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# Prevalence and predictors of Tuberculosis among diabetes patients in Nigeria; A multicentre study

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**Keywords:** Diabetes; Tuberculosis; Co-morbidity; Prevalence; Predictors; Nigeria

## Abstract

**Objective:** This study aimed to ascertain the prevalence of TB among DM patients as well as factors influencing the co-morbidity.

**Methods:** A cross-sectional study was conducted under routine programme settings in ten purposively selected health facilities in 6 states in southern Nigeria in 2018. Over a period of six months, all diagnosed DM cases aged ≥18years who attended the clinics were progressively screened for tuberculosis. Chi square test of statistical significance and binary logistic regression were used in analysis at statistical significance level of <0.05.

**Results:** A total of 3457 DM patients were screened for TB. Mean (SD) age: 59.9 (12.9) years and males 65.9%. Of those screened, 27 (0.8%) patients were diagnosed with TB: females 13(48%) and males 14(52%)]. None of the three people that tested positive for HIV had TB. Predictors of TB included being a smoker (AOR 36.4; 95% CI 9.33-1 41.85), BMI of ≥30 (AOR 23.24; 95% CI 3.98-135.77) and BMI of 25-29.9 (AOR 11.83, 95% CI 3.05-45.88).

**Conclusion:** The prevalence of TB among DM patients was higher than in the general population. Predictors were "smoking cigarette" and high BMI. The findings will aid policy makers and programme managers in planning and development of TBDM integrated services which will ultimately help mitigate the emerging DM/TB epidemic. We recommend that the NTP conduct more bi-directional studies to ascertain the magnitude and nature of TB/DM comorbidity in the country in keeping with the joint framework promoted by the UNION and WHO.

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## Introduction

Diabetes Mellitus (DM) and Tuberculosis (TB) are major killer diseases of mankind across the globe [1]. The effect of DM on the development and severity of TB remains an issue to public health and clinical medicine [2]. Diabetes prevalence is increasing globally especially in low and middle income countries due to rapid economic, social, and lifestyle changes. The global prevalence of DM among adults has increased by 20% in less than 30 years [3]. The number of people with diabetes, which was 171 million in 2000, is projected to grow to 366 million–440 million by 2030, with 75% of patients with diabetes living in low-income countries [4,5]. Diabetes poses a large financial burden in countries with limited resources. For example, in Africa, the mean annual cost for diabetes care ranges between $2144 and $11 430 (direct costs $876–1220) [6].

Tuberculosis is the third cause of death among subjects with Non-Communicable Diseases (NCD), and among the NCD, DM is one of the most important [7]. The impact of TB is such that in 1993 WHO declared TB as a global emergency [8]. Substantial progress has been made in reducing tuberculosis incidence over the past two decades. However, the disease remains a major cause of morbidity and mortality globally both in low-income and high-income countries including sub-Saharan Africa [4,9,10].

The association between these two diseases is not fully understood [11,12]. The definite pathophysiological mechanism of the effect of DM as a predisposing risk factor for TB is unknown. Nonetheless, some hypotheses are suggested including: depressed cellular immunity, dysfunction of alveolar macrophages, low levels of interferon gamma, pulmonary microangiopathy, and micronutrient deficiency [13,14]. The pathophysiology of tuberculosis is also complex. Acquisition of the infection is primarily dependent on exogenous factors while reactivation of disease is largely under the influence of immune sufficiency [15]. People with a weak immune system, as a result of chronic diseases such as diabetes, are at a higher risk of progressing from latent to active tuberculosis. Although Human Immunodeficiency Virus (HIV) infection is considered as the most potent risk factor for TB, the high prevalence of DM in the world and its effect on TB burden is greater than that of HIV infection [16].

Rates of TB are higher in people with diabetes than in the general population. Diagnosis and treatment of patients affected by both diseases can be challenging, particularly in low-income settings. Comorbidities such as DM complicate tuberculosis care. Patients with concurrent diabetes suffer worse tuberculosis treatment outcomes, a higher rate of relapse following tuberculosis treatment, and a higher risk of death from tuberculosis than patients with tuberculosis alone [17,18].

Estimating the contribution of diabetes to the incidence and prevalence of TB over time is difficult because diabetes is not a notifiable disease. Therefore, information about diabetes and glycemic control has not been routinely, universally, and systematically collected for patients with TB. This study aims to ascertain prevalence and predictors of TB among DM patients as well as some factors influencing the co-morbidity.

