RESEARCH LETTER

More cavities and a higher body mass index in diabetic compared with nondiabetic patients with tuberculosis: an observational study

Marcin Skowroński[1], Wojciech Michalski[2], Dorota Zozulińska-Ziółkiewicz[3], Anna Halicka[1], Aleksander Barinow-Wojewódzki[1]

1 Tuberculosis Department, Hospital in Ludwikowo, Wielkopolska Center of Pulmonology and Thoracic Surgery, Poznań, Poland
2 Department of Mathematical Oncology, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland
3 Department of Internal Medicine and Diabetology, Poznan University of Medical Sciences, Poznań, Poland

Correspondence to:
Marcin Skowroński, PhD, Tuberculosis Department, Hospital in Ludwikowo, Wielkopolska Center of Pulmonology and Thoracic Surgery, Ludwikowo k/Poznania, Mosina 62-050, Poland, phone: +48618132831, ext. 625, email: marcinas@gazeta.pl
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Introduction Diabetes mellitus (DM) is a risk factor for tuberculosis (TB). Patients with DM have a 3-fold higher risk of developing TB,[1] which is due to the intracellular nature of TB and immunological impairment in DM.[2] Moreover, their immunity against *Mycobacterium tuberculosis* is rather dysfunctional, with excessive and delayed responses. DM may modify the presenting features of TB—diabetic patients may have a different clinical presentation with more severe TB symptoms, more extensive lung involvement, and greater bacterial burden.[3]

The radiographic presentation of TB in diabetic patients has been found to be more severe. These patients are more likely to present with cavities, diffuse lung involvement, and atypical chest radiographic features such as lower lobe disease.[3,4]

There is clear evidence of an inverse association between body mass index (BMI) and the risk of TB.[5] The risk of TB in obese patients is almost two-thirds lower than in people with normal body weight after adjusting for DM; however, obesity is strongly and causally associated with DM risk.[6] Thus, obesity should increase the risk of TB through the "mediated effect" of DM.[6]

There is limited information on the clinical association between DM and TB in Poland, due to it being a country with a low TB burden. By 2030, it is estimated that 2.2 to 2.5 million Poles will be affected by diabetes.

We aimed to investigate whether diabetes affects the clinical manifestation of TB. Therefore, our objective was to study selected clinical features of TB, such as the duration of clinical symptoms, BMI, and radiologic presentation, in patients with DM in comparison with nondiabetic TB patients.

Patients and methods This observational study was conducted at the Tuberculosis Department of the Wielkopolska Center of Respiratory Medicine and Thoracic Surgery which delivers therapy to over 350 patients a year, with both tuberculous and nontuberculous mycobacterial infections. Patients older than 18 years with newly diagnosed TB confirmed by sputum or bronchial washing acid-fast bacilli smear and / or subsequent culture between 2015 and 2017 were consecutively recruited to the study. Diabetes was diagnosed according to the patient's clinical history. Types 1 and 2 as well as secondary forms of diabetes were all included. All patients with confirmed TB were screened for DM by measuring fasting plasma glucose levels, and an oral glucose tolerance test was performed when required. *M. tuberculosis* was cultured and identified using a *Mycobacterium* growth indicator tube. Participants were treated with the standard antituberculous treatment regimen recommended by the World Health Organization. At enrollment, a data collection form that recorded each patient's personal and demographic characteristics, clinical presentation, sputum examination results, and radiologic findings was completed. The duration of symptoms was defined as the time from initial onset of TB symptoms to hospital admission. Patients were questioned about the presence of symptoms such as cough, sputum production, hemoptysis, fever, night sweats, weight loss, loss of appetite, and dyspnea. All posteroanterior and lateral chest X-rays performed within 30 days before the start of TB treatment were reviewed by a radiologist and a respiratory physician participating in the study. An extensive parenchymal lesion was defined as involvement of more than 50% of the thoracic cavity. The cavity was considered to

TABLE 1 Distribution of selected clinical features among tuberculosis patients with and without diabetes mellitus

Parameter		TB patients without DM (n = 209)	TB patients with DM (n = 23)	*P* value
BMI, kg/m^2	Min–max	14.5–34.5	15.5–36.2	<0.001
	Median	20.1	23.3	
	IQR	18.4–22.7	20.3–25.2	
Symptom duration, mo	Min–max	0–36	1–12	0.55
	Median	4	3	
	IQR	2–7	2–6	
Cavities, n (%)	No	121 (57.9)	7 (30.4)	0.01
	Yes	88 (42.1)	16 (69.6)	
Extensive bilateral lesions, n (%)	No	132 (63.2)	15 (65.2)	0.85
	Yes	77 (36.8)	8 (34.8)	

Abbreviations: BMI, body mass index; DM, diabetes mellitus; IQR, interquartile range; TB, tuberculosis

be present when its diameter was at least 2 cm. The exclusion criteria were lung malignancy, decompensated heart failure, and any psychiatric disorders. The level of glycated hemoglobin was measured with an immunoturbidimetric assay. Written informed consent was obtained from all participants. The study was approved by the ethical committee of Poznan University of Medical Sciences (no. 353/15 dated April 9, 2015). The study was conducted in accordance with the Declaration of Helsinki.

