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Original Article

Incidence and Clinical profiles of Pulmonary and Extra-Pulmonary Tuberculosis patients in North Indian population: A hospital based Retrospective study

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ABSTRACT:

Introduction: Tuberculosis (TB) is one of the most important global health problems. The prevalence of TB is high among the developing world. This retrospective study was carried out to find the incidence and clinical profiles of pulmonary and extrapulmonary tuberculosis patients in North Indian population. **Material and methods:** A retrospective analysis of 552 patients having EPTB and PTB was undertaken from the Dept. of Respiratory Medicine, King George's Medical University, U.P., Lucknow, out of which 300 were of pulmonary tuberculosis and 252 of EPTB. Demographic characteristics, clinical features and apparent risk factors of disease were obtained from medical case records of all patients visiting the hospital from. The Study included only the confirmed cases of EPTB and PTB with or without other co-infections. **Results:** Results were tabulated and statistically studied. The prevalence of EPTB was higher among females than males as compared to PTB and this was statistically significant ($p=0.001$). No significant ($p>0.05$) association was found between EPTB and PTB according to the place of residence. However, the tobacco habit, smoking habit, alcohol use and family history were found to be significantly ($p<0.01$) associated with the type of TB. Pleural (62.3%) site of EPTB was a most common site in EPTB patients. The study shows a significant ($p=0.04$) association between age distribution and disease condition (both EPTB and PTB) among males. A similar observation was found among female patients. The prevalence of EPTB was 1.80 times significantly higher among smokers. The prevalence of EPTB was also higher among those who had a family history of tuberculosis infection in comparison with new cases. Diabetes was present in 16.7% of the EPTB patients and MDR-TB was present in 12.7%. HIV was present in 8%. Most of the patients of EPTB were new cases (88.1) in comparison with the retreatment cases (11.9). **Conclusion:** Among evaluated tuberculosis patients, maximum had EPTB. Pleural tuberculosis was the most common presentation of EPTB. Both pulmonary, as well as extrapulmonary forms of tuberculosis, affected the younger population, between 20-40 years of age, more commonly. The study shows female preponderance among EPTB cases as compared to PTB cases. In female population, EPTB affected younger age group as compared to male patients where PTB was found to be more common. A Higher proportion of EPTB cases were found to be HIV positive and suffering from diabetes as compared to PTB.

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INTRODUCTION

Tuberculosis (TB) is one of the most important global health problems. The prevalence of TB is high among the developing world. India has the highest TB burden, accounting for 1.9 million cases of the 9.1 million cases of globally [1]. Although tuberculosis is primarily the disease of affecting the lungs (Pulmonary Tuberculosis; PTB), it may have various manifestations and can affect many sites such as lymph nodes, central nervous system, bones, and gastrointestinal tract which is known as Extrapulmonary tuberculosis (EPTB) [2-3].

Diagnosis is based on one culture-positive specimen from the extrapulmonary site; or histological evidence; or strong clinical evidence consistent with active EPTB disease followed by a medical officer's decision to treat with a full course of anti-TB therapy. EPTB is a significant health problem in both developing and developed countries and prevalence of disease in India accounts for 8.3% to 13.1% [4-5]. Reports have largely focused on smear positive pulmonary TB that posed greater infectivity threat and accounted for a higher morbidity and mortality than EPTB. Sparse literature is available regarding the relative contributions of extrapulmonary disease to the total number of tuberculosis cases from India as reliable epidemiological data are lacking [6].

A call has been made for India to do more to combat the extrapulmonary form of tuberculosis. The Indian branch of Advocacy to Control TB Internationally (ACTION) says the country's TB control program is failing to take sufficient action to diagnose cases of the condition. Diagnosis of EPTB is not covered by RNTCP, and for treatment, these cases are forwarded to the DOTS regimen. Tertiary care centers appear to be an excellent place for medical education and operational research in this regard. This is much needed, as HIV-TB co-infection; multi-drug-resistant TB and EPTB continue to be major public health threats even in the era of DOTS [7].

