Innovations

Study of Disease Patterns in Pulmonary Tuberculosis Patients with Co-Existing Type 2 Diabetes Mellitus

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Abstract

Background: Tuberculosis (TB) and diabetes mellitus (DM) frequently coexist and mutually influence disease presentation and outcomes. This study aimed to determine the burden of DM among pulmonary TB patients and to compare clinical, bacteriological, and radiological features and treatment outcomes between TB patients with and without DM. **Methods:** A hospital-based prospective study was conducted at GSL Medical College and General Hospital. One hundred and twenty consecutive pulmonary TB patients were enrolled: 60 with concomitant type 2 DM (study group) and 60 without DM (control group). Baseline data included demographics, symptoms, smoking history, fasting blood sugar (FBS), post-prandial blood sugar (PPBS), HbA1c, sputum AFB grading, and chest radiography (extent, cavitation, zone involvement). Patients received anti-tuberculosis treatment per RNTCP guidelines and were followed for treatment outcomes. Group comparisons used t-tests/Chi-square tests and repeated measures as appropriate; $p < 0.05$ was considered significant. **Results:** Mean age was higher in the study group (51.3 ± 8.5 years) than in controls (41.4 ± 14.4 years) ($t = 4.07$; $p = 0.001$). Glycaemic markers were significantly elevated in the study group (Mean FBS 189.2 ± 69.1 vs 90.7 ± 12.8, $t = 10.54$, $p < 0.001$; Mean PPBS 292.9 ± 119.1 vs 125.9 ± 27.3, $t = 10.17$, $p < 0.001$; Mean HbA1c 7.38 ± 0.9 vs 5.0 ± 0.3, $t > 15$, $p < 0.001$). Diabetics had higher bacillary load (66.7% ≥2+ vs 38.3% in controls) and more extensive radiographic disease (86.7% vs 56.7%). Cavitary lesions were more frequent in diabetics (70.0% vs 33.3%, $p < 0.001$). Within the diabetic group, patients with HbA1c >7 had a higher proportion of extensive lesions (93.5% vs 79.3%). Treatment success (cured/completed) was similar between groups (study 90.0% vs control 91.7%; $p = 0.261$). Smoking was associated with more extensive and cavitary disease, particularly among diabetics. **Conclusions:** Concomitant diabetes in pulmonary TB is associated with older age, markedly worse glycaemic indices, higher sputum bacillary load and more extensive, frequently cavitary radiographic disease. Despite greater disease severity, standard RNTCP regimens achieved comparable short-term treatment success when diabetes care and adherence were ensured. Larger, age-matched and culture-based studies are needed to further evaluate long-term outcomes and drug resistance patterns.

Keywords: Tuberculosis; Diabetes mellitus; Pulmonary tuberculosis; HbA1c; Sputum smear grading; Radiographic severity; Cavitation.

Introduction

Tuberculosis (TB) is a major global health problem responsible for the ill health of millions of people every year. TB ranks as the second leading cause of death from an infectious disease worldwide. [1]The association between tuberculosis (TB) and diabetes mellitus (DM) and their synergetic role in causing human disease and suffering has been recognized for centuries in many retrospective and prospective studies. [2]The latest estimates showed that there were about 1.5 million deaths in the year 2013 due to TB, which included 5,10,000 deaths among women and 80,000 deaths among children. TB mortality is unusually high, and most of the deaths can be prevented by the various treatment regimens available.Short-course regimens of first-line drugs can cure around 95% of cases[1]. The prevalence of Diabetes was estimated to be 9% among adults in the global population, with low prevalence in low-income countries and the highest prevalence in upper-middle-income countries. Diabetes was responsible for about 1.5 million deaths in 2012 directly and 89 million Disability Adjusted Life Years (DALYs)[2]. More than 80% of diabetes deaths occur in low and middle-income countries (3). WHO projects that diabetes will be the 7th leading cause of death in 2030 [4]. Given the high prevalence of both DM and TB, it is likely that these two conditions representco-morbidity. It is well known that diabetic patients are at increased risk of developing TB and viceversa. It is reported that the rate of DM in patients with TB is 2.0-4.6 times higher than inthe general population.New cases of DM account for 64% of all cases of DM in TB (5). About 10% of patients with TB are linked to diabetes. Patients with diabetes have a greater chance (2-3-fold risk) of developing tuberculosis, a high risk of death, and relapse during and after anti-tubercular treatment, respectively(2). The DM-TB co-morbidity not only confers an increased risk for the development of new and recurrent TB disease, but also increases the risk of poor TB treatment outcomes and increased rates of recurrent disease after successful completion oftreatment[6, 7, 8, 9].These risks are known to become worse in people living with DM, especially if their blood glucose levels are high [7, 8, 9]. The stress of a severe chronic infection may enhance existing insulin resistance and unmask an underlying β-cell deficiency leading to hyperglycemia; it is therefore possiblethat the risk of DM is increased amongpeople with TB, especially in the presenceof other predisposing factors.The prevalence of tuberculosis and diabetes, individually and as coexisting comorbidities, is increasing day by day in this region. There is insufficient research in this area of study,particularly in this region. So, this study was undertaken to determine the concomitant burden of diabetes and tuberculosis among persons receiving TB care in our hospital. We also set out to compare clinical and radiological parameters of patients with TB with and without DM, as well as among patients with TB with previously known and newly detected DM.

Aims and Objectives

Aims:

- To determine the effect of DM on the clinical and radiological manifestations of pulmonary tuberculosis.

Objectives:

- To assess the clinical manifestations in patients of pulmonary tuberculosis with diabetes mellitus
- To assess radiological patterns in patients with concomitant pulmonary tuberculosis and diabetes mellitus.
- To assess the outcome in patients of pulmonary tuberculosis with diabetes mellitus.
- To compare the clinical, radiological presentations, and outcome of the disease treatment between patients with and without diabetes mellitus.

