ORIGINAL ARTICLE

Clinical Spectrum of Childhood Tuberculosis

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ABSTRACT

Objective: This study aimed to determine clinical spectrum and identification of risk factors of tuberculosis.

Study Design: Descriptive cross-sectional study.

Place & Duration of Study: Study was conducted at Children Hospital Faisalabad in Pediatric Medicine Department in children admitted under 15 years of age from March 2023 to February 2024.

Material and Methods: After taking permission from ethical review committee, full explanation of study purpose was explained to parents after fulfilling inclusion criteria. A questionnaire was designed to evaluate the associated risk factors of TB and its presentation. Then patients were investigated and confirmed according to disease protocol.

Results: A total of 102 patients were enrolled in this study group. Most of the patients were females 53 (51.95%) and male patients were 49 (48.03%). Out of them 53 children were diagnosed as having pulmonary tuberculosis and 49 were with extra pulmonary tuberculosis. Among extra pulmonary tuberculosis, tuberculous meningitis was commonest. Patients with disseminated tuberculosis were 9 (8.82%). Contact was positive only in 30% and household contact was present in 22%. Ninety-two patients were Immunized according to history but BCG scar was present only in 49 patients. Ninety-four (92.15%) patients were taking un-pasteurized milk. Severe malnutrition was found in 57 (85%) patients.

Conclusion: Pulmonary tuberculosis and tuberculous meningitis are predominant presentations of childhood tuberculosis. Poverty and lack of knowledge regarding disease are main risk factors. Effective awareness campaigns are urgently needed to address this issue to decrease burden of disease.

Key Words: *Pediatric Pulmonary tuberculosis, Extra pulmonary tuberculosis, Clinical spectrum.*

INTRODUCTION

Tuberculosis (TB) is the most important specific communicable disease in the world and major global health problem.[1] The WHO report in 2022, an estimated 214,000 children and young adolescents deaths due to tuberculosis in children less than 15 years, which means almost 600 children and young adolescents lose their lives daily in a year to this preventable disease.[1]

Pakistan (2022 population; 236 million) accounts for 70% of estimated TB incidence in Eastern Mediterranean Region and therefore regional priority in 2021, WHO estimates that more than 600,000 TB incident cases and 45,000 deaths occurred in Pakistan. However, exact figure of TB incidence in children is still under reported. [2]

Pakistan ranks 5th amongst the high burden countries in the world. The prevalence incidence and mortality per 100,000 population per year from tuberculosis in Pakistan is 340,259 and 20 respectively.[3] It has been accepted that childhood tuberculosis is rampant and important cause of morbidity and mortality in developing countries like Pakistan.[3] Owing to poor socio-economic condition starvation, overcrowding, HIV co-infection and high prevalence of TB in adult context, it has been increasing day by day.[4]

Childhood tuberculosis has got diverse and multiple unusual presentations, making its diagnosis challenging and tough. However, usual presentation is low- or high-grade fever. Majority has pulmonary TB. But extra-pulmonary tuberculosis is not uncommon among pediatric population now. There is a need to adopt an integrated approach of diagnosis including clinical, radiological, microbiological and immunological evidence.[5]

Keeping in view the fact that childhood tuberculosis has got multiple clinical presentations and being one of common problem of our country. Still there are very little local studies available in Pakistan, so we planned a study in our setup to determine the clinical presentation and risk factors of childhood tuberculosis. As children are more vulnerable to tuberculosis due to their immature immune system that's why they are more likely to develop severe form such as miliary tuberculosis and tuberculous meningitis. To avoid the complications associated with tuberculosis, we thought patient clinical features should be probed in his particular background regarding socioeconomic status, environment, risk factors and contacts he/she has encountered. This study will add-up to the local data which will increase our understanding of local mechanisms of spread and prevention.

Aims and objectives: To determine, the clinical presentation and risk factors of childhood tuberculosis.

