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Clinical characteristics of pulmonary tuberculosis in adult Pakistani patients with co-existing diabetes mellitus

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الجوانب السريرية للسل الرئوي المترافق بالسكري لدى البالغين الباكستانيين
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الخلاصة: أجرى الباحثون مراجعة لسجلات جميع مرضى السل الرئوي والسكري من أدخلوا المستشفى التعليمي في كراتشي، باكستان، خلال فترة 5 سنوات. فوجدوا أنه من بين 42 358 مريضاً، كان هناك 173 مصاباً بكل من السل والسكري معاً، وكان معدل انتشار السل بين السكريين يعادل عشرة أضعاف ما هو عليه لدى غير السكريين، وكان معدل الانتشار يزداد بازدياد مدة الإصابة بالسكري. وقد كان القسم السفلي من الرئتين هو الأكثر إصابةً يتلوه القسم العلوي والمتوسط. كما شوهدت إصابات ثنائية الجانب في نصف المرضى، وترافقت مع انصباب جنبي في ثلث المرضى، وشوهدت الكهوف في 32% من الرجال وفي 15% من النساء.

ABSTRACT A review was made of the records of all patients with pulmonary tuberculosis and diabetes mellitus admitted over a 5-year period to a teaching hospital in Karachi, Pakistan. Among 42 358 patients, the total number with both tuberculosis and diabetes was 173. The prevalence of tuberculosis in diabetic patients was 10-times higher than in non-diabetic patients and prevalence increased with duration of diabetes. The lower lung field was most frequently involved, followed by the upper and middle. Bilateral involvement was seen in half and an associated pleural effusion in one-third of the patients. Cavitating lesions were seen in 32% of men and 15% of women.

Caractéristiques cliniques de la tuberculose pulmonaire chez des patients adultes pakistanais présentant une comorbidité de diabète sucré

RÉSUMÉ On a procédé à un examen des dossiers de tous les patients atteints de tuberculose pulmonaire et de diabète sucré qui ont été admis dans un hôpital universitaire de Karachi (Pakistan) sur une période de 5 ans. Sur les 42 358 patients, le nombre total de patients atteints à la fois de tuberculose et de diabète s'élevait à 173. La prévalence de la tuberculose chez les patients diabétiques était 10 fois plus élevée que chez les patients non diabétiques et la prévalence augmentait avec la durée du diabète. Le champ pulmonaire inférieur était le plus fréquemment atteint, suivi par le champ supérieur et moyen. On a noté une atteinte bilatérale chez la moitié des patients et un épanchement pleural associé chez un tiers des patients. Des lésions cavitaires ont été observées chez 32 % des hommes et 15 % des femmes.

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Introduction

Pulmonary tuberculosis (TB) and diabetes mellitus (DM) may coexist frequently, particularly in a population at high risk of acquiring TB. DM has been reported to modify the clinical features of TB. Comparative studies of TB in diabetics have provided conflicting results. In a recent study from Mexico, diabetic patients were older, had more lower lung field lesions and had more multiple cavities [1]. In a Turkish study, DM did not affect the presenting features of pulmonary TB and was only associated with more lower lung field disease in females and in older patients [2]. Another study from Saudi Arabia showed similar symptoms, radiographic distribution and cavitory disease in diabetic and non-diabetic patients with pulmonary TB [3].

Pulmonary TB may adversely affect glycaemic control. TB infection has been shown to produce glucose intolerance that improves or normalizes with anti-TB treatment [4]. This association is not specific to TB but is seen in other respiratory infections such as pneumonia [5]. Asian patients from the Indian subcontinent have a higher incidence of insulin resistance and associated complications [6]. There is little information on whether DM affects the presentation, radiographic manifestations and clinical course of pulmonary TB for Asian patients from the Indian subcontinent.

The aims of this study were to determine whether DM alters the clinical and radiographic manifestations of pulmonary TB in Pakistani patients and to compare the prevalence of TB in hospitalized patients with and without DM.

Methods

The study was a retrospective descriptive study conducted at The Aga Khan Univer-

sity Hospital, a 450-bed teaching hospital in Karachi, Pakistan. The medical records were reviewed for all adult patients (aged 14 years and above) with a diagnosis of both pulmonary TB and DM, admitted from January 1992 to December 1996. Information about demographic data, clinical features, laboratory investigations and outcome of treatment were recorded.

Patients with diabetes were included if they had a previous history of DM and were receiving anti-diabetic therapy at the time of hospital admission or were later found to have 2 or more fasting blood glucose levels greater than 140 mg/dL and started on anti-diabetic treatment. An age- and sex-matched group of non-diabetic patients, who were hospitalized during the same time period, were used as the control group to estimate the prevalence of TB in non-diabetics.