In view of this scarcity of data sent knowledge gaps regarding extrapulmonary tuberculosis, this study is designed to evaluate the incidence of EPTB cases among all tuberculosis patients presenting in a tertiary care hospital along with it to assess the

clinical and demographic profiles of all EPTB cases in comparison to PTB cases and to find the risk factors predisposing to EPTB

MATERIALS AND METHODS

Patients and data collection: The present study is retrospective analysis and was conducted at a tertiary care teaching hospital of North India. A total of 552 patients having EPTB and PTB were undertaken from the Dept. of Respiratory Medicine attending outdoor patient's department and indoor patient's department. Demographic characteristics, clinical features and apparent risk factors of disease were obtained from medical case records of all patients visiting the hospital from January 2014 to June 2015. The Study included only the confirmed cases of EPTB and PTB with or without other co-infections. Patients having other disorders such as COPD, asthma, lung cancer and ILD (intestinal lung disease) were excluded from the study. Demographic, lifestyle and clinical characteristics of EPTB and PTB patients were obtained.

Statistical analysis: Statistical analysis: The analysis was carried out using SPSS 16.0 version (SPSS Inc., Chicago, Illinois, USA). The results are presented in mean SD and percentages. The Kolmogorov test was used to test the pattern for normal distribution. The test showed non-normal pattern of these parameters. Hence, Kruskal-Wallis test followed by Tukey's post hoc comparison tests were used to compare the levels of Procalcitonin. The P-value <0.05 was considered significant.

RESULTS

A total of 552 patients with tuberculosis were enrolled, out of which 300 were of pulmonary tuberculosis and 252 of EPTB. The prevalence of EPTB was 45.6% overall. In this study, the comparison of EPTB and PTB according to demographic profile shows no significant ($p>0.05$) difference among the age groups between EPTB and PTB. The prevalence of EPTB was higher among females than males as compared to PTB and this was statistically significant ($p=0.001$). No significant ($p>0.05$) association was found between EPTB and PTB according to the place of residence.

Table1: Comparison of Extra Pulmonary Tuberculosis and Pulmonary Tuberculosis according to demographic profile

Demographic characteristics	EPTB (n=252)		PTB (n=300)		p-value
	No.	%	No.	%	
Age in years					
<20	32	12.7	36	12.0	
20-30	44	17.5	41	13.7	
31-40	105	41.7	133	44.3	0.77
41-50	45	17.9	55	18.3	
>50	26	10.3	35	11.7	
Gender					
Male	78	31.0	161	53.7	0.001*
Female	174	69.0	139	46.3	
Place of residence					
Rural	134	53.4	164	54.7	0.76
Urban	117	46.6	136	45.3	

¹Chi-square test, *Significant

Table1 represents the demographic profile of EPTB and PTB showing age, gender, and place of residence. Tobacco habit, smoking habit, alcohol use and family history were found to be significantly ($p < 0.01$) associated with the type of TB.

Table2: Sites of EPTB between male and female

Clinical characteristics	Male (n=78)		Female (n=174)		Total	
	No.	%	No.	%	No.	%
Abdominal	4	5.12	5	2.8	9	3.6
Lymph node	30	38.4	58	33.3	88	34.9
Genitourinary	2	2.5	12	6.9	14	5.55
CNS	1	1.28	2	1.1	3	1.1
Pleural	41	52.5	97	55.7	138	54.7

Table2 represents the Clinical characteristics of the Pleural (62.3%) site of EPTB, common site in EPTB patients followed by lymph node (28.6%), Genitourinary (4.8%), abdominal (3.6%) and CNS (0.8%). All the sites were higher among females.

Table3: Proportional age distribution for EPTB and PTB according to gender

Age group	Male				Female			
	EPTB (n=78)		PTB (n=161)		EPTB (=174)		PTB (n=139)	
	No.	%	No.	%	No.	%	No.	%
<20	4	5.1	15	9.3	28	16.1	21	15.1
20-30	9	11.5	18	11.2	35	20.1	23	16.5
31-40	15	19.2	100	62.1	90	51.7	33	23.7
41-50	31	39.7	16	9.9	14	8.0	39	28.1
>50	19	24.4	12	7.5	7	4.0	23	16.5
p-value ¹	0.04*				0.02*			

Chi-square test, *Significant

Table 3 shows a significant ($p=0.04$) association between age distribution and disease condition (both EPTB and PTB) among males. A similar observation was found among female patients.

