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Clinical profile of patients of pulmonary tuberculosis with diabetes mellitus attending tertiary care centre of Western India

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ABSTRACT

Background: Tuberculosis (TB) is one of the major infectious cause of mortality. Diabetes mellitus (DM) among TB patients affects clinical improvement, sputum conversion and mortality by various immunogenic mechanisms. Thus, clinical profile and radiological findings helps for better understanding of its correlation.
Materials and Methods: It was single centre prospective study conducted for duration of 2 years. Seven hundred eighty eight TB patients screened for DM from which 95 patients following inclusion criteria considered for the study. The diagnosis of TB among these patients based on the clinical presentations and programmatic guidelines. Diagnosis of diabetes as per diagnostic criteria of American diabetes association.
Results: Of 95 patients, 74 were male and 21 were female; majority belonged to adult and middle age group. Cough was most common presentation. Right side of lung was commonly involved, while lower zones commonly affected. Consolidation seen in majority of patients on radiological evaluation. 75.8% patients declared cured while, 3.2% patients died during treatment.
Conclusion: Association of TB-DM is more common in males. Proper glycemic control helps in overall improvement and clinical outcome of patients.

1. Introduction

Tuberculosis (TB) is infectious disease and caused by Mycobacterium tuberculosis.[1] TB remains one of the major cause of mortality among communicable diseases globally causing major public health issue.[2] As per Global Tuberculosis report 2023, 7.5 million people diagnosed with tuberculosis worldwide in 2022. India is highest TB burden country in the world, nearly 27% cases of TB are diagnosed in India.[1] The lung is most commonly affected organ followed by cervical lymph nodes.[2]

Although there is decline in mortality due to TB over the period of time, it still causes a major public health problem due to increase in overall incidence of TB, increased emergence of drug resistance and presence of risk factors (undernutrition, HIV co-infection, alcoholism, smoking, diabetes).[3–6] There is gradual rise in prevalence of diabetes among Indian population. There is an increase in DALYs and mortality due to diabetes.[6] Overall prevalence of diabetes is 11.4%, affecting more 100 million peoples in India. The incidence of diabetes is increasing gradually in India as well as globally.[7]

Diabetic patients are associated with two-to-four fold increased risk of development of TB. It also increases the risk of mortality among TB patients.[8–10] Hyperglycemia suppresses the counts of total T lymphocytes, CD8+ T lymphocytes and Natural killer (NK) cells causing downregulation of immune responses. It leads to cavity formation, more bacterial load and higher severity in TB patients. Diabetes also contributes to increase in

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drug resistance to anti-tubercular treatment among TB patients.[9,11] As there is increased prevalence of TB as well as diabetes in India, it is a matter of concern in India and other low- to middle- income countries. As there is bi-directional relationship between TB and diabetes, screening for diabetes done in all TB patients in India under programmatic guidelines.[12]

In current study, we aimed to determine the clinical and radiological profile in pulmonary tuberculosis patients and relationship between diabetes and TB treatment outcomes.

2. Materials and Methods

After obtaining the approval from the institutional ethical committee of GMERS medical college, Sola, Ahmedabad, this single center prospective observational study was carried out by the Department of Respiratory Medicine at GMERS Medical College and Hospital, Sola, Ahmedabad. Patients diagnosed with tuberculosis between June 2019 and May 2021 considered for the study. Total 788 patients diagnosed for TB in the duration of 2 years. The diagnosis of TB among these patients based on the clinical presentations, radiographic features, and presence of acid-fast bacilli (AFB) or positive molecular testing for TB or histological confirmation. From these 788 patients, 95 patients following inclusion criteria were included for the study. All the participating patients were informed about study and after explaining written informed consent was taken in their native language.

2.1. Inclusion criteria

1. New microbiologically confirmed cases for pulmonary tuberculosis by sputum smear microscopy.
2. Patients newly diagnosed for diabetes or already diagnosed with diabetes.
3. Patients willing to participate in the study.

2.2. Exclusion criteria

1. Clinico-radiologically diagnosed patients of pulmonary TB.
2. Patients with only extra pulmonary TB.
3. Patients refused to give consent.

Socio-demogarphic details, clinical presentations, associated presence of diabetes, past history and addiction of participating patients were collected. Chest radiograph, sputum smear microscopy and fasting and postprandial blood glucose levels were performed. The bacteriological load in sputum, molecular diagnostic method for detection of drug resistance were also noted. Patients were followed up until the end of treatment and treatment outcome was noted.

