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## Original Research Article

## Clinical profile of extra pulmonary tuberculosis: A retrospective south Indian study

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## ABSTRACT

**Background:** 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. Although tuberculosis is primarily the disease affecting the lungs, Called Pulmonary TB (PTB), it may also affect other sites such as lymph nodes, central nervous system, bones, and gastrointestinal tract which is known as Extra pulmonary tuberculosis (EPTB). Extra-pulmonary TB patient reporting has been increased from 17% to 21% over period of 10 years which demands the evaluation of clinical profiles of EPTB in order to diagnose and implement the precise treatment plan.

**Objectives:** To Determine the clinical profile of extra pulmonary tuberculosis (EPTB) patients in South Indian population.

**Materials and Methods:** Three years' retrospective data of TB patients from 2015 – 2017 registered in 4 TB units of central Chennai was collected. The Study included the confirmed cases of EPTB without co-infections. Parameters such as Socio-demographic variables, clinical features and treatment outcome was collected. Age and gender wise comparisons was done for all the parameters using descriptive statistics.

**Results and Conclusion:** Lymphnode TB was the most common type of EPTB and significant association between age, gender and site of EPTB was found in the study necessitating well planned strategies, program-specified protocols for the diagnosis and treatment of extra pulmonary tuberculosis cases.

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## 1. Introduction

Tuberculosis (TB) is an old disease, studies of human skeletons show that it has affected humans for thousands of years. TB typically affects the lungs called as pulmonary TB (PTB), which is more common, however can also affect other sites called as extra pulmonary TB (EPTB).<sup>1</sup>

Currently TB can be defined as a multisystem disease with myriad presentations and manifestations which can affect any organ or tissue, excluding only the hair and nails.

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While the WHO has recognized TB as a global problem, this applies to TB as a whole and principally pulmonary TB.<sup>2</sup>

Although PTB is considered as a major global health problem due to its infectivity, non-communicable EPTB represents as a major diagnostic and therapeutic challenge. Diagnosis is based on culture-positive specimen from the extra pulmonary 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. Recent years, the total incidence of TB is declining, however EPTB incidence has remained stagnant through many decades indicating necessity of

guidance on uniform, evidence-informed practices for suspecting, diagnosing and managing EPTB at all levels of healthcare delivery and also at the same time seeking a high importance for disbursing appropriate treatment regimens.<sup>3</sup>

Worldwide, the burden of EPTB is high ranging from 15-20 per cent of all TB cases in human immunodeficiency virus (HIV) negative patients, while in HIV-positive people, it accounts for 40-50 per cent of new TB cases. 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%. The percentage of patients with EPTB in tertiary care centres in India is between 30% and 53%, while the percentage estimated by the national control program in India for HIV-negative adults is between 15% and 20%. EPTB becomes more important as chances of developing EPTB in immunocompromised patients are higher than in their immunocompetent counterparts.<sup>4</sup> Recent studies have suggested that the sites of EPTB may vary according to geographic location, population groups and a wide variety of host factors. There are many forms of EPTB, affecting every organ system in the body. Some forms, such as TB meningitis, Miliary TB and TB pericarditis, are life-threatening, while others such as pleural TB, lymph node TB and spinal TB can cause significant ill-health and lasting disability.<sup>5</sup>

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 extra pulmonary disease to the total number of tuberculosis cases from India as reliable epidemiological data are lacking.

The present study is aimed at determining the clinical profile of extra pulmonary tuberculosis patients in South Indian population.

## 2. Materials and Methods

It is a retrospective, record based study included all EPTB confirmed patients registered for treatment during the 3 years' study period from 1<sup>st</sup> January 2015 to 31st December 2017 at 3 Designated Microscopy centres (DMC) comprising Tuberculosis units, named Pulianthope, Tondiarpet and Tiruvitriyur of Central part of Chennai, Tamil Nadu, South India.