Table4: Distribution of type of co-infection among EPTB patients

Type of co-infection*	EPTB (n=252)		PTB (n=300)		p-value
	No.	%	No.	%	
Diabetes	42	16.7	31	10.3	0.02*
HIV	20	8.0	18	6.0	0.003*
MDR	32	12.7	90	30.0	-

*Multiple responses

Table 4 shows that the prevalence is significantly lower among males than females (Adjusted OR=0.62, 95%CI=0.40-0.96, $p=0.03$). However, the prevalence of EPTB was 1.80 times significantly higher among smokers (Adjusted OR=1.80, 95%CI=1.17-2.76, $p=0.007$). The prevalence of EPTB was also higher among those who had a family history of tuberculosis infection in comparison with new cases. Diabetes was present in 16.7% of the EPTB patients and MDR-TB was present in 12.7%. HIV was present in 8%.

Table5: Distribution of type of EPTB patients

Type	EPTB (n=252)		PTB (n=300)	
	No.	%	No.	%
New cases	222	88.1	226	75.3
Retreatment	30	11.9	74	24.7

$p=0.0001$, Majority of the patients were new cases in both the groups.

Table 5 shows that Majority of the patients of EPTB were new cases (88.1) in comparison with the retreatment cases (11.9).

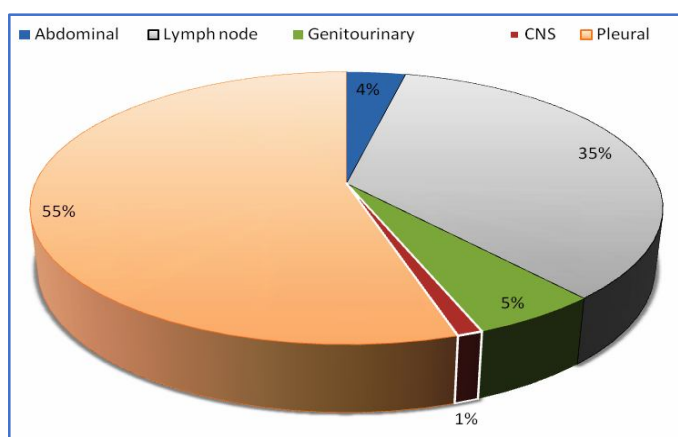


Fig. 1: sites of EPTB

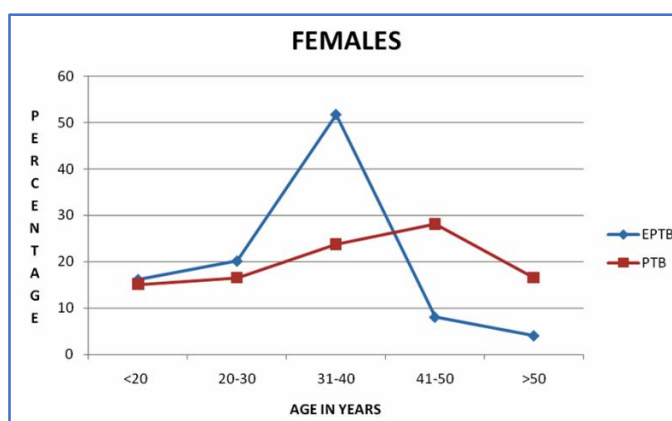


Fig. 4: Age distribution in females

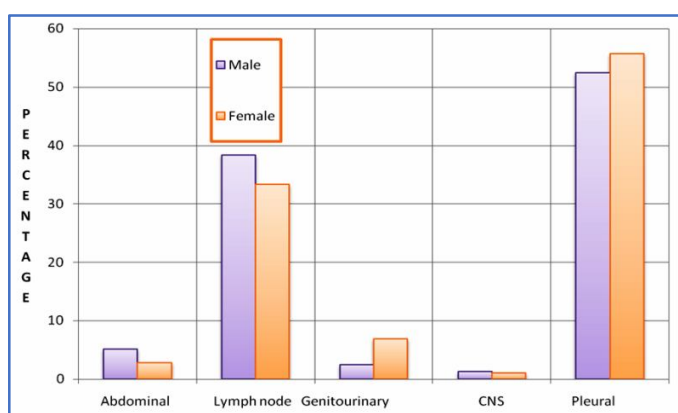


Fig.2: Sites of EPTB between male and female

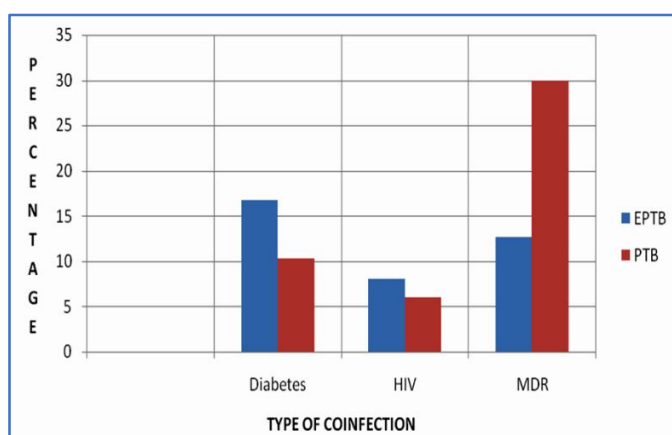


Figure 5: Distribution of type of co-infection among EPTB patients

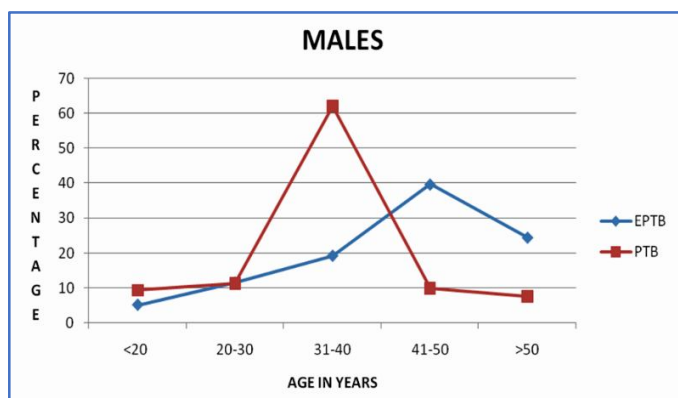


Fig. 3: Age distribution in male

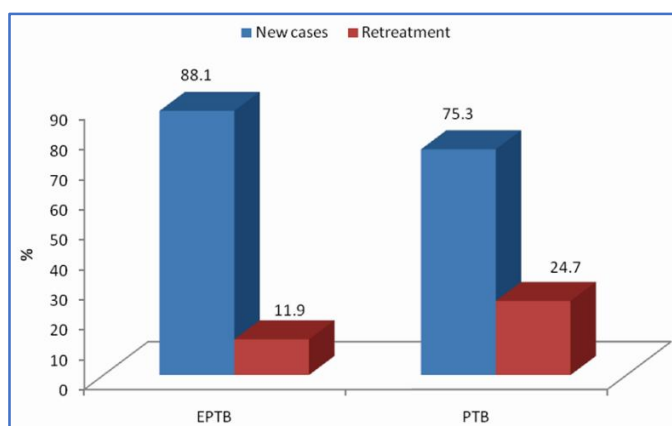


