Keywords: Tuberculosis-Diabetes Mellitus comorbidity, Hyperglycaemia, Nigeria.

Article summary:

- **Strengths and limitations of the study**
  - This is one of the few studies to document TB-DM comorbidity in Nigeria and the first to do so for Oyo State, South-west, Nigeria.
  - The high prevalence of DM among TB patients in Oyo State is a new and important finding for addressing the dual non-communicable and communicable disease burden.
  - Our study used a hospital design that enabled access to TB patients in a clinic setting and this approach is a potential opportunity for implementing concurrent regular routine screening and clinical management, lifestyle modification, and follow-up for TB-DM comorbidity.
  - Alcohol consumption and smoking are culturally undesirable behaviour, and these could have resulted in socially desirable responses.
  - The outcomes of TB management in TB-DM comorbid individuals such as cure rate, treatment success rate, or death could not be ascertained in our study, which was a cross-sectional evaluation.

Introduction

Tuberculosis remains a major global infectious disease that causes morbidity and death. The low- and middle-income countries harbor about 95% and 75% of tuberculosis (TB) and diabetes mellitus (DM) patients respectively.[1 2] Incident cases of TB were reported to be the highest among people with impaired immunity, human immunodeficiency virus (HIV) infection or DM.[2] In 2018, an estimated 10.0 million individuals were newly diagnosed with TB, 1.2 million and 250,000 people died among HIV-negative and HIV- positive people respectively, of which Africa region accounted for 24%.[3] Nigeria belongs to one of the 30 high-burden TB countries worldwide.[3] In 2018, Nigeria was among the top 8 high TB burden countries, with an estimated 429,000 incident TB cases (219 per 100,000 population); and mortality of 123,000 (64 per 100,000 population) those due to excluding TB-HIV.[3] Nigeria, with a population of more than 190 million,[4] has the highest burden of the disease globally with a total TB incidence of 418,000 (219 per 100,000).[5]

Despite the success of the TB control strategies, TB persists in several parts of the world.[5] This signifies the need to intensify control efforts that identify and address the individual and social determinants of the disease. Structural factors, such as suboptimal case detection and non-adherence to therapy, as well as host-level factors, such as HIV and diabetes mellitus (DM), that increase vulnerability to active TB are major challenges to TB control.[6 7]

In 2019, according to International Diabetes Federation (IDF),[8] there were an estimated 463.0 million and 19.4 million people with DM globally and in Africa respectively. By 2030, it is projected that 28.6 million adults in the Africa region will have DM.[8] In 2019, an estimated 4.2 million (20-79 years) and more than 366,200 deaths globally and in Africa respectively, could be attributed to DM.[8] In Nigeria, the prevalence of DM in the general population was 4.3% and 2% of total death in all ages was caused by the disease.[9]

Many studies conducted in different parts of the globe have revealed a bidirectional association between TB and DM.[10] This close link is striking in developing countries, where TB is endemic and the burden of DM is high and increasing,[10] including Nigeria.

DM directly impairs innate and adaptive immune responses that are necessary to combat the progression from infection to clinical diseases.[11] Diabetes mellitus is a known risk factor for tuberculosis,[12] and is associated with poorer tuberculosis outcomes, while tuberculosis is associated with regressing glycaemic control.[13] Hence, it is advantageous to screen and identify undiagnosed DM among TB patients and then, offer glycaemic control, in order to prevent or delay diabetes-related complications and improve TB treatment outcomes accordingly.

Despite the evidence which supports DM as a risk factor for TB, few studies have been documented in Nigeria. No study has been conducted and reported in Oyo State to the best of our knowledge. This study aimed at determining the prevalence of DM and its associated factors among patients attending Directly Observed Treatment Centres (DOTS) in Oyo State, South-west, Nigeria.

Methods

Study setting

Oyo State is in South-west Nigeria, the most populous country in sub-Saharan Africa. It has 33 Local Government Areas (LGAs) distributed over its three (3) senatorial districts. The State has 244 Directly Observed Treatment Centre-Short course (DOTS) centres across the 33 LGAs in Oyo State, comprising 200 public and 44 private DOTS centres. All the LGAs have several DOTS centres and are supported by Damien Foundation, Belgium, a leading Non-Governmental Organization (NGO) with a focus on effective TB management and control. Overall, there were 1,743 TB patients on treatment in all the DOTS clinics in Oyo State at the time of the study.

Sputum smear microscopy was the prevailing primary test for the diagnosis of pulmonary tuberculosis (PTB) in Nigeria. Smears may be prepared directly from clinical specimens or from concentrated preparations using Ziehl-Nielsen staining or Fluorescent Auramine staining) to observe acid-fast bacilli. A sputum result is positive if at least one tubercle bacillus (acid-fast/fluorescent) is detected on one or more sputum smears. The glycated haemoglobin test is used to both diagnose DM and assess control in DM.

Study design

A cross-sectional facility-based study was conducted among consenting TB patients aged 15years and above attending DOTS centres in Oyo State. Participants were systematically selected in each DOTS centre. There was no age-cut off for the study and no participant under the age of 15 years was selected. However, parents/guardians gave consent for participants who were between the ages of 15 and 17 years old. Pregnant TB patients and extra-pulmonary TB cases were excluded from the study. The fasting blood glucose level was ascertained for confirmed old and newly diagnosed pulmonary TB (PTB) patients both at any stage of anti-tuberculosis treatment.

Sampling technique

A stratified sampling approach was used to select the study participants in the first stage. The LGAs were proportionally allocated to the 3 senatorial zones of the State. Eleven (11) of the 33 LGAs in Oyo State, Nigeria was selected for the study, using simple random sampling by balloting in each of the 3 senatorial zones, namely, Oyo central (4 out of 11 LGAs were selected), Oyo north (3 out of 13 LGAs were selected) and Oyo south (4 out of 9 LGAs were selected) of the State. In the second stage, one DOTS centre was selected using simple random sampling in each of the 11 LGAs selected, and 404 patients were systematically selected, proportional to the size in each of the 11 DOTS centres selected. (Figure).

The minimum sample size of sample 364 was calculated with the formula for estimating a single population proportion ($n = Z^2 p(1 - p)/d^2$), 12.3% proportion,[14] for 0.05 precision and Z of 1.96. The final sample size was 404 TB patients after correcting for a finite population and accounting for a 10% non-response rate.