## Materials and methods

### Study Area

This was at diabetes clinics of selected health facilities in Southern regions of Nigeria spanning through all the 3 geopolitical zones and involving 6 states (two from each geopolitical zone) namely; Ogun, Ondo, Edo, Delta, Enugu and Abia states. Facilities with high DM patient load and readily accessible DOTS centre were selected in each state for the study. There are well established health facilities including; tertiary, secondary and primary facilities that care for patients including those with DM and TB. However 10 health facilities were used for the study. These were the major centres caring for both diseases in the states.

### Study design, duration and population

A hospital based cross-sectional study was done under programme implementation. The study was conducted over eight periods from February to October 2018. All diagnosed cases of diabetes mellitus aged 15 years and above who were registered with and attending Diabetes Clinics in selected health facilities within the study period and who gave informed consent were studied.

### Sampling Technique and Sample Size Determination

All diabetic patients attending DM Clinics at the selected health facilities who met the inclusion criteria were included. They were recruited consecutively as they presented at clinic throughout the period of study. A total of 3,457 patients were included in the study.

### Data Collection and analysis

Patient information were extracted from a standard globally used register and analyzed. These records were filled by trained health workers to ensure accuracy of data. Data entry, editing and analysis were done using IBM Statistical Package for Social Sciences Version 21. Results were presented in tables. Mean, Standard deviation, proportion and percentages were used as summary measures where appropriate. Chi square test was used to establish associations between characteristics of DM patients and TB status. Binary Logistic Regression was done for variables with p value of 0.2 and below. Level of statistical significance was determined by a p value of $< 0.05$.

### Ethical Consideration

The Ethics and Research Committee of University of Nigeria Teaching Hospital (UNTH), Enugu approved the study. Approval was also obtained from the State TB Control Programme in six states selected for the project. Permission was equally obtained from heads of the facilities and written informed consent obtained from the patients.

**Table 1:** Characteristics of patients

| Variables | Frequency (n =3457) | Percent (%) |
|---|---|---|
| **Age cat(years)** | | |
| <60 | 788 | 22.8 |
| ≥60 | 2669 | 77.2 |
| ***Mean(SD)*** | ***59.86(12.86)*** | |
| **Gender** | | |
| Male | 2277 | 65.9 |
| Female | 1180 | 34.1 |
| **Occupation** | | |
| Civil/public servant | 1428 | 41.3 |
| Trading/business | 1309 | 37.9 |
| Others[#] | 722 | 20.9 |

| | | |
|---|---|---|
| **BMI n = 3262** | | |
| <18.5 | 77 | 2.4 |
| 18.5 - 24.9 | 908 | 27.8 |
| 25 - 29.9 | 1266 | 38.8 |
| ≥30 | 1011 | 31.0 |
| **Current smoker** | | |
| Yes | 22 | 0.6 |
| No | 3435 | 99.4 |
| **Type of DM n = 3051** | | |
| 1 | 129 | 4.2 |
| 2 | 2922 | 95.8 |
| **HIV Status n = 3395** | | |
| Negative | 3392 | 99.9 |
| Positive | 3 | 0.1 |

#Others: farming, artisan, unemployed, clergy

## Results

Table 1 shows that higher proportion of patients were aged ≥60 years 3669(77.2%) with their mean age 59.86 years**.** Males were higher in proportion 2277(65.9%). They were predominantly Civil/public servant 1428(41.3%) and traders 1308(37,8%). Majority had BMI of 25-29.9 Kg/m$^2$ 1266 (38.8%) followed by ≥30 Kg/m$^2$ 1011(31.0%). Only 22(0.6%) currently smokes cigarette or tobacco based product. As well only 3(0.1%) tested positive for HIV. Most were Type 2 DM 2922(95.8%).

**Table 2:** Prevalence of TB [Overall and disaggregated]

| Variables | Yes | No |
|---|---|---|
| | Freq(%) | Freq(%) |
| **Overall** | 27(0.8) | 3420(99.2) |
| **DISAGGREGATED** | | |
| **Age cat(years)** | | |
| <60 | 7(0.9) | 781(99.1) |
| ≥60 | 20(0.7) | 2649(99.3) |
| **Gender** | | |
| Male | 14(0.6) | 2263(99.4) |
| Female | 13(1.1) | 1167(98.9) |
| **Occupation** | | |
| Civil/public servant | 8(0.6) | 1418(99.4) |
| Trading/business | 13(1.0) | 1296(99.0) |
| Others | 6(0.8) | 716(99.2) |
| **BMI (Kg/m$^2$)** | | |
| <18.5 | 5(6.5) | 72(93.5) |
| 18.5 - 24.9 | 10(1.1) | 888(98.9) |
| 25 - 29.9 | 6(0.5) | 1260(99.5) |
| ≥30 | 4(0.4) | 1007(99.6) |
| **Current smoker** | | |
| No | 23(0.7) | 3412(99.3) |
| Yes | 4(18.2) | 18(81.8) |
| **DM Type** | | |
| 1 | 3(2.3) | 126(97.7) |
| 2 | 7(0.2) | 2913(99.8) |
| **HIV status** | | |
| Negative | 26(0.8) | 3366(99.2) |
| Positive | 0(0.0) | 3(100.0) |

