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Diabetes mellitus and its associated factors among patients with tuberculosis 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 patients with TB 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 semistructured questionnaire. The FBG test was conducted on patients with confirmed pulmonary TB (old and newly diagnosed patients with TB) at any stage of anti-TB treatment. Background characteristics and FBG level were summarised using descriptive statistics and factors associated with TB-DM comorbidity were examined at bivariate and multivariable analyses.

Results Of the 404 patients with TB, 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 (IQR: Q1: 99, Q3: 79) mg/dL. Age, marital status and educational level were not associated with TB-DM comorbidity. In the multivariable model, only normal body mass index was independently and significantly associated with diabetes.

Conclusion TB-DM 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.

Strengths and limitations of this study

- ► Our study used a hospital design that enabled access to patients with tuberculosis (TB) 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 tuberculosis-diabetes mellitus (TB-DM) comorbidity.
- ► Alcohol consumption and smoking are culturally undesirable behaviours and thus, they might have been under-reported 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 (TB) remains a major global infectious disease that causes morbidity and death. Low-income and middle-income countries harbour about 95% and 75% of patients with TB and diabetes mellitus (DM), respectively.[1 2] Incident cases of TB were reported to be the highest among people with impaired immunity, 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 eight high-burden TB 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 (eg, suboptimal case detection and non-adherence to therapy) and host-level factors (eg, HIV and DM) that increase vulnerability to active TB are major challenges to TB control.[6 7]

In 2019, according to the International Diabetes Federation,[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] DM is a known risk factor for TB,[12] and is associated with poorer TB outcomes, while TB is associated with regressing glycaemic control.[13] Hence, it is advantageous to screen and identify undiagnosed DM among patients with TB 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-Short course (DOTS) centres 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-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 Organisation with a focus on effective TB management and control. Overall, there were 1743 patients with TB 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 patients with TB aged 15 years 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 patients with TB and extrapulmonary TB cases were excluded from the study. The fasting blood glucose (FBG) level was ascertained for confirmed old and newly diagnosed patients with PTB both at any stage of anti-TB 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 three 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 three 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 1).

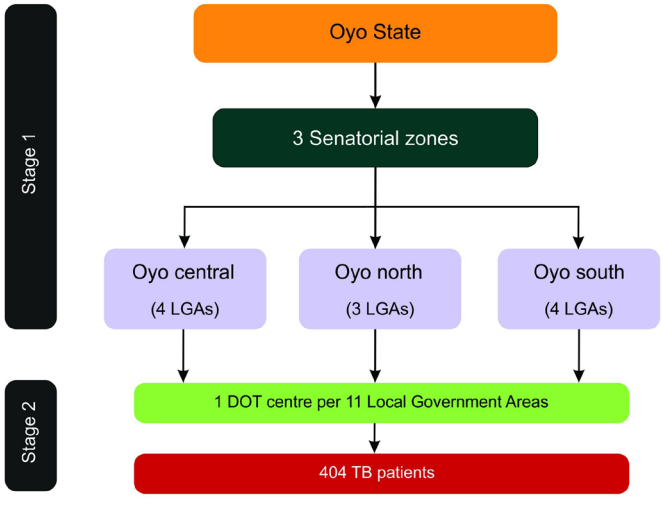

Figure 1 Sampling strategy flow chart. Oyo central senatorial zone: Akinyele, Egbeda, Ona-ara, Oyo east. Oyo north senatorial zone: Saki west, Kajola, Iseyin. Oyo south senatorial zones: Ibadan Northeast, Ibadan Northwest, Ibadan Southeast, Ibadan Southwest. DOT, Directly Observed Treatment; LGAs, local government areas.

The minimum sample size of 364 was calculated with the formula for estimating a single population proportion ($n = Z^2p(1-p)/d^2$), 12.3% proportion,[14] for 0.05 precision and Z of 1.96. The final sample size was 404 patients with TB 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 pretested interviewer-administered semistructured questionnaire to the selected patients with TB to collect information on respondents' sociodemographic characteristics, lifestyle factors, clinical characteristics and socioeconomic status (SES).

Data on 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) was obtained using standard procedures: BMI (kg/m^2) was calculated as weight (kg)/height (m^2). Blood pressure (BP) was measured in millimetres 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] (110 mg/dL to 125 mg/dL—prediabetic/impaired fasting glucose; (≥126 mg/dL—diabetic/fasting plasma glucose).