The diagnosis of TB was based on a positive culture or histopathology, a suggestive serosal fluid report or typical radiographic findings with high clinical probability of TB. The data on radiographic findings were collected using the posterior–anterior roentgenograms obtained at the time of diagnosis. In compliance with the usual clinical approach, the upper, mid and lower zones were defined by theoretical horizontal lines passing at the level of the anterior ends of the second and fourth ribs, respectively.

Statistical analysis (including prevalence rates) was performed using *Epi-Info* statistical software, version 6.0. Student's *t*-test or chi-squared test were performed where applicable.

Results

A total of 42 358 patients were admitted to The Aga Khan University Hospital, between 1992 and 1996. The number of patients discharged with a diagnosis of DM was 1458

and with a diagnosis of TB was 691. The total number of patients with both TB and DM were 173. The prevalence of TB in diabetic patients was 173/1458 (11.9%) and in non-diabetic patients was 691/40 900 (1.7%) ($P < 0.5$).

Data on 93 of the 173 patients (56 males, 37 females) with both TB and DM was available for analysis. The clinical characteristics of these patients are presented in Table 1. The majority of the patients (82%) were 40–70 years of age, with only 6% below 40 years and 12% above 70 years of age. The prevalence of TB increased progressively with the duration of DM (Table 1).

The highest prevalence was in those with DM of more than 10 years duration. Most of the patients (80%) required oral hypoglycaemic agents and hence were classified as

type 2 diabetics; about 9% required insulin and the remainder were diet-controlled.

Fever was the commonest presenting symptom of TB in this group, being high grade ($> 38\text{ }^{\circ}\text{C}$) in 55% of patients and of more than 3-months duration in 10% of patients. Positive auscultatory findings on chest examination were found in 84%, with bronchial breathing in 13%. We found 43.0% of lower lobe, 20.3% upper lobe and only 15.0% middle lobe involvement on clinical examination.

Chest radiograph findings are presented in Table 2 for the 77 patients for whom chest X-rays were available (some X-rays were unavailable for analysis as patients had been allowed to take the films). The lower lung fields were most frequently involved, followed by the upper and middle fields. Cavitating lesions were significantly more common in males (32%) than in females (15%). Erythrocyte sedimentation

Table 1 Clinical characteristics of pulmonary tuberculosis (TB) patients with diabetes mellitus (n = 93)

Characteristic	Value	
Patient characteristics		
Male: female ratio	3:2	
Mean (range) age (years)	46.1	(20–90)
Mean (range) duration of diabetes (years)	13.8	(1–17)
	No.	%
Duration of diabetes (years)		
< 2	6	7
2–5	14	15
5–10	26	28
> 10	47	51
Family history of tuberculosis		
Yes	10	11
Presenting symptoms of TB		
Fever	67	72
Cough	61	66
Dyspnoea	22	24
Haemoptysis	17	18
Weight loss	8	9

Table 2 Chest radiograph findings in pulmonary tuberculosis patients with diabetes mellitus (n = 77)

Variable	No.	%
Side affected		
Right	31	40
Left	10	13
Bilateral	36	47
Lung field affected		
Upper only	12	18
Middle only	10	15
Lower only	24	36
Upper and middle	9	13
Upper, middle and lower	1	1
Upper and lower	5	7
Middle and lower	6	9
Associated features		
Effusion	25	32
Cavity	20	26
Hilar lymphadenopathy	4	5

rate (ESR) was checked in 61 patients and was < 100 mm/h in only 13 patients. Pleural biopsy was performed in 13/25 patients with pleural effusion and was diagnostic in 11 patients.

The number of patients who died was 10 overall, giving a mortality rate in these 93 patients with DM and TB of 11%. Mortality was not influenced by the radiographic appearance. A high ESR (> 50 mm/h) was associated with a better outcome. The mean ESR for patients who died was 46 mm/h compared with 76 mm/h for patients who were cured.

The outcome of anti-TB therapy was better in type 1 DM, when compared with type 2 DM with early clearance of bacilli and improvement in cavities: after 6 months 5/9 (56%) patients with type 1 DM showed clearance of bacilli compared with 32/84 (40%) patients with type 2 DM.