Statistical analysis To describe the data, standard descriptive statistics were used: frequency and cross tables for categorical variables, quartiles and extreme values for continuous variables with a nonnormal distribution, and mean, SD, and extreme values for continuous variables with a normal distribution. The χ^2 test was used to compare categorical variables, whereas continuous variables were compared using the Mann–Whitney or *t* test, depending on their distribution. Mean values for differences were presented with 95% CIs, and medians, with interquartile ranges (IQRs). A *P* value of less than 0.05 was considered significant. The IBM SPSS Statistics package, version 23.0 (IMB Corp., Armonk, New York, United States) was used for statistical analyses.

Results A total of 232 patients (72 women and 160 men) aged 20 to 86 years (mean [SD], 48 [14.1] years) were included in the analysis. They were divided into 2 groups: a DM TB group (n = 23) and a TB control group (n = 209). In both groups, the majority of participants were men (n = 15 [65.2%] and n = 145 [69.4%], respectively). The difference in sex distribution was not significant (*P* = 0.68). The median (IQR) duration of diabetes was 4.5 (3.0–12.5) years and the median (IQR) concentration of glycated hemoglobin was 9.2% (7.6%–11.1%). The mean age difference between the groups was 7.6 years (95% CI, 1.6–13.7; mean [SD], 54.6 [13.3] years vs 46.9 [14.1] years in the DM TB and TB control groups, respectively; *P* = 0.01). There was no difference in the duration of clinical symptoms of TB (TB DM group, median [IQR] 3 [2–6] months; TB control group, median [IQR], 4 [2–7] months; *P* = 0.54) (TABLE 1). There was a significant difference in BMI between DM TB patients and controls (median [IQR], 23.3 [20.3–25.2] kg/m^2 vs median [IQR], 20.1 [18.4–22.7] kg/m^2, respectively; *P* <0.001). TB patients with diabetes were more likely to have cavities (69.6% vs 42.1%, *P* = 0.01). There was no difference in the frequency of extensive parenchymal lesions (34.8% vs 36.8%, *P* = 0.84). TB symptoms and noncommunicable comorbidities in both groups are presented in Supplementary material, *Tables S1* and *S2*.

Discussion The incidence of TB in Poland in 2020 was estimated to be 8.8 cases per 100 000 people. There has been a trend toward a steady decrease in the number of cases, with a drop of 36.7% compared with 2019.[7]

In the present study, we did not find a difference in the duration of TB symptoms between the diabetic and nondiabetic TB groups. We expected the duration of symptoms to be shorter in the group of TB patients with DM due to clinical symptom severity and extensive pulmonary involvement. Suleiman et al[8] reported a longer duration of symptoms in nondiabetic versus diabetic TB patients (4.5 vs 2.6 months; *P* <0.05). A shorter duration of symptoms in patients with DM was explained by greater pulmonary involvement, earlier development of symptoms, and earlier diagnosis. However, in a retrospective analysis of 692 patients, there was no difference in the mean duration of symptoms between TB patients with and without DM (mean, 2.16 vs 2.19 months; *P* = 0.76).[9] Likewise, Magee et al[3] did not report any differences in the duration of symptoms up to the time of diagnosis. Nonetheless, patients with TB and DM had a more severe clinical disease (odds ratio [OR], 2.26, adjusted for age, sex, HIV status, and smoking status) and a higher smear grade (adjusted OR, 2.37). Our results suggest no influence of diabetes on TB symptoms duration, which might be due to the low number of patients or a different pattern of association between TB and DM in Poland. In addition, diabetes does not always cause a delay in TB diagnosis.

We found that BMI was significantly higher in the diabetic group compared with the control group. Higher BMI in diabetic TB patients was confirmed in a prospective study (21.1 vs 17.5 kg/m^2).[10] In a study from Tanzania, where the prevalence of diabetes is as high as 16.4%, increased waist circumference (>102 cm for men and >88 cm for women) was strongly associated with diabetes (OR, 2.51; 95% CI, 1.06–5.92).[11] Despite these findings, the majority of TB patients with DM were not obese (BMI <25 kg/m^2, 94%) and they were mostly young (age <45 years, 72%). This may be due by the fact that diabetes in that region develops without a typical phenotype, or that

poorly controlled diabetes could have led to weight loss. However, Kubiak et al[12] reported that compared with nondiabetic patients, TB prevalence was 12-fold higher in overweight or obese individuals, 2.5-fold higher in normal-weight adults, and not statistically different in underweight adults.

We confirmed that patients with diabetes more frequently presented with cavities compared with controls. In a large survey, DM was more common among patients with cavities, although this result was not significant in multivariable analysis.[13] Likewise, in a prospective study of patients with TB, those with DM had severe clinical manifestations, such as cavities of any size (adjusted OR, 2.26; 95% CI, 1.04–4.90).[3] Kreisel et al[14] found that cavitation was present in 24% of patients in the diabetic group compared with only 5% in the nondiabetic group (P = 0.03). In contrast, Dousa et al[15] observed less frequent cavitary disease in diabetic patients and no relationship with glycemic control.

In conclusion, diabetic patients with TB had a higher BMI and more advanced radiologic manifestations of the disease. This is the first study to investigate the influence of diabetes on TB in Poland. The results suggest that diabetes affects the clinical presentation of TB. Diabetic patients with TB may present with higher BMI compared with nondiabetic individuals. This finding might be useful for physicians performing screening for TB in patients with diabetes.

SUPPLEMENTARY MATERIAL

Supplementary material is available at www.mp.pl/paim.

ARTICLE INFORMATION

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CONFLICT OF INTEREST None declared.

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