

## PATTERN OF EXTRA PULMONARY TUBERCULOSIS AS SEEN IN A TERTIARY CARE CENTER IN SOUTH INDIA

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### ABSTRACT

#### BACKGROUND

Tuberculosis is one of the major infectious diseases affecting the global population. It ranks alongside HIV as a leading cause of death worldwide. Around 9.6 million people were estimated to be suffering from TB in 2014, out of which 480000 were cases of multi drug resistant TB (MDR-TB).

Tuberculosis most commonly affects the lungs. It can involve almost any organ system of the body, the so called extra pulmonary TB. EPTB possess a diagnostic challenge for the clinicians because of lack of specific and usual symptoms of cough. In this study, we have analysed the pattern of EPTB in our center.

#### MATERIALS AND METHODS

It was a prospective observational study. 60 patients suffering from EPTB were included and these patients were selected on basis of radiological or histological confirmation of TB with or without AFB positivity source of data included physician prescribing records, patient medication profile, laboratory investigations and presentations. Study was conducted over a period of one year. Patients with Pulmonary Tuberculosis (PTB) and HIV were excluded.

#### CONCLUSION

Maximum number of patients were in the age group of 21 to 40 years. Males predominantly suffered from the disease. Lymph node TB was the commonest form of EPTB followed by pleural effusion

#### RESULTS

There was a slight male preponderance. Lymph node was the commonest site of involvement in EPTB, followed by pleural effusion.

#### KEYWORDS

Pulmonary Tuberculosis (PTB), Extra Pulmonary Tuberculosis (EPTB), Acid Fast Bacillus (AFB).

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#### BACKGROUND

Mycobacterium tuberculosis is a facultative intracellular pathogen that can infect several animal species, though human beings are the primary hosts. This pathogen is an aerobic, acid fast, non-encapsulated, non-motile organism. The causative organism enters the body through the respiratory tract. Though, pulmonary tuberculosis is the commonly observed form, haematogenous and lymphatic dissemination of the organism may occur. Extra Pulmonary Tuberculosis (EPTB) is the isolated occurrence of TB at body sites other than the lungs or the bronchi. Lymph node tuberculosis is the commonest form of EPTB. Sometimes, the tonsil may act as an important portal of entry.

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Then, spread of infection to the cervical, hilar and mediastinal lymph nodes may also be seen. Pleural effusion is categorized as extra pulmonary despite an intimate anatomic relationship between pleura and the lungs. Most patients with pleural effusion present with a dry cough, pleuritic chest pain and dyspnea depending upon the size of the effusion. Other sites of infection include the genitourinary tract, central nervous system, bones and joints. Almost any site other than the hair and nails may be involved

The revised National Tuberculosis Control Programme (RNTCP), based on the internationally recommended Directly Observed Treatment Short course (DOTS) strategy, was launched in 1997 and achieved a nationwide coverage by March 2006. The RNTCP provides free diagnostic services and treatment to benefit the poor and vulnerable groups of the society. Due to the paucibacillary nature of EPTB and low infectivity, not much importance is given to it. Besides, the emerging evidence of HIV/AIDS with which EPTB is quite common, it is important that the non-pulmonary component of TB be diagnosed with equal efficacy and ease.

TB still remains a major global public health problem. Extra pulmonary sites of infection include lymph nodes,

pleura, osteoarticular areas, all though any organ can be involved. The diagnosis of EPTB requires a high index of suspicion as it is paucibacillary and conventional investigations like sputum AFB and X-ray chest may not be reliable if there is no pulmonary component. Testing of body fluids for Adenosine deaminase (ADA), Polymerase Chain Reaction (PCR) or histopathological specimen showing caseating granuloma may be required to establish the diagnosis. Therefore, the disease is not only elusive but expensive investigations and invasive procedures specific for the organ may be required to arrive at a diagnosis.

Extra pulmonary tuberculosis is a milder form of disease in terms of infectivity as compared to pulmonary tuberculosis. The sputum sample can be obtained for the detection of PTB, diagnosis of EPTB may be, and however, difficult for histopathological diagnosis, the presence of granulomas, caseation and demonstration of AFB have been commonly used for confirmation. The organ involvement usually affects the selection of diagnostic procedures. Various methods like needle biopsy, excision biopsy, endoscopy, laparoscopy and biopsies under guidance of ultra sound and computed tomography may be required.<sup>1</sup> Body fluids such as pleural, peritoneal and pericardial fluids can provide valuable diagnostic results in EPTB patient; the measurement of ADA is a useful biomarker for the diagnosis of EPTB.<sup>2</sup> Interferon gamma release assays (IGRAS) are whole blood test used in diagnosis of tuberculosis. This test is sensitive, specific and rapid. They detect interferon gamma produced by lymphocytes in response to Mycobacterium tuberculosis – specific antigens.<sup>3</sup> Nucleic acid amplification tests are also used for blood or body fluids to diagnose TB.

