

## To study the profile of extra pulmonary tuberculosis at tertiary health care centre

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### Abstract

**Introduction:** Tuberculosis (TB) is a major global health problem and India being highest tuberculosis burden country, needs emphasis. The percentage of Extra pulmonary tuberculosis (EPTB) among all diagnosed TB cases in developed countries range from 12 to 28.5% while in India ranged from 30-55%. **Aims:** To Study the Socio-Demographic Profile of Extra Pulmonary Tuberculosis cases diagnosed in a tertiary health care centre, the various Clinical Presentation of Extra Pulmonary Tuberculosis and the various Risk Factors Associated with Extra Pulmonary Tuberculosis. **Materials and Methods:** The present study was a hospital based Observational Study. This Study was conducted from March 2021 to June 2022 at Department of Respiratory Medicine, Mahatma Gandhi Hospital, Jaipur. **Result:** In our study most patients were 21-40 years old (51%) & female (67%), most no. of patients were housewife (53%), upper lower class (36%) and from urban area (52%), most number of EPTB patients had fever (100%) and loss of appetite (55%) as the main clinical feature. It was found that patients had h/o ATT (22%) and no H/O ATT (78%), 31% patients were smokers, biomass fuel exposure was present in (21%) and T2DM in (14%). Lymph node Tb was present in (36%), Abdominal Tb in (24%), Pleural Tb in (14%), genitourinary Tb (12%), CNS Tb (4%). **Conclusion:** Extra pulmonary tuberculosis is a significant health issue in developing countries. In conclusion, our study shares the knowledge regarding the epidemiology of EPTB and gives understanding of the host related factors to its pathogenesis. The frequency of EPTB in this study was advanced with the maximum proportion in lymph node. Also, female case was at advanced rate of positivity for EPTB than male. Youthful grown-ups between age 21-40 yrs, and associated diabetes mellitus & smoking were significant risk factors for being EPTB positive.

**Keywords:** Extra pulmonary tuberculosis, pulmonary tuberculosis and tuberculosis

### Introduction

Tuberculosis (TB) is a major global health problem and India being highest tuberculosis burden country, needs emphasis. The percentage of Extra pulmonary tuberculosis (EPTB)

among all diagnosed TB cases in developed countries range from 12 to 28.5% while in India ranged from 30-55% <sup>[1]</sup>.

While Pulmonary Tuberculosis (PTB) is the most common presentation of tuberculosis, EPTB is also an important clinical problem in endemic countries like India. The term EPTB is used for isolated occurrence of TB at body sites other than the lungs. Diagnosis of EPTB is done as per NTEP (National Tuberculosis Elimination Programme) guidelines which is based on microbiological evidence of mycobacterium tubercle or confirmed molecular test for tuberculosis in specimen from extrapulmonary sites or histological evidence or strong clinical evidence consistent with EPTB <sup>[2]</sup>. Atypical presentation, lack of diagnostic resources for procurement of tissue or fluid for diagnosis from an accessible site and a poor yield of conventional diagnostic methods leads to a considerable delay in making the diagnosis or diagnosis may be missed. In today era due to the availability of Computed tomography, endoscopy, Magnetic resonance imaging help in localization of anatomical site for obtaining tissue for diagnosis. High prevalence of Diabetes mellitus, COPD, alcoholics, and malignancies in India making EPTB more prevalent <sup>[3]</sup>.

EPTB occurs as a result of contiguous spread of tubercle bacilli to adjoining structures, such as pleura or pericardium, lympho-hematogenous spread during primary or chronic infection. Gastrointestinal TB may also result from the ingestion of Mycobacterium Bovis infected milk particularly in the rural area where pasteurization of milk is not available <sup>[4]</sup>. Cutaneous TB could be exogenous, endogenous or through hematogenous spread. Hematogenous spread is the most frequent mechanism in genital TB. Genital TB in females, although infrequent, is a cause of infertility. The fallopian tubes are usually involved, followed by the endometrium. In countries with a high prevalence of TB, up to 25% of women with infertility may have genital TB. Central nervous system is also affected by TB.

