

Effects of Hyperglycemia on Presentations of Pulmonary Tuberculosis in Diabetic Patients.

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الخلاصة

- داء السكري هو متزامنة سريرية تمتاز بارتفاع نسبة السكر المزمن في الدم وله تأثيرات مختلفة العوامل على المناعة مما يزيد من إمكانية الإصابة بالالتهابات مع خطورة أعلى للالتهابات الجهاز التنفسي السفلية وبضمنها التدرن الرئوي.
- الهدف من الدراسة لتقييم تأثير مرض السكري على العروض السريرية والجرثومية والشعاعية للتدرن الرئوي.
الدراسة شملت (25) مريضا مصابا بالتدرن الرئوي ضمن (310) مريض مصاب بمرض السكري والذين راجعوا العيادة الخارجية لمرض السكري في مستشفى الديوانية التعليمي، تمت دراستهم خلال الفترة من الأول من تشرين الأول/ 2009 إلى الواحد والثلاثون من آذار/ 2010.
- كشفت هذه الدراسة بأن نسبة الذكور إلى الإناث هي 4:1. 16% من المرضى كانوا من النوع الأول لمرض السكري. 56% من المرضى كانوا مصابين بداء السكري لمدة أقل أو مساوية لـ (10) سنوات. 12% من المرضى كان تحليل الدم صياما لديهم أقل أو مساو لـ (6.9 mmol/l). 84% من المرضى كانت نسبة الهيموغلوبين A_{1c} أكثر أو مساوية لـ (7%) . 24% من المرضى كان لديهم تاريخ مرضي للتدرن الرئوي. 76% من المرضى كانت لديهم مسحة القشع لعصية كوخ موجبة. شمول فصوص متعددة من الرئة، وجود علل تجويفية في الرئة، تأثر المساحة السفلية، و انصباب جنبي بنسبة 64% ، 60% ، 32% و 16% على التوالي.
- استنتج من هذه الدراسة بأن مرض السكري يعدل الصورة السريرية، الجرثومية والشعاعية لمرض التدرن الرئوي. مرضى السكري لديهم درجة عالية من الخطورة لتكرار التدرن الرئوي.

Abstract

Background: Diabetes Mellitus (DM) is a clinical syndrome characterized by chronic hyperglycemia and have multifactorial effects on immunity which increase the liability for infections with higher risk of lower respiratory tract infections including pulmonary tuberculosis (PTB).

Objective: To assess the effects of hyperglycemia in DM on the clinical, bacteriological and radiological presentations of pulmonary tuberculosis.

Methods: This study enrolled 25 tuberculous patients out of 310 diabetic patients who attend to the out-patient clinic of DM at Al-Diwaniya Teaching Hospital, they were studied during the period from 1st of October 2009 to 31st of March 2010.

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Results: This study revealed that male to female ratio was 4:1. 16% of the patients were type 1 DM, 56% were diabetic ≤ 10 years, 12% had fasting blood sugar (FBS) ≤ 6.9 mmol/l, 84% had HbA_{1c} level $\geq 7.0\%$, 24% had positive history of pulmonary tuberculosis and 76% had positive sputum smear for acid fast bacilli (AFB). Multiple lobe involvement, cavitory lesions, lower lung field involvement and pleural effusion had been diagnosed in 64%, 60%, 32% and 16% of the sample respectively.

Conclusions: This study revealed that DM affects the clinical, bacteriological and radiological picture of PTB. Diabetic patients have a higher risk for recurrence of PTB.

Introduction

Hyperglycemia (elevated blood glucose level; normal range of 3.5-6.5 mmol/l) is the cardinal metabolic change in DM due to absolute or relative deficiency of insulin⁽¹⁾. PTB and many other specific infections are more common in diabetic patients with increase severity and risk of complications⁽²⁾. Several aspects of immunity are altered in diabetic patients; depression of polymorphonuclear leukocyte function particularly when acidosis is present, leukocyte adherence, chemotaxis, phagocytosis and antioxidant systems may be affected⁽³⁾. The clinical data on humoral immunity in DM are limited, but responses to vaccines appear to be normal otherwise cutaneous responses to antigen challenges and measures of T-cell function may be depressed⁽⁴⁾.

There are evidences that improving glycemic control in diabetic patients will improves immune function and the efficiency of intracellular killing of microorganisms⁽⁵⁾. Among diabetic patients undergoing heart surgery, those given insulin infusions have better neutrophil function than those given intermittent insulin therapy and this finding could be due to the fact that hyperglycemia reduces oxidative killing capacity of neutrophil⁽⁶⁾.