Methodology

Study design and setting

This was a hospital-based prospective study conducted among outpatient and inpatient attendees of the Pulmonology Department at GSL Medical College and General Hospital.

Study Population

All consecutive cases of pulmonary tuberculosis (both smear-positive and smear-negative) presenting to the department during the study period were screened. Cases were classified as follows:

Inclusion criteria

- Patients with pulmonary tuberculosis and concomitant type 2 diabetes mellitus (known diabetics or those diagnosed at presentation).

Exclusion criteria

- Children (age cut-off per institute policy).
- Non-cooperative patients.
- Patients with type 1 diabetes mellitus.
- Patients with documented HIV infection.
- Patients with other infectious lung diseases (non-tuberculous pulmonary infections).

Patients without diabetes served as the control group.

Ethical Considerations and Consent

The present study, titled *"Study of Disease Patterns in Pulmonary Tuberculosis Patients with Co-existing Type 2 Diabetes Mellitus,"* was approved by the Institutional Ethics Committee of GSL Medical College and General Hospital, Rajahmundry (Approval No: 93/IEC/GSL/2013). Written informed consent was obtained from all participants before enrollment. Patient confidentiality was strictly preserved, and all data were utilized exclusively for academic and research purposes. The study adhered to the ethical principles outlined in the Declaration of Helsinki and followed the guidelines of the Indian Council of Medical Research (ICMR) for biomedical research involving human participants.

Data Collection

A structured pro forma was used to record demographic details, clinical history, comorbidities, symptoms, past anti-tuberculosis treatment, and treatment adherence. For all participants, the following investigations were performed at baseline:

- Blood glucose: fasting and postprandial blood glucose.
- Glycated haemoglobin (HbA1c).
- Sputum microscopy for acid-fast bacilli (AFB) (two samples: spot and early morning).
- Chest radiograph (posterior–anterior view) for extent and pattern of pulmonary involvement.

All laboratory procedures and radiographic readings were performed by trained personnel according to departmental standard operating procedures.

Microbiological methods — sputum AFB microscopy

Sputum samples (early morning and spot) were processed in the RNTCP-designated microscopic centre attached to the department. Ziehl–Neelsen staining was performed as follows: selection of the purulent portion, preparation of a thin smear, fixation, application of carbon fuchsin with gentle heating until steaming for 5 minutes, washing, decolorization with 25% sulfuric acid for ~2½ minutes, washing, and counterstaining with 0.1% methylene blue for 10 seconds. Smears were air-dried and examined systematically under oil immersion. AFB were recorded as bright red bacilli against a blue background.

Smear grading (RNTCP):

No. of AFB per field(s)	**Report**
None per 100 oil immersion fields	Negative
1–9 per 100 oil immersion fields	Scanty
10–99 per 100 oil immersion fields	1+
1–10 per oil immersion field	2+
>10 per oil immersion field	3+

Diagnosis and classification (smear-positive vs. smear-negative) followed the RNTCP algorithm current at the time of study.

Radiological assessment

Chest X-rays were evaluated for laterality (unilateral/bilateral), presence or absence of cavitation, and extent of disease. Radiological extent was graded according to the National Tuberculosis Association (USA) classification:

- **Minimal:** Slight to moderate density lesions without cavitation, extent not exceeding the volume of one lung above the second chondrostean junction to the body of the 4th–5th thoracic vertebra.
- **Moderately advanced:** Lesions present in one or both lungs with total extent up to one lung volume or dense confluent lesions limited to one-third lung volume; cavitation (if present), total diameter < 4 cm.

- **Far advanced:** Lesions more extensive than the moderately advanced category.

Radiographs were read by the department radiologist (or designated reader) and findings recorded on the study proforma.

Treatment and diabetic management

Anti-tuberculosis treatment (ATT) was provided under RNTCP guidelines. Drug regimens used in the study were:

- **New (treatment-naïve) cases:**Short-course chemotherapy (SCC) — Intensive phase (2 months): Isoniazid (H), Rifampicin (R), Pyrazinamide (Z), Ethambutol (E) three times weekly; Continuation phase (4 months): Isoniazid and Rifampicin three times weekly.
- **Relapse cases:** 2 months of H, R, E, Z, and Streptomycin (S) followed by 1 month of H, R, Z, E; then 5 months of H, R, E (as per RNTCP retreatment regimen applicable at the time).

Standard drug doses used in the study were: H = 600 mg, R = 450 mg, E = 1200 mg, Z = 1500 mg, S = 750 mg. Every dose during the intensive phase was administered under direct observation; in the continuation phase, supervised dosing was provided at least once weekly per programme practice.

Patients with diabetes mellitus were managed according to standard international guidelines (oral hypoglycaemic agents and/or insulin as clinically indicated). Diabetes therapy was optimized in consultation with the treating physician/endocrinology service and documented in the record.

Treatment outcomes and definitions

Treatment outcomes were recorded as per RNTCP definitions and included: cured, treatment completed, died, failure, defaulted, transferred out, and switched to MDR-TB treatment. Operational definitions used in the study:

- **Cured:** Initially smear-positive patient who completed treatment and had negative sputum smears on at least two occasions, one of which was at the end of treatment.
- **Treatment completed:** Smear-positive patient who completed treatment with negative smears at the end of the intensive phase/at two months in the continuation phase, but had no end-of-treatment smear available; or smear-negative patients who received a full course and did not become smear-positive.
- **Died:** Patient who died from any cause during treatment.
- **Failure:** Any patient who remained or became smear-positive at five months or later after treatment initiation and was not yet on MDR-TB treatment.
- **Defaulted:** Patient who interrupted treatment for more than two consecutive months.
- **Transferred out / Switched to MDR-TB treatment:** As per programme documentation.

Follow-Up and Data Management

Patients were followed according to RNTCP schedules with periodic clinical review, sputum examinations, and radiographs as clinically indicated. All case records and laboratory results

were entered into a pre-designed database. Data quality checks were performed periodically, and source documents were maintained securely.