Tuberculous leptomeningitis being the most common form. When tuberculous meningitis extends to the spinal cord and nerve roots, it is called Radiculomyelitis. In some cases, it arises from contiguous extension of tuberculous spondylitis, or it manifests as a primary lesion from hematogenous spread. Tuberculous arthritis is usually secondary to osteomyelitis or occurs through hematogenous spread by the synovial blood vessels.

Different types of EPTB are Pleural TB, Lymph Node TB, Pericardial TB, Abdominal TB, Genitourinary TB, Bone TB, Central Nervous system TB etc. Extra- pulmonary tuberculosis accounts for 15 to 20% of all tuberculosis cases. Lymph Node TB, Pleural and ganglioner extra-pulmonary tuberculosis are the most frequent forms, followed by genitourinary tuberculosis, symptoms of extra-pulmonary tuberculosis depend on the affected organ <sup>[5]</sup>.

### Materials and Methods

- **Type of Study:** Hospital based Observational Study
- **Period of Study:** March 2021 to June 2022.
- **Place of Study:** Department of Respiratory Medicine, Mahatma Gandhi Hospital, Jaipur.
- **Plan of Study:** This was an Observational study based on tracing Profile of Extra Pulmonary TB in a Tertiary health Care Centre.
- **Sample Size:** All patients had Extra pulmonary tuberculosis in period of March 2021 to June 2022.

### Inclusion criteria

- All Extra Pulmonary Tuberculosis cases.

### Exclusion criteria

- Pulmonary Tuberculosis cases.
- Patient not willing for consent.

### Methodology

Present study was a hospital based Observational study. Data was collected using a pretested proforma meeting the objectives of the study. The purpose of the study was explained to the patient and informed consent obtained. Patients were selected for study who satisfied all

inclusion and exclusion criteria. Relevant history including symptoms and signs at presentation, past medical history, drug history and examination findings were noted. Necessary investigations were undertaken.

### Statistical Analysis

For statistical analysis data were entered into a Microsoft excel spreadsheet and then analyzed by SPSS 24.0. and GraphPad Prism version 5. A chi-squared test ( $\chi^2$  test) was any statistical hypothesis test wherein the sampling distribution of the test statistic is a chi-squared distribution when the null hypothesis is true. Without other qualification, 'chi-squared test' often is used as short for Pearson's chi-squared test. Unpaired proportions were compared by Chi-square test or Fischer's exact test, as appropriate p-value  $\leq 0.05$  was considered for statistically significant.

### Result and Discussion

Our study was an Observational study. This study was conducted from March 2021 to June 2022 at Department of Respiratory Medicine, Mahatma Gandhi Hospital, Jaipur. 100 patients were included in this study.

We found that, 51 (51.0%) patients were 21-40 years old. Age was statistically significant (p < 0.001). It was found that, the mean Age of patients was [41.3000  $\pm$  16.6912]. In our study female population [67 (67.0%)] was higher than the male population [33 (33.0%)] and it was statistically significant (p < .001) (Z=4.8083).

**Table 1:** Age group distribution in study subject

Age group	Frequency	Percent
$\leq 20$	2	2.0%
21-40	51	51.0%
41-60	27	27.0%
$\geq 61$	20	20.0%
Total	100	100.0%

**Table 2:** Distribution of Sex in study subjects

Sex	Frequency	Percent
Female	67	67.0%
Male	33	33.0%
Total	100	100.0%

Chander V, *et al.* (2012) <sup>[6]</sup> observed that Extra pulmonary tuberculosis is substantially higher in their study. Mean age of the patients was 26.67  $\pm$  11.72 years. 57 patients of 86 (66.3%) were in the age group of 15-34 years. Anita Velingker *et al.* <sup>[7]</sup> (2018) observed that EPTB was found in all age groups but majority of cases 33(47.35%) cases belonged to 30-50 years of age group. EPTB was found almost in equal frequency in both sexes, males 64(47%) and females 72(52.9%). Above study had similar observation as our study, depicting the fact that EPTB affect the younger age group more which is economically and sexually productive age group of the society thus proving it to be a major indirect setback to the economy of the nation.