MATERIAL AND METHODS

Study design: Descriptive cross-sectional study.

Settings: Pediatric medicine ward, The Children Hospital & Institute of Child health, Faisalabad.

Inclusion criteria: All children admitted under age of 15 years:

- With strong history and examination findings strongly suggestive of tuberculosis.
- Patients having labs suggestive of tuberculosis (Mantoux test, gene-Xpert).
- Patients having histology findings compatible with tuberculosis (Granulomatous inflammation with caseation).

Exclusion criteria: Any child having comorbidity like cystic fibrosis, immunodeficiency and congenital lung anomaly.

Duration of study: March 2023 to February 2024 (1 year).

Methods: After taking permission from ethical review committee The Children's Hospital & the Institute of Child Health Faisalabad, Pakistan IRB no. 51 dated 17/04/2023, full explanation of study purpose was explained to parents after fulfilling inclusion criteria. A questionnaire was designed to evaluate the associated risk factors of TB and detailed information obtained regarding history of contact with tuberculous source case, household contact, number of people sharing one room, BCG immunization, socio-economic status, education and HIV status of parents, ingestion of un-pasteurized milk and chronic illnesses other than TB. The patients were further examined for BCG scar and nutritional status via anthropometry (WHO malnutrition classification) and then investigations were sent in the form of CBC with ESR, Mantoux test (done at Children Hospital Faisalabad), gastric aspirate for gene Xpert (Allied Hospital Faisalabad). Mantoux test was excluded for patients having severe malnutrition. Patients having pleural effusion ascites and CSF (with suspicion of tuberculous meningitis) were investigated with aspiration of fluid for cytology and gene xpert. Biopsy specimen (patients having lymphadenopathy) was also sent. All patients were also screened for HIV infection. Data about the main study variables (clinical presentation,

pulmonary/extra pulmonary TB, patients labs) was recorded according to predesigned proforma.

All collected data was analyzed in terms of frequency tables with percentages and graphs. Means and standard deviations calculated with relevant graphical representation for quantitative data.

RESULTS

A total of 102 patients were enrolled in this study group. Most of the patients were females 53 (51.95%) and male patients were 49 (48.03%).

Out of these 102 patients, 92 patients (90.19%) received BCG vaccine and only 10 (9.8%) patients were unvaccinated and out of these 92 patients 49 (48.03%) patients had BCG scar.

Fifty-three (51.96%) patients were from lower socio-economic class, 47 (46.07%) patients were from middle class family and only 2 (1.96%) patients were upper class family (as determined by per capita income).

Forty-two (41.17%) patients were living below 5 marla house, 53 (51.96%) patients were living below 10 marla house and only 7 (6.86%) patients were living above 10 marla house. All houses were overcrowded.

Forty-eight (47.05%) mothers never went to school, 34 (33.33%) mothers were primary passed, 25 (24.50%) mothers were middle passed and only 5 (4.9%) mothers went to college.

Fifty-three (51.95%) patients were diagnosed as having pulmonary tuberculosis and 49 (48.03%) patients were with extra pulmonary tuberculosis (table 01).

TABLE 1: Type of tuberculosis

Male= 49		Female= 53	
Pul-monary	Extra Pulmonary	Pul-monary	Extra Pulmonary
26	23	27	26

Among extra pulmonary tuberculosis, tuberculous meningitis was found commonest that is 26 (25.49%) patients then comes abdominal tuberculosis 13 (12.74%) patients. Patients with disseminated tuberculosis were 9 (8.82%). Among disseminated miliary pattern was found in 3 (2.94%) patients. Only one female (0.98%) patient who was admitted with suspicion of lymphoma was found having tuberculous lymphadenitis (fig 01).

