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ORIGINAL RESEARCH

PULMONARY TUBERCULOSIS AND DIABETES MELLITUS PROFILE

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ABSTRACT

Background About 95% of patients with tuberculosis (TB) and 70% of patients with diabetes mellitus (DM) live in low and middle-income countries. As a result, DM and TB are increasingly occurring together. The risk of tuberculosis is two to five times greater in patients with diabetes.The purpose of this study is to analyze the characteristics of pulmonary tuberculosis in patients with diabetes and to evaluate the impact of tuberculosis on diabetes control.

Patients and Methods This is a retrospective study of 80 patients with confirmed pulmonary tuberculosis, comparing 30 patients with diabetes with 50 without diabetes.

Results Diabetes was more frequent in older patients with tuberculosis and in male patients. 63,3% had type 2 diabetes. Tuberculosis symptoms did not differ between the two groups. Involvement of basal segments of the lower lobes and cavitation occurred more frequently in patients with diabetes, but this difference was not significant. The time for conversion to negative of sputum culture was longer in control patients (44,1 ± 20,2 days) than in case (36 ± 18.3) (p = 0.08).

Conclusion Tuberculosis is frequently associated with diabetes mainly in low-income countries. The problem with this association could be accentuated in the future.

KEY WORDS: tuberculosis; diabetes; risk factor; prevalence

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INTRODUCTION

Diabetes is a risk factor for developing active TB. There is strong evidence for this association, with studies examining the incidence of TB showing it to be two to five times higher in diabetic patients than in non- diabetic patients [1, 2]. About 95% of patients with tuberculosis (TB) and 70% of patients with diabetes mellitus (DM) live in low and middle-income countries. The epidemic growth of DM has occurred in developing countries where TB is endemic [3]. As a result, DM and TB are increasingly occurring together. The prevalence of diabetes in tuberculosis patients was 29% (known diabetic cases - 20.7%, new diabetic cases - 8.3%) [3].

The purpose of this study is to analyze the epidemiological, clinical, radiological, bacteriological and progressive characteristics of pulmonary tuberculosis in patients with diabetes and to evaluate the impact of tuberculosis on diabetes control.

MATERIAL AND METHODS

This is a comparative restrospective study that was carried out in the phthisiology department of Moulay Youssef Hospital in Rabat, Morocco. This study analyzes the records of patients hospitalized for pulmonary tuberculosis between 1 January 2012 and 30 September 2014.

Inclusion Criteria

In group 1, all patients with pulmonary tuberculosis known or discovered during hospitalization for diabetes were included. The records were selected from the hospital's registry service. The selection of patients in group 2 was randomly made from a list of TB patients without diabetes hospitalized during this period.

Exclusion criteria

Patients with a factor of immunosuppression (HIV positive [human immunodeficiency virus], long-term corticosteroid, immunosuppressive therapy, etc.) were excluded from the study. These exclusion criteria were applied to both groups. The diagnosis of pulmonary tuberculosis was established on the detection of acid-fast bacilli (AFB) in bronchial secretions and / or culture positive Koch bacillus in the sputum. After their release, all patients were followed up at the outpatient clinic for the first two months minimum (intensive phase for new tuberculosis cases) then were followed up at the tuberculosis diagnostic centers of their residence areas.

Statistical Analysis

Data analysis was performed with SPSS 13.0 software. Quantitative variables with normal distribution were summarized as average with standard deviation (SD), while quantitative variables with non-Gaussian distribution were expressed as median [quartiles]. Qualitative variables were expressed as counts (proportions). Comparison tests that were used are: Student's t-test, Mann-Whitney, Chi 2 and Wilcoxon. A p <0.05 was taken as statistically significant.

RESULTS

Epidemiological data

Patients in group 1 were older. The age difference was statistically significant between the two groups. The association of tuberculosis and diabetes was more common in men with a sex ratio of 3. Number of smokers was similar in both groups. 90% of diabetic patients with tuberculosis were "new cases" versus 70% in the control group. (Table I)

Characteristic	Group I SPPT + DM N=30	Group II Isolated SPPT N=50	P values
Age	54,1 ± 15,1	41,34 ± 16,7	0,001
Sex			0,9
Men	20 (66,7)	34 (68)	
Women	10 (33,3)	16 (32)	
Smoking			0,2
Yes	10 (33,3)	24 (48)	
No	20 (66,7)	26 (52)	
History of TB			0.025
Yes	3 (10)	16 (32)	
No	27 (90)	34 (68)	
Current TB			0.038
New case	27 (90)	35 (70)	
Previously treated	3 (10)	15 (30)	
Diabetes Type			
IDD	11 (36,7)		
NIDD	19 (63,3)		
Discovery of diabetes			
OLD	27 (90)		
Concomitant TB	3 (10)		
Controlled diabetes			
Yes	8 (26,7)		
No	22 (73,3)		

Table I: Demographic, epidemiological characteristics and data on diabetes.

