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PULMONARY TUBERCULOSIS SCREENING IN PATIENTS WITH DIABETES MELLITUS

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Abstract

Background and aims: *Diabetes mellitus (DM) is a risk factor for pulmonary tuberculosis (TB), increasing the risk of progression of latent tuberculosis infection (LTBI) to active TB threefold, threatening the TB control, especially in developing countries. The aim of this study was to assess active and latent TB infection frequency in patients with DM.* ***Material and methods:*** *There were enrolled in this study 503 adult DM patients. Active TB screening was performed through anamnestic data, clinical examination and chest X-ray and latent TB infection screening was evaluated using the tuberculin skin tests (TST).* ***Results:*** *A number of 63 (12.5%) patients had type 1 DM and 440 (87.5%) had type 2 DM. Personal history of TB was present in 21 (4.2%) subjects, 5 (8.1%) with type 1 DM and 16 (3.6%) with type 2 DM. The TST was positive in 258 (51.5%) patients and 54 (10.7%) presented cough for more than two weeks at the time of examination. The chest X-ray revealed suggestive lesions for active TB in 4 (1%) subjects and lesions of inactive TB in 90 (22.4%) subjects.* ***Conclusions:*** *TB screening must receive proper attention in patients with DM, being essential for diagnosis in those with nonspecific symptoms.*

key words: *pulmonary tuberculosis, diabetes mellitus*

Background and aims

The prevalence of diabetes mellitus (DM) is increasing worldwide, from 8.8% in 2017 to 9.9% by 2045. Actually 425 million people are suffering from this disease, an increase to 629 million being estimated by 2045 [1]. In Romania, the prevalence of DM was 11.6%, according to the PREDATORR study (National Study on Diabetes, Prediabetes, Overweight, Obesity, Dyslipidemia, Hyperuricemia and Chronic Kidney Disease Prevalence in Romania) [2].

Worldwide, 2 billion people are infected with Mycobacterium tuberculosis, which means they have latent tuberculosis infection (LTBI); in 2017, 10 million new cases of tuberculosis (TB) were estimated worldwide; in Romania, there were diagnosed 14,000 new cases of TB [3].

DM increases the risk of progression of LTBI to active TB threefold [4,5], this generating important implications regarding TB control, particularly in developing countries.

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The risk factors for DM-TB comorbidity are represented by male gender, old age, marital status, smoker status, alcohol consumption, physical inactivity, urban environment, crowded areas, insanitary conditions, low educational level and reduced economic status [6-11]. Patients with DM and TB have a family history of TB, family history of DM, higher body mass index and decreased glycemic control [6,7]. Also, they are predisposed to pulmonary cavities, hemoptysis and sputum positive at diagnosis, which persist positive after one or two months of treatment [5]. Patients with type 1 DM are more prone to develop TB [12], although TB is more commonly associated with type 2 DM, given its much higher prevalence [13]. In addition, the risk of TB is higher in patients with insulin therapy, increasing with the dose [14]. Patients with HbA1c ≥ 7% have an increased risk of TB compared with those with HbA1c < 7% [15], HbA1c being higher also in patients with LTBI [16].

So far, most studies have been conducted on non-european subjects and the necessity of such studies on european subjects is required because of the low level of information that can be used in the development of medical guidelines regarding the treatment and control of DM and TB. The aim of this study was to assess active TB and LTBI frequency and its risk factors in hospitalized adult patients with DM.

Material and methods

Study design and patients

The study had a cross-sectional design and was conducted in the Department of Diabetes, Nutrition and Metabolic Diseases of the Clinical County Emergency Hospital Craiova between February 2014 and October 2015. Active TB and LTBI frequency and the DM-TB comorbidity risk factors, both individual and socio-economic, were investigated. This study is part of a complex international project – TANDEM (Concurrent Tuberculosis and Diabetes Mellitus: Unraveling the causal link and improving care), conducted in Romania during 2013 and 2017, the consortium having members in Romania, Peru, South Africa and Indonesia, and laboratories in Germany, Great Britain and Netherlands. The project was approved by the London School of Hygiene and Tropical Medicine – Interventions/Observational Research Ethics Committee and the Institutional Review Boards in each country.