The diagnosis of EPTB was established following the revised national tuberculosis control program (RNTCP) guidelines which required culture positive specimen from an extra pulmonary site or histological evidence or strong clinical evidence consistent with active EPTB followed by concerned medical officer's decision to treat with full course of anti-tubercular therapy.

### 2.1. Inclusion criterion

Confirmed EPTB (Histopathological/Clinical).

### 2.2. Exclusion criteria

#### 2.2.1. PTB

2.2.1.1. PTB with EPTB. Total 1569 cases were diagnosed as TB in the study period and amongst which 512 EPTB cases were included in the study. The proportion of this EPTB to PTB cases was also evaluated. The EPTB cases were mainly categorised as per the age, gender and site of involvement. In the study group, age was categorised into three groups using 25<sup>th</sup> and 75<sup>th</sup> percentile as lower and upper limit.

Mainly, EPTB cases were grouped into categories based on the site of involvement like pleural cavity, lymph nodes, abdominal, eye, meninges, spine/bone, disseminated/Miliary, breast and other miscellaneous sites.

### 2.3. Statistical analysis

The collected data was entered and analysed by using SPSS Version 16. Chi-square test was used to know if differences observed in different groups were statistically significant. Data was described in proportion or percentages. P value of < 0.05 was considered significant.

## 3. Results

In the 3-year study period, a total of 1569 tuberculosis cases were registered in 3 DMC's amongst which 512 (32.6%) were EPTB cases, 250 (48.8%) were males and 262 (51.2%) were females (Table 1). Over the years, there was a significant increase in the total number of cases registered. The age was ranging from 3.5 months to 88 years, with a mean of 32.43 years. 83 (16.2%) patients were in the age group 0-17 years, 294 (56.4%) patients in the age group 18-40 years and 135 (26.4%) patients were in the age group above 40 years (Table 1). It was found that there was a highly significant difference in total number of cases reported between different age groups with maximum of the cases occurring in 18-40 years of age. (P = 0.01) (Table 1 & Figure 2). Significant gender wise difference was also noticed between different age groups (p value= 0.01). Females were outnumbering in 17-40 years' group and males in above 40 years' group. However, in 0-17 year's age group it remained almost equal (Table 1 and Figure 2).

About 487 (95%) patients were newly diagnosed EPTB cases and 25 (5%) patients were found to be reactivated/recurrent EPTB cases.

The number and percentage of cases of different types of EPTB was calculated. Lymph node tuberculosis was the commonest type of tuberculosis in all the age groups accounting for 258 (50%) cases, followed by Pleura 124 (24.2%), abdomen 41 (8%), Meningeal 33 (6.4%), Bone

19 (3.7%), military 10 (2%), breast 5 cases, ocular 4 cases and others 15 cases. Others include TB Pericarditis, Genitourinary and ovarian TB. 79% of Meningeal TB was presented in the age group 18-40 years. (Table 2)

Considering the commonest EPTB types reported in this study - Lymph node TB and Pleural TB, there was a highly significant association between the gender and site of EPTB. Females reported significantly higher number of Lymph node TB cases, while males reported high number of Pleural TB cases ( $P = 0.001$ ). (Table 3 & Figure 2).

A significant association between the age and location of EPTB was also found in the study. Pleural TB was significantly higher in age group above 40 years compared to other two age groups. ( $p$  Value=0.001) (Table 2)

In this study, 68 (13.3%) cases had diabetes mellitus. 78 cases (15.2%) were found to have BMI less than 18.5, mainly Miliary TB, Meningeal TB, Pleural TB.

Amongst 512 EPTB cases, 441(86%) completed the treatment, 40 (8%) were Lost to follow up and 31 (6%) died during the course of treatment (Table 3). Most of the death occurred in the severe forms EPTB like Miliary and Meningeal TB.

