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Clinical spectrum and associated comorbidities in Tuberculosis patients: A Hospital-based study in Odisha, India

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Abstract

Background

Tuberculosis (TB) is a common infectious disease frequently associated with comorbidities. However, data on tuberculosis and comorbidities from northeast India are scarce. The study's goal is to look at the clinical spectrum of tuberculosis and the number of comorbidities in TB patients.

Methods

The present study was a prospective hospital-based observational study of all TB patients selected by consecutive sampling. The data was collected for socio-demographic characteristics and clinical data. The data were analyzed using statistical software SPSS v. 17.0, and a p-value of 0.05 was considered significant.

Results

The mean age of the 223 patients was 41.0517.04 years, with a male: female ratio of 4.18:1. Pulmonary tuberculosis (PTB) was found in 43.49 percent of patients, extrapulmonary tuberculosis (EPTB) in 52.01 percent, and disseminated TB in 4.48 percent. The most common symptomatic presentation was Fever (61.43%), followed by cough (54.26%) and breathlessness (32.73%). Of the 97 patients with PTB and ten with disseminated TB, making a total of 107 patients, 56 (67.4%) were Sputum positive. Pleural effusion (53.44 percent) was the most common type of EPTB among 116 patients, followed by central nervous system (CNS) tuberculosis (26.72 percent) and abdominal tuberculosis (8.62 percent). Diabetes mellitus (26.45 percent) and hypertension (17.48 percent) were the most common comorbidities, affecting 53.36

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percent of the patients. PTB had significantly more comorbid conditions than EPTB (66 of 107 vs. 53 of 116, p<0.05). PTB had significantly higher mean glycated haemoglobin (HbA1c) than EPTB (8.71± 2.05 vs. 7.57 ± 0.28, p0.05).

Conclusion
Comorbidities, particularly diabetes, were present in half of the patients, with PTB patients having significantly worse glycemic control than EPTB patients.

Keywords: pulmonary tuberculosis, extrapulmonary tuberculosis, comorbidity, diabetes mellitus, anti-tubercular therapy

Introduction

With an estimated 28 million cases of tuberculosis (TB) in 2015, India accounts for 25 percent of the global TB burden.(1) Approximately 40% of the Indian population is infected with tuberculosis, with the majority having a latent infection that can potentially progress to active disease.(2) While extrapulmonary tuberculosis (EPTB) accounts for a quarter of global TB incidence, the overall literature on the spectrum of extrapulmonary tuberculosis (EPTB) is limited.(3) Many countries with a high Tuberculosis burden also have a high burden of medical comorbidities. These include diseases such as liver disease, chronic kidney disease (CKD), diabetes mellitus (DM), cardiovascular disease, connective tissue disorders, lung disease like chronic obstructive pulmonary disease, and others.(4) These medical comorbidities interact with tuberculosis on multiple levels. On the one hand, these may aggravate the tubercular process, causing it to progress from latent to active or even disseminated forms, pose diagnostic challenges, and result in ineffective treatment. On the other hand, these comorbidities may limit the use of some potent anti-tubercular drugs.(4) Furthermore, TB can exacerbate comorbidities or obstruct diagnosis and/or optimal management of such comorbidities. Published research on TB and any associated comorbidities with TB from the Eastern states of India are limited, particularly in Odisha. With this context in mind, the purpose of this study was to investigate the clinical spectrum of tuberculosis and the association of these comorbidities in TB patients attending a tertiary care centre in eastern India that serves the majority of the state's patients.

Materials And Methods

The present study is a hospital-based prospective observational study conducted for all tuberculosis cases admitted to SLN Medical college and hospital, Koraput, Odisha. All the patients who were admitted in the department of general medicine were considered for enrollment. During the study period, 728 tuberculosis patients were enrolled in the DOTS (directly observed treatment, short-course) anti-tubercular therapy centre (ATT). The consecutive sampling method was used to enrol 223 patients admitted to the department of general medicine during the study period. Prior to the start of the study, written informed consent was obtained from the study participants. All cases meeting the following criteria were diagnosed with tuberculosis: If Sputum is positive for TB, if Sputum is negative for TB but conventional chest radiography is suggestive of TB, if fluid cytology is suggestive of

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TB, if fine needle aspiration cytology (FNAC)/biopsy confirms TB, and if Computed tomography (CT) scan (contrast or non-contrast)/magnetic resonance imaging (MRI) scan suggest that it's a case of TB.