Data collection

The study instrument was adapted from an earlier study. Trained data collectors administered the pre-tested interviewer-administered semi-structured questionnaire to the selected TB patients to collect information on respondents' socio-demographic characteristics, lifestyle factors, clinical characteristics, and socio-economic status.

Data on past medical history and duration of their treatment on anti-TB drugs were extracted from patients' clinical records.

Anthropometric measures: height, weight and waist circumference using standard procedures. Body Mass Index (BMI, kg/m^2) were obtained using standard procedures: BMI (kg/m^2) was calculated as Weight (kg)/Height (m^2). Blood pressure was measured in millimeters of mercury (mm Hg) using a digital BP measurement device.

All participants were tested for DM, irrespective of prior diabetes status. Screening for DM among the respondents was done by Fasting Blood Sugar (FBS) test, using an electronic glucometer and test strips (ACCU-CHEK Active by Roche), in the morning at the respective DOTS centres, in respondents who have fasted for at least 8 hours overnight. The DM status was assessed in line with the WHO recommendation for the diagnostic criteria for diabetes and intermediate hyperglycaemia.[9] (110mg/dl to 125mg/dl – prediabetic/impaired fasting glucose; (≥126mg/dl – diabetic/fasting plasma glucose).

TB patients who were diagnosed with DM were referred to DM clinics situated in Oyo State, Nigeria for prompt and appropriate management.

Data processing and analysis

The dependent variable is diabetes status (Fasting Blood Glucose level). The independent variables include age, sex, residence, education, marital status, occupation, HIV status, smoking, BMI, drinking of alcohol, family history of diabetes, physical activity (exercise) and socio-economic status. The main outcome variables were proportions of patients with a diagnosis of TB-DM and TB without DM (TB-DM co-infection status), and patients with Impaired Fasting Glucose were not included in the non-diabetic group for the analysis. Variables were summarized with descriptive statistics. Bivariate analysis using Pearson's chi-squared test or Fisher's Exact Test appropriately was conducted to determine the relationship between the dependent variable and other independent variables. Predictors of the outcome variable (DM) was identified with a multiple binary logistic regression analysis. Covariates selected for the adjusted model was predictive, hence all significant variables at 10% level of significance were carried over to the adjusted model. The SES definitions were computed through principal component analysis which aggregates possession of economic household items and divides it into quintiles. Each respondent was given a score based on the number and kinds of consumer goods owned or services enjoyed, ranging from radio, television, mobile telephone, refrigerator, cable TV, generating set, air conditioner, computer, electric iron, fan, motorcycle, car/truck, land ownership, house ownership, livestock/other farm animals/poultry and availability of electricity. These scores were derived through principal component analysis and using the first factor that has the highest proportion of information

explained (25%) to rank each participant by their score. The score was then divided into three equal categories, each comprising 33% of the population. In this case, the SES was categorized into three quintiles. Results were presented at the 5% alpha significant level. Analysis was performed using Epi info version 7 and SPSS Statistical Software.

	Diabetics n (%)	Non-diabetics n (%)	Total n (%)	P-value
Sex				
Male	16(6.3)	237(93.7)	253(62.6)	0.124
Female	16(10.6)	135(89.4)	151(37.4)	
Age				
15-24	1(1.7)	57(98.3)	58(14.4)	
25-44	11(5.1)	203(94.9)	214(53.0)	0.000
45-64	12(12.2)	86(87.8)	98(24.3)	

Ethical consideration

Ethical clearance was obtained from the Ethics Committee of the Oyo State Ministry of Health (reference number: AD 13/479/277, date: 15 November 2016). Informed consent was obtained from the study participants and guardians- for participants below the age of 18 years. Confidentiality of information obtained was maintained. Data were de-identified.

Patient and Public Involvement

Patients and the public were not involved in the design of this study. However, patients served as study participants and were recruited after obtaining informed consent.

Results

We approached a total of 426 selected patients, replaced immediately those who refused to participate in the study (n =22) until we attained our sample size of 404 (response rate =94.8% (404/426). The overall prevalence of TB-DM co-morbidity was 7.9% (32/404) [95% CI: 5.7- 10.9]. The proportion of IFG TB patients was 7.4% (30/404). The mean age of the male and female respondents was 41 (±14.2) and 36.8 (±15.0) respectively. There was a female preponderance for TB-DM co-morbidity (Table 1). The median FBG level of male and female patients with TB-DM co-morbidity was 89 (Interquartile range:148) and 88 (Interquartile range:319) respectively (Table 2). TB-DM co-morbidity among poor (10.1%) and average (6.1%) socio-economic status (SES) were lower and 9 (22%) had no formal education, and 9 (22%) had no formal education (Table 1).

Age (aOR: 2.28, 95%CI: 0.91, 5.74) and marital relationships ([being married, aOR: 2.23 95%CI: 0.45 – 10.97] and being separated/divorced/widowed, aOR: 3.80, 95%CI: 0.48 – 30.13]) were not significant predictors of being diabetic TB patient. In the multivariate model, only body mass index was independently and significantly associated with diabetes (Table 3).

≥65	8(23.5)	26(76.5)	34(8.4)	
Religion				
Christian	9(8.3)	99(91.7)	108(26.7)	0.853
Muslim	23(7.8)	273(92.2)	296(73.3)	
Educational level				
No formal Education	9(22.0)	32(78.0)	41(10.1)	
Primary school	11(9.7)	102(90.3)	113(28.0)	0.02
Secondary school	10(4.5)	205(95.3)	215(53.2)	
University/ Higher education	2(5.7)	32(94.3)	35(8.7)	
Marital status				
Single	2(2.4)	82(97.6)	84(21.0)	1.00
Married	27(8.8)	279(91.2)	306(75.4)	0.025
Divorced/Separated/Widowed	3(21.4)	11(78.6)	14(3.5)	
Place of residence				
Urban	24(8.2)	269(91.8)	293(72.5)	0.744
Rural	8(7.2)	103(92.8)	111(24.5)	
Occupation				
Govt/Privately employed	2(5.9)	32(94.1)	34(8.4)	
Self-employed	25(8.3)	277(91.7)	302(74.8)	0.296
Student	1(2.4)	40(97.6)	41(10.1)	
Unemployed	4(14.8)	23(85.2)	27(6.7)	
Average monthly income (Naira)				
< 18,000	15(6.6)	211(93.4)	226(55.9)	
18,000-50,000	9(7.6)	109(92.4)	118(29.2)	0.202
> 51,000	8(13.3)	52(86.7)	60(14.9)	
Ethnicity				
Yoruba	31(7.7)	360(92.1)	391(96.8)	0.975
Others (Hausa, Ibo, etc)	1(0.2)	12(92.3)	13(3.2)	
Socioeconomic status				
Poor	14(10.5)	120(89.6)	134(33.2)	
Average	10(7.4)	126(92.7)	136(33.7)	0.381
Rich	8(6.0)	126(94.0)	134(33.2)	

