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# A Clinical Profile of Pediatric Tuberculosis Presenting to the Emergency Department of Tertiary Care Hospital in Karachi, Pakistan

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## ABSTRACT

### Background

Tuberculosis (TB) is a preventable airborne infectious disease, and its early detection is essential to improve patient outcomes. The extent of childhood tuberculosis is unknown and is estimated to be around 6% of all incidences. Diagnosis of pediatric tuberculosis is always difficult, and no age is spared. The primary objective was to assess the clinical profile of tuberculosis patients presenting to the emergency department (ED). The secondary objective was to evaluate the frequency of BCG vaccination, history of contact, and measles among tuberculosis cases in children presenting to EDs.

### METHODS

This was a retrospective chart review of children admitted to the Aga Khan University Hospital, Karachi, Pakistan, with the discharge diagnosis of Tuberculosis from June 2010 to June 2015 as per WHO criteria. Patient demographic characters, medical history, and physical examination findings in ED, along with vital signs, were recorded from the charts. Lab parameters were recorded from an electronic database. The frequency of BCG vaccination status, history of contact and measles was also documented. A univariate and multivariate regression analysis was performed. Data analysis was done using SPSS v 22. Continuous variables were dichotomized into either normal and abnormal or yes and no. Mean, median and percentages were calculated for frequencies. A p-value of less than 0.05 was considered significant.

### RESULTS

We enrolled 264 children, the majority of 139 (53%) were below 5 years of age, 152 (58%) males and 112 (42%) females. BCG vaccination was given to 81 (30%) males and 60 (23%) female children. 183 (69%) children had pulmonary symptoms, whereas 81 children (31%) had extra extrapulmonary tuberculosis. The commonest extrapulmonary manifestation was gastrointestinal (GIT) 34 (13%), followed by central nervous system (CNS) 27 (10%) cases. Cough was found in 54 children (31%), followed by respiratory distress in 49 children (27%), and almost all were below 5 years of age. Chest X-ray was performed in all cases; 85 (32%) didn't have radiological findings. 23 children had a history of contact and measles both. Miliary TB was found in 6 (26%) cases. However, 22 (99%) of 23 didn't have BCG vaccination. History of weight loss was found in 46 (33%) who either didn't get BCG vaccination or didn't remember (no BCG scar). Of 92 children with weight loss, 31 (34%) had a contact history.

### Conclusion

Diagnosing childhood tuberculosis in the emergency department with vague/overlapping clinical presentations is a dilemma. A clinical scoring system may not identify most cases; hence suspicion must be high in all suspected cases with prolonged history, contact tracing methods, weight loss or failure to gain weight.

### KEYWORDS

Childhood Tuberculosis, Clinical presentation, Contact history

## Introduction

Tuberculosis (TB) is a preventable airborne infectious disease. Pakistan has an estimated incidence of 510,000 new cases yearly and ranks 5th among high-burden countries globally. World Health Organization (WHO) has worked to reduce the TB disease burden, mortality, and prevalence through its National TB Control Strategy to Stop TB by 2017-2020. [(1)]

WHO has disseminated its guidelines on systematic screening for active tuberculosis (TB) based on a thorough review of available evidence. Early TB detection is essential to improve health outcomes for people with this deadly disease and reduce TB transmission effectively. [(1)]

The extent of childhood tuberculosis is unknown and is estimated to constitute about 6% of all incident cases, the majority

occurring in high TB burden countries: an estimated 0.5 million cases and 64,000 deaths occurred among children in 2011. [1] The exact proportion of children with tuberculosis in Pakistan is unknown.

Diagnosis of pediatric tuberculosis is always difficult, and no age is spared; however, children younger than five years are more at risk. Presentation of pediatric tuberculosis varies from failure to thrive, fever and cough to life-threatening illnesses like miliary or tuberculous meningitis and are frequently admitted through the ED with somehow different working diagnoses and was later identified as tuberculosis. [2] Such grey cases were either undiagnosed or ignored ED by physicians. Emergency physicians often diagnose tuberculosis, military tuberculosis, and disseminated tuberculosis as pneumonia or meningitis. Secondarily the presentation of tuberculosis is different in different age groups. [3] Despite multiple studies conducted on pediatric tuberculous from Pakistan, the complex and multifaceted ED presentation of childhood tuberculosis was not looked in.

