

The relationship between tuberculosis and Diabetes Mellitus in patients

Ibrahim Kareem Khalil

MSC

Abstract :

Diabetes Mellitus is associated with higher risk of lower respiratory tract infection including pulmonary tuberculosis with features which differ from that observed in the general non-diabetic population. To assess the effect of diabetes mellitus on the clinical, bacteriological and radiological presentation of pulmonary tuberculosis diabetic population. This is a cross sectional study that enrolled 50 patients with diabetes mellitus and pulmonary tuberculosis. The patients included in this study had been randomly selected from those attending AL-Hilla Teaching Hospital in Babylon Province – Iraq during the period between the 1st of May, 2006 to the 31st of May, 2007. All of the patients had been subjected to thorough physical examination and laboratory investigations. This study revealed male to female ratio of 5:1. Sixteen percent of the sample (4 patients) was of type 2 diabetes mellitus. 56% of those with diabetes and pulmonary tuberculosis (14 patients) were diabetic for 0-10 years. 38 patients (76% of the sample) had sputum smear positive, the remaining 12 patients (24% of the sample) were smear negative / culture positive. Multiple lobe involvement was obvious in 64% of (32 patients). Lower lung field involvement had been detected in 32% of the sample (36 patients). Cavitary lesions had been diagnosed in 30 patients (60% of the sample). This study revealed that diabetes modifies the clinical and radiological picture of pulmonary tuberculosis. Diabetic patients are at higher risk of recurrence and extensive pulmonary involvement. Tuberculosis is associated with poor glycemic control. Diabetes changes the male : female ratio toward the side of male predominance. Lower lung field involvement is more common in diabetics who had pulmonary tuberculosis.

Introduction :

The relationship between tuberculosis and diabetes was noticed by Avicenna more than thousand year ago. More than a hundred years ago, half of diabetic patients who died were found on post-mortem to be suffering from pulmonary tuberculosis. Not only tuberculosis is more common among diabetics but many specific infections are more common in them, and some occur almost exclusively in diabetes mellitus patients. Other infections occur with increased severity and are associated with an increased risk of complications in patients with diabetes⁽¹⁾. The increased risk of tuberculosis in Patients with diabetes mellitus has been highlighted by several retrospective and prospective studies. In a study in Mumbai, India, tuberculosis was found to be the most common complicating illness among diabetics (5.9%) in a large cohort study of over 8000 patients with diabetes mellitus⁽²⁾. In a recent study from the Regional Institute of Medical Sciences, Imphal-India, the prevalence of pulmonary tuberculosis in diabetics was found to be 27% by radiological diagnosis and 6% by sputum positivity⁽³⁾. Taking into consideration this link between diabetes mellitus and tuberculosis on one hand and the current epidemic of diabetes mellitus in both the developing as well as the developed countries. On the other hand, could be proposed the size of this health problem. The association

between diabetes and tuberculosis indicates that the two diseases do *not* coexist incidentally but rather than diabetes predisposes to the development of pulmonary tuberculosis or vice versa⁽⁴⁾. Thus, the question that must be answered or at least discussed is do patients with tuberculosis too have a higher incidence of diabetes mellitus? There is not enough evidence to give a definitive answer, but there *are* some trends . Studies conducted after the introduction of the glucose tolerance test in the 1950s , have shown high prevalence of impaired glucose tolerance test in patients with tuberculosis with rates ranging from 2-41%. There have been reports of high prevalence rates of diabetes in cases of pulmonary tuberculosis (4-20%) and rates are higher for impaired glucose tolerance test (16- 29%). After anti-tuberculous therapy. 50% of them had normalization of glucose intolerance . Some investigators have reported an association between severity of tuberculosis and abnormal glucose tolerance test⁽⁴⁻⁵⁾ .

Objectives are:-

- 1-Assess the effect of metabolic control and duration of diabetes on the frequency tuberculosis among diabetics.
- 2-Evaluate chest X-ray findings in patients with tuberculosis and diabetes concerning about number of lobes involved, the presence of cavitary lesions, and which lobe is more frequently involved .
- 3-Determine percentage of smear positive tuberculosis compared to culture positive tuberculosis among diabetics with pulmonary tuberculosis.