Diabetes data

Type 2 Diabetes (non-insulin dependent) was in 19 patients (63.3%) and type 1Diabetes (insulin-dependent) was in the remaining 11patients (36.7%). For 27 patients (90%), diabetes was known within an average period of 7 years. The discovery of diabetes was concomitant diagnosis of tuberculosis in three patients (10%). Diabetes was uncontrolled in 22 patients (73.3%) with ketoacidosis in 5 patients. Two patients had degenerative complications such as: chronic kidney disease (1 case) and retinopathy (1 case). (Table I).

Glycemia at the beginning of antituberculous treatment was higher in diabetics: 2.4 [1.9 to 3.2] with a statistically significant difference (P<0, 001). The glycosylated hemoglobin was also high: 11.04 ± 2.5 (Table IV)

Clinical data

Clinically, there was no significant difference in the symptoms of tuberculosis between patients in the two groups, except anorexia which was statistically increased in the control group (p = 0.023). (Table II)

Characteristic	Group I SPPT + DM N=30	Group II Isolated SPPT N=50	P values
Cough			1
Yes	28 (93,3)	46 (92)	
No	2 (6,7)	4 (8)	
Sputum			0,5
Yes	21 (70)	31 (62)	
No	9 (30)	19 (38)	
Hemoptysis			0,26
Yes	14 (46,7)	17 (34)	
No	16 (53,3)	33 (66)	
Chest pain			0,081
Yes	1 (3,3)	9 (18)	
No	29 (96,7)	41 (82)	
Exertional dyspne			0,13
Yes	7 (23,3)	20 (40)	
No	23 (76,7)	30 (60)	
weight loss			0,42
Yes	23 (76,7)	42 (84)	
No	7 (23,3)	8 (16)	
Anorexia			0,023
Yes	14 (46,7)	36 (72)	
No	16 (53,3)	14 (28)	
Asthenia			0,2
Yes	13 (43,3)	29 (58)	
No	17 (56,7)	21 (42)	
Fever			0,9
Yes	19 (63,3)	31 (62)	
No	11 (36,7)	19 (38)	
BMI	22,3 ± 2,9	18,4 ± 3,5	< 0,001

Table II : Clinical characteristics

Radiological data

The involvement of bases and excavations were more frequent in diabetic TB compared to non-diabetics, but this difference was not statistically significant. A predominance of micronodules was statistically higher in the control group (p = 0.032) (Table III).

Characteristic	Group I SPPT + DM N=30	Group II Isolated SPPT N=50	P values
Radiological images			
Infiltras	13 (43,3)	28 (56)	0,27
nodules	13 (43,3)	26 (52)	0,45
alveolar opacities	5 (16,7)	10 (20)	0,71
micronodules	2 (6,7)	13 (26)	0,032
excavations	16 (53,3)	31 (62)	0,45
Site of radiological images			
Right upper third	12 (40)	39 (78)	0,001
Right middle third	8 (26,7)	25 (50)	0,04
Right lower third	9 (30)	12 (24)	0,55
Left upper third	14 (46,7)	29 (58)	0,32
Left middle third	8 (26,7)	21 (42)	0,17
Left lower third	7 (23,3)	17 (34)	0,31

Table III : Radiological characteristics

Bacteriological data
The smears were positive on direct examination in all patients in the two groups. Cultures were positive in all patients in the two groups. Resistance to treatment was observed in 2 patients without diabetes. The bacterial load at the beginning of antituberculous treatment in number of AFB / 10 fields was similar in the two groups (p = 0, 24) (Table IV)

Characteristic	Group I SPPT + DM N=30	Group II Isolated SPPT N=50	P values
Bacterial load	30 [1-100]	50 [4-100]	0,24
Glycemia	2,4 [1 ,9-3,2]	0,7 [0,6-0,8]	< 0,001
Glycosylated hemoglobin	11,04 ± 2,5		

Table IV : Characteristics of bacterial load, glycemia and glycosylated hemoglobin at the beginning of treatment.