Hyperglycemia will lead to increased susceptibility to tuberculosis and this could be related to the lowered production of interleukin-1 β and tumor necrosis factor by peripheral blood monocytes in diabetic patients⁽⁷⁾. In addition, the non-enzymatic glycosylation of tissue proteins might play a role in creating such a higher risk of tuberculosis by inducing an alteration in the nature of connective tissue in DM⁽⁸⁾.

The increased risk of tuberculosis in diabetic patients had been proved by several retrospective and prospective studies. In a large

study done in Bombay, India, tuberculosis was found to be the most common complicating illness among diabetic patients (5.9%)⁽⁹⁾. In a recent study from the Regional Institute of Medical Sciences, Imphal-India, the prevalence of pulmonary tuberculosis in diabetics was found 27% by radiological diagnosis and 6% by positive sputum smear for AFB⁽¹⁰⁾. DM occurs world-wide and the incidence of both type 1 and type 2 are rising; 171 million people had diabetes in 2000 and this expected to double by 2030, this epidemic had resulted from changes in human behaviors and lifestyle over the last century which have resulted in a dramatic increase in the incidence of diabetes worldwide⁽¹¹⁾. The epidemic is chiefly of type 2 diabetes (75%)⁽¹²⁾. After a progressive decline that began in the 19th century, the incidence of tuberculosis in the United States began to climb again in the mid-1980⁽¹³⁾. This increase in the incidence can be explained by higher frequency of tuberculosis in patients with immune-compromised states which occur in two important conditions (epidemic-like phenomena) in the last 2 decades including DM and acquired immune deficiency syndrome⁽¹³⁾.

In Congo, published study appeared that DM have an induction and aggravating effect on tuberculosis which was found to be more frequent in diabetic patients and had more pronounced radiological signs, treatment failures and death more frequent⁽¹⁴⁾. Although the relative risk of developing PTB and mortality is several times higher in diabetic patients than in nondiabetic patients, the clinical symptoms and presentation of pulmonary tuberculosis are believed to be similar in both and so far the bacteriological conversion rates and relapse rates⁽¹⁴⁾.

After the introduction of glucose tolerance test in 1950, many studies had been show prevalence rate of impaired glucose tolerance test in patients having PTB were 2-41% (50% of them had normalization of glucose intolerance after anti-tuberculous therapy)⁽¹⁵⁾ and prevalence rate of DM in patients with PTB were 4-20%⁽¹⁵⁾.

Methods

326 diabetic patients who attend to the out-patient clinic of DM at Al-Diwaniya Teaching Hospital studied during the period from 1st of October 2009 to 31st of March 2010. 16 patients excluded (2 females patients have pregnancy, 4 refuse to participate in this study, 7 had asthma and 3 had rheumatoid arthritis). 310 patients (suspect to have chest infection) had been subjected to thorough physical examination and laboratory investigations. 25 patients prove to have

PTB. Active PTB was define as a positive sputum smear and/or culture on hospital admission or within 6 weeks of admission.

All the patients included in this study were assess clinically with full history intake, examined thoroughly, investigated with sputum smear examination (3 early morning samples), sputum culture for AFB, FBS and glycated haemoglobin (HbA_{1c}) done for patients with PTB. The extent of lung field involvement with tuberculosis was assessed through evaluation of detailed chest X-ray images (taken in consideration the hazardous effects of X-ray exposure) noting unilateral or bilateral lung involvement, cavitary or no cavitary lesion and number of involved zones. The formal consents of the patients and the official requirement were taken.

Results

This study revealed that 25 diabetic patients (8.06%) have PTB, 5 patients (20%) were female and male to female ratio was 4:1 as shown in table 1 and figure 1.

Age of the patients ranged between 24-75 year-old (51.84 ± 10.71 year-old). 16 patients (64%) were 40-59 year-old. Table 2 is showing patients' distribution according to age.

Figure 2 shows patients' distribution according to type of DM, 4 patients (16%) were of type 1 and 21 patients (84%) were of type 2.

In this study, 14 patients (56%) were diabetics for ≤ 10 years. Table 3 is showing distribution of diabetic patients according to duration of DM.

3 patients (12%) included in this study had FBS ≤ 6.9 mmol/l (well controlled) and 22 patients (88%) had FBS between 7mmol - ≥ 20.6 mmol. as showing in table 4.