Table 2 shows that overall prevalence of TB among Diabetic patients was 27(0.8%). When disaggregated, prevalence were for: age [0.9% for those aged<60 years, 0.7% for those ≥60 years], Gender [0.6% for males and 1.1% for females], current smoking [o.7% for non smokers and 18.2% for smokers], BMI [6.5% for <18.5kg, 1.1% for 18.5-24.9kg and 0.4% for ≥60] and HIV status 0.8% for negative and 0.0% for positive].

**Table 3:** Factors influencing TB among DM patients

| | Presence of TB | | Bivariate analysis | Multivariate analysis |
|---|---|---|---|---|
| Variables | Yes | No | $\chi^2$ (p value) | AOR (95% CI of AOR) |
| | Freq(%) | Freq(%) | | |
| **Age cat(years)** | | | | |
| <60 | 7(0.9) | 781(99.1) | 0.15(0.697) | NA |
| ≥60 | 20(0.7) | 2649(99.3) | | |
| **Gender** | | | | |
| Male | 14(0.6) | 2263(66.0) | 2.38(0.123) | 1 |
| Female | 13(1.1) | 1167(34.0) | | 1.33(0.50-3.54) |
| **Occupation** | | | | |
| Civil/ public servant | 8(0.6) | 1418(99.4) | | |
| Trading/ business | 13(1.0) | 1296(99.0) | 1.67(0.433) | NA |
| Others | 6(0.8) | 716(99.2) | | |
| **BMI (Kg/m$^2$)** | | | | |
| <18.5 | 5(6.5) | 72(93.5) | | 1 |
| 18.5 - 24.9 | 10(1.1) | 888(98.9) | 37.80(<0.001) | 8.42(2.21-32.06) |
| 25 - 29.9 | 6(0.5) | 1260(99.5) | | 11.83(3.05-45.88) |
| ≥30 | 4(0.4) | 1007(99.6) | | 23.24(3.98-135.77) |
| **Current smoker** | | | | |
| No | 23(0.7) | 3412(99.3) | 86.51(<0.001) | 1 |
| Yes | 4(18.2) | 18(81.8) | | 36.39(9.33-141.85) |
| **DM Type** | | | | |
| 1 | 3(2.3) | 126(97.7) | 16.44(<0.001) | 1 |
| 2 | 7(0.2) | 2913(99.8) | | 3.07(0.78-12.17) |
| **RVS** | | | | |
| Negative | 26(0.8) | 3366(99.2) | FT(0.977) | NA |
| Positive | 0(0.0) | 3(100.0) | | |

FT: Fishers Exact test; AOR: Adjusted Odd Ratio; NA: Not Applicable

Table 3 shows that there were no statistical significant associations of age ($\chi2 = 0.15$; $p = 0.697$), Sex ($\chi2 = 2.38$; $p = 0.123$), Occupation ($\chi2 = 1.67$; $p = 0.433$) and HIV status screening (FT; $p = 0.977$) with prevalence of TB among DM patients. However, there were statistical significant associations with BMI ($\chi2 = 37.80$; $p < 0.001$), currently smokes cigarette ($\chi2 = 86.51$; $p < 0.001$) and type of DM ($\chi2 = 16.442$; $p < 0.001$)

Table 3 also shows that Current smokers who are diabetic, were about 36 times (AOR 36.4; 95% CI 9.33-1 41.85) likely to have TB than Diabetic nonsmokers. Those with BMI of ≥30 were about 23 times (AOR 23.24; 95% CI 3.98-135.77) and BMI of 25-29.9 about 12 times (AOR 11.83, 95% CI 3.05-45.88) likely and those 18.5-24.9 about 8 times (AOR 8.42, 95% CI 2.21-32.06) likely to have TB than those of BMI <18.5 kg/$m^2$.

## Discussion

Former studies conducted in various parts of the world have shown that Tuberculosis and Diabetes co-morbidity are major public health problems, constitute a major economic burden and poses a threat to even medical practice. A wide range of estimates on the burden and associated factors of the two co-morbid conditions were reported [19,20].