Characteristics	**Diabetics n (%)**	**Total**	**OR (95% C.I)**	
Told in the past that you have DM?				
Yes	19(82.6)	23	134.46 (40.02 – 451.73)	
No	13(3.4)	381	1.00	
Smoking				
Yes	9(8.5)	106	1.11 (0.49 – 2.48)	
No	23(7.7)	298	1.00	

Table 1: Socio-demographic characteristics of diabetic and non-diabetic Tuberculosis patients (n=404)

Drinking Alcohol			
Yes	9(7.0)	128	0.83 (0.37 – 1.85)
No	23(8.3)	276	1.00
Duration of TB treatment			
< 1 month	26(8.3)	314	0.79 (0.32 – 1.98)
> 1 month	6(7.5)	90	1.00
Do you take any other stimulant?			
Yes	3(7.0)	43	0.86 (0.25 – 2.95)
No	29(8.0)	361	1.00
Habit of exercise			
Yes	4(5.3)	75	0.61 (0.21 – 1.78)
No	28(8.5)	329	1.00
BMI (Kg/m^2)			
Underweight	8(4.8)	167	1.00
Normal	22(10.3)	213	2.29 (0.99 – 5.28)
Overweight/Obese	2(8.3)	24	1.81 (0.36 – 9.06)
Family History of Diabetes Mellitus			
Yes	1(50.0)	2	12.00 (0.73 – 196.00)
No	31(7.7)	402	1.00
Close contact with TB patient			
Yes	2(3.8)	53	0.42 (0.10 – 1.81)
No	30(8.6)	351	1.00

Table 2: Factors associated with diabetes status among TB patients

Table 3: Multivariable analysis of the predictors of DM

*=statistically significant at ≤5%

Characteristics	Adjusted Odds Ratio (95% CI)	p-value
Age group		
<40 **(ref)**	1.00	
40+	2.28 (0.91, 5.74)	0.080
Educational level		
No formal education	2.72 (0.49 – 15.08)	0.252
Primary school	1.06 (0.21 - 5.41)	0.945
Secondary school	0.60 (0.12 - 3.00)	0.532
University/higher education **(ref)**	1.00	
Marital Status		
Single **(ref)**	1.00	
Married	2.23 (0.45 – 10.97)	0.323
Divorced/Separated/Widowed	3.80 (0.48 – 30.13)	0.206
BMI (Kg/m^2)		
Underweight **(ref)**	1.00	
Normal	2.91 (1.18-7.14)	0.020
Overweight/Obese	1.75 (0.33 – 9.39)	0.514

Discussion

Our study revealed that the prevalence of DM among diagnosed TB patients was 7.9%. Factors associated with TB-DM co-morbidity were age (being at least 40 years of age), marital status and poverty. Although, the above-mentioned factors were not shown to be of significant risk at the multivariate level. Screening for DM in TB patients could improve DM

case detection and early initiation of treatment, education of patients and correction of hyperglycaemia, which potentially could have positive effects on the outcome of TB treatment.

In Nigeria, the most recent prevalence of DM in the general population was 4.3%. [9] This is similar to 4.6% as reported by Shittu et al in a similar population in the Oke-Ogun geo-political zone of Oyo State, Nigeria.[15] The prevalence of DM in this study is quite alarming (7.9%), it is comparable to the studies conducted in Uganda (8.5%),[16] and Ethiopia (8.3%).[17] However, the current findings were lower than what was reported from Taiwan (29.5%),[18] Southern-Mexico (29.3%),[19] Kerala-India (44%),[20] Lagos, Nigeria (12.3%).[14] The reported finding in Tanzania was lower (4%).[21] Reasons for the observed variation in prevalence might be related to differences in background between populations (rural and urban settings) and screening methods (RBS, FBS and Oral Glucose Tolerance Test etc.) used in DM diagnosis.

The prevalence of IFG in this study was 7.4%. This finding is similar to the study done in Taian, Dingxi, Jinan, Shijiazhuang, Guiyang- China (7.8%),[22] Gujarat-India (7%),[23] higher than Kolar-India (3.1%),[24] but lower than the study findings from Gondar-Ethiopia (29.6%), Addis Ababa-Ethiopia (26.7%) and Tamil Nadu-India (24.5%),[25-27] respectively. Individuals with Impaired Fasting Glucose are at high risk of progressing to type 2 DM, although this is not inevitable,[9] and this may go further to indicate an increased risk of DM in the future in Nigeria. The observed DM and IFG prevalence in our study pose threats to gains made in TB control; hence, necessitates integrated health services approach to effectively address the burden of the two diseases.

The TB-DM co-morbidity demonstrated an association with older age. The occurrence of DM in older people is consistent with studies done in Addis Ababa–Ethiopia,[26] Ethiopia,[28] Kerala-India,[20] Tamil Nadu–India,[27] Brazil,[29] Southern-Mexico,[19] and China.[30] This may be because DM is an age-related illness that occurs in persons above 40years. This is consistent with earlier studies which determined the risk factors for TB.[31] Old age is related to immunosuppression and is one of the risk factors for both TB and DM.[8 2] In Nigeria, for example, the risk of developing DM increases three to four folds after the age of 44 years,[15] a consistent finding with this study where age group > 44 years had a higher proportion of TB with DM co-morbidity. This goes to strongly suggest that the health care system in Nigeria should improve its content and delivery of services with respect to older age groups.

A slightly higher preponderance of TB-DM co-morbidity among females than males in this study is similar to those found in studies done in Ethiopia,[17] and Mexico.[32] The prevalence and complication of diabetes are more pronounced in females than males as a result of gender-associated adiposity.[33] Unlike for men, increased androgen levels induce insulin resistance in women,[33] and increase the risk of type 2 diabetes and cardiovascular diseases.[34] Women have a higher percentage of body fat and more often develop peripheral adiposity, whereas men accumulate fat centrally.[35] Women generally have poorer glycemic control.[36 37] The health system in Nigeria should be geared towards ensuring that concerned females are

duly educated on preventive measures against DM and encouraged to utilise available health services to halt the trend of DM among this female gender in Nigeria.