**MATERIALS & METHODS**

The study was carried out in the department of Pulmonary Medicine, Jubilee Mission Medical College and Research Institute, Thrissur. It was a Prospective and Observational Study.

Based on inclusion and Exclusion criteria, 60 Patients suffering from EPTB were selected after obtaining their informed written consent. Ethical clearance was taken from the Institution Ethical Committee (IEC), Jubilee Mission Medical College. Jubilee Mission Medical College is a tertiary care hospital which caters to a lot of patients namely from Thrissur, Malappuram and Palakkad.

**Inclusion Criteria-**

1. Patients with a clinical and or histopathological / proven diagnosis of EPTB.
2. Associated with or without AFB smear positively/ culture positivity.

**Exclusion Criteria-**

1. Patient with PTB.
2. Patients with HIV 60 patients who fulfilled the criteria were enrolled in the study.

The diagnosis of EPTB cases followed the program guidelines which required one culture positive specimen from extra pulmonary site, or histological evidence of caseating granulomas or clinical evidence of TB, followed by the medical officers’ decision to treat with a full course of anti TB therapy, data such as demographic details, site of EPTB and treatment category were documented. Most of the patients received category I DOTS treatment whereas, patients who were treated earlier were put on category II DOTS. Very few of the patients received private medication i.e. AKT4.

**Statistical Analysis**

To calculate the test for linear trend, Chi- square test was used.

**RESULTS**

Age wise distribution of the patients was as follows:

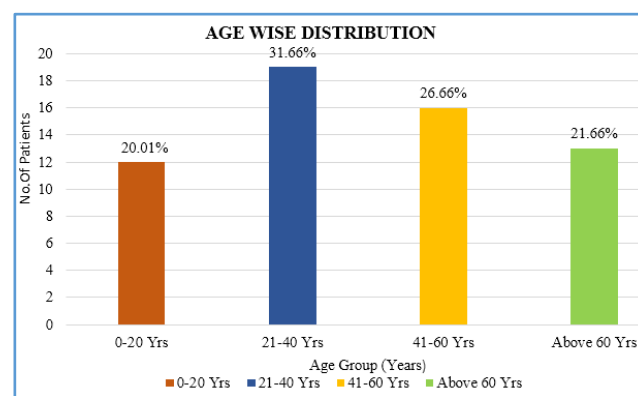


Figure 1

Maximum number of patient were in the age group of 21-40 years (31.66%) male predominantly suffered from the diseases (51.66% as compared to 48.33%).



Figure 2

Lymph node tuberculosis was the commonest site of EPTB observed in our study (35%) followed by Pleural effusion (26.66%).

Sl. No.	Site of EPTB	Number of Patients (N= + 60 )	Percentage (%)
1.	Lymph Node	21	35
2.	Pleural effusion	16	26.66
3.	Bone and joints	8	13.33
4.	Abdomen	6	10
5.	Urinary	4	6.66
6.	CNS	3	5
7.	Pericardial	2	3.33

**Table 1**

The following table depicts the relationship between age group and site of EPTB.

Age Group	Site of EPTB						
	Lymph Node	Pleural Effusion	Bone & Focal	Abdomen	Urinary	CNS	CVS
0-20 Years	5	2	1	3	0	1	
21 - 40 Years	10	3	2	2	2	0	
41 - 60 years	6	7	1	0	0	1	
61 - 80 Years	0	4	4	1	1	0	

**Table 2**

Most of the lymph node TB patient belonged to the age group of 21 - 60 years whereas pleural effusion was seen in the age group of 41 - 60 years.

The Patients received the following treatment schedule.

Sl. No.	Category of Treatment	Number of Patients	Percentage %
1.	Category I DOTS	43	71.66
2.	Category II DOTS	6	10
3.	Private regimen	11	18.33

**Table 3**

71.66% of the patients received Category I DOTS. 10% of the patients were put on retreatment schedule and 18.33% of the patients were on a private regimen.

**DISCUSSION**

Tuberculosis can involve any organ system in the body. While pulmonary tuberculosis is the most common presentation, Extra Pulmonary tuberculosis (EPTB) is also an important clinical problem. Diagnosis of EPTB has always been a challenge due to the paucity of bacilli and difficulty in obtaining a specimen for histopathological confirmation.<sup>4</sup> Nearly one percent of the world’s population is newly infected with TB each year. Mycobacteria invade many organs during primary infection but, therefore remain dormant if the host has an effective immune system. Reactivation is accelerated in patients with latent disease, under conditions where the immune system is suppressed. The category wise treatment is similar for both PTB and

EPTB cases. Newly detected cases put on Category I DOTS and patients who have been treated earlier are put on Category II DOTS.