Patients&Methods:

This a cross sectional study.had enrolled 50 diabetic patients who had active pulmonary tuberculosis and attend Al Hilla Teaching Hospital in Babylon province/Iraq, during the period between 1st of May,2006 to 31 of May,2007. Active tuberculosis was defined as a positive sputum smear and /or culture on hospital admission or within 6 weeks of admission. All the patients participated in this study were asked by a detailed questionnaire about their personal information , history of diabetes and their recent chest complaints.The patients included in this study had been examined thoroughly, and sent for sputum smear examination (3 early morning samples for each patient), culture for acid fast bacilli, fasting plasma glucose, and glycated hemoglobin (HbA1C) .the extent of lung field involvement with pulmonary tuberculosis was assessed through the evaluation of detailed chest Xray reports noting unilateral or bilateral lung involvement, cavitary or no cavitary disease, and the number of lobes involved with pulmonary tuberculosis.

Results:

This study had enrolled 50 diabetic patients with pulmonary tuberculosis , 10 of them were female (20% of the sample), with a male to female ratio of about 5:1. Age of the patients ranged between 24 - 75 year -old (51.84 ± 10.71 year-old) . 32 patients (64% of the sample) were 40-59 year- old . Table-1 show patients' distribution according to their age.

Table -1 : Patients' distribution according to their age .

Age group (yrs)	No	%
20-29	2	4
30-39	6	12
40-49	14	28
50-59	18	36
60-69	4	8
70-79	6	12
Total	50	100
Mean $\pm$ SD	51.84 $\pm$ 10.71 yrs	

8 diabetic patients were of type 1 diabetes (16% of the sample) and the remaining 42 patients (84% of the sample) belonged to type 2 diabetes.

In this study , duration of diabetes mellitus ranged between 0.5 – 30 years (10.94 $\pm$ 8.09 years). 14 patients (56% of the sample) were either newly discovered diabetics or they were diabetics for 10 years or less . Table -2 show patients distribution according to duration of diabetes .

Table -2 : Patients' distribution according to duration of diabetes

Duration (yrs)	No	%
0-5	16	32
6-10	12	24
11-15	6	12
16-20	4	8
21-25	8	16

26-30	4	8
Total	50	100
Mean $\pm$ SD = 10.94 $\pm$ 8.09 yrs		

Fasting blood sugar of tuberculous patients included in this study ranged between 82-396 mg/dl (206.24 $\pm$ 80.37 mg/dl) . just 12% of diabetic patients included in this study (3patients) had Fasting blood glucose 120 mg/dl or less , i.e. controlled fasting blood glucose.

Table-3 show patients distribution according to fasting blood glucose level .

Table -3 : Patients' distribution according to their fasting plasma glucose

Fasting blood glucose	No	%
50-99	2	4
100-149	8	16
150-199	12	24
200-249	18	36
250-299	4	8
300-349	4	8
350-399	2	4
Total	50	100
Mean $\pm$ SD	206.24 $\pm$ 80.37 mg/dl	

The level of glycated hemoglobin in diabetics with pulmonary tuberculosis, HbA1c level ranged between 4.9-18.8% (9.33 $\pm$ 2.48. 84% of diabetics with pulmonary tuberculosis (42 patients) had HbA1c level of 7.0% or more. Table-4 show patients distribution according to their HbA1c level. 12 out of 50 patients with diabetes and active pulmonary tuberculosis (24% of the sample) had history of previous pulmonary tuberculosis sometime in their life. 4 of them received inadequate anti-tuberculous therapy because of their non- or poor compliance (8% the sample, 33% 38 patients (76% of the of those with previous history of pulmonary tuberculosis). sample) were sputum smear positive for tuberculous bacilli. All of the remaining 12 patients with sputum smear negative results for tuberculous bacilli had positive culture for tuberculosis (24% of the sample, 100% of those with smear negative results). Multiple lobe involvement was obvious in 64% of the patients included in this study (32 patients). lower lung field invol 32% of the sample (16 patients). Cavitory lesions had been diagnosed in 30 patients (60% of the sample). 3 of 4 patients with type 1

diabetes (75% of type 1 patients, 12% of the whole sample) had cavitory lesion on their chest x-ray. 16% of the sample had pleural effusion (4 patients). Table-5 showed frequency of different chest X-ray findings.

