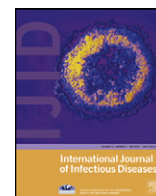


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Tuberculosis and diabetes in Guyana

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SUMMARY

Objectives: This study was conducted to determine the prevalence of diabetes mellitus among tuberculosis (TB) patients attending three TB clinics in Guyana.**Methods:** A cross-sectional study was conducted among TB patients attending TB clinics in three regions in Guyana. A structured questionnaire was used to collect demographic, clinical, and risk factor data. Random blood sugar testing was done using the OneTouch UltraSmart glucometer (LifeScan, Inc., 2002).**Results:** One hundred TB patients were recruited; 90 had pulmonary TB and 10 had extrapulmonary disease. Fourteen patients were classified as diabetic: 12 had been previously diagnosed as diabetic by a physician and two had abnormally high random blood sugar at the time of enrolment. Of the 12 known diabetics, seven had been diagnosed before TB was discovered, three were identified at the time TB was diagnosed, and two after TB was diagnosed. All 14 diabetic patients presented with pulmonary TB. Thirty-one patients were HIV-positive and 28 of these had pulmonary TB, whereas three had extrapulmonary TB. None of the diabetics were infected with HIV. TB-diabetic patients tended to be older than non-diabetics (median age 44 vs. 36.5 years), were more likely to have been incarcerated at the time of TB diagnosis than non-diabetics ($p = 0.06$), and were more likely to have an elevated (random) blood sugar level ($p = 0.02$). Clinically, diabetes did not influence the presentation of TB.**Conclusions:** This study clearly highlights that diabetes and HIV are frequent in Guyanese TB patients. Routine screening of TB patients for diabetes and diabetic patients for TB should be speedily implemented. The National TB Programme should work closely with the diabetes clinics so that TB patients who are diabetics are optimally managed.

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1. Introduction

The World Health Organization (WHO) estimated that there were approximately 8.8 million new tuberculosis (TB) cases and 1.6 million deaths worldwide in 2005. Almost 2 billion people are estimated to be infected with the TB bacilli.¹ The lifetime risk of progression to active TB in healthy persons is estimated to be 5–10%.² In persons with weakened immune systems, the annual and lifetime risks of progression of latent TB to active disease are considerably higher.³ Conditions that weaken the immune response, such as HIV infection, the use of corticosteroids or chemotherapy for cancers, and other chronic disease such as diabetes mellitus, have all been linked to the progression of latent TB to active disease.^{4,5}

Many studies have examined the relationship between diabetes and TB. Diabetics, especially those with type 2 diabetes mellitus, have been shown to be at increased risk of TB infection in several settings.^{6,7} In Canada, type 2 diabetes mellitus was an important independent predictor for TB in Saskatchewan women aged 20–59.⁷ Studies have demonstrated that prevalence rates of diabetes in TB patients can vary from as low as 3% in Conakry to as high as 29% in Mexico.^{8–10} In fact, in some studies, TB–diabetes co-morbidities have been shown to be much more frequent than TB–HIV co-infections.^{10,11} While diabetes clearly increases TB risk, the exact mechanism by which this occurs is poorly understood. The high prevalence of diabetes in TB patients has led to some suggestions of the likelihood that active TB may be a risk factor for diabetes, if not playing a direct role in the pathogenesis of this disease.¹²

Guyana is at a point of epidemiological transition with high incidences of infectious diseases such as malaria, tuberculosis, and HIV, and a high burden of chronic diseases such as diabetes and cardiovascular diseases (Guyana Ministry of Health report). The burden of TB and diabetes overlap geographically in the more

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densely populated coastal areas of the country. Guyana is one of the high incidence countries for TB in the Western Hemisphere with an estimated incidence of TB of 185/100 000 population (WHO 2004 TB country profile for Guyana). While Guyana's 2005 TB treatment guidelines clearly identify diabetes as a risk factor for TB in Guyana, the true relationship between TB and diabetes has never been established among Guyanese TB patients.

