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The impact of diabetes mellitus on outcomes of adult tuberculosis patients: a cross-sectional study

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Abstract. Background. Both diabetes mellitus (DM) and tuberculosis (TB) are major public health problems and among the leading causes of morbidity and mortality worldwide. The TB-DM coexistence is known to complicate TB care, control and prevention. Globally, 10.4 million TB cases exists, of them 10 % are linked to DM. People with DM are at four to five times higher risk of getting infected with tuberculosis and evidence show poor TB treatment outcomes. This study purposed to evaluate the impact of diabetes mellitus on treatment outcomes in patients with active tuberculosis. Materials and methods. A cross-sectional study was conducted in a tertiary health care center in Tirana, Albania. We analyzed the medical records of 140 patients hospitalized during in 2018–2019 with a diagnosis of pulmonary tuberculosis. Study subjects were adult tuberculosis patients hospitalized in our hospital and undergoing antituberculosis treatment. Data from study subjects were obtained by interview method using semistructured questionnaire consisting of socio-demographic and clinical parameters. To determine DM risk factors, one variable and multivariable logistic regression analysis was done with 95% confidence interval and p-value < 0.05 considered significant. **Results.** Out of 140 patients, the prevalence of DM was found to be 9.3 % (n = 13) with average glucose values X = 145 mg/dl (min 120 — max 175 mg/dl), SD = 30. No significant differences were found between sex, residence, type and site of TB. Increasing age (p < 0.02), male sex (p = 0.04), and clinical manifestations like type of TB (p = 0.82), multilobe involvement (p = 0.243), other lung diseases (p = 0.154) are not significantly associated with DM-TB comorbidity. Conclusion. The prevalence of DM among TB patients in this study is high. The expanding burden of diabetes is increasing the risk of contracting tuberculosis and has a strong impact on TB treatment outcomes. The results of our study show that patients with TB-DM were at higher risk of treatment failure and mortality compared to those with TB without diabetes. Bidirectional screening for TB and DM along with planning and implementation of preventive and curative strategies will help early detection and prevent complications of comorbidity.

Keywords: diabetes mellitus; tuberculosis; burden; prevalence; outcomes

Introduction

Tuberculosis (TB) is still the largest infectious disease killer in the world accounting for millions of morbidity and mortality figures each year [1]. The burden of this global epidemic is high especially in low- and middle-income countries where ending TB is a distant reality [1–5]. One of the key challenges in ending TB is the changing epidemiological and demographic transition with ageing populations, increasing burden of non-communicable diseases, exacerbating comorbidities like diabetes mellitus (DM) and other cardiometabolic diseases [5, 6].

Nowadays, DM is considered an epidemic because of the high and rapidly increasing prevalence of the disease. The global DM prevalence in 20-79 years old in 2021 was estimated to be 10.5 % (536.6 million people), rising to 12.2 % (783.2 million) in 2045 [4]. The majority living in low- and middle-income countries, the same as TB. As a known risk factor, DM triples the risk of developing TB [3, 5-8].

Likewise, DM is associated with a higher risk of severe clinical presentation, failure in TB treatment or relapse, failure in culture conversion at 6 months and deaths in TB

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patients, more precisely pulmonary TB patients [8]. Additionally, DM may accelerate the emergence of drug-resistant TB among those receiving TB treatment [5]. Consequently, 15 % of the global TB cases are attributed to DM [9, 10].

In a recent systematic review on type 2 DM and TB, the prevalence of DM among TB patients ranged from 1.8 to 45 %, while TB prevalence among people with DM ranged from 0.1 to 6.0 % [11] underscoring the need for immediate bidirectional screening of TB and DM along with planning and implementation of preventive and curative strategies.

Conversely, TB may increase existing insulin resistance, trigger the onset of DM in predisposed individuals and worsen glycaemic control in diabetic cases. Moreover, the effectiveness of TB and DM medications may be decreased due to drug-drug interactions, contributing to TB treatment failure and uncontrolled glycaemia [3].