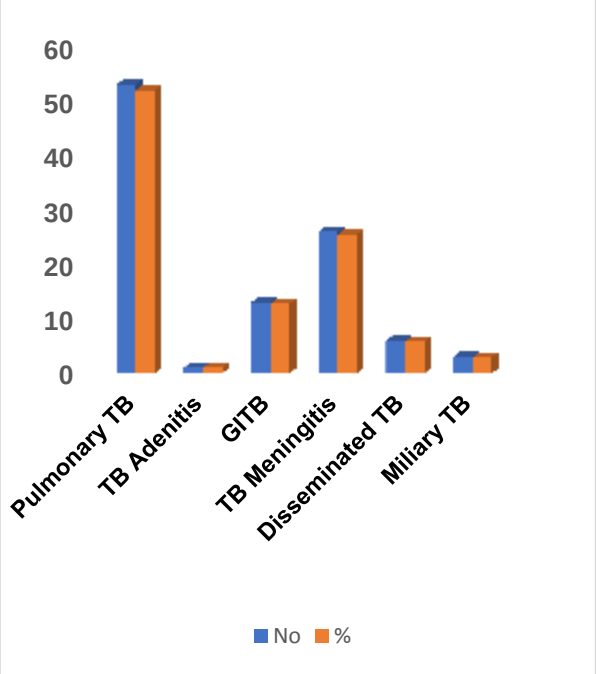

Fig 01: Pattern of TB

Highest proportion of patients were found between 1 to 5 years that is 59 (57.8%) patients then between 5-10 years 24 (23.5%) patients then between 10 to 15 years 19 (18.6%) patients.

Contact was positive only in 30% and household contact was present in 22%. Ninety-four (92.15%) patients were taking un-pasteurized milk. Severe malnutrition was found in 57 (85%) patients. MAM was found in 24 (23.52%) patients and only 21 (20.58%) patients were having adequate nutritional status.

Regarding clinical presentation fever was present in highest percentage of patients that is 94 (92.15%), cough was present in 70 (68.62%), 67 (85.29%) patients presented with fatigue, weight loss was present in 64 (62.17%) patients, 30 (29.41%) presented with fits, 22 (39.21%) patients was presented with night sweats, clubbing was present in 47 (46.07%) patients, hepatomegaly was present in 28 (27.45%) patients, splenomegaly was present in 9 (9.82%) patients, lymphadenopathy was present in 17 (16.66%)

patients, ascites was present in 11 (10.78%) patients, 3 (2.9%) patients presented with hemiplegia (table 2).

TABLE 2: Clinical Presentation of Study Subjects

Clinical features	Frequency	Percentage
Fever	94	92.15
Cough	70	68.62
Fatigue	67	85.29
Weight loss	64	62.17
Night sweats	22	39.21
Convulsions	30	29.41
Liver enlargement	28	27.45
Splenomegaly	09	08.82
Ascites	11	10.78
Lymphadenopathy	17	16.66
Hemiplegia	03	02.9
Clubbing	47	46.07

Forty-five patients who were tested with Mantoux test only 7 (15.55%) were positive. Gene Xpert was sent for 90 patients and only 23 (25.55%) were found positive. 48 (47.05%) were having leukocytosis that i.e. above 11,000. 11 (10.78%) patients were having ESR above 100 and 30 (29.14%) patients were having ESR between 52-70 and rest were having between 20-40. Lymph node biopsy was sent in 7 patients 4 (57.14%) showed granulomatous inflammation.

On chest X-ray 23 (22.5%) patients showed only hilar lymphadenopathy, 13 (12.74%) patients showed opacity. 11 (10.7%) showed opacity with hilar lymphadenopathy, 07 (6.8%) patients showed pleural effusion, 05 (4.9%) patients showed lung collapse, 3 (2.9%) patients showed miliary pattern, 01 (0.98%) had cavity and 39 (38.23%) x-rays were normal.