This study revealed that prevalence of TB was 0.8% [800 per 100,000]. This is higher than that from general population in Nigeria which is estimated at incidence of *322 per 100 000* general population [9] and 361 per 100,000 for persons aged 14 years and above [21]. This is expected as DM has been documented as major risk factor for developing active TB and reactivation of latent ones [4]. Even though HIV has been documented to be the strongest risk factor for TB at an individual level, DM is seen as most important at the population level. Diabetes triples a person's risk of developing both active and latent TB [16,19,22]. This finding may be due to increasing global prevalence of Diabetes. The implication of this is that since both DM and TB are major killer diseases, mortality rates will continue to soar especially in low income settings like Nigeria. Also the co-morbidity will continue to pose a great threat to global tuberculosis control since it is associated with poor tuberculosis treatment outcomes including higher rate of relapse and higher risk of death from tuberculosis when compared with patients with tuberculosis alone [17,18].

This finding from present study was supported by other studies [11,19,23-27]. A study involving systematic review of bidirectional screening for TB-DM co-morbidity found that TB prevalence among DM patients ranged from 1.7% to 36% [11]. A similar review done on 13 observational studies reported that DM was associated with an increased risk of TB [19]. In Tanzania, 1.3% of screened adults with DM had TB, 7–fold greater than the general population [23]. A modeling study estimated that up to 15% of TB cases in South Africa (SA) might be attributed to DM [24]. Several case–control studies have shown that the odds of developing tuberculosis in diabetic patients ranges from 2·44 to 8·33 compared with non-diabetic patients [25-27].The prevalence of TB in patients with DM in China was 342.7 per 100,000 persons, compared with 42.8 per 100,000 persons in the local general population [16,28]..Another meta-analysis showed that diabetic patients were 3·1 times more likely to have tuberculosis than controls [19]. A similar study in India estimated that DM accounts for 14.8% of pulmonary TB cases, while HIV infection accounts for 3.4% of cases [29]. A prospective cohort study showed that patients with DM and TB have more severe clinical manifestations, delayed sputum conversion and a higher probability of treatment failure, recurrence and relapse. In Hong Kong, in a 5-year study of 42,000 elderly individuals, the adjusted hazard of active tuberculosis was higher in diabetic patients than in individuals without diabetes [28].

Present study reported that about 52% of males and 48% of females were infected just like a study done in Ethiopia in which smear positive pulmonary TB among diabetic patients were 52% for males and 48% for females [30]. Females were about 1.3 times more likely to have TB than males from current study. However, the difference was not marginal or statistically significant. This finding is surprising as many other studies have documented higher prevalence among males. Globally, tuberculosis notification data for 2012 show a male-to-female ratio of 1.9:1 [31]. Of the 20 high-burden countries for which data are available, the median male-to-female ratio is 1.8:1, with only Afghanistan reporting a ratio of <1:1 [1]. A multicenter case-control study in West Africa found male-to-female ratios of 2.03:1 among cases [32]. Another study reported that male to female ratio in patients of pulmonary tuberculosis was 2:1, which was also maintained when smear positive and smear negative were studied separately [33]. This difference among sexes were attributed by previous studies to various factors including differences in social roles, risk behaviors, and activities. Males travel more frequently; have more social contacts; spend more time in settings that may be conducive to transmission, such as bars; and engage in professions associated with a higher risk for tuberculosis, such as mining [11].

Smoking Cigarette was identified as a predictor. Smokers were about 36 times more likely to have TB than non smokers. Diabetes and cigarette smoking independently increased the risk of death among TB patients. Previous reports had similar findings. Estimating the combined impact of diabetes and smoking yielded a hazard ratio of 5.78 [34].The adjusted relative risk of a pretreatment positive smear for a smoker compared with a non-smoker was 2.19 (95% CI 1.38–3.47) in non-diabetic patients and 2.23 (95% CI 1.29–3.87) in diabetic culture-positive pulmonary TB patients. The adjusted relative risk for a positive smear among diabetic smokers was 5.61 (95% CI 3.35–9.41) compared with non-diabetic non-smokers [35]. The odd ratio of tuberculosis among diabetes patients was 7.6 (95% CI 1.46–39) in cigarette smokers as compared to nonsmokers [36].

Another predictor was BMI. Those with BMI of ≥30 were about 23 times, BMI of 25-29.9 about 12 times and those 18.5-24.9 about 8 times likely to have TB than those of BMI <18.5 kg/$m^2$. These findings can be explained partly by skewed distribution of these characteristics A previous study documented that TB patients with DM usually have a higher body weight before initiating treatment and even more so after treatment [16].

## Conclusion

The prevalence of TB among DM patients was higher than in the general population. Predictors were "smoking cigarette" and high BMI. The findings will aid policy makers and programme managers in planning and development of TB and DM integrated services which will ultimately help mitigate the emerging DM/TB epidemic. We recommend that the NTP conduct more bi-directional studies to ascertain the magnitude and nature of TB/DM comorbidity in the country in keeping with the joint framework promoted by the UNION and WHO.

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