After obtaining valid informed consent, information was gathered. The parameters and outcomes of socio-demographic, clinical, and laboratory studies were evaluated. Age, gender, ethnicity, and occupational background were all included in the demographic data. Clinical data included symptoms related to tuberculosis's primary aetiology, risk factors, and/or associated comorbidities. For all the study participants complete blood count, the sputum analysis for acid-fast bacilli (AFB), blood glucose test, blood urea, serum creatinine, liver function tests, electrolytes, coagulation, and urine analysis were performed in the laboratory. Fluid cytology, FNAC, biopsy, urine for AFB, chest X-ray, abdominal ultrasonography (USG), and other biochemical tests and radiological diagnostics were performed as needed.

Statistical analysis

The data collected from the study participants were entered into Microsoft Excel and was used to describe the socio-demographic characteristics of the study population. The statistical analysis was carried out using statistical software SPSS Statistics v17.0 Continuous data were presented as mean (with standard deviation) and categorical data as count (with percentage). The inferential statistics chi-square test was used to analyze categorical variables. A p-value less than 0.05 was regarded as significant.

Results

The case group included 223 patients (age = 41.05 ± 17.02 years), with the majority (80.71 percent) being males and the male-to-female ratio was 4.18:1. For both gender, the most common age group was 18-30 years. There were 97 (43.49 percent) pulmonary tuberculosis (PTB) patients, 116 (52.01 percent) extrapulmonary tuberculosis (EPTB) patients, and ten (4.48 percent) disseminated tuberculosis patients among the 223. In the current study, all cases of disseminated tuberculosis had pulmonary involvement. For the purposes of comparing PTB and EPTB, disseminated cases were included in the PTB category. Seven of the ten cases of disseminated tuberculosis had comorbid condition with HIV infection, where all patients were having a CD4 count of less than 50 cells/L. Both PTB and EPTB were more common in men than in women. Furthermore, while PTB was more common in 180 male patients (92 of 180, or 51.11 percent), EPTB was more common in female patients (34 of 43, or 79.06 percent). PTB patients had a higher mean age (42.79 ±16.1 years) than EPTB patients (38.88 ± 17.39 years), but the difference was statistically insignificant. The average length of stay in the hospital for TB patients was 7.48 ± 4.66 days. The average length of PTB, EPTB, and disseminated TB stay was 6.1 ± 4.73 days, 6.86 ± 4.7 days, and 13.29 ± 5.09 days, respectively.

In the study, patients' most common symptom was low-grade fever, with an evening rise in temperature (61.43 percent), followed by cough (54.26 percent), breathlessness (32.73 percent), and altered sensorium (17.48 percent) (Table 1).

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Table-1 Symptoms of TB patients

	Number of TB patients (%)			
Presenting symptom	PTB (n=97)	EPTB (n=116)	Disseminated (n=10)	Total (n=223)
Abdominal distension	1	10	0	11 (4.93%)
Altered sensorium	1	33	5	39 (17.48%)
Breathlessness	26	45	2	73 (32.73%)
Chest discomfort	13	17	0	30 (13.45%)
Chest pain	9	10	0	19 (8.52%)
Chronic diarrhea	0	3	1	4 (1.79%)
Cough	80	41	0	121 (54.26%)
Fever	73	64	0	137 (61.43%)
Generalized weakness	13	9	0	22 (9.86%)
Hemoptysis	22	0	0	22 (9.86%)
Jaundice	1	14	0	15 (6.72%)
Oliguria	1	7	0	8 (3.58%)
Weight loss	5	0	5	10 (4.48%)

In this study, the most common predisposing behavioural risks were smoking (59.64 percent), alcohol abuse (56.50 percent), and tobacco use (42.15 percent). Alcohol consumption was significantly higher in PTB in comparison to EPTB ($p < 0.05$). Nineteen seventy three percent (19.73 percent) of the patients lacked such a risk factor (Table 2).