Positive family history is a known risk factor for DM.[38] However, there was no significant association with DM among TB patients who have a family history/genetic predisposition to DM. This finding is in contrast with the study done in Tamil Nadu-India and China.[27 39]

Tuberculosis is a disease of poverty. In our study, two-thirds of the respondents were of low and average socioeconomic status. This portends a lack of adequate resources to a large proportion of the participants and could be a challenge for persons living with diabetes in Nigeria. Therefore, these should be considered in the management of the disease which comes at a huge personal out-of-pocket cost.

Most of the respondents (78.0%) had no formal education. Many factors are shown to affect the health of individuals and communities, namely, low educational level, which relates to poor health, higher stress level and lower self-esteem.[40] Educational programmes that embody and emphasize awareness of DM and its preventative measures and complications, self-care management behaviour (adherence to diabetic medications, healthy diet, regular exercise and follow up should be effectively propagated across all levels. The death of a spouse currently ranks as the life-event needing the most intense social readjustment and poses health risks.[41]

Strengths and limitation

This is one of the few studies on TB-DM comorbidity conducted and documented in Nigeria, at the time of the study. The findings are generalizable to similar settings in Nigeria and other low-and-middle-income countries. Alcohol consumption and smoking are culturally undesirable behaviour, and these could have resulted in socially desirable responses. The outcomes of TB management in TB-DM comorbid individuals such as cure rate, treatment success rate or death could not be ascertained in our study being a cross-sectional evaluation.

Conclusion

There was a high prevalence of DM among TB patients. Age, educational level, and marital status were associated with TB-DM co-morbidity in this study. Although not revealed to be significant risk factors at the multivariate level, a current single relationship from a previous married relationship, that is, being divorced, separated, or widowed, could pose potential health risks. Those in a married spousal relationship tends to benefit from social support towards adhering to healthy behavioural lifestyle. Hence, we recommend that physicians should also be aware of possible long-term health risks emerging after widowhood such as changes in lifestyle, diet, and adiposity, which may be remedied by attention to healthy behaviour.

We hope that data obtained would be used to inform a new holistic national treatment guideline for TB, inclusive of routine screening for DM and active management of the glycaemia in those found in TB-DM co-morbid individuals. These would result in improved treatment outcomes and management in PTB patients.

Patient and Public Involvement

Patients and public were not involved in the design of this study. However, patients served as study participants and were recruited after obtaining an informed consent.

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Authors' contributions

MOA and AK were involved in the conception, design, and execution of the study. MOA, AK, and NA were involved in the analysis and data interpretation. OA contributed to data interpretation, drafting, formatting and final revision of the manuscript for intellectual content. MOA, OA, and AU reviewed the manuscript for intellectual content. All authors read and agreed to the final version of the manuscript.

Data Availability Statement

All relevant data to the study are included in the article or uploaded as supplementary information.

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Competing interests

None declared.

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Figure: Sampling strategy flow chart

Oyo central senatorial zone: Akinyele, Egbeda, Ona-ara, Oyo east

Oyo north senatorial zone: Saki west, Kajola, Iseyin

Oyo south senatorial zones: Ibadan Northeast, Ibadan Northwest, Ibadan Southeast, Ibadan Southwest.

1

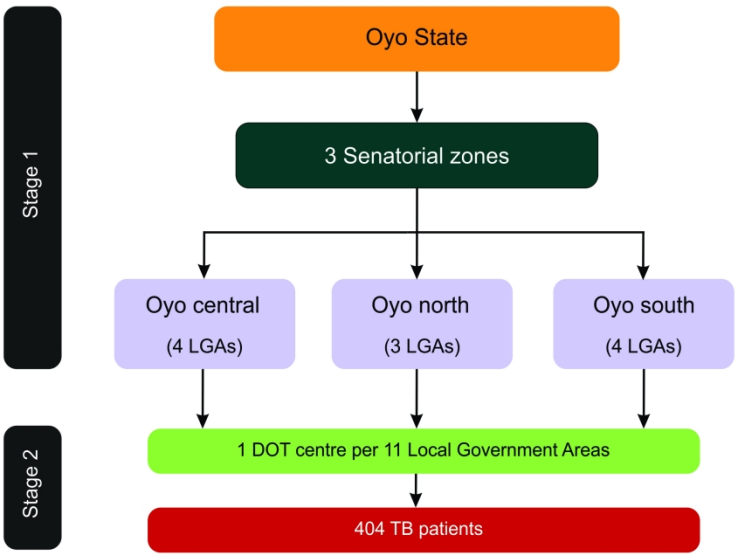

Figure
Sampling strategy flow chart

210x297mm (300 x 300 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*6*
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6-7
		(*b*) Describe any methods used to examine subgroups and interactions	6-7
		(*c*) Explain how missing data were addressed	Not Applicable (N/A)
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	6-7
		(*e*) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—e.g. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	(Uploaded)
Descriptive data	14*	(a) Give characteristics of study participants (e.g. demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	N/A
Outcome data	15*	Report numbers of outcome events or summary measures	9-10

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10
		(*b*) Report category boundaries when continuous variables were categorized	10
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	10
Discussion			
Key results	18	Summarise key results with reference to study objectives	11-12
Limitations	19	Discuss limitations of the study, considering sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12-13
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	13

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Diabetes Mellitus and Its Associated Factors among Tuberculosis Patients Attending Directly Observed Treatment Centres in Oyo State, Nigeria: A cross sectional evaluation

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Diabetes Mellitus and Its Associated Factors among Tuberculosis Patients Attending Directly Observed Treatment Centres in Oyo State, Nigeria: A cross sectional evaluation

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Abstract

Objective

Diabetes mellitus (DM) and Tuberculosis (TB) comorbidity is evolving into an emerging epidemic globally. In Nigeria, a high burden of both diseases respectively exists with limited information on Tuberculosis-Diabetes Mellitus (TB-DM) comorbidity. We determined the fasting blood glucose (FBG) level among patients with TB and factors associated with TB-DM comorbidity in Oyo State, South-west Nigeria.