Statistical Analysis

Data were entered into Microsoft Excel and analysed using IBM SPSS Statistics version 26. Descriptive statistics (means ± SD or medians and interquartile ranges for continuous variables; frequencies and percentages for categorical variables) were computed. Between-group comparisons used the Chi-square test or Fisher's exact test for categorical variables and the independent-samples t-test or Mann–Whitney U test for continuous variables, depending on distribution. Multivariable analysis (binary logistic regression) was performed to identify independent predictors of adverse outcomes where appropriate. A two-tailed p-value < 0.05 was considered statistically significant.

Results

The study cohort (n=120) demonstrated important epidemiological and clinical differences between pulmonary TB patients with and without diabetes. Patients in the diabetic (study) group were older (mean 51.3 ± 8.5 years) than controls (41.4 ± 14.4 years; t = 4.07, p = 0.001), and most diabetics were >40 years with peak incidence in the 41–60 year bands, whereas controls were concentrated under 40 years. A male predominance was seen overall (74.2%), present in both groups. Smoking was common (40% overall; 56.7% when current + ex-smokers combined) and distributed in both arms; smokers in the study group showed a higher proportion of extensive and cavitary disease. Clinically, cough, fever and breathlessness were the predominant symptoms in both groups; presentation delays were common, with the majority seeking care after 2–8 weeks. Glycaemic indices were markedly higher in the study group (mean FBS 189.2 ± 69.1 mg/dL, PPBS 292.9 ± 119.1 mg/dL, HbA1c 7.38 ± 0.9) compared with controls (FBS 90.7 ± 12.8, PPBS 125.9 ± 27.3, HbA1c 5.0 ± 0.3), all differences being highly significant (p ≤ 0.001). Microbiologically, diabetics carried a higher bacillary burden (66.7% with smear ≥2+), while controls more often had low-grade or negative smears. Radiographically, extensive disease (moderate + far advanced) was substantially more frequent among diabetics (86.7% vs 56.7% in controls; p values for extent by age strata 0.046, 0.022 and 0.000 for minimal/moderate/far advanced as reported), and cavitary lesions were more common in diabetics (70.0% vs 33.3%, statistically significant). Lower-zone involvement was also more frequent in diabetics (61.7% vs 46.7%). Within the diabetic group, poor glycemic control (HbA1c >7) correlated with a higher proportion of extensive lesions (93.5% vs 79.3%). Despite greater disease severity in diabetics, treatment success rates (cure/completion) were comparable between groups (study 90.0% vs control 91.7%; p = 0.261), though relapse and default rates warrant ongoing surveillance. Overall, the tables and charts show that diabetes is associated with older age, worse glycemic control, higher sputum bacillary load, and more extensiveand more frequently cavitaryradiographic disease, with smoking and poor glycemic control amplifying these adverse patterns.

Table 1: Mean Age Distribution

Group	N value	Mean age	't' value	Significance
Study	60	51.3 ± 8.5	4.07	0.001*
Control	60	41.4 ± 14.4		

P<0.05* is considered statistically significant

Table 2: Age distribution

Age	Study group	Control group	Total
<40 years	5 (8.33)	31(51.67)	36 (30)
41-50 years	27 (45)	13 (21.67)	40 (33.33)
51-60 years	24 (40)	10 (16.67)	34 (28.33)
>60 years	4 (6.67)	6 (10)	10 (8.33)
Total	60 (100)	60 (100)	120 (100)

Chart 1: Gender distribution

Table 3: Smoking status

	Study group	Control group	Total
Smokers	21(35)	27 (45)	48 (40)
Ex smokers	13 (21.67)	7 (11.67)	20 (16.67)
Non smokers	26 (43.33)	26 (43.33)	52 (43.33)

Chart 2: Symptoms

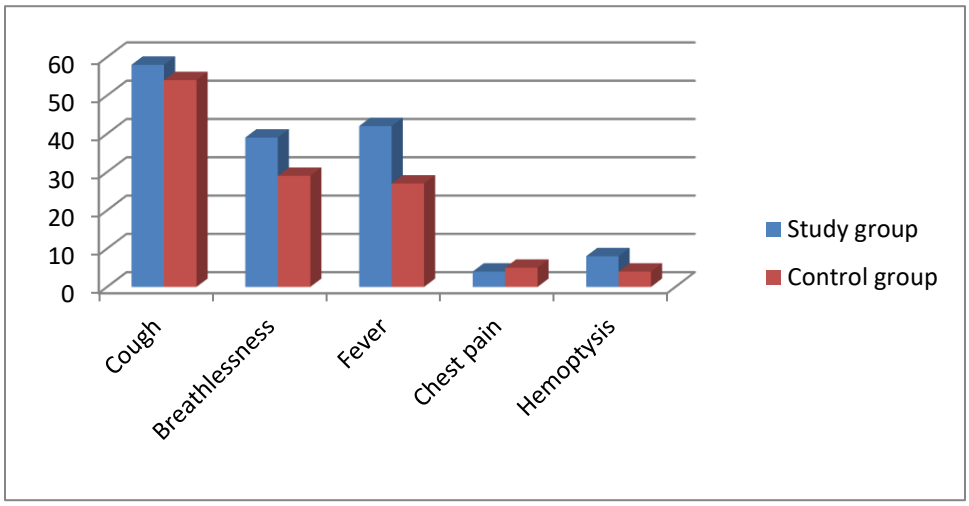

Table 4: Blood sugar and glycosylated hemoglobin levels

	Study group	Control group	't'value	Significance
Mean FBS	189.2 ± 69.09	90.71 ± 12.8	10.54	0.001*
Mean PPBS	292.9 ± 119.1	125.86 ± 27.3	10.17	0.001*
Mean HbA1C	7.38 ± 0.9	5.0 ± 0.3	>15	0.001*

