



## Clinical spectrum and outcome of extra-pulmonary tuberculosis in children.

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## INTRODUCTION

Tuberculosis (TB) is known to be one of the most ancient and lethal diseases globally. TB is a matter of great concern in Pakistan as Pakistan stands 5<sup>th</sup> among highest TB prevalent countries.<sup>1</sup> It is a major clinically challenging health problem among pediatric age group but it is considered to be a preventable and treatable disease. About 1/3<sup>rd</sup> population of world is estimated to be infected by mycobacterium tuberculosis (MTB).<sup>2</sup> TB carries significant danger to public health all around the world and threat resonates even more among developing countries. Persons infected with MTB could either remain asymptomatic or advance to active TB disease. EPTB or EPTB along with pulmonary involvement form a small proportion (19-39%) of all active TB cases as most of the patients are found to have pulmonary TB (PTB).<sup>3</sup> When TB is diagnosed clinically and

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**ABSTRACT... Objective:** To determine the types, clinical spectrum and outcome of Extra-Pulmonary Tuberculosis (EPTB) in children admitted at a tertiary care hospital. **Study Design:** Cross Sectional study. **Setting:** The Children's Hospital and The Institute of Child Health, Lahore. **Period:** May to December 2019. **Material & Methods:** A total of 63 patients diagnosed with EPTB aged 1 month to 16 years were included. All patients with lung involvement were excluded from the study. Anti-tuberculous therapy (ATT) was started in all patients and outcome was monitored during the hospital stay. **Results:** In a total of 63 patients, mean age was 9.03+3.1 years. There were 35 (55.5%) male and 28 (44.4%) female. The mean duration of symptoms at the time of presentation was 5.93+2.4 months. The common sites of EPTB were meninges noted in 17(26.9%), pleural in 13 (20.6%), abdominal in 12 (19.04%), lymph nodes in 11 (17.4%), disseminated in 6 (9.52%) and bone and joints in 4 (6.34%) patients. The most common systemic complaints were fever in 58 (92.06%), weight loss in 48 (76.1%) and anorexia in 45 (71.4%). After treatment, fifty-four patients improved and discharged while 9 (14.2%) patients died. **Conclusion:** The commonest sites of EPTB were meninges, pleural, abdomen and lymph nodes. Fever, weight loss and anorexia were the most frequent systemic complaints. Most of the patients recovered while the most common cause of mortality was tuberculous meningitis.

**Key words:** Anti-Tuberculous Therapy, Disseminated Tuberculosis, Extra-Pulmonary Tuberculosis.

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bacteriologically in other parts of body except lungs, it is called EPTB.

EPTB cases are increasing in numbers among all TB cases in children.<sup>4</sup> There are multiple risk factors which are associated with EPTB, such as male gender, younger age and HIV infection.<sup>5,6</sup> The sites of EPTB are variable in different age groups, but common sites are lymph nodes, meninges, abdomen, pleura, bones and joints.<sup>7,8</sup>

Although PTB is most common among all types of TB, EPTB also affects significant number of cases.<sup>9,10</sup> If patients have both pulmonary and EPTB, they are classified as pulmonary TB. Children with EPTB are less infectious as compared to pulmonary TB, however, they are at higher risk to develop severe EPTB, such as tuberculous meningitis (TBM).<sup>11,12</sup> Among pediatric age

groups, diagnosis of EPTB could be challenging as majority of the signs and symptoms of EPTB are non-specific while sensitivity of diagnostic modalities remain low because of paucibacillary nature of this ailment, and might be similar to other diseases.<sup>9</sup> It is always better to have high index of suspicion while early initiation of the treatment is considered to be the most significant factor reducing the morbidity as well the mortality among TB cases. Exploring TB data among children in a country like Pakistan is considered vital so the aim of this study was to determine the types, clinical spectrum and outcome of EPTB in children admitted at a tertiary care hospital.

### MATERIAL & METHODS

This cross-sectional study was conducted at Department of Paediatric Medicine, Children's Hospital and The Institute of Child Health, Lahore from May to December 2019. Approval from institutional ethical committee was taken for this study (2020-EME/IUH140). Informed consent was acquired from parents or guardians of all study participants for inclusion in this study.

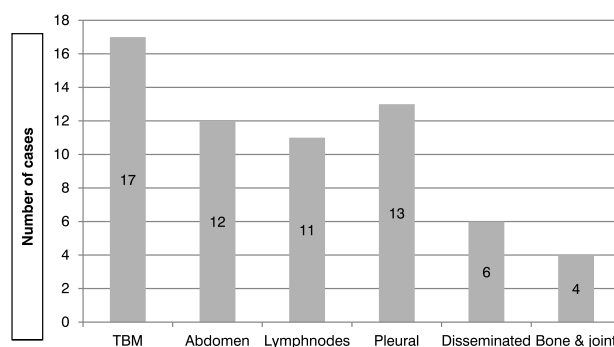
In this study 63 patients diagnosed with EPTB were included. When TB was diagnosed clinically and bacteriologically in other parts of the body except lungs, it was labeled as EPTB.<sup>3</sup> A special proforma was designed to record all study data. Assessment was done by a detailed history and examination, asked about BCG vaccination status, history of contact with TB patient along with nutritional assessment. Complete workup in the form of complete blood count with ESR and chest X-ray were done. Montoux test were done in all patients. Other tests were done according to site of involvement such as ascitic tap, ultrasound abdomen and CT abdomen for abdominal TB. For CNS involvement, cerebrospinal fluid (CSF) analysis and CT brain were done, Lymph node biopsy, pleural tap, X-rays and MRI for bone and joints were performed. Anti-tuberculous therapy (ATT) as 4 drugs was started in all patients. It consisted of Rifampicin, Isoniazid, Ethambutol and Pyrazinamide for initial 2 months and Rifampicin and Isoniazid were continued for a period of 9 to 12 months. All cases were monitored for outcome during hospital stay.