Table-2 Behavioural risk factor in TB patients

Behavioral risk	**PTB (n=97)**	**EPTB (n=116)**	**Disseminated= (n=10)**	**Total (n=223)**	**P-value (PTB+disseminated vs EPTB)**
Smoking	65	66	2	133 (59.64%)	p>0.05
Alcohol consumption	68	51	7	126 (56.50%)	P<0.05
Tobacco chewing	39	49	6	94 (42.15%)	P>0.05
IV drug users	1	1	3	5 (2.24%)	P>0.05
High risk sexual history	3	0	2	5 (2.24%)	P<0.05
None	20	23	1	44 (19.73%)	P>0.05

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Tubercular pleural effusion (53.44 percent) was the most common type of EPTB among 116 patients, followed by CNS tuberculosis (26.72 percent) and abdominal tuberculosis (8.62 percent) (Table 3).

Table-3 Incidence of different types of EPTB

	Number of patient (%)		
Type of EPTB	Male	Female	Total
Abdominal tuberculosis	6	4	10 (8.62%)
CNS tuberculosis	21	10	31 (26.72%)
Pericardial effusion	2	2	4 (3.44%)
Pleural effusion	42	20	62 (53.44%)
Spine tuberculosis	2	1	3 (2.58%)
Tubercular lymphadenopathy	3	3	6 (5.17%)
Total	76	40	116

Diabetes mellitus (26.45 percent) and hypertension (17.48 percent) were the most common medical comorbidities in the current study, affecting 53.36 percent of the patients. PTB had significantly more comorbid conditions than EPTB (66 of 107 vs. 53 of 116, $p < 0.05$).

Furthermore, the average age of study participants with comorbidity was significantly higher than that of those without (46.11 ± 18.01 vs. 34.41 ± 16.52, $p < 0.05$). Except for ischemic heart disease, all comorbid conditions were more common in PTB than in EPTB; however, both diabetes mellitus and chronic kidney disease were found significantly higher in PTB than in EPTB (Table 4).

Table-4 Distribution of comorbid medical conditions

Comorbidity	**PTB + disseminated n=107**	**EPTB N=116**	**Total (% of n=223)**	**Mean age (years)**	**P-value**
Diabetes mellitus	45	14	59 (26.45%)	45.88	P<0.05
Hypertension	23	16	39 (17.48%)	53.92	p>0.05
Ischemic heart disease	1	4	5 (2.24%)	48.4	p>0.05
Chronic liver disease	11	11	22 (9.86%)	44.34	p>0.05
Chronic kidney disease	7	1	8 (3.58%)	44.6	P<0.05

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Chronic obstructive pulmonary disease	5	3	8 (3.58%)	57.59	p>0.05
Connective tissue disorder	3	0	3 (1.34%)	26	p>0.05
Hypothyroidism	4	4	8 (3.58%)	43.6	p>0.05
HIV*	6	0	6 (2.69%)	29.3	
	Overall PTB + disseminated	Overall EPTB			
Comorbidity	66	53	119 (53.36%)	46.11±18.01	
No comorbidity	41	63	104 (46.63%)	34.41±16.52	
P-value			0.03	0.04	
Grand total	107	116	223		

PTB had significantly higher mean HbA1c than EPTB (8.71 ± 2.05 vs. 7.57 ± 0.28, p<0.05). Of the 97 (43.49%) patients with pulmonary tuberculosis and ten (4.48%) with disseminated tuberculosis, for a total of 107 patients, 72 (67.28%) were Sputum positive, with the rest being Sputum negative. When pulmonary tuberculosis, comorbid conditions (46 of 72 vs. 24 of 35, p>0.05), the presence of diabetes (26 of 72 vs. 19 of 35, p>0.05), and mean HbA1c (8.94 ± 1.5 vs. 8.15 ± 3.40, p>0.05) were higher in sputum-positive in PTB patients, but the findings were not statistically significant (Table 5).

Table-5 Comparision between sputum positive and sputum negative PTB

	Number of patients (%)			
Type of PTB	Comorbidity	No Comorbidity	Total	**P-value**
Sputum positive (SP)	46	26	72	0.06
Sputum negative (SN)	24	11	35	
Total	70	37	107	
Number of patients (%)				
Type of PTB	Diabetes	No diabetes	Total	**P-value**
SP	26	46	72	0.07
SN	19	16	35	
Total	45	62	107	

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All patients received ATT, with 174 (78.02 percent) receiving Category I ATT (79 (45.40 percent) having PTB and 95 (54.59 percent) having EPTB) and the remaining 49 receiving Category II ATT (28 (57.14 percent) having PTB and 21 (42.85 percent) having EPTB). When retreatment cases (those on Category II) were compared to new cases, the proportion of PTB in the retreatment group was significantly higher ($P<0.05$).