Methods

A cross-sectional study was conducted among TB patients aged 15 years and above, who were selected using multistage sampling. Data were collected on patients' biodata, anthropometric measurements and FBG levels using a pretested semi-structured questionnaire. The FBG test was conducted on confirmed Pulmonary TB patients (old and newly diagnosed TB patients) at any stage of anti-tuberculosis treatment. Background characteristics and FBG level were summarized using descriptive statistics and factors associated with TB-DM comorbidity were examined at bivariate and multivariable analyses.

Results

Of the 404 TB patients, 30 (7.4%) had impaired fasting glucose and 32 (7.9%) were diagnosed with diabetes. The mean age of the male and female respondents was 41 (±14.2) and 36.8 (±15.0) respectively. Females were more likely than males to have diabetes (10.6% vs. 6.3%). Median FBG level for the patients was 88 (Interquartile range: Q1: 99, Q3:79) mg/dl. Age, marital status, and educational level were not associated with TB-DM co-morbidity. In the multivariable model, only normal body mass index was independently and significantly associated with diabetes.

Conclusion

Tuberculosis-Diabetes Mellitus was prevalent among the studied population in South-west Nigeria. We recommend the integration of DM screening within the continuum of care for TB management.

Keywords: Tuberculosis-Diabetes Mellitus comorbidity, Hyperglycaemia, Nigeria.

Article summary:

- **Strengths and limitations of the study**
  - Our study used a hospital design that enabled access to TB patients in a clinic setting and this approach is a potential opportunity for implementing concurrent regular routine screening and clinical management, lifestyle modification, and follow-up for TB-DM comorbidity.
  - Alcohol consumption and smoking are culturally undesirable behaviours and thus, they might have been underreported by participants.
  - The outcomes of TB management in TB-DM comorbid individuals such as cure rate, treatment success rate, or death could not be ascertained in our study, which was a cross-sectional evaluation.

Introduction

Tuberculosis remains a major global infectious disease that causes morbidity and death. Low- and middle-income countries harbor about 95% and 75% of tuberculosis (TB) and diabetes mellitus (DM) patients respectively.[1 2] Incident cases of TB were reported to be the highest among people with impaired immunity, human immunodeficiency virus (HIV) infection or DM.[2] In 2018, an estimated 10.0 million individuals were newly diagnosed with TB, 1.2 million and 250,000 people died among HIV-negative and HIV- positive people respectively, of which Africa accounted for 24%.[3] Nigeria belongs to one of the 30 high-burden TB countries worldwide.[3] In 2018, Nigeria was among the top 8 high TB burden countries, with an estimated 429,000 new TB cases (219 per 100,000 population), and mortality of 123,000 (64 per 100,000 population) excluding TB-HIV cases.[3] Nigeria, with a population of more than 190 million,[4] has the highest burden of the disease globally with a total TB incidence of 418,000 (219 per 100,000).[5]

Despite the success of the TB control strategies, TB persists in several parts of the world.[5] This signifies the need to intensify control efforts that identify and address the individual and social determinants of the disease. Structural factors, (e.g., suboptimal case detection and non-adherence to therapy), and host-level factors, (e.g., HIV and diabetes mellitus [DM]) that increase vulnerability to active TB are major challenges to TB control.[6 7]

In 2019, according to International Diabetes Federation (IDF),[8] there were an estimated 463.0 million and 19.4 million people with DM globally and in Africa respectively. By 2030, it is projected that 28.6 million adults in Africa will have DM.[8] In 2019, an estimated 4.2 million (20-79 years) and more than 366,200 deaths globally and in Africa respectively, could be attributed to DM.[8] In Nigeria, the prevalence of DM in the general population was 4.3%, and 2% of total death in all ages was caused by the disease.[9]

Many studies conducted in different parts of the globe have revealed a bidirectional association between TB and DM.[10] This close link is striking in developing countries, where TB is endemic and the burden of DM is high and increasing,[10] including Nigeria.

DM directly impairs innate and adaptive immune responses that are necessary to combat the progression from infection to clinical diseases.[11] Diabetes mellitus is a known risk factor for tuberculosis,[12] and is associated with poorer tuberculosis outcomes, while tuberculosis is associated with regressing glycaemic control.[13] Hence, it is advantageous to screen and identify undiagnosed DM among TB patients and then, offer glycaemic control, in order to prevent or delay diabetes-related complications and improve TB treatment outcomes accordingly.

Despite the evidence which supports DM as a risk factor for TB, few studies have been documented in Nigeria. No study has been conducted and reported in Oyo State to the best of our knowledge. This study aimed at determining the prevalence of DM and its associated factors among patients attending Directly Observed Treatment Centres (DOTS) in Oyo State, South-west, Nigeria.

Methods

Study setting

Oyo State is in South-west Nigeria, the most populous country in sub-Saharan Africa. It has 33 Local Government Areas (LGAs) distributed over its three (3) senatorial districts. The State has 244 Directly Observed Treatment Centre-Short course (DOTS) centres across the 33 LGAs in Oyo State, comprising 200 public and 44 private DOTS centres. All the LGAs have several DOTS centres and are supported by Damien Foundation, Belgium, a leading Non-Governmental Organization (NGO) with a focus on effective TB management and control. Overall, there were 1,743 TB patients on treatment in all the DOTS clinics in Oyo State at the time of the study.

Sputum smear microscopy was the prevailing primary test for the diagnosis of pulmonary tuberculosis (PTB) in Nigeria. Smears may be prepared directly from clinical specimens or from concentrated preparations using Ziehl-Nielsen staining or Fluorescent Auramine staining technique to observe acid-fast bacilli. A sputum result is positive if at least one tubercle bacillus (acid-fast/fluorescent) is detected on one or more sputum smears. The glycated haemoglobin test is used to both diagnose DM and assess control in DM.

Study design

A cross-sectional facility-based study was conducted among consenting TB patients aged 15years and above attending DOTS centres in Oyo State. Participants were systematically selected in each DOTS centre. There was no age-cut off for the study and no participant under the age of 15 years was selected. However, parents/guardians gave consent for participants who were between the ages of 15 and 17 years old. Pregnant TB patients and extra-pulmonary TB cases were excluded from the study. The fasting blood glucose level was ascertained for confirmed old and newly diagnosed pulmonary TB (PTB) patients both at any stage of anti-tuberculosis treatment.