The objectives of this study were: (1) to determine the prevalence of diabetes among TB patients attending chest clinics in Georgetown, Linden, and New Amsterdam (the three main cities in Guyana), and (2) to describe the epidemiology of TB–diabetes co-morbidity and the clinical presentation of TB in diabetics.

2. Methods

This study was conducted during the months of May and June 2006 at three of the largest TB clinics located in Georgetown, New Amsterdam, and Linden. A cross-sectional design was utilized. A detailed questionnaire was used to collect socio-demographic, clinical, and risk factor data for both TB and diabetes. Clinics were visited by investigators on scheduled clinic days and all TB patients in attendance during these visits were eligible for participation in the study. Patients were informed of the nature of the study and verbal consent was solicited prior to patient recruitment. For minors, consent was sought from parents. University of Guyana medical students who were part of the investigator group used the study questionnaire to collect patient data, and a random blood sugar test was performed on enrolled patients (by clinic personnel) on completion of the interview. Random blood sugar testing was done using the OneTouch UltraSmart glucometer (2002; LifeScan, Inc., Milpitas, CA, USA). Patient charts were reviewed to verify particulars and to confirm the results of laboratory tests. Patients with abnormal random blood sugar readings were referred to the clinic's attending physician for further evaluation.

Diabetics were defined as persons who were either diagnosed by a physician or who had an abnormally high random blood sugar (>200 mg/dl) at the time of study enrolment. TB patients were those with a clinical, radiological, or microbiological diagnosis of TB and who were placed on anti-TB therapy according to national guidelines.

Approval to conduct the investigation was obtained from the National TB Programme (NTP) of Guyana. Study participation was voluntary with informed consent. No patient identifying data were recorded on questionnaires. Patient charts were reviewed at the clinic and only pertinent data were extracted.

An electronic database was created in EpiInfo version 3.2.2 (Centers for Disease Control and Prevention, Atlanta, GA, USA) and was used for data analysis. The socio-demographic characteristics of study participants were described using univariate analyses. The frequency of common risk factors and clinical manifestations were examined. Bivariate analyses compared the socio-demographics, risk factors, and clinical presentations of TB patients who were diabetics with TB non-diabetics. The Chi-square test and Student's *t*-test were used to compare qualitative and numerical variables, respectively.

3. Results

One hundred TB patients were recruited: 70 from Georgetown, 24 from New Amsterdam, and six from Linden TB clinics. Ninety patients had pulmonary TB and 10 had extrapulmonary disease.

Fourteen of the 100 (14%) patients were classified as diabetic. Twelve of these had been previously diagnosed by a physician and two had abnormally high random blood sugar at the time of enrolment. Of the 12 known diabetics, seven had been diagnosed before their TB was discovered, three were diagnosed at the time

Table 1
Demographic characteristics of TB patients (*n*=100)

	All TB patients (<i>n</i> =100)	Patients with TB and DM (<i>n</i> =14)	Patients with TB only (<i>n</i> =86)
Female	44%	35.7%	45.3%
Male	56%	64.3%	54.7%
Age group, years			
0–14	6%	7.1%	5.8%
15–24	14%	7.1%	15.1%
25–34	23%	7.1%	25.6%
35–55	28%	35.7%	26.7%
45–54	20%	21.5%	19.8%
55 and older	9%	21.5%	7.0%
Ethnicity			
African	52%	35.7%	54.7%
Indian	32%	42.9%	30.2%
Mixed	10%	7.1%	10.5%
Amerindian	6%	14.3%	4.7%

TB, tuberculosis; DM, diabetes mellitus.

TB was diagnosed, and two after TB was diagnosed. Seven of the 12 known diabetics were being managed with oral anti-diabetic drugs (type 2 diabetes). All diabetics presented with pulmonary TB.

Thirty-one (31%) patients were HIV-positive; 28 of these had pulmonary TB and three had extrapulmonary TB. However, none of the diabetics were infected with HIV.