DISCUSSION

In this era of modern tuberculosis diagnostic capability, still there is significant burden of disease in pediatric population which attributes to disease diversity in presentation.[2]

TB effects mostly the poor as we closely observed the risk factors among our admitted patients. Poverty remained a highest risk factors as poor patients have to live in small poorly ventilated over crowded homes. People are unable to send their children to schools due to low socio-economic status and this led to illiteracy. Illiterate mothers are unaware of food quality and diversity. In this way, a positive vicious cycle develops that is malnutrition leading to TB and TB leading to malnutrition.

Among 102 childhood tuberculosis cases female remained predominant as compared to male. This coincides with the recent TB data collected by NIH[4] that also showed female predominance. Although, the reason is still unclear however, this epidemiology is a public health issue of importance that impact transmission dynamics and disease control initiatives.

Our study emphasizes variability in disease presentation of tuberculosis in pediatric population and its various risk factors.

Generally, age of majority of tuberculosis patients both pulmonary and extra pulmonary ranged between 1-5 years. This is similar to other studies done for pediatric tuberculosis like one conducted in Gilgit Baltistan, Pakistan[6] and another retrospective study done in Uganda showing 54% of TB patients below 5-year age.[7] Another study done in Kashmir India showed contrary results, where maximum number of TB patients were observed in 6 to 11 years age group (39.7%).[8] In our study, most types of tuberculosis individually including tuberculous meningitis, pulmonary TB, abdominal TB, belonged to dominant age group of <5 years children.

There is slight dominance of pulmonary tuberculosis (51.95%) as compared to extra pulmonary tuberculosis (48.03%) in our study. Many of the other studies across the world as well as in Pakistan also showed consistent results like one done in Kashmir India showed (57.35%) of tuberculosis children had pulmonary TB among all age groups.[8] Another study done in India by Gupta et al showed highest ratio of pulmonary tuberculosis (58%) among other types of TB.[9] A retrospective study done in Mexico which is a low prevalence area showed high proportion of pulmonary TB as compared to extra-pulmonary tb.[10] Contrary to our results, Shah in Nepal in 2018 found extra pulmonary tuberculosis more common (59.38%) then pulmonary TB (40.62%).[11] Another Indian study, conducted in Delhi found extra-pulmonary TB (70.2%), three times more common than pulmonary TB.[12] These differences in occurrence of pulmonary TB and extra pulmonary TB may be due to age distribution in

studies presence of other comorbidities, malnutrition and efficacy and availability of diagnostic methods. Pulmonary TB cases are easier to diagnose than extra-pulmonary TB due to non-specific symptoms of extra pulmonary TB which are missed in younger patients.

Tuberculous meningitis is the most common type of extra-pulmonary TB in our study (25.49%) while abdominal TB comes next (12.74%) then comes the patients with the disseminated TB (8.82%). This is similar to results of studies done in Children Hospital Lahore and Kashmir India.[8,13] Abdominal TB is (24.14%) and lymph nodes TB (19%), pleural TB (15.52%). Lymphadenitis was the commonest type of extrapulmonary tuberculosis found in Sudan Khartoum study, also in Madrid a low prevalence region had lymphadenitis the most common form of EPTB.[2] With 34.5%, a multicenter study of Sindh Pakistan also had lymphadenitis TB among all forms of EPTB at top.[14] This variability in type of extrapulmonary TB could be due to different regions and centers all over world. In our study, tuberculous lymphadenitis was missing they are managed in out-patient department.

History of giving BCG vaccine at birth was good, confirmed by EPI card, showing (90.19%) coverage but out of that only (48.03%) had BCG scar while another study done in children hospital Lahore showed 38.09% BCG scar rate.[13] In a Kashmiri India study, it is (69.85%).[8]

Another European study showed that among all BCG vaccinated children only (76%) had scar.[15] Our concern about relationship of vaccination and BCG scar formation is based on the fact that children who do not have a scar have more chances of developing severe disease as compared to non-BCG scar children. Our results are consistent with the results of a metanalysis done in south Africa by Benn, which showed that among vaccinated children, scar positive patients had good survival.[16] Poor scar formation after vaccination can be due to faulty technique, loss of cold chain and poor nutrition.