In our study 31% patients were smokers and 14% were k/c/o DM2 among 100 EPTB patients examined.

**Table 3:** Distribution of Personal Hx/Risk factors present in study subjects

Type of EPTB	No. of Patients	Personal Hx/Risk Factor				
		Smoking	Alcohol	Biomass fuel Exposure	DM2	No risk factor
Lymph node	36	6	0	3	3	18
Pleural	14	3	0	9	3	3
Abdominal	24	9	3	6	0	6

Genitourinary	12	3	3	0	6	6
CNS	4	4	3	0	0	0
Bone	2	0	0	0	2	0
Breast & Axilla	8	6	0	3	0	0

Suman Thapa *et al.* 2021<sup>[8]</sup> observed that Smoking and diabetes was present in 90 (43.06%) and 25 (11.96%) patients, respectively. 64 (71.11%) of the smokers were current smokers. As compared to the above study our study had lesser prevalence of smoking and DM2 depicting that smoking and DM2 are relative risk factors for EPTB. More studies are needed to find the association of DM2 and smoking with EPTB.

Most number of the patients had Fever (100 patients) (100%) in all type of EPTB patients which was statistically significant. LOA & LOW was present in 45 patients (45%) patients. Our study showed that, the most number of the patients had Fever in Lymph node Tb group (36) compared to Abd. Pain in Abdominal Tb group (24) which was statistically significant ( $p < .00001$ ) ( $Z = 6.1284$ ).

**Table 4:** Distribution of Predominant symptoms according to site of EPTB

Site of EPTB	No.	Fever	Abd. Pain	Loose motion	Loa	Low	Headache	Seizure	Malaise	Aub	Urinary retention	Chest pain	Back pain
Lymph node	36	36	0	0	33	33	0	0	2	0	0	0	0
Pleural cavity	14	14	0	0	0	0	0	0	0	0	0	14	0
CNS	4	4	0	0	0	0	4	4	0	0	0	0	0
Bone (Potts spine)	2	2	0	0	0	0	0	0	0	0	0	0	2
Abdomen	24	24	24	8	6	6	0	0	6	0	0	0	0
Genitourinary system	12	12	0	0	3	3	0	0	1	8	2	0	0
Breast & Axilla	8	8	0	0	3	3	0	0	0	0	0	3	0

Pınar Aysert Yıldız *et al.*<sup>[9]</sup> found in contrast to our study that Fever was present in 11 (17.5) Lymph node Tb patients, 11 (28.2) Bone Tb patients, 11 (39.3) CNS Tb patients and 14 (60.9) Pleural Tb patients. Above study showed that EPTB patients presented with less symptoms while in our study EPTB patients presented with more symptoms.

Suman Thapa *et al.* 2021<sup>[8]</sup> Fever was the commonest presentation in 166 (79.42%) followed by anorexia in 108 (51.67%), weight loss 104 (49.76%). In above study most number of patients presented with fever, anorexia and weight loss, similarly our in study most number of patients presented with fever, LOA, LOW depicting that fever, LOA & LOW are common symptoms with which EPTB patients presents. This shows changing trend in clinical presentation of EPTB.

Our study showed that, most number of the patients were Housewife [53 (53.0%)] which was statistically significant ( $p < .00001$ ) ( $Z = 8.0764$ ).

It was found that, most number of the patients were Upper Lower Class [36(36.0%)] which was statistically significant ( $p < .00001$ ) ( $Z = 6.721$ ). Our study showed that, most number of the patients were Urban area [52 (52.0%)] this was not statistically significant ( $p = .56868$ ) ( $Z = 0.5657$ ).