Table -4 : Patients' distribution according to glycated hemoglobin (HbA1c) level

HbA1c level %	No	%
4.0-7.9	10	20
8.0-11.9	24	48
12.0-15.9	10	20
16.0-19.9	6	12
Total	50	100
Mean $\pm$ SD	9.33 $\pm$ 2.48 %	

Table -5 Frequency of different chest X-ray findings

X-ray findings	No	%
Multiple lobe involvement	32	64
Lower lung field involvement	16	32
Cavitory lesions	30	60
Pleural effusion	8	16

Discussion:

Diabetics mellitus had noticed with a higher than usual risk of developing tuberculosis^(17,19,22). The frequency of tuberculous patients having diabetes concurrently tends to increase, and the relative risk of diabetics having

tuberculosis is also high, a three to four times higher prevalence of tuberculosis had been observed in diabetic patients compared with non-diabetics[23-24]. Physicians giving diagnosis and treatment of diabetes mellitus should understand that diabetics belong to the high risk group of developing tuberculosis and perform chest X-ray examination periodically(17, 19, 23-24]. There is evidence that diabetes is associated with a progressive shift of male predominance in pulmonary tuberculosis. Perez et al showed that in the non-diabetic population, male incidence is of about 51%, compared to 75% frequency of tuberculosis among male diabetics[25]. This study revealed a male to female ratio of 5:1, a finding that is quite higher than the results of other similar studies which showed a male to female ratio of 2.2-3:1[23,26-27]. This study revealed that those 40-59 year old age groups are the major age group of diabetics affected by pulmonary tuberculosis. This finding is similar to the results of an Indian study that had been done by Patel et al, in the late 1970s, showing that 40-60 year old age group is the major affected group with about 57% of that study sample (251 diabetic patients with pulmonary tuberculosis) were 40-60 year old[28]. Many other studies showed that relative risk of having pulmonary tuberculosis is higher among diabetics aging less than 50 years old, specifically: 30-49 year old with a relative risk of 9.88 and 4.72 in the 30-39 year and 40-49 year age group respectively, compared to somewhat lower relative risk in older age groups, 1.76 relative risk in those over 49 years old[29]. Regarding the effect of type of diabetes on the course and presentation of pulmonary tuberculosis, there is evidence that there are significant differences between type 1 and type 2 groups of diabetes mellitus patients when comparing the clinical and characteristics of pulmonary tuberculosis. An acute onset and rapid progression, formation of extensive lesions with multiple but small cavity areas are typical for type 1 diabetes patients[30]. This study showed that 16% of the sample was type 1 and 75% of type 1 diabetics included in this study had multiple cavitary lesions. Duration of diabetes plays an important role in the development of chronic diabetic complications that may alter the physiology of the system. Diabetic autonomic neuropathy can lead to abnormal basal airway tone due to alteration in vagal pathways and thus cause a reduced bronchial reactivity and bronchodilation and thus can play an important role in creating this higher risk of respiratory tract infection including tuberculosis among diabetic patients[31-32]. 56% of the sample included in this study was either newly diagnosed or had diabetes for less than 10 years. This frequency is similar to the estimated frequency in the study of Patel et al[28]. Most of the patients included in this study had poor glycemic control in terms of uncontrolled fasting plasma glucose (88% of the sample had plasma glucose level higher than 120mg/dl) and level of HbA1c (84% of the sample had HbA1c level more than 7.0%). Tamura et al concluded that in patients who had diabetes mellitus and whose HbA1c was $\geq 9.0\%$, proportion of smear positive cases was higher and period until culture negative conversion was longer than in patients who had diabetes mellitus and whose HbA1c was less than 9.0% [33]. This high percentage of poor glycemic control among the patients included in this study could be related to the fact that tuberculosis can aggravate diabetes and increases the frequency of complications compared with diabetics without tuberculosis [34]. Nakamoto found that 13 of 19 patients included in his study (68.4%) had poor glycemic control [35]. This study revealed that 8 patients (32% of the sample) had previous history of tuberculosis which is a percentage that can be considered as being higher than what is seen in non-diabetic patients [36]. Diabetes is associated with high risk of recurrent tuberculosis. The important idea is that many of those with recurrent tuberculosis will have infection with resistant strains of mycobacterium[31,36]