The median age of the study patients was 38 years (range 3–71 years) and 56% were males. The majority of patients (84%) were of African and East Indian descent (Table 1). Forty-four (44%) TB patients were unemployed and 15% were homeless.

TB-diabetic patients tended to be older than non-diabetics (median age 44 vs. 36.5 years). Otherwise, both groups were similar demographically.

The clinical presentation of pulmonary TB in the 90 patients was typical, with most reporting cough of greater than 2 weeks duration (82.2%), weight loss (80%), night sweats (72.2%), and fever (64.4%) (Table 2). In this study most patients (54.4%) were acid-fast bacillus (AFB) sputum smear-negative, but in 10% of the cases there was no record that sputum smear microscopy had been done.

The clinical presentation of pulmonary TB among diabetics was compared to that of TB patients who were not diabetics (Table 2). Diabetes did not significantly impact on the clinical manifestations of TB. Likewise there was no significant difference for AFB sputum smear microscopy results between diabetics and non-diabetics.

Symptoms suggestive of diabetes were not appreciably different between pulmonary TB patients who were diabetics and those who were non-diabetics (Table 3), with the exception of polyuria (Table 3). However, the mean random blood sugar of diabetics was higher than that of non-diabetics (243.1 mg/dl vs. 97.8 mg/dl; *p* = 0.02). In addition, diabetics with pulmonary TB were more

Table 2
Clinical features of pulmonary TB patients (*n*=90)

	All patients with pulmonary TB (<i>n</i> =90)	Patients with pulmonary TB and DM (<i>n</i> =14)	Patients with pulmonary TB only (<i>n</i> =76)
Cough	82.2%	85.7%	81.6%
Weight loss	80%	78.6%	80.3%
Night sweats	72.2%	71.4%	72.4%
Fever	64.4%	78.6%	61.8%
Chest pain	61.1%	57.1%	61.8%
Bloody sputum	36.7%	42.9%	35.5%
AFB sputum smear results			
Negative	54.4%	57.1%	54.0%
Positive	35.6%	28.6%	36.8%
Unknown	10%	14.3%	9.2%

TB, tuberculosis; DM, diabetes mellitus; AFB, acid-fast bacillus.

Table 3
Clinical features and risk factors for diabetic and non-diabetic pulmonary TB patients ($n = 90$)

	All TB patients with pulmonary TB ($n = 90$)	Patients with pulmonary TB and DM ($n = 14$)	Patients with Pulmonary TB only ($n = 76$)
Polyuria	45.6%	57.1%	43.4%
Excessive thirst	42.2%	50%	40.8%
Hunger	5.6%	14.3%	3.9%
Family history of diabetes	44.4%	78.6%	38.2% ^a
Mean random blood sugar, mg/dl	–	243.1	97.8 ^a

TB, tuberculosis; DM, diabetes mellitus.

^a Chi-square p -value 0.02; p -value t -test < 0.001 .

Table 4
Behavioral and other risk factors for TB patients ($n = 100$)

	All TB patients ($n = 100$)	Patients with TB and DM ($n = 14$)	Patients with TB only ($n = 86$)
Previous abnormal CXR	57%	64.3%	55.8%
Alcohol use	44%	50%	43.0%
Unemployment	44%	35.7%	45.3%
Exposure to an infectious case	43%	35.7%	44.2%
Non-injecting drug use	19%	7.1%	20.9%
Imprisonment at time of TB diagnosis	18%	35.7%	15.1% ^a
Homelessness	15%	14.3%	15.1%
Steroid use	11%	14.3%	10.5%

TB, tuberculosis; DM, diabetes mellitus; CXR, chest X-ray.

^a $p = 0.06$.

likely to have a family history of diabetes than non-diabetics with pulmonary TB (78.6% vs. 38.2%; Chi-square $p = 0.02$).