P<0.05* is considered statistically significant

Table 5: Level of blood sugar control in the study group

HbA1C	N	%
<7	29	48.33
>7	31	51.67

Table 6: Distribution of category

	Study	Control	Total
New	43 (71.67)	43 (71.67)	86 (71.67)
Relapse	17 (28.33)	16 (26.67)	33 (27.5)
Treatment after default	0	1(1.67)	1(0.8)
P value	0.597		

P<0.05* is considered statistically significant

Chart 4: Sputum for AFB grading

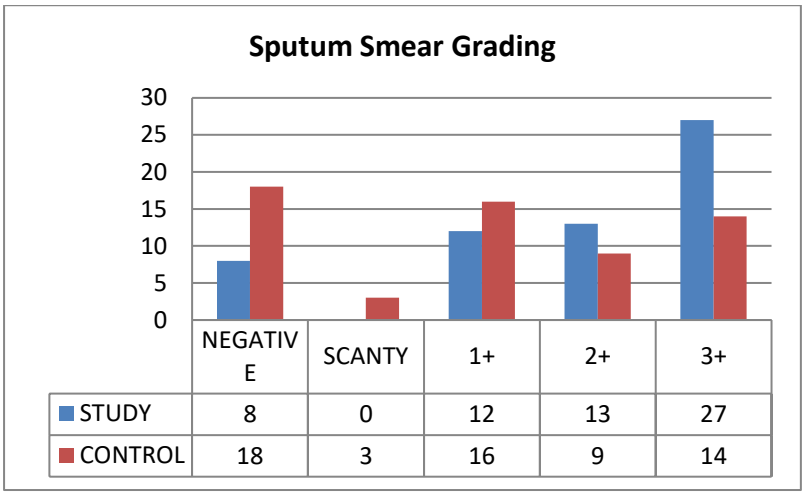

Chart 5: Imaging

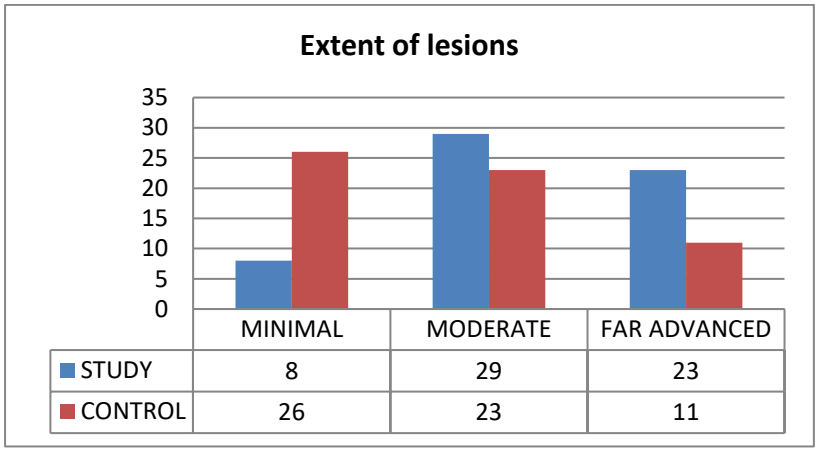

Table 7: Extent of lesions

	Minimal		Moderate		Far advanced	
	Study	**Control**	**Study**	**Control**	**Study**	**Control**
<40 years	1	10	3	14	1	7
41-50 years	5	6	12	4	10	3
51-60 years	1	7	12	3	11	0
>60 years	1	3	2	2	0	1
P value	0.046		0.022		0.000*	