Sampling technique

A stratified sampling approach was used to select the study participants in the first stage. The LGAs were proportionally allocated to the 3 senatorial zones of the State. Eleven of the 33 LGAs in Oyo State, Nigeria were selected for the study, using simple random sampling by balloting in each of the 3 senatorial zones, namely, Oyo central (4 out of 11 LGAs were selected), Oyo north (3 out of 13 LGAs were selected) and Oyo south (4 out of 9 LGAs were selected) of the State. In the second stage, one DOTS centre was selected using simple random sampling in each of the 11 LGAs selected, and 404 patients were systematically selected, proportional to the size in each of the 11 DOTS centres selected. (Figure).

The minimum sample size of 364 was calculated with the formula for estimating a single population proportion ($n = Z^2 p(1 - p)/d^2$), 12.3% proportion,[14] for 0.05 precision and Z of 1.96. The final sample size was 404 TB patients after correcting for a finite population and accounting for a 10% non-response rate.

Data collection

The study instrument was adapted from an earlier study. Trained data collectors administered the pre-tested interviewer-administered semi-structured questionnaire to the selected TB patients to collect information on respondents' socio-demographic characteristics, lifestyle factors, clinical characteristics, and socio-economic status.

Data on past medical history and duration of their treatment on anti-TB drugs were extracted from patients' clinical records.

Anthropometric measures: height, weight and waist circumference using standard procedures. Body Mass Index (BMI, kg/m^2) were obtained using standard procedures: BMI (kg/m^2) was calculated as Weight (kg)/Height (m^2). Blood pressure was measured in millimeters of mercury (mm Hg) using a digital BP measurement device.

All participants were tested for DM, irrespective of prior diabetes status. Screening for DM among the respondents was done by Fasting Blood Sugar (FBS) test, using an electronic glucometer and test strips (ACCU-CHEK Active by Roche), in the morning at the respective DOTS centres, in respondents who have fasted for at least 8 hours overnight. The DM status was assessed in line with the WHO recommendation for the diagnostic criteria for diabetes and intermediate hyperglycaemia.[9] (110mg/dl to 125mg/dl – prediabetic/impaired fasting glucose; (≥126mg/dl – diabetic/fasting plasma glucose).

TB patients who were diagnosed with DM were referred to DM clinics situated in Oyo State, Nigeria for prompt and appropriate management.

Data processing and analysis

The dependent variable is diabetes status (Fasting Blood Glucose level). The independent variables included age, sex, residence, education, marital status, occupation, HIV status, smoking, BMI, drinking of alcohol, family history of diabetes, physical activity (exercise) and socio-economic status. The main outcome variables were proportions of patients with a diagnosis of TB-DM and TB without DM (TB-DM co-infection status), and patients with Impaired Fasting Glucose were not included in the non-diabetic group for the analysis. Variables were summarized with descriptive statistics. Bivariate analysis using Pearson's chi-squared test or Fisher's Exact Test was conducted to determine the relationship between the dependent variable and other independent variables. Predictors of the outcome variable (DM) were identified with a multiple binary logistic regression analysis. Covariates selected for the adjusted model were predictive at 10% level of significance and were carried over to the adjusted model. The SES definitions were computed through principal component analysis which aggregates possession of economic household items and divides it into quintiles. Each respondent was given a score based on the number and kinds of consumer goods owned or services enjoyed, ranging from radio, television, mobile telephone, refrigerator, cable TV, generating set, air conditioner, computer, electric iron, fan, motorcycle, car/truck, land ownership, house ownership, livestock/other farm animals/poultry and availability of electricity. These scores were derived through principal component analysis and using the first factor that has the highest proportion of information explained (25%) to rank each

participant by their score. The score was then divided into three equal categories, each comprising 33% of the population. In this case, SES was categorized into three quintiles. Results were presented at the 5% alpha significant level. Analysis was performed using Epi info version 7 and SPSS Statistical Software.

Ethical consideration

	Diabetics n (%)	Non-diabetics n (%)	Total n (%)	P-value
Sex				
Male	16(6.3)	237(93.7)	253(62.6)	0.124
Female	16(10.6)	135(89.4)	151(37.4)	
Age				
15-24	1(1.7)	57(98.3)	58(14.4)	

Ethical clearance was obtained from the Ethics Committee of the Oyo State Ministry of Health (reference number: AD 13/479/277, date: 15 November 2016). Informed consent was obtained from the study participants and guardians- for participants below the age of 18 years. Confidentiality of information obtained was maintained; data were de-identified.

Patient and Public Involvement

Patients and the public were not involved in the design of this study. However, patients served as study participants and were recruited after obtaining informed consent.

Results

We approached a total of 426 selected patients, replaced immediately those who refused to participate in the study (n =22) until we attained our sample size of 404 (response rate =94.8% (404/426). The overall prevalence of TB-DM comorbidity was 7.9% (32/404) [95% CI: 5.7- 10.9]. The proportion of IFG TB patients was 7.4% (30/404). The mean age of the male and female respondents was 41 (±14.2) and 36.8 (±15.0) respectively. There was a female preponderance for TB-DM comorbidity (Table 1). There was a female preponderance for TB-DM comorbidity. 22% of these individuals (n=9) had no formal education (Table 1). TB-DM comorbidity among those in poor (10.5%) and average (7.4%) socio-economic status (SES) were higher than the rich (Table 1). Compared to underweight participants, participants with normal body mass index had 129% higher odds of being diabetic and overweight patients with TB-DM comorbidity had 81% higher odds of being diabetic, but these were not statistically significant (Table 2).

Age (aOR: 2.28, 95%CI: 0.91, 5.74) and marital relationships ([being married, aOR: 2.23, 95% CI: 0.45 – 10.97] and being separated/divorced/widowed, aOR: 3.80, 95% CI: 0.48 – 30.13]) were not significant predictors of being a diabetic TB patient. In the multivariate model, only normal body mass index was independently and significantly associated with diabetes (Table 3).