TB patients in this study reported high levels of alcohol use (44%), unemployment (44%), non-injecting drug use (19%), homelessness (15%), and imprisonment at the time of their TB diagnosis (18%) (Table 4). TB-diabetics in this study were more likely to have been imprisoned at the time of their TB diagnosis than non-diabetics (35.7% vs. 15.1%, Chi-square $p = 0.06$).

4. Discussion

In this study of 100 TB patients, 14% were diabetic. Factors associated with diabetes in TB patients were age, history of being incarcerated at the time of TB diagnosis, and a family history of diabetes. TB-diabetics were also more likely to present with an elevated random blood sugar than non-diabetics.

In this study, the prevalence of diabetes in TB patients is similar to that reported from Indonesia, but much lower than that found in Mexico.^{6,9–11} While the prevalence of diabetes in Guyana is unknown, these differences may reflect differences in prevalence of diabetes in the general population of these countries. Previous studies have shown no association between TB–diabetes comorbidity and demographic factors such as gender, sex, and ethnicity.¹³ Older age, however, has consistently been linked to an increased risk of diabetes in TB patients.^{8,11,13} Likewise a family history of diabetes has also been shown to be an important predictor of diabetes in TB patients.⁸

In this study, there was no noticeable impact of diabetes on the clinical presentation of pulmonary TB, including the frequency of sputum smear-positive TB. The clinical impact of diabetes on pulmonary TB is uncertain. Some studies have reported no clinical, radiological, or bacteriological impact of diabetes on TB,^{8,13} whereas others have described higher frequencies of certain

clinical symptoms and lower lung field lesions, cavities, and AFB smear positivity in TB–diabetes co-morbid patients.^{14,15} Symptoms suggestive of diabetes with the exception of polyuria were not more common in diabetics than non-diabetics. The majority of the TB diabetics in this study were receiving treatment for diabetes, which may have influenced the frequency of diabetes symptoms.

In Guyana the frequency of diabetes is unknown and so there are no population-based prevalence data available against which the prevalence of diabetes encountered in this study could be compared. Nevertheless, the high burden of TB–diabetes comorbidity clearly points to the need for routine screening of TB patients for this condition. The use of point-of-care testing for diabetes at TB chest clinics is feasible and should be encouraged, as this is not currently routinely done in Guyana. TB clinicians and nurses should demonstrate a particularly high index of suspicion for diabetes, especially in patients aged 40 years and older and those with a family history of diabetes. Given these associations and the influence of diabetes on the progression of latent TB to active TB, a case can be made for the institution of routine screening for TB among diabetics and the provision of preventive therapy to diabetics who have latent TB. Being imprisoned at the time of TB diagnosis was linked to diabetes, probably indicating the acquisition of infection during the period of incarceration.

Finally, TB patients in this sample were from the socially deprived sections of the population with a high prevalence of unemployment, homelessness, and history of being incarcerated. Likewise lifestyle factors such as alcohol use, cigarette smoking, and illicit drug use were frequent among TB patients. Anecdotal reports suggest that these types of patient are more difficult to manage and less likely to adhere to therapy. It is incumbent on the NTP of Guyana to develop appropriate strategies for getting treatment to this population.

In terms of limitations, this study was completed as part of the requirements for the University of Guyana's Bachelor of Medicine degree program (MBBS). Only a limited period of time was allotted to the data collection, analysis, and report writing; as such it was not possible to interview all the patients who were on treatment at the three clinics. Likewise the use of a random blood sugar instead of a fasting sugar may have resulted in a misclassification of two of the patients as diabetic. This study relied on patient recall of presenting symptoms and may have been affected by recall bias.

In conclusion, this study clearly highlights that diabetes is frequent in TB patients. Consequently routine screening of TB patients for diabetes should be speedily implemented. The use of adequately calibrated glucometers to perform random blood sugar tests at chest clinics is feasible and is recommended. Likewise routine screening of diabetics for TB should be encouraged, and isoniazid prophylaxis should be considered for diabetics with a latent infection. The NTP must work closely with the diabetes clinics so that TB–diabetics are optimally managed.

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Conflict of interest: No conflict of interest to declare.

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