Treatment data
All patients in both groups began a TB treatment according to the protocol of the National Tuberculosis Program, (2RHZE/4RH) for new TB cases and 2RHZE/1RHZE/ 5RHE for previously treated cases.

Antidiabetic medication was initiated when diabetes was inaugural. Among the patients on oral antidiabetic agents (OAD), the insulin use was required in 19 patients with diabetes (63.3%) with an improvement in blood glucose within the first month of antituberculous treatment.

Evolutive data
When comparing the time of sputum smear conversion in the two groups, it was longer in non-diabetic (44.1 ± 20.2 days vs 36 ± 18.3 days, p = 0.08). Thus, negativity at 30 days was observed in only 36.7% of diabetics against 60% of non-diabetics. This difference was statistically significant (p = 0.043). Treatment duration was not different in the two groups. However, chest X-rays after two months of antituberculous treatment showed improvement in 90% of diabetics against 62% in non-diabetics (p = 0.017).
Side effects of antituberculous treatment occurred in two diabetic patients, it was a completely reversible skin rash after antihistamines. Side effects were observed in eleven patients without diabetes which were 5 cases of hepatotoxicity, 3 cases of skin rash and 3 cases of uncontrollable vomiting. (Table V)

Characteristic	Group I SPPT + DM n=30	Group II Isolated SPPT n=50	P values
Side effects of anti-tuberculosis treatment			0,12
Yes	2 (6,7)	11 (22)	
No	28 (93,3)	39 (78)	
Weight gain			0,09
Yes	23 (76,7)	29 (58)	
No	7 (23,3)	21 (42)	
Reduction or disappearance of initial symptoms			0,13
Yes	25 (83,3)	34 (68)	
No	5 (16,7)	16 (32)	
BK+ sputum the 15th day	22 (73,3)	38 (76)	0,8
BK+ sputum the 1st month	11 (36,7)	30 (60)	0,043
BK+ sputum the 2d months	4 (13,3)	15 (30)	0,9
Glycemia the 1st month of treatment antibacillary	1,64 ± 0,6	-	-
Chest X-ray the 2d months			0,017
Improvement	27 (90)	31 (62)	
Stagnation	3 (10)	12 (24)	
Aggravation	0	7 (14)	
Delay of sputum smear conversion (days)	36 ± 18,3	44,1 ± 20,2	0,08

Table V: progressive profile of pulmonary smear-positive during the first two months (attack phase)

Three deaths (6%) occurred in non-diabetics. They occurred after an average of 31.3 days of hospitalization. They were secondary to a state of severe hypo-protidemia in one case, a massive hemoptysis in one case and acute respiratory failure on MDR-TB in another case.

DISCUSSION
The prevalence of diabetes in tuberculosis patients was 29% (known diabetes cases- 20.7%, new Diabetes cases - 8.3%). Diabetes was significantly associated with older age, family history of diabetes, consumption of alcohol and sputum positivity [3]. The results were similar to those of Touré [4] in Senegal which reported that between 1994 and 1998, at a rate of 4.7%, diabetes was the most common risk factor of pulmonary tuberculosis. Wang and et al. [5], found that 31.2% of patients with pulmonary tuberculosis were diabetics. Stevenson et al. found that 14.8% of pulmonary tuberculosis in India occurred in diabetics and that the bacillus tuberculosis was associated with diabetes in 20.2% of cases [6]. Calculations from an epidemiological model in India suggested that DM accounts for 14.8% of pulmonary TB and 20.2% of smear-positive TB. [7]

The only study to be published on the direct interaction between TB and DM in sub-Saharan Africa was performed in Tanzania in 1990 and found DM to be at least four times as common in patients with TB compared to the general population. [8] We cannot appreciate the incidence of tuberculosis in diabetics through this study because diabetic patients were cured from tuberculosis.
Diabetes is a risk factor for developing active TB. There is strong evidence for this association, with studies examining the incidence of TB showing it to be two to five times higher in diabetic patients than in non- diabetic patients. [1, 2]

Our comparative study showed that TB patients with diabetes were older than those without diabetes (54 vs. 32 years). For Pérez et al. [9] Mboussa et al. [10] Touré et al. [4], the average age of diabetics was 51, 45 and 51.5 years. A male predominance in diabetic tuberculosis was noted with a sex ratio of 3, as was the case in other studies [4, 10]. In contrast, Maalej et al. [11] observed a female predominance.

Touré et al. [4] found that fever; dyspnea and anorexia were more frequently found among control group. In our study, only anorexia was statistically increased in control group.