P<0.05* is considered statistically significant

Chart 6: Relation between sugar levels and extent of radiological shadows

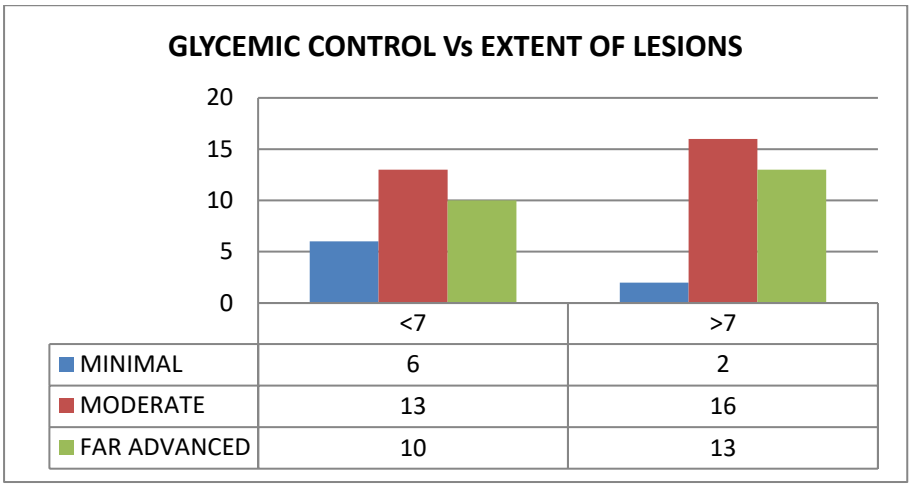

Chart 7: Type of lesions

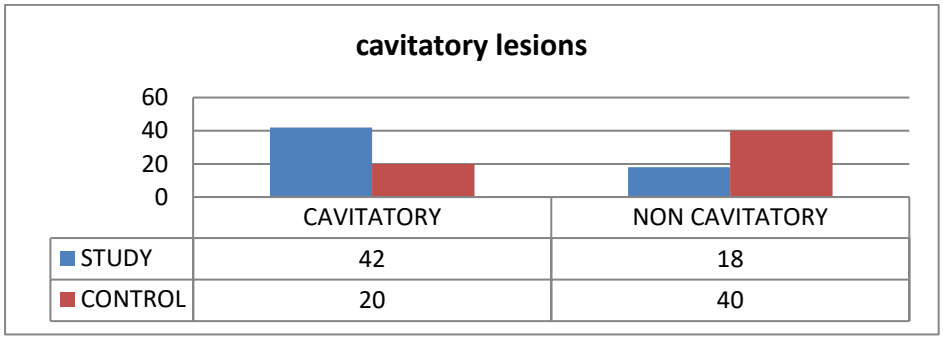

Chart 8: Level of sugar control Vs extent of cavitations

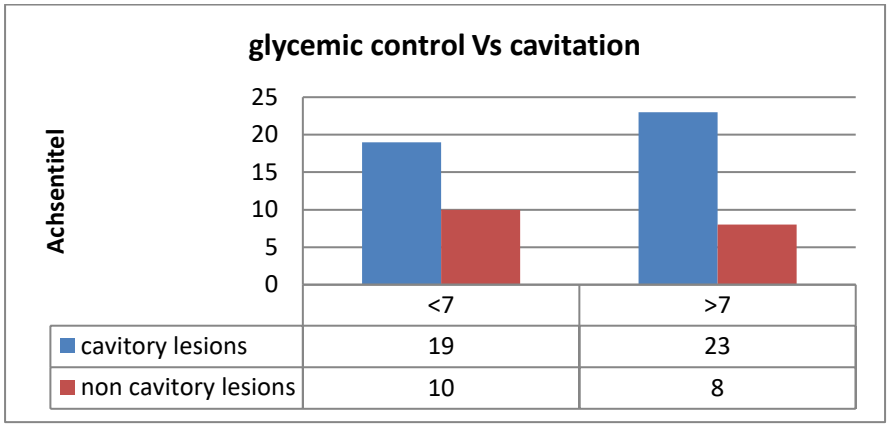

Table 8: Distribution of lesions

	Study	**Control**
Right	13 (21.67)	9 (15)
Left	22 (36.67)	16 (26.67)
Bilateral	24 (40)	35 (58.33)
P value	0.188	

P<0.05* is considered statistically significant

Chart 9: Distribution of lesions according to zones

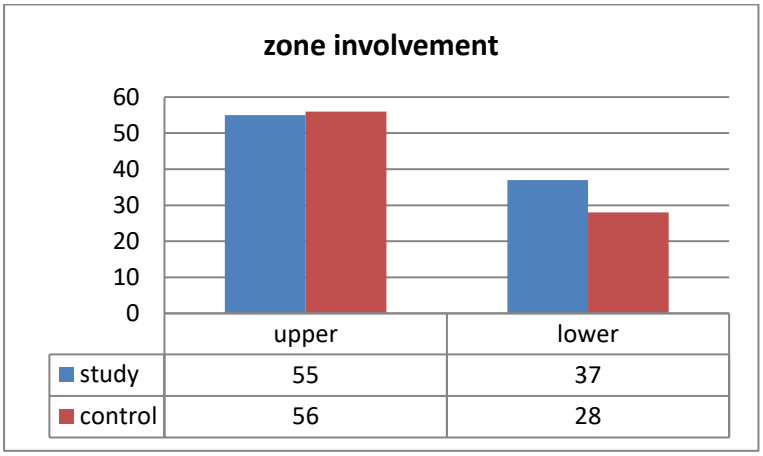

Table 9: Level of Sugar Control Vs Zone Involvement

HbA1C	Upper zone	Lower zone
<7 (n=29)	26 (89.66)	19 (65.51)
>7 (n=31)	29 (93.54)	18 (58.06)
P value	0.701	

P<0.05* is considered statistically significant

Table 10: Outcomes

	Study	Control
Cured	47 (78.33)	39(65)
Completed	7(11.67)	16(26.67)
Defaulted	4 (6.67)	4 (6.67)
Failure	1 (1.67)	0
Death	1 (1.67)	1 (1.67)
P value	0.261	

P<0.05* is considered statistically significant

Table 11: Smoking status Vs extent of lesions

	Study			Control		
	Minimal	**Moderate**	**Far advanced**	**Minimal**	**Moderate**	**Far advanced**
Smokers	2 (9.52)	12 (57.14)	7 (33.33)	13 (48.14)	11 (40.74)	3 (11.11)
Ex smokers	2 (15.38)	3 (23.08)	8 (61.54)	3 (42.86)	3 (42.86)	1 (14.28)
Non smokers	4 (15.38)	14 (53.85)	8 (30.76)	10 (38.46)	9 (34.61)	7 (26.92)

Table 12: Smoking status Vs type of lesions

	Study group		Control group	
	Cavitatory	**Non cavitatory**	**Cavitatory**	**Non cavitatory**
Smokers	17 (80.95)	4 (19.05)	7 (25.93)	20 (74.07)
Ex smokers	9 (69.23)	4 (30.77)	3 (42.86)	4 (57.14)
Non smokers	16 (61.54)	10 (38.46)	10 (38.46)	16 (61.54)