In this study, a number of 503 adult patients with DM were enrolled randomly for screening. Their participation in this study was entirely voluntary. The subject signed an informed consent prior to the enrollment, in full knowledge, after having been informed of all relevant aspects in the decision-making process. Once the eligibility was established, the subject was included in the study and the specific procedures started. Eligible subjects once enrolled in the study were not replaced by others even if they did not complete all of the protocol steps.

The inclusion criteria in the study were: adult patients with DM (aged over 18) who signed the informed consent of patients to be included in the study. The exclusion criteria were gestational or other forms of diabetes.

Laboratory, anthropometric and clinical data collection

Blood and urine samples were collected to study genetic material (DNA or RNA). The samples will be stored for a period of 25 years in order to carry out further research on the basic relationship between DM and TB. LTBI screening was evaluated using the tuberculin skin tests (TST). Active TB screening was performed through chest X-ray, clinical examination, anamnestic data and sputum examination.

The patients participated in an interview in which they were asked questions about their socio-economic, medical and TB status (if they had been previously treated for TB, if they had TB risk factors or symptoms of active TB).

For each patient a record of the following data was made:

- General data: age, gender, environment;
- History of DM: the DM type and duration, the type of antidiabetic treatment: oral antidiabetic (OAD) medication, insulin; antihypertensive, lipid-lowering, antiplatelet therapy;
- DM complications: amputations, by-pass or lower limb stent, unhealed wounds (duration > 3 months), history of myocardial infarction or stroke, by-pass or cardiac stent or cardiac surgery, angina or heart failure, cataract or previous laser therapy, treatment or history of glaucoma, blindness (non-traumatic), impaired vision, past or currently treated chronic kidney disease (CKD);
- TB symptoms: presence of cough (how long he coughs, the productive nature of coughing, sputum appearance: present/absent blood), dyspnea, night sweats, chest pain, weight loss over the last 3 months, history of TB (how many times he has had TB, how long ago he had TB);
- Exposure to TB: first-degree relative contacts with TB, proximity to patients with TB (prolonged contact with persons with active TB – more than 5 hours/week, outside the house), if he lived with someone with active TB;
- Smoking status: current smoker (patient who smoked more than one cigarette daily or occasionally or gave up smoking for less than a year before) / former smoker (patient who have quit smoking for more than a year before) / non-smoker (patient who never smoked), how long he gave up smoking, the age at which he started to smoke; number of cigarettes/day;
- Alcohol: alcohol consumption in the last 12 months, frequency of alcohol consumption;
- Socio-economic data: married/unmarried, level of education (no formal education; less than primary school; primary school; secondary school; high school; college/university; postgraduate studies), labor market status over the last 12 months (budgetary, employee, independent, unpaid, student, household, retired, unemployed – able to work), he is living alone/not (who is living with), where he lived (living in his own house, living with his family, rented accommodation), possession of a bank account, the main source of water for drinking and cooking (connection to the public network, private fountain, public source of the city network, public fountain, from neighbors, water vendor, spring, stream, river, lake, pond, rain water, bottled water), type of toilet (tank toilet, traditional toilet, latrine with ventilation, bowl/bucket, without toilet), if he owns a stove, refrigerator, microwave oven, washing machine, air conditioning, fan, computer, TV, DVD player, radio/CD player, camera, mobile phone, bicycle, motorcycle/scooter, car/truck;
- Systolic blood pressure (SBP), diastolic blood pressure (DBP); hypertension was defined as SBP ≥ 140mmHg and/or DBP ≥ 90mmHg or if they are taking antihypertensive therapy;
- Anthropometric data: weight, height, waist circumference (WC); body mass index (BMI) was calculated; overweight was defined as BMI between 25 and 29,9 kg /

