EFFECTS OF DIABETES MELLITUS IN PULMONARY TUBERCULOSIS

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ABSTRACT

We studied the effects of Diabetes on Tuberculosis. For this, we had taken 50 patients with Tuberculosis and Diabetes both and 50 controls who had only Diabetes but no TB infection. The cases and the controls were divided into 2 categories: Controlled and uncontrolled diabetes. For this the cut off used was HbA1c of 7%. Chest X rays were also taken from the TB patients and it was compared with other studies. The study showed that Tuberculosis is more common in uncontrolled Diabetic patients as compared to patients with controlled Diabetes. The p value is <0.01 which suggests the statistically significant result. Other interesting findings is that in tuberculosis patients having uncontrolled diabetes, bilateral lobe involvement is more common. This is due to the decrease in the immunity in diabetes. The most common involvement on chest x ray was consolidation followed by cavity followed by nodule.

KEYWORDS: Diabetes Mellitus, Tuberculosis, Infection.

ABBREVIATIONS
TB= TUBERCULOSIS; DM = DIABETES MELLITUS.

BACKGROUND
Diabetes Mellitus (DM) is a problem of great significance in Tuberculosis because this metabolic disorder lowers the body resistance to tuberculosis to great extent. At present, an epidemic of DM is rising both in developed and developing countries. With recognition of this explosive increase in no. of people diagnosed with DM all over the world, a whole new field of related interaction between DM and pulmonary Tuberculosis has been thrown open.[1] Many individual infections are more common in people with diabetes, including pneumonia, pyelonephritis, soft tissue infections, including the "diabetic foot," Necrotizing fasciitis and mucocutaneous Candida infections. Others occur almost exclusively in diabetics are invasive (malignant) otitis externa, rhino cerebral mucormycosis and emphysematous infections (cholecystitis and pyelonephritis). Some infections result in increased severity when they occur in diabetic patients and are associated with increased complications. Pulmonary Tuberculosis in DM is characterized by alteration in host defense in entire body and in the lung locally as well as in the function of respiratory epithelium and ciliary motility. It is characterized by serious clinical features, longer duration, more frequent complications and increased mortality. Pulmonary Tuberculosis mortality in diabetic patient is approximately four fold higher than general population. This importance of hyperglycemia has to be emphasized because an alteration in host defense and consequently increased susceptibility to infection.[2] Nolan et al in 1978 reported that granulocyte from ambulatory hospitalized diabetics with fasting blood glucose more than 200 mg/dl had an impaired ability to engulf and kill opsonized tubercle bacilli. He also mentioned that the granulocyte functions improved after intensive management of diabetes.[3] Infection is associated with impaired carbohydrate tolerance[4-6] and contributes to approximately 25% of deaths associated with DKA.[7-9] With the advent of anti-diabetic drugs and modern anti-microbial and also with better diagnostic techniques, there is no doubt in improvement in mortality status regarding pulmonary Tuberculosis but morbidity continues to remain an immense problem.

AIMS
To study the impact of Diabetes Mellitus on Pulmonary Tuberculosis.

OBJECTIVES
1. To study the clinical impact of Diabetes Mellitus on Pulmonary Tuberculosis.
2. To study the radiological features of patient of pulmonary tuberculosis with diabetes mellitus.
3. To study the management of Pulmonary Tuberculosis with Diabetes Mellitus.

METHODS
The present study was carried out in the department of medicine, B. J. Medical College and Civil Hospital, Ahmedabad from November 2011 to September 2013. In this study total 50 patients of age >12 years and either sex were selected randomly from patients admitted in the medicine department at civil hospital or coming to OPD. Inclusion criteria was patients with diabetes, known case, associated with pulmonary tuberculosis determinate by clinical, radiological and/or pathological means were included in the study. Patients with upper and lower respiratory tract infection or patient having extra pulmonary manifestation without pulmonary tuberculosis, newly diagnosed cases of diabetes mellitus and patients with less than 12 years of age were excluded. Also, 50 patients without tuberculosis with diabetes mellitus were taken for control from the same hospital. After taking detailed medical history, all patients underwent detail physical examination and routine laboratory investigations like Hb, total WBC count, differential WBC count, ESR, Random blood sugar, fasting and post prandial blood sugar, renal function test, urine examination, sputum examination for AFB and other microorganism were carried out in almost all patients. A plain x-ray of chest in Posterior-anterior view was obtained in almost all patients. Ultrasonography and computer tomography was done whenever indicated. Body fluid examination and its culture was carried our whenever indicated. Electrocardiogram, fundus examination and urine albumin level were done in almost all patients to observe complications of DM. Diagnosis was made on the basis of clinical examination, radiological and/or laboratory investigations.

RESULTS AND DATA ANALYSIS
As per table 1, the mean age of the group is 51.96 with a standard deviation of $\pm$ 12.48 years. In the study conducted by Dr. Prabhakar Singh in 2005, the mean age of patients of the study group was 50.2 years with a standard deviation of $\pm$11.1 years.[10]

As per table 2, in the present study 54% patients had consolidation type of lesion on chest x ray. In the study conducted by Gupta et al. on CXR of diabetic sputum positive Tuberculosis patients, 59.2% had consolidation type of lesion. This is similar to our results.