Our primary objective of this study was to assess the clinical profile of tuberculosis patients presenting to the pediatric emergency department. The secondary objective was to evaluate the relation of BCG vaccination, history of contact, and measles to clinical presentation.

## METHODS

### Study design.

This was an analytic retrospective chart review of all children admitted to the Aga Khan University Hospital with the discharge diagnosis of Childhood Tuberculosis from June 2010 to June 2015 after the approval from the hospital ethical review board. The sample size was calculated on the surveysystem.com calculator with confidence level and confidence intervals of 95% and six respectively, with a population size of the study center was 26,000, and the sample size calculated was 264. The study includes children younger than 16 years of either gender who presented to pediatric emergency with history and clinical findings suggestive of tuberculosis and had a final diagnosis of tuberculosis at the time of discharge from the hospital or in follow-up as per WHO criteria. Neonates and children with other diagnoses or who were either discharged from ED or died were excluded from this study.

### Sampling Technique

Samples were collected through convenience sampling, and the sample size calculated was extracted from the medical records of the study institution; it was reviewed after ethical approval by the primary and co-investigators on a designed proforma. Charts were extracted from the record room using the International classification of disease for pediatric tuberculosis. A pilot study on ten charts was done before starting the actual research to see the data questionnaires' errors and confounding stability.

Patient demographic characters, medical history, and physical examination findings in ED, along with vital signs and laboratory variables, were recorded from the charts. CXR, CBC, ESR, sputum analysis, and other lab parameters were recorded from an electronic database. Data analysis was done using SPSS v 22We collected all data on SPSS v22. Mean, median and percentages were calculated for frequencies. A P-value of less than 0.05 is considered significant. Continuous variables will be dichotomized into either normal and abnormal or yes and no.

## RESULTS

We enrolled 264 children who presented to pediatric emergency with suspected tuberculosis involving any system. Most children were below five years of age (139, 53%). There were 152 (58%) males and 112 (42%) females. Regarding gender distribution of BCG vaccination, we found 81 (30%) male and 60 (23%) female children.

Table I describe the systemic involvement among all children with gender distribution and common clinical manifestations in ED. 183 (69%) children had pulmonary symptoms, while 81 (31%) had extra extrapulmonary tuberculosis. The most typical extrapulmonary manifestation was GIT 34 (13%), followed by CNS 27 (10%) cases. Among the respiratory features, the cough was found in 54 (31%), followed by respiratory distress in 49 (27%), and almost all of them were below five years of age.

CXR was performed in all cases; 85 (32%) didn't have radiological findings. However, hilar enlargement was identified in 62 (34%) cases.

The frequency of BCG vaccination status, history of contact, measles with age, gender, and systemic involvement are described in tables II, III & IV.

There were 23 99%) children who had a history of contact with an adult TB case and measles both, among that miliary tuberculosis was found in 6 (26%) cases. However, 22 (99%) of 23 didn't have BCG vaccination.

There was a significant history of weight loss 46 (33%) among children who either didn't get BCG vaccination or didn't remember (no BCG scar, 123); out of 92 children with weight loss, 31 (34%) had contact history.

We had 139 (53%) children who were below five years of age. Out of this, 27 (19.5%) were malnourished, most 15 (56%) female and 12 (44%) males.