m^2; obesity was defined as BMI ≥30 kg / m^2; WC ≥80 cm for women and ≥94 cm for men defined abdominal obesity;
- Positive pulmonary auscultation, the presence of BCG scar;
- Screening of LTBI: TST, considered positive at a value ≥10 mm;
- HbA1c, hemoglobin;
- Albumin/creatinine ratio (ACR), creatinine, uroculture; the estimated glomerular filtration rate (eGFR) (CKD-EPI) was calculated;
- Total cholesterol (TC), triglycerides; hypercholesterolaemia was defined as TC ≥200 mg/dl;
- Chest X-ray;
- Additional investigations – sputum examination: if the patient had productive cough, chest X-ray suggestive of TB or clinical suspicion of active TB, 2 sputum samples were collected, which were microscopically and on Lowenstein-Jensen solid medium culture analyzed;
- Mortality and withdrawal from study.

Statistical analysis

The statistical analysis was performed using SPSS Statistics version 22.0 (IBM, Armonk, New York, USA). The data was analyzed according to the type of DM. The Student's T-test was used to compare the mean values. Two-tailed p <0.05 was considered statistically significant.

Results

The general characteristics of the patients are presented in Table 1. Of the 503 patients, there were more females (52.9%) than males, with higher frequency of type 2 DM (87.5%) than type 1. The mean (±SD) age of the subjects was 57.57±11.99 years. The mean (±SD) DM duration was 9.05±8.13 years, with a mean (±SD) HbA1c of 9.86±2.29%. Most of the patients with type 2 DM (69.5%) had insulin treatment at the moment of the enrollment, the percentage being explained by the fact that the main cause of hospitalization of these subjects was the glycemic imbalance, requiring transient insulin therapy or for a longer period of time. The mean (±SD) BMI was 29.71±6.41 kg/m^2, most of the patients (77.7%) being overweight or obese, and 85.6% with the WC above normal and nearly three-quarters of the patients were hypertensive (71.4%). The mean (±SD) eGFR was 84.93±24.12 ml/min/1.73m^2, 15.8% of the patients having the eGFR <60 ml/min/1.73m^2.

Table 1. General characteristics of the patients according to DM type.

		Type of DM		p value	Total
		Type 1 DM	Type 2 DM		
Overall (no, %)		63 (12.5%)	440 (87.5%)		503 (100%)
Gender	Men	33 (52.4%)	204 (46.4%)		237 (47.1%)
	Women	30 (47.6%)	236 (53.6%)		266 (52.9%)
Age (categories)	< 40 years	25 (39.8%)	15 (3.4%)		40 (8%)
	40-59 years	30 (47.6%)	204 (46.4%)		234 (46.5%)
	60-79 years	8 (12.7%)	216 (49.1%)		224 (44.5%)
	≥ 80 years	0 (0%)	5 (1.1%)		5 (1%)
Age (years) (mean±SD)		42.60±13.21	59.71±10.15	**p<0.001**	57.57±11.99
Environment	Urban	34 (54.8%)	236 (54%)		270 (54.1%)
	Rural	28 (45.2%)	201 (46%)		229 (45.9%)
	Missing	1	3		4

Table 1. *Continued*.