Discussion

The majority of patients in the current study were male (80.71 percent), with a male-to-female ratio of 4.18:1. The average age was 41.04 ± 17.02 years, with the 18-30 age group being the most common. Males have a higher prevalence of tuberculosis worldwide, including the most recent Indian data.(1) The precise reason for this is still being researched.(5)

According to the most recent Revised National Tuberculosis Control Program (RNTCP) data, the third decade is the most common age group for tuberculosis in India. A large systematic review and a large population-based study from Europe support this.(2,6) However, tuberculosis in the elderly is on the rise, as evidenced by national and international data.(7) EPTB was more common in females than males in the current study, contrary to the norm of male predominance. A recent gap analysis of South Asian EPTB studies revealed the same trend of female predominance in EPTB, particularly pleural effusion.(8) Smoking (59.64 percent) was the most common predisposing behavioural risk in tuberculosis patients, followed by alcohol consumption (56.50 percent) and tobacco chewing (42.15 percent). Tobacco use has long been linked to tuberculosis.The first strong association was found in a systematic review conducted in 2005, with recent population-based studies from China showing a two-fold risk of pulmonary tuberculosis in with smoking.(8,9) Alcohol use has also been linked to tuberculosis, with a large systematic review indicating a causal link [9]. According to a recent meta-analysis, alcohol use caused 2.35 deaths and 22.02 incident cases of tuberculosis per 100,000 people in 2014.(10)

In the current study, Sputum was negative in 35 of 107 (32.71 percent) of pulmonary tuberculosis patients. Patients with radiologically active lesions but no evidence of acid-fast bacilli in the Sputum face a diagnostic and treatment challenge.(11–13) These patients could be culture positive or negative. In a population-based study from Brazil, sputum-negative pulmonary tuberculosis was linked to a high incidence of HIV coinfection.(14) Furthermore, in a Dutch population-based study, patients with smear-negative and culture-positive TB were responsible for 13% of total TB transmission.(15) This emphasizes the significance of this subset of TB patients. The majority (53.44 percent) of all extrapulmonary cases in the current study were tubercular pleural effusions, which was followed by abdominal tuberculosis. This is consistent with the majority of Indian data from Karnataka and Himachal Pradesh.(3,16) However, a Bhopal study found that TB lymphadenitis was more common than pleural effusion.(17)

Diabetes mellitus (26.45 percent) and hypertension (17.48 percent) were the most

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common medical comorbidities in the current study, affecting 53.36 percent of the patients. Comorbid conditions were significantly more associated with PTB than with EPTB in TB patients. Diabetes mellitus (DM) and chronic kidney disease (CKD) were significantly more linked to PTB than EPTB. PTB had significantly higher mean HbA1c levels than EPTB. Diabetes and tuberculosis are well-known intersecting epidemics. Diabetes was found to be an independent risk factor for mortality in TB in a retrospective cohort study.(4)

Tuberculosis and chronic kidney disease (CKD) are linked to each other [17]. Tuberculosis has been shown in an Indian study to be a risk factor for causing chronic kidney disease and more prevalent in the community with chronic kidney disease.(18,19) PTB had a higher prevalence of chronic liver disease (CLD) and cardiovascular disease (CVD), though the difference was insignificant. Cirrhosis of the liver has also been associated with increased risk of tuberculosis. In a large Taiwanese nationwide cohort study, 957 cirrhosis patients developed tuberculosis, which was found significantly higher than the non cirrhosis patients (P 0.001).(20) Tuberculosis has been linked to an increased risk of CVD. Another nationwide cohort study from Taiwan with a three-year follow-up found that the presence of TB increases the risk of ischemic stroke.(21) Another study found that latent tuberculosis infection is linked to increased acute myocardial infarction risk.(22)

The study has few limitations also, because the study was conducted in a tertiary care centre with patients ranging from moderate to severe with multiple comorbidities, there is a possibility of inherent bias.

Conclusions

Tuberculosis was more prevalent in young men. In PTB patients, the Sputum was found positive twice as common as compared to sputum-negative cases but pleural effusion was the most common type of EPTB. Medical comorbidities were discovered in nearly half of the patients, with PTB being significantly more common than EPTB. Diabetes mellitus was the most common comorbidity in PTB compared to EPTB and was associated with significantly worse glycemic control. PTB was found in a significantly higher proportion of retreatment cases.

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