Univariate and multivariate logistic regression was done in miliary and disseminated tuberculosis against

| | Male | Female | Total |
|---|---|---|---|
| **Respiratory Symptoms** (n=183) | | (P-0.003) | |
| Cough | 24 | 30 | 54 |
| Distress | 26 | 23 | 49 |
| Chest Pain | 19 | 21 | 40 |
| Purulent/Bloody Sputum | 22 | 18 | 40 |
| No Respiratory Symptoms | 61 | 20 | 81 |
| | **152** | **112** | **264** |
| **CNS Symptoms** (n=27) | | (P-0.393) | |
| Headache | 03 | 02 | 05 |
| Vertigo | 00 | 01 | 01 |
| Seizures | 06 | 02 | 08 |
| Visual disturbance | 01 | 01 | 02 |
| Unconscious | 01 | 01 | 02 |
| Drowsiness | 08 | 01 | 09 |
| No CNS Symptoms | 133 | 104 | 237 |
| | **152** | **112** | **264** |
| **GIT** (n=34) | | (P-0.513) | |
| Abdominal Distension | 04 | 01 | 05 |
| Vomiting | 08 | 03 | 11 |
| Diarrhea | 06 | 02 | 08 |
| Bleeding PR | 04 | 02 | 06 |
| Abdominal Pain | 03 | 01 | 04 |
| No GI Symptoms | 127 | 103 | 230 |
| | **152** | **112** | **264** |
| **Lymph Nodes** (n=24) | | (P-0.002) | |
| Isolated Cervical LN | 03 | 00 | 03 |
| Generalized Lymphadenopathy | 19 | 02 | 21 |
| No LN involvement | 130 | 110 | 240 |
| | **152** | **112** | **264** |
| | | | |
| **Skeletal** (n=26) | | (P-0.315) | |
| Long Bone | 04 | 02 | 06 |
| Vertebral | 12 | 06 | 18 |
| Digits | 00 | 02 | 02 |
| No Skeletal Involvement | 136 | 102 | 238 |
| | **152** | **112** | **264** |
| **CXR** (n=179) | | (P-0.006) | |
| Patchy Consolidation | 13 | 10 | 23 |
| Generalized Infiltrates | 22 | 23 | 45 |
| Hilar enlargement | 31 | 31 | 62 |
| Miliary Pattern | 13 | 12 | 25 |
| Pleural Effusion | 08 | 14 | 22 |
| Pulmonary edema | 01 | 01 | 02 |
| No Radiological Findings | 64 | 21 | 85 |
| | **152** | **112** | **264** |

**Table I: Description of Systemic Involvement and Chest Radiology.**

| | BCG Vaccination | | | Total |
|---|---|---|---|---|
| | Given | Not Given | Not Known | |
| **Hx of Measles** | | | | |
| Present | 07 | 31 | 00 | 38 |
| Absent | 134 | 55 | 37 | 226 |
| **Hx of Contact** | | | | |
| Present | 21 | 46 | 04 | 71 |
| Absent | 79 | 19 | 22 | 120 |
| | 41 | 21 | 11 | 73 |
| | P-value of 0.000 (both) | | | |

**Table II: Frequencies of BCG Vaccination with Measles and Contact History**

| | Age in Years | | | | Total |
|---|---|---|---|---|---|
| | < 1 year (40) | 1-5 years (99) | 6-10 years (70) | >10 years (55) | |
| **Hx of Measles** | | | | | |
| Present (M=19) (F=19) | 11 | 17 | 06 | 04 | 38 |
| Absent (M=133) (F=93) | 29 | 82 | 64 | 51 | 226 |
| P-value of 0.016 | | | | | |
| **Hx of Contact** | | | | | |
| Present (M=38) (F=33) | 14 | 25 | 16 | 16 | 71 |
| Absent (M=70) (F=50) | 09 | 38 | 42 | 31 | 120 |
| Not Known (M=44) (F=29) | 17 | 36 | 12 | 08 | 73 |
| P-value of 0.000 | | | | | |
| **BCG Given** | | | | | |
| Yes (M=81) (F=60) | 23 | 57 | 34 | 27 | 141 |
| No (M=55) (F=31) | 15 | 34 | 21 | 16 | 86 |
| Not Known (M=16) (F=21) | 02 | 08 | 15 | 12 | 37 |
| P-value of 0.071 | | | | | |

**Table III: Relationship between BCG Vaccination, Measles, and Contact History with Ages.**

the common factors like age, gender, history of contact, BCG vaccination and measles. (Table V & VI).