As per table 3, only 4% cases had upper zone involvement and 16% had Lower zone. Most cases (64%) had bilateral involvement which can be correlated with other two studies, besides that unilateral involvement of lung more than one zone was 10%. Compared to this, the CXR of non-DM patients studied by Gupta et al. only 1.2% of the cases had Lower zone involvement, while 7.4% in DM-TB group of Gupta et al. and 16% of cases of this study. While non DM-TB group had 30% Upper zone involvement studied by Gupta et al. which is higher than Upper zone involvement in DM-TB group (22.2%) by himself and 4% in this study.

From table 4, it can be seen that out of 50 cases with TB and DM both, 37 cases had uncontrolled Diabetes and only 13 had controlled Diabetes. In the control group, 5 people had uncontrolled Diabetes and 45 people had controlled Diabetes. On applying the student chi square test, the p value turns out to be <0.01 showing that uncontrolled Diabetes has high chances of having Pulmonary tuberculosis when compared to controlled Diabetes.

Table 1: Age and Sex wise distribution of Tuberculosis in Diabetic patients.

Age Group Years	Male		Female	
	Present study	**Prabhakar Singh**	**Present study**	**Prabhakar Singh**
21-30	01(02)	00(00)	01(02)	00(00)
31-40	08(16)	10(20)	01(02)	02(04)
41-50	08(16)	10(20)	06(12)	00(00)
51-60	13(26)	18(36)	03(06)	02(04)
61-70	03(06)	06(12)	03(06)	00(00)
>70	03(06)	02(04)	00(00)	00(00)
Total	36(72)	46(92)	14(92)	04(08)
Mean Age	51.97	50.12	52.14	45

Table 2: Radiological characteristics (Type of Lesion).

Type of lesion	Present study N=50	Prabhakar Singh N=50	Gupta et al N=27
Nodular	05(10%)	8(16%)	04(14.8%)
Consolidation	27(54%)	30(60%)	16(59.2%)
Cavity	13(26%)	12(24%)	7(26%)
Hydro-Pneumonia thorax	05(10%)	-	-

Table 3: Radiological Characteristics (Number of Zones involved).

Number of Zones involved	Present study N=50	Prabhakar S. N=50	Gupta et al N=27
Upper Zone	02(4%)	06(12%)	06(22.2%)
Mid Zone	03(06%)	00(00%)	00(00%)
Lower Zone	08(16%)	04(08%)	02(7.4%)
>1 Zone	05(10%)	10(20%)	19(70.3%)
Bilaterally	32(64%)	30(60%)	-

Table 4: Distribution of Tuberculosis in controlled and uncontrolled Diabetes patients.

	Uncontrolled Diabetes	Controlled Diabetes	P value
Tuberculosis present	37	13	
Tuberculosis absent	5	45	<0.01
Total	42	58	

DISCUSSION

Uncontrolled diabetes has high chances of having pulmonary tuberculosis as compared to patients having controlled diabetes. (p value is <0.01 and hence the result is statistically significant).

Most of the patients having Tuberculosis and Diabetes have bilateral lobe involvement and the most common lesion in CXR is consolidation followed by cavity followed by nodules.

Tuberculosis in diabetes mellitus is usually due to reactivation of an old focus rather than through fresh contact, so lower lobe involvement is more common in pulmonary TB with DM. Rifampicin accelerates the metabolism of oral hypoglycemic agents, as it is a potent hepatic enzyme-inducing agent. So rifampicin shortens the plasma half-life of sulphonylureas. It was also known to cause early hyperglycemia in non-diabetic patients with or without pulmonary tuberculosis, and also to augment intestinal absorption of glucose. Some of the adverse effects of Rifampicin in Type I diabetes mellitus may well be applicable to the altered glycemic control in Type II diabetes mellitus, as well isoniazid, or pyrazinamide, was attributed to the increased insulin requirement in Type I diabetes mellitus. Malabsorption of rifampicin was also reported in poorly controlled diabetes mellitus. Another Rifamycin, Rifabutin is a less potent inducer of CYP 3A4 liver enzyme as compared to rifampicin, while being equally safe and effective for treatment of TB. Its main usefulness lies in the fact that it has lesser drug interactions with sulphonylureas than rifampicin. Apart from causing pancreatic hypo function and peripheral insulin insensitivity, long-term administration of ATT interfered with hydrolysis and absorption of carbohydrates in small intestine in patients with pulmonary tuberculosis. Unfortunately, the liability of these diabetic patients persisted in spite of the best control of tuberculosis by tuberculostatics. Isoniazid antagonizes sulphonylureas and impairs insulin release and action and rifampicin shortens the plasma half-life of sulphonylureas. Biguanides are contraindicated, as metformin produces weight loss indicating the role of malabsorption, particularly in high doses, and it is also an anorectic. Biguanides as well as sulphonylureas are contraindicated in hepatic disease, which is a common adverse effect of ATT. Marked weight loss, increasing age, longer duration of diabetes mellitus, higher insulin and caloric needs in tuberculosis are other important indications for withholding oral anti-diabetic therapy in diabetes mellitus.

CONCLUSION

The prevalence of Tuberculosis is more in patients with uncontrolled Diabetes when compared to patients with proper control of Diabetes (p value <0.01). Bilateral lobe involvement in lungs is more common due to decreased immunity. Also, the most common lesion on chest x ray is consolidation.

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