		Type of DM		p value	Total
		Type 1 DM	Type 2 DM		
DM duration (categories)	New case	10 (15.9%)	61 (13.9%)		71 (14.1 %)
	< 1 year	6 (9.5%)	29 (6.6%)		35 (7%)
	1-5 years	5 (7.9%)	79 (18%)		84 (16.7%)
	6-15 years	19 (30.2%)	188 (42.6%)		207 (41.1%)
	> 15 years	23 (36.5%)	83 (18.9%)		106 (21.1%)
DM duration (years) (mean±SD)		13.25±12.00	8.44±7.22	**p=0.003**	9.05±8.13
DM treatment	No medication	0 (0%)	9 (2%)		9 (1.8%)
	Metformin	12 (19%)	312 (70.9%)		324 (64.4%)
	Other OADs: - Gliclazide - Glimepiride - Gliquidone - Repaglinide - Acarbose - Sitagliptin - Exenatide QW - Exenatide BID - Lixixenatide	0 (0%) 0 (0%) 0 (0%) 0 (0%) 0 (0%) 0 (0%) 0 (0%) 0 (0%) 0 (0%) 0 (0%)	198 (45%) 149 (33.9%) 28 (6.4%) 13 (3%) 4 (0.9%) 8 (1.8%) 14 (3.2%) 5 (1.1%) 5 (1.1%) 1 (0.2%)		198 (39.4%) 149 (29.6%) 28 (5.6%) 13 (2.6%) 4 (0.8%) 8 (1.6%) 14 (2.8%) 5 (1%) 5 (1%) 1 (0.2%)
	Insulin	63 (100%)	306 (69.5%)		369 (73.4%)
DM comorbidities and complications	Amputations (non-traumatic)	3 (4.8%)	17 (3.9%)		20 (4%)
	Lower extremity bypass / stent	1 (1.6%)	2 (0.5%)		3 (0.6%)
	Unhealed wounds	3 (4.8%)	16 (3.7%)		19 (3.8%)
	Miocardial infarction	2 (3.2%)	33 (7.5%)		35 (7%)
	Stroke	2 (3.2%)	51 (11.6%)		53 (10.6%)
	Heart bypass/stent	0 (0%)	10 (2.3%)		10 (2%)
	Heart failure	3 (4.8%)	93 (21.3%)		96 (19.2%)
	Cataract / laser eye surgery	14 (22.2%)	82 (18.7%)		96 (19.2%)
	Glaucoma	4 (6.3%)	33 (7.5%)		37 (7.4%)
	Blindness (non-traumatic)	1 (1.6%)	3 (0.7%)		4 (0.8%)
	Visual impairment	17 (27%)	161 (36.8%)		178 (35.5%)
BMI (categories)	Underweight	3 (4.9%)	11 (2.5%)		14 (2.8%)
	Normal	31 (50.8%)	66 (15.1%)		97 (19.5%)
	Overweight	20 (32.8%)	141 (32.4%)		161 (32.4%)
	Obese	7 (11.5%)	218 (50%)		225 (45.3%)
	Missing	2	4		6
BMI (kg/m^2) (mean±SD)		24.79±4.87	30.40±6.30	**p<0.001**	29.71±6.41
Abdominal obesity	Total	34 (55.7%)	387 (89.8%)		421 (85.6%)
	Missing	2	9		11
Waist circumference (cm) (mean±SD)		88.90±13.78	105.17±14.35	**p<0.001**	103.15±15.24
Hypertension		25 (39.7%)	334 (75.9%)		359 (71.4%)
BP ≥ 140/90 mmHg		15 (23.8%)	213 (48.4%)		228 (45.3%)
Patients on antihypertensive therapy		20 (80%)	295 (88.3%)		315 (87.7%)
SBP (mmHg) (mean±SD)		124.97±19.78	138.59±20.67	**p<0.001**	136.89±21.03
DBP (mmHg) (mean±SD)		74.02±11.37	81.31±12.80	**p<0.001**	80.40±12.85
Hypercholesterolaemia		35 (55.6%)	299 (68%)		334 (66.4%)
Total cholesterol ≥200 mg/dl		24 (39.3%)	196 (46.4%)		220 (45.5%)

Table 1. *Continued*.