**Table 5:** Distribution of socioeconomic status in study subjects

Socio economic status (kuppusswamy scale)	Frequency	Percentage
Upper	3	3.0%
Upper Middle	15	15.0%

Lower Middle	43	43.0%
Upper Lower	36	36.0%
Lower	3	3.0%
Total	100	100.0%

Khan AH, *et al.* (2019) <sup>[10]</sup> found that extra-pulmonary tuberculosis (EPTB) represents about 14% of all cases of tuberculosis (TB). Those living in urban areas (1.272 [1.109-1.459];  $p = 0.001$ ) and Upper lower class with no formal education (1.361 [1.018-1.820];  $p = 0.037$ ).

In our study, most number of patients had Lymph node Tb [36 (36%)] which was statistically significant ( $p = 0.00174$ ) ( $Z = 3.1277$ ) and secondly had Abdominal Tb (24%) (Ileocecal junction, Liver, Spleen) and thirdly Pleural Tb (14%) which was statistically significant ( $p = 0.0002$ ) ( $Z = 3.7148$ ). Apart from this we found tubercular infection on rare sites including Breast (4%), CNS & Bone (6%), Rt. Axillary cyst and Rt. Axillary sinus tract (4%), Genitourinary system (12%)-Prostate gland (2), Urinary bladder (2), Uterine Endometrium (8).

**Table 6:** Distribution of Site of Disease

Site of Disease	Affected Organ	Frequency	Percent
Abdomen	Abdomen	7	7.0%
	Ileo-caecal junction, colon	6	6.0%
	Liver	3	3.0%
	Intestine	4	4.0%
	Liver/spleen	4	4.0%
	Total	24	24.0%
Breast	Left breast lump	4	4.0%
Pleura	Left side Pleura	8	8.0%
	Right side pleura	6	6.0%
	Total	14	14.0%
Lymph Node	Lymph node	36	36.0%
CNS & Bone	Meninges	4	4.0%
	Potts spine	2	2.0%
	Total	6	6.0%
Axilla	Right Axillary cyst	2	2.0%
	Right axillary sinus tract	2	2.0%
	Total	4	4.0%
Genitourinary System	Prostate gland	2	2.0%
	Urinary Bladder	2	2.0%
	Uterine Endometrium	8	8.0%
	Total	12	12.0%

Teyim Pride Mbuh *et al.* (2019) <sup>[11]</sup> The most affected site were the lymph nodes (68.9%) and there was a statistically significant different between the positivity of lymph node aspirates and all other EPTB specimens tested [ $p = 0.001$ , CI 55.4-82.4, OR=] this was closely followed by the pleural cavity 7 (15.6%). Above study showed that Lymph node was more affected with EPTB, similarly our study also that EPTB affects lymph node more than other organs depicting that Lymph node is the most common site affected by EPTB.

In our study, Pleural fluid characteristics of patients was, mean sugar [74.3000± 32.3503], mean ADA of patients was [46.7395± 31.8291], Protein of patients was [4.6095± .8286], LDH of patients was [524.2476± 310.5783] and cell count of patients was [2638.5714± 3875.0875].

Kiran Gupta *et al.*, (2020) <sup>[12]</sup> found in their study that the mean ± SD of ADA and protein in body fluid which was calculated to be as 84.81±44.55 IU/L, 4.67±0.94 gm/dL. In body fluid the mean ± SD value for glucose in test group was 80.73±42.2 mg/dL. The mean ± SD of LDH in tubercular pleural effusion cases was 3404.2±9201.67 IU/L. Above study shows that

ADA and LDH is found higher & glucose is lower in tubercular pleural effusion, similarly our study shows the same result depicting that high ADA & LDH and low glucose in pleural fluid indicated tubercular etiology.