Discussion

Our study describes the characteristics of pulmonary TB in Pakistani adult diabetics with a diagnosis of both TB and DM. In our hospitalized patients, TB prevalence was 11.9% in patients with DM, 10-times more common than in those without DM. In a large cohort of Korean diabetic patients (over 8000) the relative risk of developing bacteriological confirmed pulmonary TB was 5 times higher in diabetics than in matched controls [6]. In a random sample of 100 Indian diabetic patients, TB was diagnosed by a positive sputum result in 6% and by radiological examination in 27% [7]. In a 1–7 year follow-up study of 1250 African diabetic patients, 5.4% developed pulmonary TB [8]. The prevalence was higher in those with a lower body mass index, in type 1 DM compared with type 2 DM and in those whose diabetes was poorly controlled.

The majority of our patients who developed TB were middle-aged (30–60 years), similar to other studies. In the Indian study, a majority of patients were above 40 years of age [7]. In both the Korean [6] and Japanese [9] studies, the prevalence was particularly high in the age groups 40–50 years compared to the other age groups. In our study, the prevalence of TB increased progressively with duration of diabetes. The highest prevalence was seen in those who had been diagnosed with DM for more than 10 years. Comparative studies of type 1 DM and type 2 DM have shown that the prevalence of type 1 DM was 8-times higher in TB patients than in the general population, whereas the prevalence of type 2 DM was similar [10]. TB patients with type 1 DM have a more acute course of TB, rapid progression, and formation of extensive lesions with multiple cavities [11]. There was early clearance of bacilli and improvement in cavities in type 1 DM compared with type 2 DM.

The reason for increased susceptibility of diabetics to TB may be multifactorial. Alveolar macrophages play a critical role in eliminating mycobacterial infection in collaboration with lymphocytes. Alveolar macrophages have been found to be less activated in TB patients complicated with DM which may contribute to increased susceptibility [12]. In a study of 64 TB patients with DM a higher depression of cellular immunity was evidenced by fewer T lymphocytes and their decreased capacity for blast-cell transformation than those with TB alone [13]. Differences in cytokine production have also been observed. Interferon (IFN)-gamma production by CD4+ T-cell was reduced in patients with TB but those with poor diabetic control produced significantly less IFN-gamma than did patients with good diabetic control. In a longitudinal study, IFN-gamma production returned to normal

by 6 months in patients with TB alone and in well controlled diabetic TB patients but remained suppressed in poorly controlled diabetic TB patients [8]. Changes in pulmonary vasculature and alveolar oxygen pressure may also be contributory. Histological features of disseminated microangiopathy were observed in the lung preparations of 47 patients with destructive TB and DM [14].

The presence of DM does not seem to modify the presenting symptoms of pulmonary TB [2,3]. Fever with cough and sputum remain the common presenting features. Tuberculin reaction was found to be similar [2]. Data on bacteriological results are variable. Some studies showed no difference in bacteriology results, bacilli negative conversion rate or TB relapse rate in diabetic patients [14]. Other studies have shown that in diabetic patients the proportion of smear positive cases was higher, the culture-negative conversion period was longer [15], relapse rates were higher [16] and TB relapses were frequently associated with resistant strains [14]. In a case-control study from New York the relative risk of multi-drug resistant TB was found to be 8.6 (confidence interval, 3.1 to 23.6) in the diabetic group compared with the control group [17]. In patients with pulmonary TB, the most common underlying disease was DM [15]. In an inner-city cohort, presence of underlying illness (DM, chronic obstructive pulmonary disease, renal failure) and immunosuppression were important predictors of survival for patients with pulmonary TB [18].

Upper zone involvement and presence of cavitations are typical features of active pulmonary TB. In patients with DM and other systemic diseases, chest radiograph changes may be atypical. In our study, lower lung field involvement was the most frequent change, with upper and middle changes less common. Bilateral changes were present in half of the patients and an associated effusion was present in one-third. In a comparative study of pulmonary TB patients with and without DM, being a diabetic was found to be the most important factor determining lower lung field lesions [1]. In a second study, lower lung field TB was only seen in older diabetic patients (above 40 years) and female sex [2]. Other studies have, however, failed to show any differences in localization of TB lesions [3,19]. Cavitation was seen in only 26% of our patients. A higher rate of multiple cavitation has been reported in many studies [1,2,19] but not in others [3]. Among diabetics, patients with type 1 diabetes were found to have more extensive lesions with multiple cavities [11].

In conclusion, pulmonary TB may occur more often among patients with diabetics than those without, mostly between 40 and 70 years of age. Fever and cough are the common presenting symptoms. Lower lung field and bilateral or multi-lobar involvement is common. An associated effusion may be present. The mortality rate was 10% but was not associated with a particular radiographic appearance.

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