Discussion

A total of one hundred and twenty patients have been evaluated in the present study, out of which sixty are cases having both pulmonary tuberculosis and diabetes mellitus, and sixty are controls having pulmonary tuberculosis without diabetes mellitus. The clinical historyof these patients was noted. Blood sugars and HbA1C (glycosylated hemoglobin) were estimated. Sputum for microscopy was done, and grading was done for the smears according to the number of bacilli present. Chest imaging was done, and the extent of lung lesions was assessed and categorized ascavitatory or non-cavitatory, and the extent was assessed as unilateral or bilateral,and was noted and tabulated for analysis. In the present study, both new and retreatment cases of pulmonary tuberculosis with or without diabetes mellitus were considered. The mean age of the study group was 51.3 ± 8.5, and of the control group was 41.4 ± 14.4 (Table 1).In earlier studies by Jagadish Rawat et al at Uttarakhand in India, the mean age group in patients with coexisting tuberculosis and diabetes was 53.34 ± 14.06, and it was 44.35 ± 18.14 in controls without diabetes mellitus. [56]In a similar study by Viswanathan et al., from Chennai, found that the median age group in the study group was 50 years, whereas in the control group it was 48 years.[57]Mohammad A shaikh from Saudi Arabia observed that the mean age group in tuberculosis patients with diabetes was 48.2 ± 12.0 and without diabetes was 32.3 ± 12.4. [58]In the present study, the number of patients above 40 years of age was 91.67% and the peak incidence was in the age groups of 41-50 and 51- 60 years. 85% of the total cases were in this age group. 51.67% of controls are in the age group of 40.(Table 2)Similar observations are made by Nissapatorn et al., in their comparative study,i.e, 75.3% of cases fall in the age group >45 years.[65]In a review done by Jabbar et al, 82% of patients with concomitant tuberculosis and diabetes were 40-70 years of age, with only 6% below 40 years and 12% above 70 years.[59]Patients in the study group were found to be older than those in the control group. Usually, diabetes mellitus is more common in people aged 40 years. The risk of tuberculosis increases progressively with increased duration of diabetes mellitus. Lower frequencies of DM among TB patients by age > 60 years may simply reflect reduced overall survival among patients with DM.Male preponderance was observed in our overall study. Out of 120 individuals, 89 are males, accounting for 74.17% and 31 are females, accounting for 25.83%. (chart 1)This male predominance was also observed in each of the study and control groups when tabulated separately. In the study

group, 73.33% are males (n=44) and 26.67% are females (n=16). In the control group, 74.17% are males (n=46) and 25.83% are females (n=14).The male-to-female ratio in the study group was 2.75, and in the control group was 3.28.(chart 1). Similar observations were made in the earlier studies as well.

In the present study, the male-to-female ratio was found to be 2.75:1 among patients with tuberculosis and diabetes, and 3.28:1 among those with tuberculosis without diabetes. These findings suggest a higher proportion of males affected in both groups, with the disparity more pronounced in non-diabetic tuberculosis patients.

When compared with published literature, Mohammad et al. reported a ratio of **3.1:1** in TB with diabetes and **1.5:1** in TB without diabetes, indicating relatively fewer males in the non-diabetic group. Jagdish Rawat et al. observed a ratio of **1.16:1** for TB with diabetes and **2.05:1** for TB without diabetes, again showing male predominance in both groups but with different magnitudes. Similarly, Nissapatorn et al. reported ratios of **2.2:1** and **1.9:1** for TB with and without diabetes, respectively, consistent with an overall male preponderance.

Taken together, these studies—including the present one—demonstrate that male patients are more commonly affected by tuberculosis irrespective of diabetic status, although the degree of male predominance varies across different cohorts.The higher prevalence of DM among men than in women might be a cumulative effect of other risk factors such as smoking, tobacco use, and alcohol consumption, which impact both TB and DM.Anotherpossible explanation for this male preponderance may be attributable to males usually having more social, cultural, and outdoor activities than women, which predispose them to a higher transmission rate of tuberculosis. Lack of access to health care facilities by women may be the reason for underdiagnosis of the disease inthe female population.Smokers are more commonly associated with tuberculosis than non-smokers. 56.67% of our study individuals are smokers, either current or ex-smokers, compared to 43.33% non-smokers. (Table 3) This association is maintained even in the study and control groups. Smokers are more than non-smokers in both the study and control groups.Smoking as a common risk factor for tuberculosis and diabetes has been mentioned in earlier studies. Smoking increases the incidence of new cases[67]and mortality from tuberculosis[68].A cohort study of 97,244 individuals followed up for 5.5 years in Mumbai9 found that smoking, particularly bidi smoking, more than doubles the risk of death fromtuberculosis in men [69]In the study group, 35% are smokers, 21.67% are ex-smokers, and 43.33% are non-smokers. In the control group 45% are smokers, 11.67% are ex-smokers, and 43.33% are non-smokers. (Table 3)There was statistically no difference between diabetic and non-diabetic groups with respect to smoking in this study.In a study done by Tatar et al, they have noticed that smoking was found at a higher rate in non-diabetics than in diabetics. In their study, 30.8% diabetics are smokers compared to 50% smokers in non-diabetics.[63]

Disease presentation

Pulmonary tuberculosis patients commonly presentwith complaints of cough, fever, shortness of breath, loss of weight and appetite, and occasionally with hemoptysis. In this study, a detailed history of the patient's symptoms was noted and tabulated. The predominant symptoms in the study group were cough (96.67%), followed by a history of fever (70%) and breathlessness (65%). Other symptoms noted are hemoptysis (13.33%) and chest pain (6.67%)(chart 2)In a study done in Pakistan, among diabetic patients with tuberculosis most common symptoms noted were fever (75%), cough (56%) anddyspnea (13%), hemoptysis (17%) and loss of weight (11%) being the associated symptoms.[60]On comparing the symptom patterns of the patients from the present study with the previously mentioned studies, there is no significant difference in the presentation of symptoms in patients, except for minor variations between groups. The presence of diabetes mellitus does not seem to modify the clinical presentation of pulmonary tuberculosis. Fever with cough and sputum remain the most common presenting symptoms. Observations in this study were consistent with the observations of two retrospective studies conducted by Bacakoğlu F et al(70) and Maâlej S et al (71), respectively, who concluded that the presence of diabetes mellitus would not affect patients' symptoms. Recently, in a major prospective clinical trial, patients with DM and TB were found to have more symptoms than non-diabeticpatients. [50]It was observed that 75% of cases presented to the hospital within 2-8 weeks. (chart 3)This may be due to a lack of health consciousness & proper education. The majority of patients do not turn up to the hospital unless the lesion sufficiently advances, compelling them to seek medical advice.Mean FBS value in diabetics with tuberculosis is 189 ± 69.09, whereas in non-diabetics, it is 90.71 ± 12.8. Mean PPBS value is 292.9 ± 119.1 and 125.86 ± 27.3 among the study and control group, respectively (Table 4).Diabetes has been identified as a condition that may cause previous TB patients or people with latent TB to reactivate the infection. Moreover, the risk of TB increases with the severity of diabetes. Tatar D et al in their study observed that elevated levels of ketone bodies in the blood because of diabetes will provide a suitable condition for the reactivation of TB[63]. The majority of cases have higher glucose levels at the time of admission. Ketoacidosis is noted in some cases. According to Amrit Guptan and Ashok Shah, the diabetics who develop pulmonary tuberculosis have higher blood sugar levels and develop complications like coma and diabetic microangiopathies[72]. Zakeya Abdulbaqi Bukhary, in his review, quoted that active TB may worsen blood sugar control with increasedrisk of developing sepsis in diabetic patients[73]. There are similarnumbers of new cases seen in the study and control groups. Even though the relapses in the study group are more compared to the control group, their association is not statistically significant. 71.67% of cases in the study group were new cases, whereas 28.33% of subjects were re-treatment cases. In the control group, 71.67% were new cases, 26.67% were retreatment cases, and 1.67% were treatment after default. (Table 6)V Nissapatorn et al, 2005 interpreted similar results in their study in 1651 patients, that there is no statistical difference in diabetic and non-diabetic patients with tuberculosis regarding categorization of