19 out of 25 patients with diabetes and pulmonary tuberculosis that had been included in this study (76% of the sample) had been proven bacteriologically to have active pulmonary tuberculosis as being sputum smear positive. On the other hand, the rest of the sample had been proven bacteriologically by being smear negative/culture positive cases (6 patients, 24% of the sample). The incidence of smear positive and culture positive pulmonary tuberculosis is under controversy. Some studies, like that made by Kim et al in Korea, showed that there is higher proportion of bacteriologically proven pulmonary tuberculosis among diabetic patients compared to non-diabetic patients; they found that the relative risk of developing bacteriologically proven pulmonary tuberculosis was 5.15 when compared with non-diabetics[29] This finding had been explained by higher proportion that had been included in that study. In contrast, Bacakogolu et al in another study found that fewer diabetic patients were smear positive results compared to the non-diabetic complications without giving any clear explanation. Pulmonary tuberculosis is found predominantly in the upper lobes. Lower lung field tuberculosis occurs but is often misdiagnosed as pneumonia, carcinoma or lung abscesses[38]. Sosman and Steid first suggested that tuberculosis in diabetics tended to predominantly in the lower lobes. The incidence of lower lung field tuberculosis has been reported to comprise approximately 7% of patients with active pulmonary tuberculosis[37,40-41]. This study indicated that 32% of diabetics with active pulmonary tuberculosis had lower lobes pulmonary tuberculosis, a proportion that is much higher than the estimated incidence in the non-diabetic population.

References:

Avieenna quoted by **Maims J. p.268.**

Bacakoglu F, Basoglu 00, Cok G, Sayiner A, Ates M. Pulmonary tuberculosis in patients with diabetes mellitus. *Respiration* 2001; 68(6): 595-600 .

Banyai AL. Diabetes and pulmonary tuberculosis. *Am Rev Tubercul* 1931; 24: 650- 67?

Back NJ, Kim CS, Kang MW, Park SH, Pyum HW. The prevalence of radiologically suspected pulmonary tuberculosis in diabetic patients. *Tuberc Res Dis (Korean)* 1977; 24:118-55.

Bloom JD. Glucose intolerance in pulmonary tuberculosis. *Am Rev Res Dis* 1969; 100: 38- 41?

Delamaire M, Maugendre D, Moreno M, Le Goff MC, Allannic H, Genetet B. Impaired leucocyte functions in diabetic patients. *Diabet Med* 1997; 14: 29-34.

Ezung T, Devi NT, Singh NT, Singh TB. Pulmonary tuberculosis and diabetes mellitus: a study. *J of Indian Medical Association.* 2002; 100:376.

Gallacher SJ, Thomson G, Fraser WD, Fisher BM, Gemmell CG, MacCuish AC. Neutrophil bactericidal function in diabetes mellitus: evidence for association with blood glucose control. *Diabet Med* 1995; 12: 9 16-20.

Goswami R, Kochupillai N. Endocrin implications of tuberculosis. In: Sharma SK, \Mohan A, eds. Tuberculosis. New Delhi: Jaypee Brothers Medical publishers (P) Ltd. 2001, 386.

Goswami R, Kochupillai N. Endocrine implications of tuberculosis. In: Sharma SK,

Joshi N, Cputo GM, Weitekamp MR, Karchmer AW. Infections in patients with diabetes mellitus. N Engl J Med. 1999; (4 341(25): 1906-12.

Kim SJ, Hong YP, Lew WJ, Yang SC, Lee EG. Incidence of pulmonary tuberculosis among diabetics. Tuberc Lung Dis 1995; 76:529-33.