For diagnostic purpose, fluorescence microscopy was done for sputum smear microscopic examination. Bacteriological load in sputum graded as shown in Table 1. For diagnosis of TB among suspected cases, guidelines by National Tuberculosis Elimination Programme (NTEP) was followed.[13] Cartridge based nucleic acid amplification test (CB-NAAT) performed for diagnosis of rifampicin resistance. First line- and second line- line probe assay (LPA) performed for diagnosis of isoniazid and rifampicin resistance and to detection of resistance to fluoroquinolone and aminoglycosides respectively. Patient diagnosed for diabetes according to diagnostic criteria of American diabetes association.[14]

2.3. Definitions:[15]

1. Drug sensitive tuberculosis (DS TB): Patients showing sensitivity to all four first-line anti tubercular drugs.
2. Isoniazid-resistant tuberculosis (Hr-TB): Patients having resistance to Isoniazid with confirmed susceptibility to Rifampicin.
3. Multidrug resistant tuberculosis (MDR-TB): Patients having resistance to Isoniazid and Rifampicin, with or without resistance to other first-line anti-tubercular drugs.
4. Extensive drug resistant tuberculosis (XDR-TB): A MDR-TB patients having additional resistance to any of the fluoroquinolones and any one of the second-line injectable drugs (Amikacin, kanamycin or capreomycin).

All the data collected and analyzed using Microsoft excel 2016. The categorical variables were expressed as frequency and percentage and quantitative data were presented as mean ±standard deviation (SD).

3. Results

From 95 patients, 74 patients were male, while 21 patients were female with male-to-female ratio was 3.5:1. Among these 95 patients, 12 patients newly diagnosed for diabetes mellitus during diagnosis of TB, while 83 tuberculosis patients already diagnosed for diabetes mellitus. Forty-seven patients had previous history of tuberculosis at least once during their lifetime.

Patients aged 18 years and more were included for the study. Mean age was 45.1 ±14.5 years. Majority of patients belonged to adult (26 – 44 years) and middle age (45 – 59 years) group. Ten patients aged 25 years or less. Between age group of 26 years to 44 years and 45 years to 59 years of age, 35 patients seen in each group. Fifteen patients belonged to older age (≥ 60 years and more).

Tuberculosis patients having diabetes most commonly presented with cough. Eighty (84.2%) patients presented with cough with or without expectorations. It followed by fever, which was seen in 60 (63.2%) patients. Nearly half of the patients presented with weight loss. Anorexia was presenting complain in 40 (42.1%) patients. Hemoptysis and

dyspnea on exertion was seen in 29 (30.5%) and 10 (10.5%) patients respectively. Other presenting complaints were chest pain (9.4%), generalized weakness (7.3%), headache (6.3%), diarrhea (5.3%) nausea and abdominal pain (3.1%) among these patients. Fifty-nine (62.1%) patients had at least one presenting symptom for 3 months and less.

Sputum smear was examined by fluorescence microscopy for detection of acid-fast bacilli. Sputum graded as scanty, 1+, 2+ and 3+. Majority patients (40 patients; 42.2%) had 3+ sputum grading. Sputum smear examination of 16 (16.8%) patients had scanty, 20 patients (21%) had 1+ and 19 (20%) patients had 2+ grading.

Chest radiograph was done in all the patients. Right side of lung was involved in 46 (48.4%) patients; left sided lung field was involved in 23 (24.2%) patients, while 26 (27.4%) patients had bilateral lung involvement. Lower zone involvement seen in majority of tuberculosis patients having diabetes. More than half of the patients (49 patients) had lower zone involvement. Upper zone was involved in 17 (17.8%) patients, upper and mid zone was involved in only 1 (1.1%) patient. Mid zone was involved in three (3.2%) patients, while mid zone and lower zone was involved in 25 (26.3%) patients. Consolidation, infiltrations, and cavity found on chest radiograph among majority of cases. Consolidation was present in 40 (42.1%) patients, infiltrative changes were found in 38 (40%) patients. Cavity seen in 16 (16.8%) patients, while cavity with air fluid level was seen among 10 (10.5%) patients. Each pleural effusion and pneumothorax was found in 2 (2.1%) patients.

Eighty-one (85.3%) patients treated for drug sensitive TB and put on category one anti tubercular treatment as per programmatic guidelines. Two (2.2%) patients had Hr-TB. Nine (9.5%) patients diagnosed as MDR TB, 1 (1.1%) patient had XDR-TB, while two (2.2%) patients diagnosed with non-tuberculous mycobacterium tuberculosis.

All the patients followed up until assignment of treatment outcome. Seventy-two (75.8%) patients were declared cured after end of the treatment. Treatment completed in 12 (12.6%) patients, 3 patients died during the course of treatment. Four patients were patients were lost to follow up. Among 4 patients there was treatment failure.

Table 1: Sputum grading for fluorescence microscopy

S.No.	Microscopy used	Grading	Result
1	Zero AFB / 1 length	Negative	Negative
2	1-19 AFB/ 1 length	Scanty	Positive
3	20-199 AFB/ 1 length	1+	Positive
4	5-50 AFB/ 1 field on average	2+	Positive
5	50 AFB/ 1 field on average	3+	Positive

Table 2: Epidemiological and clinical characteristics of study population

Patients characteristics	No. of patients (in percentage)
Age group	
18 - 25 (Young adult)	10
26 - 44 (Adult)	35
45 - 59 (Middle age)	35
≥ 60 (Old age)	15
Gender distribution	
Male	74
Female	21
Symptoms	
Cough	80 (84.2)
Fever	60 (63.2)
Weight loss	47 (49.5)
Anorexia	40 (42.1)
Hemoptysis	29 (30.5)
Dyspnea	10 (10.5)
Chest pain	9 (9.4)
Weakness	7 (7.3)
Headache	6 (6.3)
Diarrhea	5 (5.3)
Abdominal pain, nausea, vomiting	3 (3.1)
Diagnosis	
New	12 (12.6)
Already diagnosed	83 (87.4

Table 3: Radio-microbiological profile of study population.