Fig. 6: Distribution of type of EPTB patients

DISCUSSION

The present study was aimed at understanding the clinical-epidemiological profile of extra-pulmonary tuberculosis in comparison with pulmonary tuberculosis in patients presenting to a tertiary care center. Though the percentage of EPTB cases estimated by the national control program in India for HIV-negative adults is between 15% and 20%, the percentage of patients with EPTB in tertiary care centers in India varies between 30% and 53% [7]. In our study, among 552

tuberculosis patients evaluated, 252 (45.6%) had EPTB. This data is in concordance with the tuberculosis trends seen in various studies especially from tertiary care centers across India. For example, at the Tuberculosis Clinic at the All India Institute of Medical Sciences, (AIIMS), New Delhi (n=1137) and the Sri Venkateswara Institute of Medical Sciences (SVIMS), Tirupati (n=612), patients with EPTB constituted 53 and 30.4 per cent respectively during the period 1994-2002 (unpublished observations). Since several patients are referred to tertiary care centers for confirmation of diagnosis, these high figures could be a result of referral bias [8].

Site: Various studies have suggested that the sites of EPTB may vary according to geographic location, population groups and a wide variety of host factors [9-12]. Pleural tuberculosis was the most common presentation of EPTB in our study (54.7%) followed by lymph nodes (34.9%), followed by genitourinary, abdominal and CNS TB respectively.