25-44	11(5.1)	203(94.9)	214(53.0)	0.000
45-64	12(12.2)	86(87.8)	98(24.3)	
≥65	8(23.5)	26(76.5)	34(8.4)	
Religion				
Christian	9(8.3)	99(91.7)	108(26.7)	0.853
Muslim	23(7.8)	273(92.2)	296(73.3)	
Characteristics	**Diabetics**	**Total**		
Education level	**n (%)**			**OR (95% C.I)**
No formal Education	9(22.0)	32(78.0)	41(10.0)	
Primary school	11(9.7)	102(90.3)	113(28.0)	0.02
Secondary school	10(4.5)	205(95.3)	215(53.2)	
University/ Higher education	2(5.7)	32(94.3)	35(8.7)	
Marital status				
Single	2(2.4)	82(97.6)	84(21.0)	
Married	27(8.8)	279(91.2)	306(75.4)	0.025
Divorced/Separated/Widowed	3(21.4)	11(78.6)	14(3.5)	
Place of residence				
Urban	24(8.2)	269(91.8)	293(72.5)	0.744
Rural	8(7.2)	103(92.8)	111(24.5)	
Occupation				
Govt/Privately employed	2(5.9)	32(94.1)	34(8.4)	
Self-employed	25(8.3)	277(91.7)	302(74.8)	0.296
Student	1(2.4)	40(97.6)	41(10.1)	
Unemployed	4(14.8)	23(85.2)	27(6.7)	
Average monthly income (Naira)				
< 18,000	15(6.6)	211(93.4)	226(55.9)	
18,000-50,000	9(7.6)	109(92.4)	118(29.2)	0.202
> 51,000	8(13.3)	52(86.7)	60(14.9)	
Ethnicity				
Yoruba	31(7.7)	360(92.1)	391(96.8)	0.975
Others (Hausa, Ibo, etc)	1(0.2)	12(92.3)	13(3.2)	
Socioeconomic status				
Poor	14(10.5)	120(89.6)	134(33.2)	
Average	10(7.4)	126(92.7)	136(33.7)	0.381
Rich	8(6.0)	126(94.0)	134(33.2)	

Table 1: Socio-demographic characteristics of diabetic and non-diabetic Tuberculosis patients (n=404)

Table 2: Factors associated with diabetes status among TB patients

Characteristics			Adjusted Odds Ratio (95% CI)	p-value
Told in the past that you have DM?				
Yes	19(82.6)	23	134.46 (40.02 – 451.73)	
No	13(3.4)	381	1.00	
Smoking				
Yes	9(8.5)	106	1.11 (0.49 – 2.48)	
No	23(7.7)	298	1.00	
Drinking Alcohol				
Yes	9(7.0)	128	0.83 (0.37 – 1.85)	
No	23(8.3)	276	1.00	
Duration of TB treatment				
< 1 month	26(8.3)	314	0.79 (0.32 – 1.98)	
> 1 month	6(7.5)	90	1.00	
Do you take any other stimulant?				
Yes	3(7.0)	43	0.86 (0.25 – 2.95)	
No	29(8.0)	361	1.00	
Habit of exercise				
Yes	4(5.3)	75	0.61 (0.21 – 1.78)	
No	28(8.5)	329	1.00	
BMI (Kg/m^2)				
Underweight	8(4.8)	167	1.00	
Normal	22(10.3)	213	2.29 (0.99 – 5.28)	
Overweight/Obese	2(8.3)	24	1.81 (0.36 – 9.06)	
Family History of Diabetes Mellitus				
Yes	1(50.0)	2	12.00 (0.73 – 196.00)	
No	31(7.7)	402	1.00	
Close contact with TB patient				
Yes	2(3.8)	53	0.42 (0.10 – 1.81)	
No	30(8.6)	351	1.00	

Table 3: Multivariable analysis of the predictors of DM

Age group		
<40 **(ref)**	1.00	
40+	2.28 (0.91, 5.74)	0.080
Educational level		
No formal education	2.72 (0.49 – 15.08)	0.252
Primary school	1.06 (0.21 - 5.41)	0.945
Secondary school	0.60 (0.12 - 3.00)	0.532
University/higher education **(ref)**	1.00	
Marital Status		
Single **(ref)**	1.00	
Married	2.23 (0.45 – 10.97)	0.323
Divorced/Separated/Widowed	3.80 (0.48 – 30.13)	0.206
BMI (Kg/m^2)		
Underweight **(ref)**	1.00	
Normal	2.91 (1.18-7.14)	0.020
Overweight/Obese	1.75 (0.33 – 9.39)	0.514

*=statistically significant at ≤5%

Discussion

Our study revealed that the prevalence of DM among diagnosed TB patients was 7.9%. There was a high proportion of TB-DM comorbidity among women, older persons (at least 44 years), persons with informal education, and those in a single relationship (Divorced/ Separated/Widowed). Although, the above-mentioned factors were not shown to be of significant risk at the multivariate level. Screening for DM in TB patients could improve DM

case detection and early initiation of treatment, education of patients and correction of hyperglycaemia, which potentially could have positive effects on the outcome of TB treatment.

In Nigeria, the most recent prevalence of DM in the general population was 4.3%. [9] This is similar to 4.6% as reported by Shittu et al in a similar population in the Oke-Ogun geo-political zone of Oyo State, Nigeria.[15] The prevalence of DM in this study is quite alarming (7.9%), it is comparable to the studies conducted in Uganda (8.5%),[16] and Ethiopia (8.3%).[17] However, the current findings were lower than what was reported from Taiwan (29.5%),[18] Southern-Mexico (29.3%),[19] Kerala-India (44%),[20] Lagos, Nigeria (12.3%).[14] The reported finding in Tanzania was lower (4%).[21] Reasons for the observed variation in the prevalence might be related to differences in background between populations (rural and urban settings) and screening methods (RBS, FBS and Oral Glucose Tolerance Test etc.) used in DM diagnosis.

The prevalence of IFG in this study was 7.4%. This finding is similar to the study done in Taian, Dingxi, Jinan, Shijiazhuang, Guiyang- China (7.8%),[22] Gujarat-India (7%),[23] higher than Kolar-India (3.1%),[24] but lower than the study findings from Gondar-Ethiopia (29.6%), Addis Ababa-Ethiopia (26.7%) and Tamil Nadu-India (24.5%),[25-27] respectively. Individuals with impaired fasting glucose (IFG) are at high risk of progressing to type 2 DM, although this is not inevitable,[9] and this may go further to indicate an increased risk of DM in the future in Nigeria. The observed prevalence of DM and IFG in our study pose threats to gains made in TB control which necessitates an integrated health services approach to effectively address the burden of the two diseases.

The TB-DM comorbidity demonstrated an association with age, although older age (40+ years) was not an independent predictor of developing DM in TB patients). The occurrence of DM in older people has been reported in studies done in Addis Ababa–Ethiopia,[26] Dessie-Ethiopia,[28] Kerala-India,[20] Tamil Nadu–India,[27] Brazil,[29] Southern-Mexico,[19] and China.[30] This may be because DM is an age-related illness that occurs in persons above 40 years. Earlier studies which determined the risk factors for TB also corroborated this detail.[31] Old age is related to immunosuppression and is one of the risk factors for both TB and DM.[8 2] In Nigeria, for example, the risk of developing DM increases three to four folds after the age of 44 years,[15] a consistent finding with this study where age group > 44 years had a higher proportion of TB with DM comorbidity. This strongly suggests that the health care system in Nigeria should improve its content and delivery of services with respect to older age groups.