Table 5 shows distribution of diabetic patients according to glycated haemoglobin (HbA_{1c}) level, 21 patients (84%) had level $\geq 7.0\%$.

Figure 3 shows distribution of diabetic patients according to past history of PTB, 6 out of 25 patients (24%) had positive history.

Figure 4 shows distribution of diabetic patients according to the result of sputum smear examination, 17 patients (68%) had positive sputum smear for AFB and 8 patients (32%) with negative sputum smear but had positive culture for AFB.

16 patients (64%) had multiple zones involvement. Lower lung field involvement had been detected in 8 patients (32%). Cavitary lesions had been diagnosed in 15 patients (60%), 3 of them had type 1 DM. 4 patients (16%) had pleural effusion.

Table (1) Distribution of diabetic patients according to gender and presence of PTB

	PTB	%	No PTB	%	Total no.	%	P-value
Male	20	6.45	171	55.16	191	61.61	0.04
Female	5	1.61	114	36.78	119	38.39	
Total no.	25	8.06	285	91.94	310	100	

P-value less than 0.05 is considered significant.

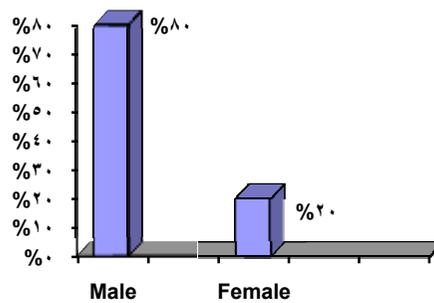


Figure (1) Distribution of diabetic patients with PTB according to gender.

Table (2) Distribution of diabetic patients with PTB according to age.

		No.	%
Age group (year)	≤29	1	4
	30-39	3	12
	40-49	7	28
	50-59	9	36
	60-69	2	8
	≥70	3	12
Total		25	100

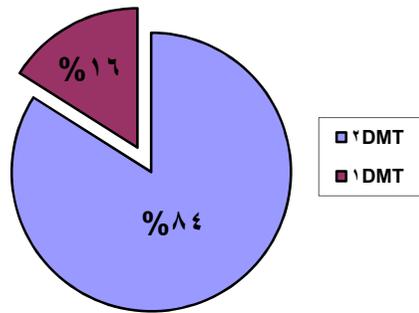


Figure (2) Distribution of diabetic patients with PTB according to type of DM.

Table (3) Distribution of diabetic patients with PTB according to duration (year)of DM.

		No.	%
Duration (years)	0-5	8	32
	6 - 10	6	24
	11 - 15	3	12
	16 - 20	2	8
	21 - 25	4	16
	26 - 30	2	8
Total		25	100

Table (4) Distribution of diabetic patients with PTB according to FBS (mmol/l).

		No.	%
FBS (mmol/l)	≤6.9	3	12
	7-8.5	2	8
	8.6-11.5	6	24
	11.6-14.5	9	36
	14.6-17.5	2	8
	17.6-20.5	2	8
	≥20.6	1	4
Total		25	100

Table (5) Distribution of diabetic patients with PTB according to glycated haemoglobin (HbA_{1c}) level.

		No.	%
HbA _{1c} level %	4.0-6.9	4	16
	7-11.9	13	52
	12.0-15.9	5	20
	16.0-19.9	3	12
Total		25	100

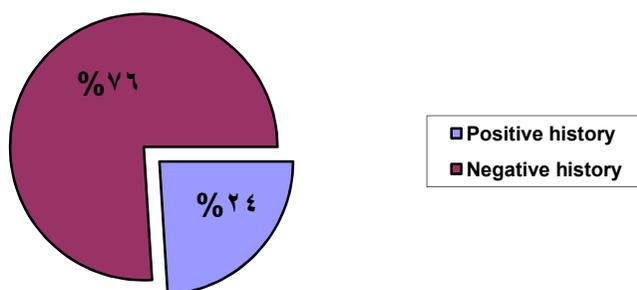


Figure (3) Distribution of diabetic patients with PTB according to past history of PTB.

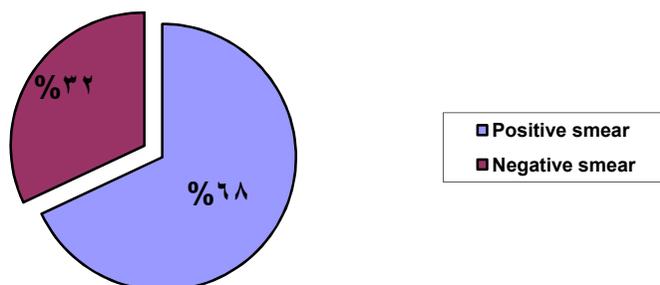


Figure (4) Distribution of diabetic patients with PTB according to result of sputum smear examination.