History of contact with tuberculous patients was present in 30% of our study patients while in Sudanian study it was found very high, around 60%.[2] History of TB contact in another study done in Kashmir India showed 47.8%, Lahore children hospital study is 61.9% and another study in Gilgit Baltistan showed 15%.[6,8,13] These variability among different studies could be due to recall bias, poor interpretation of symptoms, or wrong diagnosis.

Nutritional status was very poor of majority of our study population, with severe acute malnutrition reaching up to 85% and moderate acute malnutrition up to 23.52%. reflecting strong association of malnutrition with tuberculosis. Malnutrition was also high in other studies done like Gilgit Baltistan 24%, similarly in 2021 Khuawar et al., while studying tuberculosis as a forecaster of childhood malnutrition in Sindh, Pakistan observed that 13% children infected with TB were found with low BMI and low nutrition marker.[6,14] Its proportion is further high in Lahore children hospital study with 77.7% children infected with TB were found malnourished.[13] It appears that malnutrition is a predictor of tuberculosis disease and is associated with worse outcome. The case fatality ratio of SAM children is higher in TB comorbidity.[17]

Regarding signs and symptoms fever was present in 90% and cough was 70%, weight loss was present in 62.17%, fits were present in 39.21%. Clubbing was present in 46.07% (this was not only due to bronchiectasis but also due to malnutrition and hypalbuminaemia)[18], our findings are consistent with other studies like in 2019 in Bangladesh Ahsan et al found fever 94.12%, cough 84.34%, cold 70.59%, vomiting 49.02% among tuberculosis children.[19] Among extrapulmonary tuberculosis patients, again fever 92.06%, weight loss 76.1% and anorexia 71.4% was found in TB patients in a study conducted in Lahore children hospital in 2019.[13] In a Brazilian study of clinical and epidemiological features of tuberculosis in children and adolescents, weight loss followed by expectoration followed by fever were the most commonly found symptoms.[20] A tertiary care paediatric hospital in Sudan found prolonged fever as the most common presenting feature in 170 (97.7%), followed by weight loss in 139 (79.9%), cough in 125 (71.8%) and lymphadenopathy in 103 (59.2%).[2]

All these variations might be due to, different systemic involvement, age and sex differences, subjective variation in history taking, study conducted in specific centres.

Among patients who were tested with Mantoux test only 15.55 % were found positive, similar rate was found in Sudan study patients, but its positivity rate was high in children hospital study 68.2%, also kaba oz et al in turkey found positive Mantoux test in 63.8% of tuberculous patients.[2,13,21] This low rate of positive Mantoux test could be due to high prevalence of malnutrition.

As TB is a paucibacillary disease, so Gene Xpert test done on gastric aspirate was found positive only in 25.55%patients, while south Indian study had 31 %positive Gene Xpert rate, so clinical expertise is still more important despite availability of these tests.[5]

Forty-eight (47.05%) were having leukocytosis i.e. above 11,000. 11 (10.78%) patients were having ESR above 100 and 30 (29.14%) patients were having ESR between 52-70 and rest were having between 20-40. Lymph node biopsy was sent in 7 patients 4 (57.14%) showed granulomatous inflammation.

CONCLUSION

The most common form of tuberculosis found in our study is pulmonary tuberculosis. TBM is the most dominant presentation of extrapulmonary TB. The main risk factors responsible for both pulmonary and extrapulmonary TB are low socio-economic status leading to malnutrition, poor education and non-availability of timely health care facility access. So, we have to strengthen our social welfare institutes and NGOs to improve all these interlinked parameters. Healthcare professionals should be trained and updated regarding diagnosis of tuberculosis and implementation of treatment according to WHO guidelines.

Conflict of interest: None

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