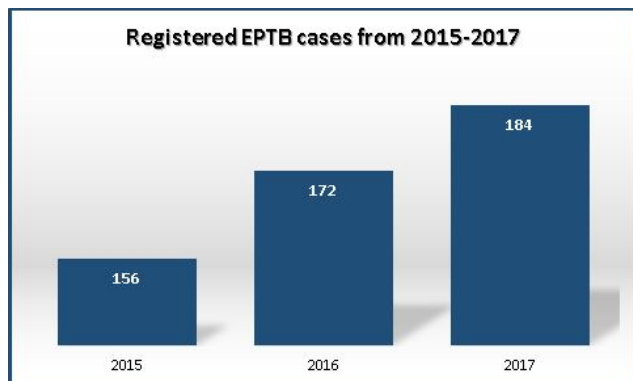


Fig. 1: Registered EPTB cases from 2015-2017

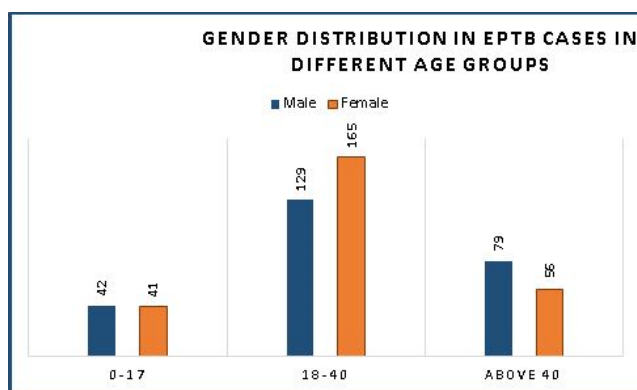


Fig. 2: Association of age & gender

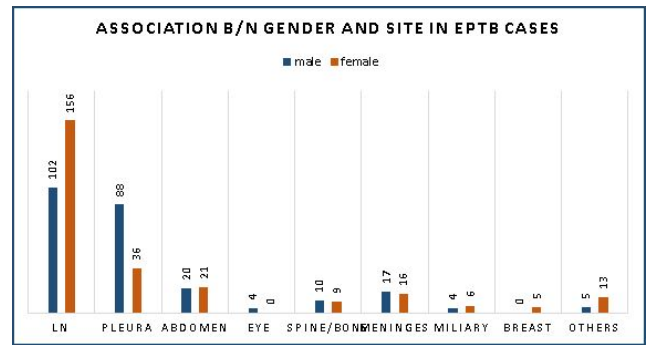


Fig. 3: Association of site and gender

#### 4. Discussion

The study was done to understand the demographic and clinical characteristics of various EPTB patients at 3 DMC's of central Chennai. Firstly, males (250, 48.8%) and females (262, 51.2%) contributed to nearly an equal number of cases, with a slight marginal increase in females. The similar marginal increase in the females has also been found in other studies as well.<sup>5,6</sup>

The majority of cases (294, 57.4%) belonged to the age group of 18-40 years, who are young and working individuals, highlighting the socioeconomic burden of extrapulmonary tuberculosis. Similar reports of higher incidence of EPTB in younger adult individuals are reported by other studies as well.<sup>5,7</sup>

Secondly, lymph node tuberculosis was the commonest type of EPTB in all the age groups accounting for 50.3% of total 512 registered cases. Pleural TB being the second commonest, increased significantly in number in the age group above 40 years to reach almost to equal number as Lymph node TB. This raises the possibility that the risk of reactivation in pleura may be higher as the age increases which was also noticed in other studies.<sup>3,7</sup> Various studies have been found to have same results, however few recorded a different pattern. A study from England showed that lymph node involvement was the most common site in the body.<sup>8</sup> However, a study from Hong Kong showed the most common sites were pleura, followed by lymph node; and one-third of all cases had pulmonary tuberculosis. A study in Holland showed that the most common sites of EPTB were pleura and lymph node, equally (17%).<sup>9</sup> Maltezou and his colleagues found the lymph node was the most common site of EPTB in children and EPTB constituted 9% of all cases with TB Lymph node involvement in EPTB was correlated with HIV co-infection, female gender, young age and Asian race.<sup>10-12</sup>