Kossii lu E, Karachunskii MA, Kaminskaia GO, et al. Pulmonary tuberculosis in patient with different types of diabetes mellitus. Probl Tuberk 2002; 5: 2 1-4.

Koziel H, Koziel MJ. Pulmonary complications of diabetes mellitus, pneumonia. Infect Dis Clin North Am 1995; 9(1):65-96.

Mboussa J, Monabeka H, Kombo M, et al. Course of pulmonary tuberculosis in diabetics. Rev Pneumol Clin 2003; 59(1): 39-44.

Mbossa J, Monabcka H, Kombo M, et al. Course of tuberculosis in diabetics. Rev Pneumol Clin 2003; 359: 39.

McMahon MM, Bistrian BR. Host defenses and susceptibility to infection in patients with diabetes mellitus. Infect Dis Clin North Am

Muchova J, Liptakova A, Orszaghova Z, et al 1995; 9: 1-9 Antioxidant systems in polymorphonuclear leucocytes of type 2 diabetes mellitus. Diabet Med 1999; 16: 74-78.

Nakamoto A, Saito A. Diagnosis and management of tuberculosis in diabetics. Nippon Rinsho 1998; 56(12): 3205-8.

Nichols GP. Diabetes among young tuberculous patients. Am Rev Tuberci 195;76:1016-30?

Morris JT, Seaworth BJ, McAllister CK. Pulmonary tuberculosis in diabetics. Chest 1992; 102: 539-41.

Oluboyo P0, Erasmus RT. The significance of glucose intolerance in pulmonary tuberculosis. Tubercle. 1990; 71: 135-8.

Parmer M. Lower Lung field tuberculosis. A, Rev Respir Dis 1967;96:310-3.

Perez-Guzman C, Vargus MH, Torres-Cruz A, et al. diabetes modifies the male: Lung Dis. 2003; 7(4): 354-8. female ratio in pulmonary tuberculosis. Int J Tuberc

Putel JC. Complications in 8793 cases of diabetes mellitus: 14 years study in Bombay Hospital, Bombay, India. Ind J Med Sci. 1989; 43: 177.

Sridhar CB. Kini Usha. Subbhash Kavitha. Comparative cytological study of lymph node tuberculosis in HIV infected individuals and in patients with diabetes in a developing country. Diagn Cytopathol. 2002; 26(2): 75-80.

Rassias AJ, Marrin CA. Arruda J, Whalen PK, Beach M, Yeager MP. Insulin infusion improves neutrophil function in diabetic cardiac surgery patients. *Anesth Analg* 1999; 88: 1011-1016.

Rom WN, Garay SM. Tuberculosis. *N Engl J Med*. 1996; 334(26): 1752.

Patel JC, Ugini SS. Diabetes and tuberculosis in J Tub. Volume XXIV (4): 155-30- Tamura M, Shirayama R, Kasahara R, et al. A study on relation between active pulmonary tuberculosis and underlying diseases. *Kekkaku* 2001; 76(9): 6 19-24.

Root HF. The association of diabetes and tuberculosis. *New Engl J Med* 1934; 210:1, 78. 127.

Valerius NH, Eff C, Hansen NE, et al. Neutrophil and lymphocyte function in patients with diabetes mellitus. *Acta Med Scand* 1982; 211:463-467.

Weaver R. Unusual radiographic presentation of pulmonary tuberculosis in diabetic patients. *A, Rev Respir Dis* 1974; 109: 162-3.

Williams G, Pickup JC, eds. Handbook of diabetes. London: Blackwell science. 1998; 1- 6.

Tulltk JA. Diabetes mellitus in the tropics. E. & S Livingstone: London, 1962, p 131.

Yamagishi F. Medical risk factors of tuberculosis and countermeasures. *Kekkaku* 2002; 77(12): 799-804.

Yoon SJ, Lee YH, Chung ST, et al. Clinical study of pulmonary tuberculosis complicating diabetes mellitus. *Tuberc Resp Dis (Korean)* (1985; 32: 93-100.

Zack MB, Fulkerson LL, Stein E. Glucose intolerance in pulmonary tuberculosis. *Am Rev Respir Dis*. 1973; 108: 1164-69.