In Albania, the prevalence of DM in the general population has rapidly increased from 0.8 % in 1980 to 3 % in 2006. International Diabetes Federation reported that in 2019 the prevalence of diabetes in Albania among people aged 20–79 years was 9 % with another 43 % estimated to have undiagnosed DM. DM is ranked among the top five diseases in terms of mortality and morbidity at national level [12]. Currently TB continues to be a public health challenge in Albania regardless of the seemingly generally stable epidemiological situation. Recent research of our hospital shows that during the 10-year period 2009–2018, TB incidence increased from 14 to 15.5 and the total number of TB cases increased from 440 to 447 [13].

In response to this dual epidemic, the country has adopted the World Health Organization and International Union against TB and Lung Diseases (IULTD) collaborative framework for the care and control of TB and DM [14].

There is a lack of literature in our setting on the burden of TB-DM comorbidity and associated risk factors. Therefore, this study was conducted to better understand DM and TB relationship, to assess the prevalence of DM among TB patients and the impact of diabetes on TB treatment outcomes.

Materials and methods Study design

This study used analytical cross-sectional study design. Period of time: 2018–2019

Study setting

This study was conducted in University Hospital "Shefqet Ndroqi" Tirana. This Hospital is specialized in pulmonary disease, specially for TB cases.

The study subject was a sample of 140 TB patients who were diagnosed with TB during a period from 2018 to 2019.

TB diagnosis was made based on the standard diagnostic procedures as defined in the National TB Control Program and WHO Guidelines [15, 16]. Thus, TB patients diagnosed, both bacteriological confirmed (by smear microscopy and Expert MTB/RIF) and clinically diagnosed (abnormalities by X-ray, extra-pulmonary cases without laboratory confirmation and physicians' decision) were included in this study [17]. Data collection was done randomly.

We analyzed the clinical records of 140 patients hospitalized during the period 2018–2019 for the diagnosis pulmonary tuberculosis.

Were used specific files, from which 39 variables of interest were listed such as: age, gender, clinical complaints, DM parameters (fasting and random blood sugar test results, HbA1c test), biochemical analyses, outcomes of TB etc.

In this study, DM was the outcome variable and the socio-demographic and clinical variables were the risk factors for DM among TB patients. A structured data abstraction tool was used to collect the following clinical and socio-demographic variables. The DM screening results which were collected from the TB patients' medical record was classified using the WHO diagnostic criteria for DM. Hence, fasting blood glucose level ≥ 126 mg/dl was considered as DM and fasting blood glucose levels of 110-125 mg/dl as prediabetes [19].

In our hospital, all the patients with active tuberculosis, are routinely screened for DM by collecting blood for diabetes tests like fasting blood glucose test, 2-h postprandial glucose test and HbA1c test. Those with fasting blood glucose level \geq 126 mg/dl, postprandial > 200 mg/dl and HbA1c test > 6.5 % are consulted by the endocrinologist for confirmation of DM diagnosis, follow-ups and appropriate management. Local ethics committee approval was obtained for the study (number: 2018-38).

Data analysis

Our database was cleaned, coded and processed with the statistical package SPSS21. A logic check was used to identify errors made during data entry, and appropriate corrections made. All data were divided into two groups: categorical and continuous numerical. Statistical tests were used for data analysis. Categorical data were analyzed using frequencies and proportions, and Chi-square test used to assess for any association of DM with socio-demographic and clinical characteristics. One-way ANOVA to see significant differences between the mean values of a continuous numeric variable and a categorical variable (more than two categories). To determine the strength of association, both one variable and multivariable logistic regression analysis was performed, with significance level set at 5 %.

Results

Demographic profile of study participants

Among the study participants 99 (70.7%) were male and 41 (29.3%) were female. The mean of age of all cases was 43.4 (min 16 - max 84), SD = 19. Young patients (15–24 years old) were 37 (26.4%) of cases. The majority 110 cases (78.6%) were resident in urban area (Table 1).