		Type of DM		p value	Total
		Type 1 DM	Type 2 DM		
Patients on statins		18 (28.6%)	176 (40%)		194 (38.6%)
Triglycerides ≥150 mg/dl		15 (24.2%)	230 (54%)		245 (50.2%)
HbA1c (categories)	< 7%	4 (6.7%)	45 (10.4%)		49 (10%)
	7-8.9%	15 (25%)	123 (28.5%)		138 (28%)
	9-10.9%	23 (38.3%)	131 (30.3%)		154 (31.3%)
	11-12.9%	6 (10%)	86 (19.9%)		92 (18.7%)
	≥ 13%	12 (20%)	47 (10.9%)		59 (12%)
	Missing	3	8		11
HbA1c (%) (mean±SD)		10.17±2.27	9.81±2.29	p=0.265	9.86±2.29
eGFR (ml/min/1.73m^2)	≥ 60	57 (90.4%)	367 (83.4%)		424 (84.3%)
	30-59.9	5 (8%)	58 (13.2%)		63 (12.5%)
	< 30	1 (1.6%)	15 (3.4%)		16 (3.2%)
eGFR (ml/min/1.73m^2) (mean±SD)		98.14±24.78	83.03±23.45	**p<0.001**	84.93±24.12
ACR (categories)	< 30 mg/g	50 (81.9%)	302 (69.5%)		352 (71.1%)
	30-299 mg/g	7 (11.5%)	94 (21.7%)		101 (20.4%)
	≥ 300 mg/g	4 (6.6%)	38 (8.8%)		42 (8.5%)
	Missing	2	6		8
Urinary tract infection (UTI)	Total	6 (9.8%)	64 (15.5%)		70 (14.8%)
	Escherichia coli	2 (33.3%)	44 (68.7%)		46 (65.7%)
	Other agents	4 (66.7%)	20 (31.3%)		24 (34.3%)
	Missing	2	28		30

Lifestyle and socio-economic factors are very important both in DM and TB development. Almost half (49.1%) of the subjects were current smokers or former smokers. Also, 61% of patients consumed alcohol in the last 12 months, 10.8% of them daily. Water source, type of toilet, educational level (which may be an important factor in adherence to the recommendation to avoid the contact with infected patients) may sustain the increased number of infected patients (Table 2).

Table 2. Lifestyle and socio-economic risk factors according to DM type.

		Type of DM		Total
		Type 1 DM	Type 2 DM	
Smoking status	Smokers	21 (33.3%)	60 (13.7%)	81 (16.2%)
	Former smokers	20 (31.8%)	143 (32.7%)	163 (32.6%)
	Non-smokers	22 (34.9%)	234 (53.6%)	256 (51.2%)
	Missing		3	3
Alcohol consumption	Total	40 (64.5%)	265 (60.5%)	305 (61%)
	Missing		2	2
Frequency of alcohol consumption	Daily	5/40 (12.5%)	28/265 (10.6%)	33/305 (10.8%)
	1-6 days/week	8/40 (20%)	92/265 (34.7%)	100/305 (32.8%)
	Less than 3 days/month	27/40 (67.5%)	145/265 (54.7%)	172/305 (56.4%)
Educational level completed	No formal education	0 (0%)	10 (2.2%)	10 (2%)
	Less than primary school	2 (3.2%)	5 (1.5%)	7 (1.4%)
	Primary school	6 (9.5%)	56 (12.9%)	62 (12.5%)
	Secondary school	19 (30.1%)	170 (39.3%)	189 (38.2%)
	High school	26 (41.3%)	148 (34.2%)	174 (35.2%)
	College/University/ Post graduate studies	10 (15.9%)	43 (9.9%)	53 (10.7%)
	Missing		8	8

Table 2. *Continued*.