Radio-microbiological characteristics	No. of patients (in Percentage)
Sputum microscopy	
Scanty	16 (16.8)
+1	20 (21)
+2	19 (19.95)
+3	40 (42)
Lung field distribution	
Right	46 (48.3)
Left	23 (24.15)
Bilateral	26 (27.3)
Radiological field distribution	
Upper only	17 (17.85)
Upper and middle zone	1 (1.05)
Middle only	4 (4.2)
Middle and lower zone	24 (25.2)
Lower only	50 (52.5)
Radiological findings	
Consolidation	40 (42)
Infiltrations	38 (39.9)
Cavity	16 (16.8)
Cavity With air fluid Level	10 (10.5)
Effusion	2 (2.1)
Pneumothorax	2 (2.1)

4. Discussion

From global incidence of TB, more than $1/4^{th}$ of TB cases occur in India.[1] India is also facing epidemic of diabetes mellitus, with having 2^{nd} largest diabetes population.[16] 1 out of 5-tuberculosis patient suffers from diabetes.[12] Although the incidence of tuberculosis is decreasing gradually, it is still considerably higher than the National Strategic Plan 2017-2025.[17] In TB patients poor glycemic control may lead to unfavorable treatment outcomes.[18,19]

Diabetes in TB patients was more common among males compared to females. Male preponderance was seen in studies done in other parts of India,[20,21] Brazil[22] and Thailand.[23] Contrast to above finding female preponderance found in study done in Iran.[24] As the males are more involved in outdoor works, they may be at higher risk of development of TB.[20] Various studies have found that diabetes is more common among males.[25] These may be the possible reasons for male predominance. Patients aged between 41 years to 60 years were more affected. Similar findings present in other Indian studies[20,21] and study done in Brazil by Beraldo et al.,[22] But in study from Thailand it was found in patients aged > 60 years.[23]

In patients with TB-DM association, cough was most common presenting feature, followed by fever and weight loss. Cough was commonest presenting feature in study done in Tamil Nadu,[21] in study by Buasroung et al. as well as in study done in Iran by Baghaei et al.[23,24] Other common presenting features were anorexia, hemoptysis and dyspnea, which ranged from 63.8% to 85%, 8.7% to 27.7% and 16.7% to 49% respectively.[21,23,24,26] In our study, 42.1% patients had anorexia, 30.5% had hemoptysis and 10.5% patients had dyspnea.

Right side of lung affected more in patients of our study, while in other Indian study both lungs were affected more.[20,21] Lower zone was affected more than the upper and mod zone. More than 50% patients had lower zone involvement, while other studies comparing radiological involvement has shown upper lobe predominance in TB-DM patients.[27,28] Consolidation was common radiological finding in TB-DM patients. It was found is more than 40% of cases. It was comparable with study done in Thailand by Buasroung et al. and other studies.[23,27,28] Other radiological findings were cavity and infiltrative changes. Each pleural effusion and pneumothorax seen in around 2.1% cases.

More than 75% patients declared cured in our study. In other Indian study 1/4th of patients and in Malaysian study 60.89% patients were declared cured.[21,29] 3.2% patients died during the course of the treatment. While mortality in study done by George et al. was 15%, by Buasroung et al. in Thailand was 14.3% and by Ahmad et al. in Malaysia was 10.57%.[21,23,29]

During our single centre prospective study the strength of the study was, we collected various data, such as thorough assessment of presenting clinical features, microbiological data, hematological data, histopathology and radiological imaging to confirm our diagnosis of TB and DM in our patients. There were few limitations of our study as well. First, although our study show better treatment outcomes in TB-DM patients and patient followed up till declaration of treatment outcome, vigilant follow up of these patients require for detection of recurrence of TB among diabetic patients after treatment completion. Second, the comparison of DM patients with non-DM patient was not done, which could helped further for better understanding differences between both groups. Third, in our study sample size was 95, prospective multi-centre study require further for enrollment of more patients and getting better understanding of TB-DM correlation.

5. Conclusion

The study has shown that in high prevalence countries DM is common association in TB patients. It is more common in males and affects working age population. Patients with DM have more radiological findings of consolidation and cavity. As the poor glycemic control is one of the risk factor for delay in sputum conversion and increased mortality, TB patients screened routinely for detection of DM and for keeping glycemic control during the course of the treatment.

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7. Conflicts of Interest

The authors declare no conflicts interest.

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