cases as new and relapse. [65]Viswanathan AA et al also found a similar presentation in their study among 209 patients in Mumbai, India.[57]S. Kumpatla et al, 2013, in their screening study in 7083 diabetic patients, observed that among patients who were found to have tuberculosis coupled with diabetes mellitus 90% are new cases and 10% are retreatment cases.[62]. M. V. Jali et al conducted a cross-sectional study in South India and observed that 79.8 % are new cases and 17.9% are retreatment cases among diabetics with tuberculosis.[61]Ogbera AO et al in their observational study in 4000 patients compared clinical and biochemical parameters in tuberculosis patients and noticed that the majority of cases of recurrent TB were seen in newly diagnosed DM compared to known diabetics, indicating that perhaps the onset of hyperglycemia and consequent lowering of immune response reactivated TB disease.[5]Majority of cases (85%) are among the age group 41 – 60 years, while the majority of controls (51.67%) are <40 years old. This correlates well with the age distribution in the respective groups of our study. Incidence of relapses increased with advancing age; more relapses are seen in patients aged> 50 years. This is explained by the duration of diabetes mellitus, with which the incidence and recurrence of tuberculosis are increased progressively.

Diagnostic microscopy

In the study group,66.67% of caseshave smear grading ≥ 2+. 61.67% of controls have smears ≤1+ and negative smears. (chart 4) It implies that high bacillary load is seen in diabetics compared to non-diabetics. This observation is also in agreement with the observations of many earlier authors. Zakeya Abdulbaqi Bukhary, in his review, mentioned that Sputum microscopic examination results are more frequently positive among diabetic patients and associated with positive culture for Tuberculosis two months after starting the anti-TB treatment than in non-diabetic individuals.[73]Rani Balasubramanian et al, in their prospective study among 100 tuberculosis patients with diabetes, found that 89% of their cases had smear grading ≥ 2+.[74]Chen-yuan Chiang et al observed similar results in their study,i.e, sputum positivity is more in diabetics compared to non-diabetics. 67.3% of their study population is sputum positive compared to 48.9% in the control population. They observed more smear negativity amongnon-diabeticsas compared to diabetics (25.5% in diabetics vs 42.7% in non-diabetics)[75]Similar observation was made in this study also. The diabetic group has more smear-negative pulmonary tuberculosis cases compared to the diabetic group. The percentages are 13.33% in the study group and 21.67% in the control group.Some authors reported a higher frequency of negative sputum smears among TB DM cases [50],while others found DM as an independent risk factor for numerous acid-fast bacilli on the sputum smear examination[63], and some showed no association between DM and patients' bacteriology results [70]. These conflicting results might be due to variations in the glycemic control status of the study subjects at the time of examination.[76]

Radiographic manifestations

Chest X-ray is graded as minimal, moderate, and far advanced based on lesions in tuberculosis. Extensive lesions (moderate and far advanced) are far more common in the diabetic group (86.66%) compared to the diabetic group (56.66%).(chart 5) They are particularly increasing with age upto 60 years; later, the incidence of moderate and advanced lesions decreased after 60 years of age. (Table 7). Chen-Yuan Chiang et al in a study among 1209 culture-positive tuberculosis patients, found that TB patients with DM were significantly more likely to have opacity over lower lung fields and extensive parenchymal lesions (moderately or far advanced) compared to those without DM. In their study, 70.9% of diabetics have extensive lesions in contrast to 62.8% in non-diabetics. [75]In an Indonesian study done by Bachti Alisjahbana, similar observations are made,i.e,52.6% of diabetics in their study had severe chest radiographic abnormalities compared to 50.9% of non-diabetics. [50]In the present study, it has also been observed that patients with uncontrolled diabetes with high HbA1C >7 had more extensive lesions (93.54%) than those with controlled sugar levels (79.3%) within the study group. (chart 6). The association between diabetes control level and clinical manifestations was mentioned by two studies so far, Chen-Yuan et al and Park et al in their respective studies. In a similar study of the association of glycemic control and extension of pulmonary lesions by Chen-Yuan Chiang et al, their results were consistent with those of the present study, further ascertaining the fact that parenchymal lesions of the lung are far advanced in patients of tuberculosis with poorly controlled sugar levels. The proportion of patients with extensive (moderately advanced or far advanced) pulmonary parenchymal lesions was 62.7% among those without DM, 58.5% in those with DM with HbA1C 7, 74.4% with HbA1C 7–9, and 76.8% with HbA1C 9.[75]Similar observation was made by Park SW et al those uncontrolled diabetics had more cavitary lesions (p=0.008) and higher positive smear rates compared with non-diabetics. [76]

Our study is consistent with the earlier studies.