		Type of DM		Total
		Type 1 DM	Type 2 DM	
Marital status	Married	45 (71.4%)	348 (80.4%)	393 (79.2%)
	Unmarried	18 (28.6%)	85 (19.6%)	103 (20.8%)
	Missing		7	7
Home ownership	Own house	40 (63.5%)	349 (81%)	389 (78.%)
	House with family	22 (34.9%)	79 (18.3%)	101 (20.5%)
	Rented house	1 (1.6%)	3 (0.7%)	4 (0.8%)
	Missing		9	9
Labor market status	Employee	8 (12.7%)	57 (13.2%)	65 (13.1%)
	Household	20 (31.7%)	89 (20.6%)	109 (22%)
	Retired	28 (44.4%)	271 (62.7%)	299 (60.5%)
	Other	7 (11.2%)	15 (3.5%)	22 (4.4%)
	Missing		8	8
Possession of a bank account	Total	24 (38.1%)	142 (32.9%)	166 (33.5%)
	Missing		8	8
Water source	Public network	19 (30.2%)	194 (44.8%)	213 (43%)
	Fountain	29 (46%)	183 (42.3%)	212 (42.7%)
	Other	15 (23.8%)	56 (12.9%)	71 (14.3%)
	Missing		7	7
Type of toilet	Tank toilet	36 (57.1%)	212 (49.1%)	248 (50.1%)
	Traditional toilet	27 (42.9%)	220 (50.9%)	247 (49.9%)
	Missing		8	8
Household assets	Stove	63 (100%)	431 (98%)	494 (98.2%)
	Refrigerator	62 (98.4%)	430 (97.7%)	492 (97.8%)
	Microwave oven	36 (57.1%)	236 (53.6%)	272 (54.1%)
	Washing machine	53 (84.1%)	379 (86.1%)	432 (85.9%)
	Air conditioning	12 (19%)	73 (16.6%)	85 (16.9%)
	Fan	18 (28.6%)	158 (35.9%)	176 (35%)
	Computer	39 (61.9%)	195 (44.3%)	234 (46.5%)
	TV	62 (98.4%)	428 (97.3%)	490 (97.4%)
	DVD player	26 (41.3%)	101 (23%)	127 (25.2%)
	Radio/CD player	42 (66.7%)	261 (59.3%)	303 (60.2%)
	Camera	19 (30.2%)	114 (25.9%)	133 (26.4%)
	Mobile phone	60 (95.2%)	360 (81.8%)	420 (83.5%)
	Bicycle	31 (49.2%)	184 (41.8%)	215 (42.7%)
	Motorcycle/scooter	8 (12.7%)	47 (10.7%)	55 (10.9%)
	Car/truck	29 (46%)	199 (45.2%)	228 (45.3%)

Table 3. TB risk factors, symptoms, screening according to DM type.

		Type of DM		p value	Total
		Type 1 DM	Type 2 DM		
History of TB	Total	5 (7.9%)	16 (3.7%)		21 (4.2%)
	Missing		8		8
Number of times the patient had TB	Once	4/5 (80%)	15/16 (93.8%)		19/21 (90.4%)
	Twice	0/5 (0%)	1/16 (6.2%)		1/21 (4.8%)
	Three times	1/5 (20%)	0/16 (0%)		1/21 (4.8%)
Patients with TB contacts (parents, children, brothers with TB)	Total	4 (6.3%)	29 (6.7%)		33 (6.6%)
	Missing		8		8
Proximity to patients with TB	Total	7 (11.1%)	35 (8.1%)		42 (8.5%)
	Missing		6		6

Table 3. *Continued*.