We showed that, 4 patients who underwent Abdominal Colonic biopsy-chronic inflammatory infiltrates, granuloma formation [4(16.6%)] which was statistically significant ( $p < 0.0232$ ) ( $Z = 2.2736$ ). In our study, 6 patients who underwent Genitourinary Endometrial curettages showed-granulomatous inflammation possibly tuberculosis [6(50.0%)].

Our study showed that, 4 patients had Breast & Axilla Trucut biopsy-left breast lump showed-chronic granulomatous mastitis [4 (50.0%)] 36 patients who underwent lymph node biopsy & FNAC showed granulomatous changes.

Ali Essa Shaker (2021) *et al.* <sup>[13]</sup> A total of 74 patients (18 males, 56 females), mean age 29.72 suspected to had extrapulmonary TB underwent biopsies from different tissue types. The biopsies from the 74 patients were taken from different tissues according to the site of lesion, 49 (66.2%) biopsies were taken from lymph node, 12 biopsies (16.2%) was taken from mass in the axilla, 6 (8.1%) from abscess, 4 (5.4%) from the intestine, 3 (4.1%) from fistula. Histopathological reports of the biopsies, there were 54 (73%) patients had positive histopathological (granuloma) result and 20 (27%) patients had negative results (non-granuloma). The sensitivity of histopathological examination of the biopsies was 91.02%. Above study showed that most common histopathological finding in biopsy samples of EPTB patients was granuloma formation similarly in our study most number of biopsy samples showed granuloma formation depicting that granuloma formation in histopathology of biopsy is strong clue for the diagnosis of EPTB.

In our study, number of the patients who underwent CECT Abdomen-Enlarged periportal and peripancreatic lymphadenopathy [3 (12.5%)] was found but it was not statistically significant ( $p = 0.6818$ ) ( $Z = 0.409$ ), multiple homogenously enhancing LN, IC junction thickening, 4 (16.6%) patients had-thickening in proximal jejunal loops, confluent enlarged mesenteric & periportal LN, 3 (12.5%) patients had Diffuse small bowel wall thickening with loculated ascites, bulky ovaries, 3 (12.5%) patients had Edematous thickening in distal ileal loops, IC junction and caecum and 3 (12.5%) patients had lymphadenopathy. In our study, all patients who underwent MRI brain & spine (4 Patients)-[2 (50.0%)] had Linear periventricular enhancement seen and [2 (50%)] had Vertebral collapse L4-5, Collection present in B/L paraspinal spaces. Our study showed that, most number of the patients who underwent USG-lymphadenopathy was found [36-36%] this was statistically significant.

Sanjay Gambhir *et al.* 2016 <sup>[14]</sup> observed that Radiological investigations play a crucial role in the early and correct identification of EPTB. Imaging modalities of choice are computed tomography (CT; lymphadenopathy and abdominal TB) and magnetic resonance imaging (MRI; CNS and musculoskeletal TB). MRI is also indicated in paediatric or pregnant patients, in whom radiation is to be avoided. In addition, bone scanning is performed in skeletal TB. Above study and our study similarly find that radiological investigations play a crucial role in diagnosing EPTB by localizing the site of EPTB and making tissue sample extraction easier for further microbiological, molecular and histopathological examination.

## Conclusion

Extra pulmonary tuberculosis is a significant health issue in developing countries. In conclusion, our study shares the knowledge regarding the epidemiology of EPTB and gives understanding of the host related factors to its pathogenesis. The frequency of EPTB in this study was advanced with the maximum proportion in lymph node. Also, female case was at advanced rate of positivity for EPTB than male. Youthful grown-ups between age 21-40 yrs, and associated diabetes mellitus & smoking were significant risk factors for being EPTB positive and tuberculosis can also involve rare sites in body. Grounded on the above conclusions there are following recommendations: Newer individual tests like molecular characterization etc. which are sensitive and specific and easy to use for early discovery and

diagnosis of EPTB should be used.

- Tuberculosis affected almost all organs of body in our study so, attempt should be made for the diagnosis through histopathology, microbiology and molecular testing.

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