### RESULTS

In a total of 63 patients, mean age was 9.03±3.1 years. There were 35 (55.5%) male and 28 (44.4%) female, representing male to female ratio of 1.25:1. The mean duration of symptoms at the time of presentation was 5.93±2.4 months. Out of all patients, 49(77.7%) patients were malnourished, BCG vaccination was done in 24 (38.09%) and Mantoux test was positive in 43 (68.2%) patients. History of contact with a TB patient was found in 39 (61.9%) patients. (Table-I).

Clinical Profile		Number (%)
Gender	Male	35 (55.5%)
	Female	28 (44.4%)
Age	1 month – 1 year	9 (14.2%)
	1—5 year	11 (17.4%)
	5—10 year	28 (44.4%)
	10—16 year	15 (23.8%)
Nutritional status	Normal	14 (22.2%)
	Malnourished	49 (77.7%)
BCG vaccination status	Vaccinated	24 (38.09%)
	Not vaccinated	39 (61.9%)
Mantoux test	Positive(>10mm)	43 (68.2%)
	Negative	20 (31.7%)

**Table-I. Clinical profile of children with extra-pulmonary tuberculosis (n= 63).**



**Figure-I. Sites of extra-pulmonary tuberculosis in children (n=63).**

The most common systemic complaints were fever in 58 (92.06%), weight loss in 48 (76.1%) and anorexia in 45 (71.4%). Investigations revealed low hemoglobin <9gm/dl in 32 (50.7%) patients, increased ESR in 43 (68.2%), raised TLC > 11,000/

mm3 in 35 (55.5%), hypoalbuminemia < 2.5gm/dl in 25 (39.6%) and deranged transaminases in 27 (42.8%).

Out of 63 patients, 54 (85.7%) improved and discharged. During stay, 9 (14.2%) patients died, 5 of TBM, 2 of disseminated TB and 2 due to complications of abdominal TB.

## DISCUSSION

EPTB is a common disease in pediatric age group due to dissemination of MTB from primary focus in lungs, after acquiring primary infection. In our study most of the patients were male (55.5%), however other researchers have also found female gender to be more commonly involved in EPTB cases (51.6%).<sup>13</sup> Common sites of EPTB in our study were meninges, pleural and abdominal followed by lymph nodes. Similar findings were reported from Bangladesh where 27.8% patients had TBM.<sup>13</sup> In another study from Saudi Arabia, the common sites of involvement in EPTB cases were lymph nodes (42%), bone (13.7%), abdominal (13.3%) and pleural (12.1%) followed by meninges.<sup>14</sup> A Turkish study noted tuberculous lymphadenitis predominance in EPTB children (32%) followed by abdominal and TBM.<sup>15</sup> Another study from Ghana revealed disseminated TB as the commonest site 32.8% followed by pleural 18.4%.<sup>16</sup> So, all these studies show variation in terms of most frequent sites of EPTB and this is why it is vital to conduct studies among different populations for determination of most common sites of EPTB.

The common systemic presenting complaints were fever, anorexia and weight loss in our study. Another local study by Hanif et al described the same presenting complaints of fever, weight loss and anorexia.<sup>17</sup> Similar results were reported by an Indonesian study.<sup>18</sup>

Malnutrition is a predefined risk factor for TB in children. In our study, 77.7% of patients were malnourished. A Pakistani study from Sindh province reported a remarkable proportion of participants (90%) with TB to be underweight.<sup>19</sup>

Although tuberculin skin test is very commonly

used by physicians all over the world, its application and interpretation always remain difficult and challenging and depends on multiple factors. In our study 68.2% patients had a positive Mantoux test. Other studies from the region also showed comparable results. Study done in Turkey reported it as 58.9%<sup>15</sup>, while in a study from Philippines it was positive in 87.9% patients.<sup>20</sup> In our study, the most affected age group was 5-10 years of age. The same finding was also observed by Santos et al in which most of the cases were 5-10 year of age.<sup>20</sup>

In our study, the mortality was observed in 14.28% patients and the commonest reason was TBM with its complications. In another study, almost same, 16.7% mortality was observed and the commonest cause was TBM.<sup>20</sup> Study from Saudi Arabia also revealed the highest mortality due to TBM (52%) followed by disseminated TB (47%).<sup>14</sup> Similar findings were observed from a Bangladeshi study where case fatality rate of 14.29% was observed and 6.59% deaths were due to TBM.<sup>13</sup> As we know that TBM might constitute a minor proportion (around 1%) of all TB patients, TBM is thought to cause major suffering with increased rates of morbidity as well as mortality. Prognosis of TBM is not very good while those who survive frequently have serious disabilities. Early identification and treatment of TBM is vital as delayed diagnosis can lead to unfavorable outcomes like mortality, neurological sequelae and neurocognitive diseases as was found in the present study where TBM was the commonest cause of death.

## CONCLUSION






Extra-pulmonary Tuberculosis is a common illness in children especially above 5 years of age in developing countries. The most common sites of EPTB were meninges, pleural, abdominal, lymph nodes and disseminated TB followed by bones and joints. As symptoms of EPTB are usually nonspecific in initial stages of disease, there is usually a delay in the diagnosis. A high index of suspicion should be there especially in countries with high prevalence of TB.

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### AUTHORSHIP AND CONTRIBUTION DECLARATION

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2	Aysha Mansoor Lodhi	Literature review, Data analysis.	
3	Wajiha Rizwan	Data interpretation, Discussion, Proof reading.	
4	Carol Ruth	Data collection, References.	
5	Meher Muzaffar	Data Collection.	
6	Arooj Mir	Data Collection.	