A few studies reported that patients with TB and DM were significantly underweight and have more weight loss. [3,12,13] Alisjahbana et al. have reported a significantly higher median BMI in TB-DM patients when compared to non-diabetic TB patients. [14] These results were also observed in our study.

The most frequently found diabetes type by Baldé et al. [15] was type 2 diabetes (85%),while in our study it was 63.3%. In the reported cases, diabetes is most often the preceded diagnosis of TB. However, in three cases (10%), diagnosis of diabetes was brought after the TB, this results were similar to those of Baldé et al. [15], which also found that an average diabetes duration was 5 years at diagnosis of TB. In our study, this delay was 7 years on average. This length was shorter than those reported in Ethiopia [16] and India [17], respectively 7.6 and 10 years. These differences could reflect differences of practice variable from one country to another concerning the systematic or oriented screening and early diagnosis of diabetes.

The radiographic presentation of tuberculosis depends on many factors, including duration of illness and host immune status [18]. Evidence concerning radiological appearances in TB patient groups with and without concurrent DM is conflicting. Some studies suggest that TB patients with DM are more likely to present atypical images, [19] whereas others suggest there are no differences in the radiological findings. [20] Sosman and Steidl [21] reported that a large proportion of diabetic patients with tuberculosis had lower-lung involvement, whereas non-diabetic patients usually had upper-lobe infiltrates. Subsequent studies [22, 23] widely believed that pulmonary tuberculosis in diabetic patients presented with an atypical radiographic pattern and distribution, particularly lower-lung involvement. Clinically, this is important because lower-lobe tuberculosis might be misdiagnosed as community-acquired pneumonia or cancer [18].

We observed a basal predominance of radiographic abnormalities in diabetic patients with tuberculosis, which was the case in other studies [11, 4, 24]. For Bacakoglu et al. the involvement of bases was correlated to the female gender and age and not to diabetes itself [25]. The excavated character of the lesions was more common among diabetics in our series. This result has been reported in most studies [24, 26].

If diabetes alters immunity to tuberculosis, leading to higher baseline mycobacterial burdens and longer times to culture conversion with treatment, it might lead to a higher rate of relapse. [18] Four small retrospective studies suggest that baseline mycobacterial burdens might be higher in diabetic patients than in controls. [11, 27, 28, 29] However, in our study that followed patients in the hospital for two months, we noticed that the period of smear negativity (Direct examination of microscopy) was longer in patients without diabetes. The challenge of balancing diabetes may explain this result. Hyperglycemia is a known factor in diabetes as altering the immune particularly cellular immunity. Thus, Singla et al. [30] observed retardation smear negativity at the 3 months of treatment for 98.9% of diabetics. This difference is not observed in all series in the literature [25]. Rekha et al. [31] observed that at 2 months of quadruple therapy, rates of smear negativity were comparable among TB patients with and without diabetes, respectively 61% for diabetics and 58% for non-diabetics. In our study, 13,3% of patients with diabetes have kept positive smear at 2 months of treatment, against 30% in patients without diabetes. Llate negativity is correlated with an equilibration delay of diabetes. Diabetes and tuberculosis interact: tuberculosis worsens diabetes by the occurrence of complications of diabetes such as acute decompensation with acetonuria requiring the use and / or increased insulin doses. This occurred in 63,3% of our patients. In the study by Touré et al. [4], 78% of patients were treated with insulin.

CONCLUSION

Tuberculosis is frequently associated with diabetes mainly in low-income countries; the problem with this association could be accentuated in the future. Screening patients with Tuberculosis for fasting blood sugar estimation will help in early detection of diabetes. Strategies are needed to ensure that optimal care is provided to patients with both diseases.

LIST OF ABREVIATIONS

AFB Acid-Fast Bacilli,
BK Bacillus Kokh,
BMI Body Mass Index,
DM Diabetes Mellitus,
IDD Insulin-Dependent Diabetes,
NIDD Non-Insulin Dependent Diabetes,
SPPT Smear-Positive Pulmonary TB,
TB Tuberculosis.

AUTHORS' CONTRIBUTIONS

The participation of each author corresponds to the criteria of authorship and contributorship emphasized in the Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly work in Medical Journals of the International Committee of Medical Journal Editors. Indeed, all the authors have actively participated in the redaction, the revision of the manuscript and provided approval for this final revised version.

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PATIENT CONSENT

Written informed consent was obtained from patients for publication of this study.

COMPETING INTERESTS

The authors declare no competing interests.

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