Table (6) Frequency of chest X-ray findings in diabetic patients with PTB.

	No.	%
Multiple zone involvement	16	64
Cavitary lesions	15	60
Lower lung field involvement	8	32
Pleural effusion	4	16

Discussion

It is well known that diabetic patients have a higher than usual risk for developing pulmonary tuberculosis⁽¹⁶⁾. The frequency of tuberculous patients having DM tends to increase and the relative risk of diabetic patients having tuberculosis have (three to four times) higher prevalence rate when compared with non-diabetics⁽¹⁷⁾.

This study revealed a males to females ratio were 4:1 (males patients are the common visitors to diabetic clinics than females in our country) which is higher than the results of study done by Back et al that showed a males to females ratio were 2.2:3.1⁽¹⁸⁾. The frequency of PTB was 75% in diabetic males as reported by Perez et al study⁽¹⁹⁾.

This study revealed that 40-59 year old age group are the major age group of diabetic patients affected by PTB (the most important productive aging group in our country and may have strong positive history for contact with tuberculous patients) which is similar to the results of study had been done by Patel et al showing that 40-60 year old age group is the major affected group (57%)⁽²⁰⁾.

There is evidence that there are significant differences between patients with type 1 and type 2 DM concerning the clinical and characteristic of PTB. A more acute onset, rapid progression and formation of extensive lesions with multiple small decay areas are typical for patients with type 1 DM⁽²¹⁾. This study showed that 16% of the patients have type 1 DM and 75% of them had multiple cavitary lesions, this can be explained by more defective immune system in state of absolute deficiency of insulin which may increase the activity of tuberculous bacilli.

Duration of diabetes play an important role in the development of chronic diabetic complications which may alter the physiology of respiratory system. Diabetic autonomic neuropathy can lead to abnormal basal airway tone due to alteration in vagal pathways and thus cause reduction in bronchial reactivity, bronchodilatation and thus can play an important role in creating

this higher risk of respiratory tract infection including tuberculosis among diabetic patients as reported in this study which supported by Koziel et al study⁽²²⁾. 56% of diabetic patients included in this study had DM for ≤ 10 years which is goes with the result of Banyai et al study⁽²³⁾.

Most of the patients included in this study had poor glyceimic control, 88% of diabetic patients had FBS level ≥ 7 mmol/l and 84% had HbA_{1c} level $\geq 7.0\%$. Tamura et al concluded that diabetic patients with HbA_{1c} $\geq 9.0\%$ and positive sputum smear for AFB was higher than in diabetic patients with HbA_{1c} $\leq 9.0\%$ ⁽²⁴⁾. This high percentage of poor glyceimic control among diabetic patients included in this study related to the fact that PTB can aggravate DM and increases the frequency of complications and this supported by Mboussa et al study⁽²⁵⁾. Nakamoto found that 13 of 19 patients included in his study (68.4%) had poor glyceimic control⁽²⁶⁾.

This study revealed that 6 diabetic patients (24%) had previous history of PTB which is higher than the reported result of study which done by Goswami et al (15%)⁽²⁷⁾. This high risk of recurrence of PTB can be explained by dietary and environmental factors.

76% of diabetic patients with pulmonary tuberculosis included in this study had been proven bacteriologically to have active PTB with sputum smear positive for AFB. Study done by Kim et al in Korea showed that positive sputum smear for AFB was 68% in diabetic patients⁽²⁸⁾. In contrast, Bacakogolu et al found that fewer diabetic patients were smear positive compared to non-diabetic patients without any clear explanation for their finding⁽²⁹⁾.

This study revealed that 32% of diabetic patients had lower lung field involvement which is supported by result of Sosman and Steid study who were suggested that tuberculosis in diabetic patients predominantly in the lower zones⁽³⁰⁾.

Conclusions

Hyperglycemia in DM affects the clinical, bacteriological and radiological presentation of PTB with male predominance. Diabetic patients are at higher risk of recurrence and extensive PTB involvement with predominance of lower lung field involvement. PTB is associated with poor glyceimic control in diabetic patients.

Recommendations

Diabetic patients belong to high risk group for developing PTB and chest X-ray examination should be done annually and more frequently for patients with positive history of PTB.

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