A slightly higher preponderance of TB-DM comorbidity among females than males in this study is similar to those found in studies done in Ethiopia,[17] and Mexico.[32] The prevalence and complication of diabetes are more pronounced in females than males as a result of gender-associated adiposity.[33] Unlike for men, increased androgen levels induce insulin resistance in women,[33] and increase the risk of type 2 diabetes and cardiovascular diseases.[34] Women have a higher percentage of body fat and more often develop peripheral adiposity, whereas men accumulate fat centrally.[35] Women generally have poorer glycemic control.[36 37] The health system in Nigeria should be geared towards ensuring that concerned females are

duly educated on preventive measures against DM and encouraged to utilise available health services to halt the trend of DM among Nigerian women.

Positive family history is a known risk factor for DM.[38] However, there was no significant association with DM among TB patients who have a family history/genetic predisposition to DM. This finding is in contrast with studies conducted in Tamil Nadu-India and China.[27 39]

Tuberculosis is a disease of poverty. In our study, two-thirds of the respondents were of low and average socioeconomic status. This portends a lack of adequate resources to a large proportion of the participants and could be a challenge for persons living with diabetes in Nigeria. Therefore, these should be considered in the management of the disease which comes at a huge personal out-of-pocket cost.

Most of the diabetic respondents (22.0%) had no formal education compared to those with higher level of education. Many factors are shown to affect the health of individuals and communities, namely, low educational level, which relates to poor health, higher stress level and lower self-esteem.[40] Educational programmes that embody and emphasize awareness of DM and its preventative measures and complications, self-care management behaviour (adherence to diabetic medications, healthy diet, regular exercise and follow up should be effectively propagated across all levels). The death of a spouse currently ranks as the life-event needing the most intense social readjustment and poses health risks.[41]

Strengths and limitation

This is one of the few studies on TB-DM comorbidity conducted and documented in Nigeria, at the time of the study. The findings are generalizable to similar settings in Nigeria and other low-and-middle-income countries. Alcohol consumption and smoking are culturally undesirable behaviours and, thus, they might have been underreported by participants. The outcomes of TB management in TB-DM comorbid individuals such as cure rate, treatment success rate or death could not be ascertained in our study, as it is a cross-sectional evaluation.

Conclusion

There was a high prevalence of DM among TB patients. Age, marital status, and educational level were not associated with TB-DM co-morbidity. Although not revealed to be significant risk factors at the multivariate level, a current single relationship from a previous married relationship; that is, being divorced, separated, or widowed could pose potential health risks. Those in a married spousal relationship tend to benefit from social support towards adhering to a healthy behavioural lifestyle. Hence, we recommend that physicians should also be aware of possible long-term health risks emerging after widowhood such as changes in lifestyle, diet, and adiposity, which may be remedied by attention to healthy behaviour.

We hope that data obtained would be used to inform a new holistic national treatment guideline for TB, inclusive of routine screening for DM and active management of the glycaemia in those found in TB-DM co-morbid individuals. These would result in improved treatment outcomes and management in PTB patients.

Patient and Public Involvement

Patients and the public were not involved in the design of this study. However, patients served as study participants and were recruited after obtaining an informed consent.

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Authors' contributions

MOA and AK were involved in the conception, design, and execution of the study. MOA, AK, and NA were involved in the analysis and data interpretation. OA contributed to data interpretation, drafting, formatting and final revision of the manuscript for intellectual content. MOA, OA, and AU reviewed the manuscript for intellectual content. All authors read and agreed to the final version of the manuscript.

Data Availability Statement

All relevant data to the study are included in the article or uploaded as supplementary information.

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Competing interests

None declared.

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Figure: Sampling strategy flow chart

Oyo central senatorial zone: Akinyele, Egbeda, Ona-ara, Oyo east

Oyo north senatorial zone: Saki west, Kajola, Iseyin

Oyo south senatorial zones: Ibadan Northeast, Ibadan Northwest, Ibadan Southeast, Ibadan Southwest.

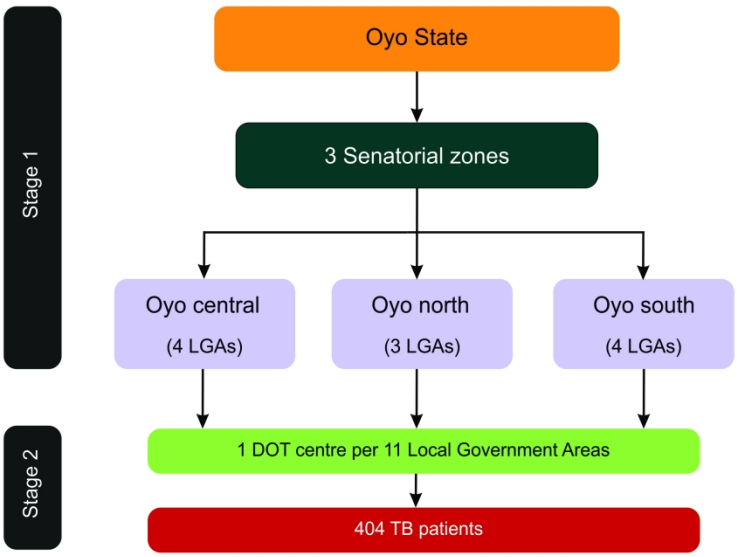

Figure
Sampling strategy flow chart

210x297mm (300 x 300 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*6*
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6-7
		(*b*) Describe any methods used to examine subgroups and interactions	6-7
		(*c*) Explain how missing data were addressed	Not Applicable (N/A)
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	6-7
		(*e*) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—e.g. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	(Uploaded)
Descriptive data	14*	(a) Give characteristics of study participants (e.g. demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	N/A
Outcome data	15*	Report numbers of outcome events or summary measures	9-10

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10
		(*b*) Report category boundaries when continuous variables were categorized	10
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	10
Discussion			
Key results	18	Summarise key results with reference to study objectives	11-12
Limitations	19	Discuss limitations of the study, considering sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12-13
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	13

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.