Almost all 123 (87.9 %) were new TB patients and 90 (64.3 %) were diagnosed with pulmonary TB (Table 2). The prevalence of DM among TB patients was 13 (9.3 %) with average glucose values X = 145 mg/dl (min 120 — max 175 mg/dl), SD = 30. Average age of cases (TB with DM) was X = 60.6 years, SD = 14.99, compared to cases (TB without DM) X = 41.7, SD = 19. Significance p = 0.01. No difference significance between sex, residence, type and site



of TB. Compared to the younger (15–24) age group, being older > 55 years old was associated with OR = 2, p = 0.02 of being with DM, respectively.

Prevalence of DM among TB cases

The prevalence of DM among TB patients was 13/140 (9.3%). Among those with both TB and DM, 10 (76.9%) were known DM and the rest diagnosed during routine DM screening. In addition, 4 (2.85%) TB cases were found to be in the prediabetes stage. DM prevalence was higher among males: 10 cases (77%), compared to females 3 (23%), and increased with age from 7.6% in the 15-24 age group to 76.9% among those ≥ 55 years. There was no significant difference between place of residence and type of TB (Table 3).

Factors associated with DM among TB cases

The factors associated with being DM are summarized in Table 3. Compared to the younger 15–24 age group, being older, 45–54 and \geq 55 was associated with OR: 3.7 [1.4–13.2], p = 0.02 and OR 5.2 [2.1–15.0], p = 0.001 of being DM, respectively.

Discussion

In the absence of precedent studies on TB-DM comorbidity in our setting, we conducted a study with the focus on evaluation of the influence of DM and its associated risk factors in TB patients. This study has provided valuable information about the burden of DM among adult TB patients.

The prevalence of DM among TB cases in the current study was 9.3 % which is higher than the occurrence of DM in the general population [14].

Different studies conducted in different countries with specific socio-economic and demographic characteristics of the respective populations and variation in diagnostic methods for DM, show contradicting results consisting in lower [20–23] and higher DM prevalence among TB cases [24–27].

In our study, 3 patients (23 %) of the TB-DM cases were not aware of their DM condition before TB diagnosis. All the diabetic patients among TB cases, in our study are type 2 DM.

This result is related to the fact that most DM patients in Albania are suffering from type 2 DM and half of them are undiagnosed [28].

The routine DM screening in TB patients aided to find DM cases, who may have otherwise been missed or presented later with complicated DM [29]. In our study we also identified in total, four cases of impaired fasting blood glucose and impaired glucose tolerance also called prediabetes. In the literature different studies indicate that TB cases can experience temporary hyperglycaemia as a result of a stress reaction to TB infection or even hyperglycaemic effect of some anti-TB drugs [30–32].

Furthermore, impaired glucose tolerance or new DM could result from TB pancreatitis and TB-related endocrine hypofunction [30]. But this hyperglycemic condition could be partly or completely reversible after TB treatment completion [30–32].

Table 1. Demographic profile of study participants

Sex	Frequency	Percentage				
Male	99	70.7				
Female	41	29.3				
Age range, years						
15–24	37	26.4				
25–34	22	15.7				
35–44	15	10.7				
45–54	15	10.7				
55–64	23	16.4				
> 65	28	20.0				
Residence						
Urban	110	78.6				
Rural	30	21.4				

Table 2. The prevalence of DM among TB cases

<u> </u>						
Type of TB	Frequency	Percentage				
New	123	87.9				
Recurrent	16	11.4				
Previously treated	1	0.7				
Presence of diabetes						
Yes	13	9.3				
No	127	90.7				
TB sites						
Extrapulmonary	50	35.7				
Pulmonary	90	64.3				

Table 3. The factors associated with DM

Variables		DM		P-value	
		Yes	No	(χ² test)	
Sex	Male	10	89	0.043	
	Female	3	38		
Age group	15–24	1	36	0.027	
	25–34	0	22		
	35–44	0	15		
	45–54	2	13		
	55–64	5	18		
	> 65	5	23		
Residence	Urban	9	101	0.00	
	Rural	4	26	0.29	
Type of TB	New	12	111		
	Recurrent	1	15	0.82	
	Previously treated	0	1		
TB sites	Extrapulmonary	3	47	0.24	
	Pulmonary	10	80	0.24	



In this study, age was independently associated with DM among TB cases. TB cases aged 45-54 and ≥ 55 were 5 and 7 times more likely to have DM, respectively, in comparison to younger TB cases. This finding is consistent to previous studies which noted higher odds of DM in older TB patients [20, 25, 33].