Patients with TB 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 (FBG 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 SES The main outcome variables were proportions of patients with a diagnosis of tuberculosis-diabetes mellitus (TB-DM) and TB without DM (TB-DM coinfection status), and patients with impaired fasting glucose were not included in the non-diabetic group for the analysis. Variables were summarised with descriptive statistics. Bivariate analysis using Pearson's χ^2 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 categorised into three quintiles. Results were presented at the 5% alpha significant level. Analysis was performed using Epi info V.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 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 to 10.9). The proportion of patients with impaired fasting glucose (IFG) TB 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. About 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%) SES were higher than the rich (table 1). Compared with underweight participants, participants with normal BMI 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 to 5.74) and marital relationships (being married, aOR: 2.23, 95% CI: 0.45 to 10.97 and being separated/divorced/widowed, aOR: 3.80, 95%

Table 1 Sociodemographic characteristics of patients with tuberculosis with diabetes and without diabetes (n=404)

	Diabetics	Non-diabetics	Total	P value
	N (%)	N (%)	N (%)	
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)	0.000
25–44	11 (5.1)	203 (94.9)	214 (53.0)	
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)	0.02
Primary school	11 (9.7)	102 (90.3)	113 (28.0)	
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)	0.025
Married	27 (8.8)	279 (91.2)	306 (75.4)	
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				
Government/privately employed	2 (5.9)	32 (94.1)	34 (8.4)	0.296
Self-employed	25 (8.3)	277 (91.7)	302 (74.8)	
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)	0.202
18 000–50 000	9 (7.6)	109 (92.4)	118 (29.2)	
>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)	0.381
Average	10 (7.4)	126 (92.7)	136 (33.7)	
Rich	8 (6.0)	126 (94.0)	134 (33.2)	

CI: 0.48 to 30.13) were not significant predictors of being a patient with diabetic TB. In the multivariable model, only normal BMI was independently and significantly associated with diabetes (table 3).

Table 2 Factors associated with diabetes status among patients with TB

Characteristics	Diabetics, n (%)	Total	OR (95% CI)
Told in the past that you have DM?			
Yes	19 (82.6)	23	134.46 (40.02 to 451.73)
No	13 (3.4)	381	1.00
Smoking			
Yes	9 (8.5)	106	1.11 (0.49 to 2.48)
No	23 (7.7)	298	1.00
Drinking alcohol			
Yes	9 (7.0)	128	0.83 (0.37 to 1.85)
No	23 (8.3)	276	1.00
Duration of TB treatment			
<1 month	26 (8.3)	314	0.79 (0.32 to 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 to 2.95)
No	29 (8.0)	361	1.00
Habit of exercise			
Yes	4 (5.3)	75	0.61 (0.21 to 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 to 5.28)
Overweight/obese	2 (8.3)	24	1.81 (0.36 to 9.06)
Family history of DM			
Yes	1 (50.0)	2	12.00 (0.73 to 196.00)
No	31 (7.7)	402	1.00
Close contact with patient with TB			
Yes	2 (3.8)	53	0.42 (0.10 to 1.81)
No	30 (8.6)	351	1.00

BMI, body mass index; DM, diabetes mellitus; TB, tuberculosis.

DISCUSSION

Our study revealed that the prevalence of DM among patients diagnosed with TB 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 abovementioned factors were not shown to be of significant risk at the multivariable level. Screening for DM in patients with TB 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 geopolitical zone of Oyo State, Nigeria.[15] The prevalence of DM in this study is quite alarming (7.9%),

Table 3 Multivariable analysis of the predictors of DM

Characteristics	Adjusted OR (95% CI)	P value
Age group		
<40 (ref)	1.00	0.080
40+	2.28 (0.91 to 5.74)	
Educational level		
No formal education	2.72 (0.49 to 15.08)	0.252
Primary school	1.06 (0.21 to 5.41)	0.945
Secondary school	0.60 (0.12 to 3.00)	0.532
University/higher education (ref)	1.00	
Marital status		
Single (ref)	1.00	0.323
Married	2.23 (0.45 to 10.97)	0.206
Divorced/separated/widowed	3.80 (0.48 to 30.13)	
BMI (kg/m^2)		
Underweight (ref)	1.00	0.020
Normal	2.91 (1.18 to 7.14)	0.514
Overweight/obese	1.75 (0.33 to 9.39)	

*Statistically significant at ≤5%.
BMI, body mass index; DM, diabetes mellitus.

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 (Random Blood Sugar (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 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 patients with TB). 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.[2 8] In Nigeria, for example, the risk of developing DM increases threefold to fourfold 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 healthcare 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 glycaemic 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 use 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 patients with TB 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]

TB is a disease of poverty. In our study, two-thirds of the respondents were of low and average SES. 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 with 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 emphasise 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 generalisable to similar settings in Nigeria and other low-income and middle-income countries. Alcohol consumption and smoking are culturally undesirable behaviours and, thus, they might have been

under-reported 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 patients with TB. Age, marital status and educational level were not associated with TB-DM comorbidity. Although not revealed to be significant risk factors at the multivariable 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 comorbid individuals. These would result in improved treatment outcomes and management in patients with PTB.

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Contributors MOA, AK were involved in the conception, design and execution of the study. MOA, AK and NBA were involved in the data analysis and data interpretation. MOA and OOA contributed to the data interpretation, drafting, formatting and final revision of the manuscript for intellectual content. MOA, OOA and AU reviewed the manuscript for intellectual content. All authors read and agreed to final version of the manuscript. MOA is the guarantor and accepts full responsibility for the work.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and 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). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

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

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