## DISCUSSION

BCG vaccination is an essential shield against lethal pediatric tuberculosis but cannot prevent pulmonary tuberculosis completely. Hence this is the most typical presentation followed by abdominal tuberculosis and CNS involvement. Lung involvement is joint among those with a history of contact and recent measles infection; the vast majority didn't have BCG vaccination. Children younger than five years are more prone to this disease.

Tanju et al. [04] described that almost half of all TB cases presented to ED before diagnosis and get access to definitive care. Many are discharged

| | Systemic Findings | | | | | | Total |
|---|---|---|---|---|---|---|---|
| | Chest | GIT | CNS | Lymph Node | Skeleton | CVS | |
| **Hx of Contact** | | | | | | | |
| Present | 39 | 10 | 08 | 07 | 06 | 02 | 72 |
| Absent | 76 | 16 | 11 | 11 | 12 | 04 | 130 |
| Not Known | 41 | 08 | 07 | 06 | 08 | 01 | 71 |
| **Hx of BCG** | | | | | | | |
| Present | 79 | 18 | 13 | 12 | 16 | 03 | 141 |
| Absent | 54 | 12 | 07 | 08 | 08 | 03 | 92 |
| Not Known | 23 | 04 | 06 | 04 | 02 | 01 | 40 |
| **Hx of Measles** | | | | | | | |
| Present | 29 | 07 | 04 | 04 | 03 | 01 | 48 |
| Absent | 127 | 27 | 23 | 20 | 23 | 06 | 226 |
| Not Known | | | | | | | |

**Table IV: Relation of BCG Vaccination, Measles, and Contact History with Systemic Findings.**

| Factors | Univariate | | Multivariate | |
|---|---|---|---|---|
| | OR [95% CI] | P-value | OR [95% CI] | P-value |
| Ref Age <1 Year | | | - | - |
| 1 to 5 Years | 3.21 [0.7 -14.82] | 0.135 | | |
| 6 to 10 Years | 3.64 [0.76 -17.3] | 0.105 | | |
| >10 Years | 2.44 [0.47 -12.76] | 0.291 | | |
| Gender (Male) | 2.15 [1.13 -4.82] | **0.048*** | 2.32 [1.02 -5.29] | **0.045*** |
| Hx Contact (Present) | 0.83 [0.37 -1.83] | 0.637 | | |
| BCG Given (Present) | 0.39 [1.66 -2.41] | 0.798 | - | - |
| BCG Scar (Present) | 0.87 [0.42 -1.81] | 0.707 | - | - |
| Hx of Measles (Present) | 2.61 [1.11 -6.17] | **0.029*** | 2.87 [1.19 -6.89] | **0.019*** |
| ***Binary Logistic Regression Analysis*** | | | | |
| ***Sig=Significance at 5% with 95% Confidence interval*** | | | | |
| ***OR= Odd Ratio*** | | | | |

**Table V: Univariate and multivariate Binary logistic regression analysis for Disseminated Tuberculosis**

from ED with some of tuberculosis symptoms and are subsequently hospitalized. Such missed opportunity for early identification and diagnosis and management highlights the concern of delays or clinical deterioration.

There is an increased risk of disease progression and extrapulmonary manifestation during the early years (<2 years) with approx. Of 40–50% risk of progression. The surrounding infects most children within 2–12 months of initial infection contact with pulmonary TB, i.e. 60–80% of all cases. [05]