		Type of DM		p value	Total
		Type 1 DM	Type 2 DM		
Patients who lived in the same house with TB contact	Total	5 (8.1%)	21 (4.9%)		26 (5.3%)
	Missing	1	8		9
Weight loss	< 5 kg	14 (22.2%)	127 (29.4%)		141 (28.5%)
	5-10 kg	11 (17.5%)	64 (14.8%)		75 (15.2%)
	≥ 10 kg	3 (4.8%)	22 (5.1%)		25 (5.1%)
	Missing		8		8
Cough	Total	16 (25.4%)	71 (16.4%)		87 (17.6%)
	Missing		8		8
Productive cough	Total	7/16 (43.8%)	29/71 (40.8%)		36/87 (41.4%)
	Missing		11		11
Sputum with blood		1/7 (14.3%)	1/29 (3.4%)		2/36 (5.6%)
Cough duration	< 1 week	3/16 (18.8%)	10/71 (14.1%)		13/87 (14.9%)
	1 week	6/16 (37.5%)	14/71 (19.7%)		20/87 (23%)
	2 weeks	1/16 (6.2%)	9/71 (12.7%)		10/87 (11.5%)
	3 weeks	1/16 (6.2%)	12/71 (16.9%)		13/87 (14.9%)
	> 3 weeks	5/16 (31.3%)	26/71 (36.6%)		31/87(35.7%)
BCG scar		62 (98.4%)	438 (99.5%)		500 (99.4%)
Positive pulmonary auscultation		2 (3.2%)	22 (5%)		24 (4.8%)
Positive TST	Total	34 (54.8%)	224 (51%)		258 (51.5%)
	Missing	1	1		2
TST (mm) (mean±SD)		9.63±7.34	8.75±7.03	p=0.378	8.86±7.07
Chest X-ray result	Normal	41 (77.3%)	251 (72.2%)		292 (72.8%)
	Abnormal – possible active TB	0 (0%)	4 (1.2%)		4 (1%)
	Abnormal – possible inactive TB	10 (18.9%)	80 (22.9%)		90 (22.4%)
	Abnormal – does not suggest TB	2 (3.8%)	13 (3.7%)		15 (3.8%)
	Missing	10	92		102

Personal history of TB was present in 4.2% of patients. In addition, 5.3% of subjects reported that they lived in the same house with a person with active TB. TST was positive in 51.5% of patients and 10.7% presented cough for more than two weeks at the time of enrollment, an unspecific symptom, part of the TB symptom screening. During the last 3 months, 48.7% of patients experienced unintentional weight loss which can also be attributed to the glycemic imbalance, 93.6% of the patients being hospitalized for symptoms of hyperglycemia. The chest X-ray revealed lesions that were suggestive for active TB in 1% of the patients and lesions of inactive TB in 22.4% of them (Table 3).

Discussion

So far, most studies about the association of DM and TB have been conducted in Asia, Africa and the US. There are few studies conducted in Europe, hence the need for researchers to discover new data from this region in order to prevent, early diagnose, and effectively treat these patients. This is the first study conducted in Romania that aimed TB screening among patients with DM. We found an increased frequency of active TB among hospitalized patients with DM, 4 (1%) patients being

diagnosed with active TB based on chest X-ray, a much higher percentage than the frequency of new cases of TB in the adult general population of Romania, this being about 0.1% (16,000 new cases in 2015, according to World Health Organization [17]).

A retrospective study published in 2012 performed on a group of UK subjects pointed out that DM is associated with a threefold higher risk of developing TB [18]. The data comes from the Oxford Record Linkage Study and revealed 12 cases of TB among 7943 patients with DM, which corresponds to a frequency of 0.15%, lower than in our study. We must take into account the incidence of TB in the UK, which is only 8.9/100,000 inhabitants/year, corresponding to 5,900 cases of TB, compared to Romania, where the incidence of TB is 72/100,000 inhabitants/year [3]. Our data was similar with another study conducted in the UK in the 1950's, which revealed a frequency of TB of 1.82% among patients with DM [19], at that time the incidence of TB in UK being high also in the general population. A study performed in Sweden showed a frequency of TB among patients with DM of 3.6%, much higher compared to 0.88% in the general population [20].

Our study has limitations. The study participants were only hospitalized patients, in a hospital in Craiova city, and the results cannot be generalized to the entire population of the country. More studies are needed in order to discover additional data regarding the association of DM and TB, researching both TB screening among patients with DM and DM screening among patients with TB.

Conclusions

This study highlights a large number of patients with DM-TB comorbidity. Both DM and TB should receive proper attention, TB screening being necessary in patients with DM, these having nonspecific symptoms. Bidirectional screening programs are required in order to diagnose and effectively treat the patients with DM and TB comorbidity. Preventive measures should be implemented for both DM and TB, some risk factors could be modified by lifestyle changes (diet, smoking cessation, alcohol consumption, exercise), which must be maintained for all the duration of their life.

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