Thirdly, lymph node TB was relatively a more common site in both the genders, however an increased proportion of Pleural TB was found in males corresponding to habit related occurrences like tobacco smoking. There was no significant gender wise difference in other EPTB sites like

**Table 1:** Association of age & gender

|          | Male | %    | Female | %     | Total      |
|----------|------|------|--------|-------|------------|
| 0-17     | 42   | 16.8 | 41     | 15.65 | 83(16.2%)  |
| 18-40    | 129  | 51.6 | 165    | 62.97 | 294(57.4%) |
| above 40 | 79   | 31.6 | 56     | 21.4  | 135(26.4%) |
| Total    | 250  |      | 262    |       | 512        |

**Table 2:** Age wise Site predilection of extra pulmonary tuberculosis.

|          | LN  | Pleura | Abdomen | Eye | Spine/bone | Meninges | Miliary | Breast | Others |
|----------|-----|--------|---------|-----|------------|----------|---------|--------|--------|
| above 40 | 55  | 48     | 11      | 1   | 9          | 3        | 1       | 2      | 5      |
| 18-40    | 157 | 59     | 23      | 3   | 9          | 26       | 4       | 3      | 10     |
| 0-17     | 46  | 17     | 7       | 0   | 1          | 4        | 5       | 0      | 3      |
| Total    | 258 | 124    | 41      | 4   | 19         | 33       | 10      | 5      | 18     |

**Table 3:** Association of site and gender

|        | LN  | Pleura | Abdomen | Eye | Spine/bone | Meninges | Miliar | Breast | Others |
|--------|-----|--------|---------|-----|------------|----------|--------|--------|--------|
| Male   | 102 | 88     | 20      | 4   | 10         | 17       | 4      | 0      | 5      |
| Female | 156 | 36     | 21      | 0   | 9          | 16       | 6      | 5      | 13     |
| Total  | 258 | 124    | 41      | 4   | 19         | 33       | 10     | 5      | 18     |

abdomen, bones and joints etc in contradiction to a study by Prakasha et al.<sup>7,12,13</sup>

In the present study, there is a gradual, but sustained increase in the number of extrapulmonary cases diagnosed and treated (86% treatment complete) under RNTCP could be due to well-defined program-specified protocols and ongoing medical education to increase the total number of EPTB cases detected in the community and treated under the program by gaining the confidence of treating practitioners. Similar trend has been observed in other studies also.<sup>6,7,13,14</sup>

The main limitation of the study is that the detailed clinical signs, symptoms and habits could not be evaluated, since the data was collected from TB treatment card having limited details. The findings cannot be generalized to the community as the cases selected were already registered in the DMC centres. HIV co-infected cases were also not assessed as they did not get registered in the study areas mentioned.

However, it gives valuable information which can be utilized by the health administrators for the pattern and changing trend of reporting EPTB cases

## 5. Conclusion

EPTB still constitutes an important clinical problem. In the current study, we assessed the age, gender and site of predilection of EPTB patients. The burden of EPTB is more among the productive age group. The difference in the occurrence of various types of EPTB cases in different age groups and sexes without the declining trend highlights the importance of strengthening the services for this vulnerable group. Extra pulmonary tuberculosis is known to be a diagnostic and therapeutic challenge which necessitates well planned strategies, program-specified protocols for the

diagnosis and treatment of extra pulmonary tuberculosis cases.

In conclusion, over the years, annual case detection has improved for extra pulmonary TB under Revised National TB Control Programme employing a DOTS strategy. Cure of infectious disease is likely to have contributed in a relative rise of the annual EPTB case detection. DOTS effected an acceptable treatment outcome in EPTB case management.

## 6. Conflict of Interest

The authors declare no relevant conflicts of interest.

## 7. Source of Funding

None.

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