A total number of 60 patients with extra pulmonary tuberculosis were included in the study. The patients were divided into four age group viz 0 – 20 years, 21 – 40 years, 41 – 60 years, and above 60 years. Majority of cases (31.66%) belonged to the age group of 21 – 40 years highlighting the social-economic impact of EPTB. This is statistically significant with P value of 0.05. Prakash et al, had shown higher incidence of EPTB in younger age group.<sup>5</sup>

In our study, male had a slightly higher incidence as compared to the female (48.33%) in the ratio of 1.06:1. S Rama Prakash, G Suresh et al, also found males and females contributed to an equal member of cases. Older studies revealed that males were much more affected with EPTB as compared to females. Uir Azam Khan, Bazit et al reported equal number of cases in both males and females.<sup>6,3</sup> In the present study most common sites involved were lymph node TB and pleural effusion. This was similar to the study done by V. K. Arora.<sup>7</sup> Priyadarshini B G et al, reported that lymph node, pleura, abdomen, hip and skin are the common involvement of TB in South Indians.<sup>8</sup>

Lymph node tuberculosis (16.66%) were mostly found in the age group of 21 – 40 years. But, pleural TB (11.66%) were commonest type of EPTB in the age group 41-60 years. The incidence of pleural TB increases as the age increases. Present study revealed that abdominal TB affects patients below 40 years of age. S Rama Prakash et al, also found similar reports in his study.<sup>2</sup> In a similar conducted by Archana Rao K, Deepa S et al., on extra pulmonary tuberculosis: an observational study in a tertiary care hospital.<sup>9</sup> This study includes the patients of all types of extra pulmonary tuberculosis in all age groups, evaluated at Mysore Medical College and Research Institute, Mysore, Karnataka. This study includes the patients with EPTB. Samples are collected for the study included pus, pleural fluid, aspirates from joints, urine, CSF, tissue from lymph node. Collected specimens were examined by fluorescent microscopy and Ziel-Neelsen staining and subjected to biochemical examinations. Haematological examination for erythrocyte sedimentation rate(ESR), differential leucocyte count (DLC), total leucocyte count (TC), and investigations like USG chest, abdomen, computed tomography (CT) scan, magnetic resonance imaging (MRI) were performed in required cases. Radiological investigations (chest X-ray) were taken in all cases. Among 4500 cases of tuberculosis, 710 cases are diagnosed as extra pulmonary TB. Of 710 cases, 415 were males and 295 were females, among them 42 were children below 16 years age. In this study male to female ratio was about 1.5:1. The patients were divided in to four age groups as 0-14 years, 15-44 years, 45-65 years and more than 65 years. Pleural TB was the commonest type of extra pulmonary TB 37% (n=268) in the age group of 45-65 years and it also present in age group of >65 years. Followed by lymph node tuberculosis was seen in all age groups accounting for 29% (n=210). Abdominal TB accounted for 19.1% (n=137) was commonly seen in the

age group of 25-45 years. TB orchitis (N=4, 0.6%) is least common site of EPTB. Cervical lymphadenitis was the commonest presentation (n=28, 3.9%) of EPTB in children below one year. Extra pulmonary tuberculosis most commonly effected with patients belonged to the age group of 15-45 years. This age group is considered to be productive age group posing a major burden on family and economic conditions. The morbidity and psychological burden on this age group may be increased due to the complications of EPTB like bone deformities, pelvic inflammatory disease and infertility. In this study most of the patients belonged to lower socioeconomic status of life. Confirmation of EPTB is challenging for a number of reasons: the difficulty to obtain an adequate sample; the processing of the sample for various diagnostic tests resulting in non-uniform distribution of microorganisms; the paucibacillary nature of the specimens; the presence of inhibitors that undermine the performance of nucleic acid amplification-based techniques; and the lack of an efficient sample processing technique universally applicable on all type of extra pulmonary samples.<sup>9</sup>

Study by Manoj Grover, Neelima Bhagat, et al,<sup>10</sup> on Treatment pathways of extra pulmonary patients diagnosed at a tertiary care hospital in Delhi. The study was conducted in a directly observed treatment short course (DOTS) cum microscopy centre is located at the chest clinic of a teaching hospital. In this study, 150 newly diagnosed EPTB patients were included. Lymph node (96; 64%) was the most common site of EPTB, followed by pleura (25; 16.7%), abdomen (14; 9.3%), bone and joint (7; 4.7%), skin (5; 3.3%), eye (2; 1.3%) and female reproductive organs (1; 0.7%). Mean age of the patients who participated in this study was 23.2 years (SD=11.1 year). There were more female (82; 54.7%) patients than males (68; 45.3%) involved in the study.<sup>10</sup>

## CONCLUSION

Tuberculosis still remains an important global health problem. EPTB has low infectivity as compared to PTB, yet it cannot be disregarded as it contributes substantially to the disease load. The liability of EPTB is more among the younger age group, affecting the socio- economic burden and highlighting the significance of reinforcement of services for this susceptible group. The pattern of EPTB varies from region to region. It has become a diagnostic dilemma in this

era of HIV/AIDS. Proper counseling, awareness programs, high index of suspicion and timely management of the disease are necessary for reducing morbidity and mortality.

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