The relation between smoking, diabetes and extent of radiological imagingwas observed and noted that higher percentage of smokers have extensive lesions and cavitatory lesions (particularly more pronounced in diabetics) than non smokers.

In study group 90.47% of smokers have extensive lesions compared to 84.61% of non smokers. In control group 51.85% of smokers and 61.53% of non smokers have extensive lesions. (table 11)

It was noted that 80.95% of smokers in study group have cavitatory lesions and only 25.93% of smokers in control group have cavitations. (table 12)

Association between smoking and tuberculosis was established earlier by many studies. Jayadeep Patra and his colleagues conducted a meta analysis of 72,684 individuals by

analyzing 14 national studies in 14 high TB burden countries to assess the association between tobacco smoking, alcohol drinking, diabetes, low body mass index and the risk of self-reported symptoms of active BMI are significant individual risk factors but in combination areassociated with triple or quadruple the risk of development of recent active TB. (77).The risk of tuberculosis and mortality from tuberculosis was reduced after smoking cessation. This correlation was mentioned by Chi-Pang Wen[78], Khan AH[79].Radiological lesions were classified as unilateral and bilateral and it was noticed that unilateral involvement is more common than bilateral involvement. The percentage of individuals with unilateral lung lesions on x-ray was 60% and those with bilateral pulmonary lesions were 40%. In the control group, the percentage of patients with unilateral to bilateral pulmonary lesions is 41.67% and 58.33% respectively. (Table 8). Jabbar et al observed more unilateral involvement than bilateral in tubercular diabetics, which was similar to our study. In their observation among 77 tubercular diabetics,[41] (53%) had unilateral lesions while 36 individuals had bilateral lesions, accounting for 47%.[59].Qazi M A et al also observed a similar difference in their study. 82% of individuals have unilateral involvement compared to 17% having bilateral involvement. [64]Localization of the radiological lesions was interpreted using two different classifications. First, commonly, the upper-mid and lower zones are separated by a horizontal line passing at the level of the second and fourth ribs, respectively. The lower lung field (LLF) was separately defined as the area below an imaginary line traced across the hila and including the parahilar regions on a standard posteroanterior chest roentgenogram. This was to allow comparisons to be made with previous reports that used the same definition. The lower lung field included the middle lobe and the lingula in addition to the lower lobes. [80]**In the present study, involvement of upper zones was almost similar in both study and control groups. It is 91.67% in the study and 93.33% in the control groups. Lower zone involvement is more in the study group compared to the control group. 61.67% of diabetics have lower zone involvement, whereas only 46.67% of non-diabetics have lower zone involvement. (chart 9)**

Similar observations (lower zones are more frequently involved in diabetics than non-diabetics) were made earlier by Qazi et al, Chen Yuan Chan et al, Rawat et al, Perez–Guzman et al, and several other studies. [64, 75, 56, 81]

Response to treatment

Out of 120 individuals subjected to study, 8 are defaulters, 4 are in the study group, and 4 are in the control group.Two patients died during the course of treatment, one in the study and the other in the control group. Treatment adherence was estimated to be 91.67% in both study and control groups. Microscopic examination of sputum samples was performed at the end of the treatmentfor all the live subjects; only one in the study group had positive results (failure). The treatment success rate was estimated to be 90% in the study group and 91.67% in the control group. Cure rate among new smear-positive cases in the study group was 91.4% and 96.67% in the control group. The default rate in our study was a total of 8 patients,

4 in each of the control and study groups. The percentage of defaulters was 6.67% in both study and control groups.(Table 10). Bachti Alisjahbana et al in a study of "the effect of type 2 diabetes mellitus on the presentation and treatment response of pulmonary tuberculosis," comprising 94 patients with tuberculosis and diabetes and 540 cases without diabetes, made similar conclusions in which the cure rate among the diabetics and non-diabetics with tuberculosis were 74.5% and 80.6% respectively, with 2 deaths overall.This was similar to our study, implying that the cure rate will be similar in both groups, provided strict glycemic control and adherence to the treatment.[50]

This study has shown that the RNTCP regimen was adequate in type 2 diabetes mellitus patients, as the treatment success rate was 89.97% (including 11.67% of smear-negative patients who completed the treatment according to RNTCP guidelines). Similar observation was made by Rani Balasubramanian et al 2007 in their study to evaluate the effect of intermittent regimen in new pulmonary tuberculosis cases with diabetes mellitus. 94% of their patients were cured, and 4% relapsed. They also quoted that the majority of their patients responded to anti-tubercular treatment despite poor diabetic control.[74]

Limitations

The sample size in this study was too small to come to a definite conclusion. A large-scale population-based study is required to know the exact influence of diabetes on the disease process and characteristics of tuberculosis. The study group and control group were not age-matched because of the small sample size. To avoid the sample selection bias, control group age matching was not tried. Drug sensitivity to anti-tubercular drugs could not be compared in this study, as sputum culture and sensitivity were not done.

Conclusion:

There are no significant differences in presentation of the disease between diabetics and non-diabetics. But the extent of the disease is more among diabetics with tuberculosis in comparison to their non diabetic counterparts. The bacillary load in diabetics is also higher in comparison to non-diabetic tuberculosis cases. If the diabetic patients presenting with tuberculosis are not properly managed with adequate anti diabetic treatment, there are chances of the development of more cavitated and extensive tubercular lesions, and also they may land in ATT failure and consequently multi-drug resistant tuberculosis. However, with good glycemic control, the cure rate will be as good as the cure rate seen in non-diabetics. A population-based randomized control trial will be more useful to assess the detail effects of diabetes and glycemic state of the patients on the clinical presentation, disease severity and outcome of tuberculosis.

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