This finding is similar to study conducted by Chandaret *al.*, where pleural TB was found to be the most common type of EPTB in 53 cases (61.6%), followed by lymph node TB in 20 cases (23.2%) and abdominal TB in 8 cases (9.3%) [13]. In study done by Prakashaet *al.*, too, the total number of different types of EPTB cases included pleural (n= 148, 28.03%), lymph node (n = 131, 24.81%), abdomen (n = 51, 9.66%), CNS (n = 66, 12.50%), bones and joints (n = 65, 12.31%) and others (n= 67, 12.69%). In the pediatric population, lymph nodes are found to be more commonly involved than pleura [7]. As our sample included adult patients, above 12 years of age, this variation in size distribution is expected. This also raises the possibility that the probability of reactivation in pleura may be higher as the age increases [7].

Risk factors

Age distribution: Both pulmonary as well as extrapulmonary forms of tuberculosis affected the younger population, between 20-40 years of age, more commonly. No particular age group was found to be free of EPTB, although the major contribution to EPTB in our study comes from adolescent and early adult age group, 58% in EPTB and 54% in PTB. A similar finding of involvement of younger age in EPTB has been observed in Minnesota [14] in which 43% of the EPTB patients were in the age 15-24 years. In another study carried out in Fars Province, Southern Republic of Iran, highest number of EPTB patients was in the age 15-24 years (30.7%) followed by age group 25-34 (24.3%) [15]. A study from South Delhi, India also shows the similar finding; 38% of the patients were in the age 15-24 years followed by 25% in age 25-34 years [16].

Gender prediction: We found a significant female preponderance among EPTB cases (females 69%, males 31%) as compared to PTB cases (females 46.3%, males 53.7%). The likelihood of development of EPTB was approximately one and half times higher among females than in males. (Adjusted Odds Ratio 0.62 95%CI 0.40-0.96 p-value 0.03). Gender differences observed in our study confirm the findings of previous studies in both developing [17, 18] and developed countries [19, 20]. This may be a consequence of gender differences in both exposures to TB infection and prevalence of susceptibility risk factors (e.g., smoking) [17]. Other possible factors accounting

for the difference are a stigma associated with having TB and lack of access to health care, especially for females, in some developing countries like India [18].

Age with gender: Since the gender distributions were different for PTB and EPTB, we examined age distributions after stratifying by gender type. We found that in the female population, EPTB affected younger age group as compared to male patients where PTB was found to be more common. This finding was clinically significant. Similar observations have been made in past. Recent Indian studies have also noted a higher prevalence of EPTB in children than adults (47% vs 16% respectively), with the greater affection of females (63% vs 33% respectively) [21]. In contrast, a higher prevalence of PTB has been observed in elderly than younger patients (16:1 respectively), with a male preponderance of disease (3:1 respectively) [22]. Thus, demography of disease has not changed over the years.

Co-morbidities: A Higher proportion of EPTB cases were found to be HIV positive and suffering from diabetes as compared to PTB. A recent study from a large tertiary hospital in South India reported that EPTB showed an increasing trend among HIV-infected patients [23]. However, data studying the association between EPTB and diabetes is lacking. More studies are needed to evaluate the role of immunosuppression in the development of EPTB. A Higher percentage of drug resistant tuberculosis (MDR-TB) was seen in PTB patients.

New and retreatment: Most of the cases (222, 88%) received Category-I treatment, highlighting the faith of treating doctors to use four drugs in the intensive phase even in extrapulmonary cases. This is a significant positive step in terms of attracting more cases to the program and will also help to reduce the number of retreatment cases in the future [7].

CONCLUSION

This study was carried out to understand the clinical-epidemiological profile of extra-pulmonary tuberculosis in comparison with pulmonary tuberculosis in patients presenting to a tertiary care center. In our study, among 552 tuberculosis patients evaluated, 252 (45.6%) had EPTB which is much higher than estimated by the national control program in India. Pleural tuberculosis was the most common presentation of EPTB. Both pulmonary, as well as extrapulmonary forms of tuberculosis, affected the younger population, between 20-40 years of age, more commonly. The study shows female preponderance among EPTB cases as compared to PTB cases. In female population, EPTB affected younger age group as compared to male patients where PTB was found to be more common. A Higher proportion of EPTB cases was found to be HIV positive and suffering from diabetes as compared to PTB.

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