Nearly three fourth of the TB-DM cases in the current study were \geq 45 years old but this age group account for only 47 % of the study population. This can be explained by the fact that type 2 DM mostly affects older adults and also increasing age and a decline of immune function increase their vulnerability to develop both TB and DM [30].

Tuberculosis patients experience significant psychological stress that can negatively impact their quality of life, control of previously known diabetes and tuberculosis treatment compliance. The magnitude of distress is higher in diabetics with acute TB and warrants proper screening and intervention [34].

Conclusions

This study showed a significant prevalence of DM in TB patients that increase with age and can reach 80 % among patients > 55 years. At the same time, we concluded that age is an important determinant of DM in TB patients.

TB patients with DM have more severe clinical presentation and worse treatment outcomes with higher risk of treatment failure and relapse. Additionally, DM may accelerate the emergence of drug-resistant TB among those receiving TB treatment.

This indicates a need for the provision of integrated service, a key and timely intervention for tackling this dual burden.

Limitations of the study. Due to the nature of the study, data were collected retrospectively from existing TB medical records. Thus, some information may be missing. In our study we could not examined the level of psychological stress and health-related quality of life of diabetic patients with acute TB and the effect of antituberculosis therapy on them.

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Вплив супутнього цукрового діабету на результати лікування дорослих хворих із туберкульозом: перехресне дослідження

Резюме. Актуальність. Як цукровий діабет (ЦД), так і туберкульоз залишаються серйозними проблемами охорони здоров'я та одними з основних причин захворюваності й смертності в усьому світі. Відомо, що наявність ЦД на тлі туберкульозу ускладнює процес лікування і профілактики останнього. В усьому світі зареєстровано 10,4 млн випадків туберкульозу, з них 10% пов'язані з ЦД. Люди з ЦД мають вищий (у 4-5 разів) ризик інфікування туберкульозом. Дані літератури свідчать про погані результати лікування туберкульозу на тлі ЦД. Мета: оцінити вплив цукрового діабету на результати лікування хворих із активним туберкульозом. Матеріали та методи. Перехресне дослідження було проведено в центрі третинної медичної допомоги в Тирані, Албанія. Проаналізовано медичні карти 140 пацієнтів, госпіталізованих протягом 2018–2019 років з діагнозом туберкульозу легень. Об'єктами дослідження були дорослі хворі на туберкульоз, які були госпіталізовані в клініку та проходили протитуберкульозне лікування. Дані дослідження були отримані методом інтерв'ю за допомогою структурованої анкети, що складається з соціально-демографічних та клінічних параметрів. Для визначення факторів ризику цукрового діабету проведено один змінний і багатофакторний логіс-

тичний регресійний аналіз із визначенням 95% довірчого інтервалу та р \leq 0,05. *Результати*. При обстеженні 140 пацієнтів було виявлено, що поширеність ЦД становить 9.3% (n = 13) із середніми значеннями глюкози X = 145 мг/дл (мін. 120 — макс. 175 мг/дл), SD = 30. Не встановлено достовірної різниці між статтю, місцем проживання, стадією і локалізацією туберкульозу. Більший вік (p < 0.02), чоловіча стать (p = 0.04) і клінічні прояви, такі як тип туберкульозу (р = 0,82), інші захворювання легень (p = 0,154), не мають істотного зв'язку із супутньою патологією ЦД і туберкульозу. Висновки. Установлено значну поширеність цукрового діабету серед хворих на туберкульоз. Наявність цукрового діабету збільшує ризик зараження туберкульозом і має вагомий вплив на результати лікування останнього. Результати дослідження показують, що ефективність лікування хворих на туберкульоз і ЦД менша порівняно з особами з туберкульозом без цукрового діабету. Скринінг на туберкульоз та цукровий діабет разом із плануванням і впровадженням профілактичних та лікувальних стратегій дозволить своєчасно виявляти ускладнення й запобігати їм.

Ключові слова: цукровий діабет; туберкульоз; коморбідність; поширеність