Contact tracing among pediatric tuberculosis is always a difficult task, especially in resource limit settings [06]. Childhood contact is defined as children living near index case for at least 20 minutes per day, for five days a week for at least one month, while index case is defined as an individual aged>15 years with sputum positive for Mycobacterium Tuberculosis [6]. Pre-school children living with their families acquire this disease. (06) Most children under five years had a history of contact, 68% as mentioned in the local study (06), and 57% from Guillermo E et al. [07], almost similar fact in this study, i.e., 55%, who either didn't have contact tracing or

| Factors | Univariate | | Multivariate | |
|---|---|---|---|---|
| | OR [95% CI] | P-value | OR [95% CI] | P-value |
| Ref Age <1 Year | | | - | - |
| 1 to 5 Years | 3.21 [0.7 -14.82] | 0.135 | | |
| 6 to 10 Years | 3.64 [0.76 -17.3] | 0.105 | | |
| >10 Years | 2.44 [0.47 -12.76] | 0.291 | | |
| Gender (Male) | 4.33 [1.44 -12.99] | **0.009*** | 4.38 [1.43 -13.41] | **0.01*** |
| Hx Contact (Present) | 0.83 [0.37 -1.83] | 0.637 | | |
| BCG Given | 0.29 [0.12 -0.71] | **0.007*** | 0.83 [0.21 -3.24] | **0.789** |
| BCG Scar | 0.2 [0.08 -0.52] | **0.001*** | 0.23 [0.06 -0.94] | **0.04*** |
| HX Measles | 0.8 [0.23 -2.8] | 0.721 | | |
| ***Binary Logistic Regression Analysis*** | | | | |
| ***Sig=Significance at 5% with 95% Confidence interval*** | | | | |
| ***OR= Odd Ratio*** | | | | |

**Table VI: Univariate and multivariate Binary logistic regression analysis for Millary Tuberculosis**

didn't remember child contact with an open case of tuberculosis. This difference might be due to the fact that data were gathered from a public sector hospital with larger sample size and a vast number of tuberculosis and poor socioeconomic status.

We found more children (53%) immunized with BCG, as compared to 36% from Siddiqui et al. [08] Males are more vaccinated as compared to female children with a ratio of 1.3:1, almost the same exact figure as described by Siddiqui et al. [08], again females are more malnourished this may represent the continuity of similar male dominant and same old traditions of less care toward our female children, in both privileged and under-privileged component of our society during the past decade.

Though the majority of children with tuberculosis had no clinical symptoms, respiratory symptoms are the most typical clinical manifestation of childhood tuberculosis, as we found 69% similarly. The commonest extra-pulmonary pediatric tuberculosis was lymphadenopathy (67%), followed by CNS manifestation (13%) and military or disseminated tuberculosis (5%) and skeletal (4%) TB. [11] However, Bano I et al. [10] identified pulmonary tuberculosis in 68%. Lymph node involvement was found in 13%, abdominal tuberculosis in 6.5%, tuberculous meningitis among 03%, and disseminated tuberculosis was isolated in only 3% of their study population. [12]

Considering the immunization status in extra-pulmonary tuberculosis, tuberculous meningitis is the most severe entity along with miliary or disseminated tuberculosis. Children who are unimmunized with BCG vaccine during their early days of life are more prone to this deadly disease, and we found 16% of such cases close to 14% by Siddiqui et al. [08]. However, among non-vaccinated children to BCG, the rate of this deadly involvement increases many-fold. A meta-analysis stratified its efficacy of 50% in most forms of pediatric tuberculosis, however, provides better coverage against tuberculous meningitis, miliary, or disseminated tuberculosis, i.e. 64-78%. [12]

## CONCLUSION

Diagnosing childhood tuberculosis presenting to a busy emergency with vague or overlapping clinical presentations is a dilemma. The different clinical scoring scales to identify tuberculosis may not work in ED. Hence the high level of suspicion must be in the mind of every ED physician, especially with prolonged history, contact tracing methods, weight loss or failure to gain weight.

## LIMITATIONS

The number of cases may not reflect the actual magnitude of this disease, the reason behind this might be that the study center is a private hospital, and only those cases visit such EDs who have acute symptoms. Hence quite a few cases were identified. We may not generalize our results to the community by enlarging; our study population was just 1% of the total annual children attending the pediatric emergency.

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