

# Pulmonary Tuberculosis in Children with Severe Acute Malnutrition: A Prospective Hospital-based Study

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## ABSTRACT

**Background:** Tuberculosis is one of the common infectious diseases in under-five children especially with severe acute malnutrition (SAM). Pulmonary tuberculosis (PTB) presenting as pneumonia in undernourished children especially in communities where TB is highly endemic is still a less recognized entity.

**Objective:** To study the prevalence of pulmonary tuberculosis in severe acute malnourished children with acute pneumonia.

**Materials and methods:** Prospective hospital-based observational study done at Nutritional Rehabilitation Centre (NRC), Department of Pediatrics, Karnataka Institute of Medical Sciences (KIMS), Hubli, Karnataka, India from January 2016 to December 2016.

**Inclusion criteria:** Severe acute malnourished children of 1 month to 59 months of age with acute pneumonia with/without HIV infection.

**Exclusion criteria:** Children with severe acute malnutrition already diagnosed to have any form of tuberculosis and on ATT. All enrolled children's detailed history and examination was taken in a predesigned Proforma. A detailed history, examination and investigations like complete hemogram, Mantoux test, chest X-ray, gastric lavage for AFB, Xpert MTB/RIF, was done in all enrolled children.

**Results:** Total of 152 SAM children admitted during the study period, of these 29 (19.07%) fulfilled inclusion/exclusion criteria, with a mean age of  $14.29 \pm 9.63$  months and male (14) to female (15) ratio of 0.9:1. The prevalence of pulmonary tuberculosis in SAM with acute pneumonia was 10.34% (3/29). All three were males, 2 cases were  $\leq 12$  months. Clinical symptoms/signs in order of frequency were fever (100%), respiratory distress (100%) and cough (66.66%). Risk factors for the development of tuberculosis were (i) presence of contact history (2/3) ( $p = 0.007$ ) and (ii) positive Mantoux test (2/3) ( $p = 0.02$ ), respectively. Though tuberculosis was more in children with absent BCG scar however it was statistically not significant (2/3). All three were bacteriologically confirmed (Xpert MTB/RIF assay) and rifampicin sensitive. Smear for AFB was positive in only one child.

**Conclusion:** Pulmonary tuberculosis should be considered in SAM children with acute pneumonia. Family history of contact with tuberculosis and positive Mantoux test was significant risk factors. XpertMTB/RIF was found superior in isolating TB bacilli as compared to smear for AFB.

**Keywords:** Pneumonia, Severe acute malnutrition, Tuberculosis, Xpert MTB/RIF assay.

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## INTRODUCTION

Globally, 10 million new tuberculosis (TB) cases occurred in 2017 of which 2.7 million cases occurred in India.<sup>1</sup> India comes under a group of high TB prevalence countries. Malnourished children are more in India next only to African countries. Combination of malnutrition and tuberculosis is very lethal.<sup>2</sup> In India, more than 33% of under-five deaths were associated with malnutrition.<sup>3</sup>

SAM affects both acquired and innate host defense mechanisms.<sup>4,5</sup> The causative organisms are different for both in well-nourished and severely malnourished children.<sup>6,7</sup> The clinical features of pneumonia in SAM children are often subtle<sup>8</sup> and duration also often less than 2 weeks.<sup>9</sup>

In SAM children with CAP, besides usual bacterial pathogens, TB is more common.<sup>9-12</sup> Many clinical autopsy<sup>13-18</sup> studies showed more TB cases presenting as pneumonia. Despite these evidences, pulmonary tuberculosis presenting as pneumonia in undernourished children especially in communities where TB is highly endemic is still a less recognized entity, although this is very important in the management of such children as mortality also accounts very high. Hence, this study was undertaken to find the prevalence of pulmonary tuberculosis in severe acute malnourished children with acute pneumonia.

## MATERIALS AND METHODS

A hospital-based observational study conducted at Nutritional Rehabilitation Centre (NRC), Department of Pediatrics, KIMS, Hubli,

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**Conflict of interest:** None

from January 2016 to December 2016. The study was approved by the Ethics Committee of the Institute.

### Inclusion Criteria

Severe acute malnourished children of 1 month to 59 months of age with acute pneumonia with/without HIV infection.

### Exclusion Criteria

Children with severe acute malnutrition already diagnosed to have any form of tuberculosis and on ATT.

All children who fulfilled inclusion/exclusion criteria were enrolled into the study. All enrolled children's detailed history,

the examination was taken in a predesigned Proforma and investigations like complete hemogram with ESR, Mantoux test, chest X-ray, gastric lavage for AFB and Xpert MTB/RIF done for all children. Diagnosis of tuberculosis was done as per RNTCP guidelines.<sup>19</sup> Severe acute malnutrition and pneumonia was defined according to WHO SAM criteria<sup>20</sup> and WHO criteria of acute respiratory infection.<sup>21</sup> Mantoux test: 2TU units of PPD RT 23 was given as an intradermal injection in the middle third of the flexor aspect of the left forearm and test evaluated 48–72 hours after administration of PPD. Gastric lavage was sent for both smear AFB and Xpert MTB/RIF assay ( using Cepheid Xpert® MTB/RIF assay).

**Data Analysis**

Data was collected in a preformed proforma, statistical analysis was done using Statistical Presentation System Software (IBM SPSS Statistics 22.0, New York). For quantitative data mean and standard deviation (SD) were calculated. Statistical test like Fisher exact test was used for comparing differences between categorical variables. For interpretation of results, significance was adopted at *p* value < 0.05 at 95% confidence interval.

**RESULTS**

Total of 29 children fulfilled the inclusion/exclusion criteria (Flowchart 1).

Table 1 shows the baseline characteristics of malnourished children. The mean age 14.29 ± 9.63 months and male to female ratio of 0.9:1. The prevalence of pulmonary tuberculosis in SAM with acute pneumonia was 10.34% (3/29).

Table 2 shows the clinical features of confirmed TB cases. All three were males, two cases were ≤12 months. Clinical symptoms/signs in order of frequency were fever (100%), respiratory distress (100%), cough (66.66%).

Risk factors for the development of tuberculosis were the presence of contact history (two out of three) (*p* = 0.007) and positive Mantoux test (two out of three) (*p* = 0.02), respectively. Though tuberculosis was more in children with absent BCG scar however it was statistically not significant (*p* = 0.06). Xpert MTB/RIF assay was positive in all three cases whereas a smear for AFB was positive in only one child.

**DISCUSSION**

Pneumonia is the leading cause of childhood mortality across the world and malnutrition is a recognized risk for pneumonia and death.<sup>22</sup> Unlike the cause of pneumonia in well-nourished children, Gram-negative bacteria form a predominant cause in malnourished children.<sup>6</sup> A few data also suggest that Mycobacterium tuberculosis

is an important cause of pneumonia in severely malnourished children.<sup>6,11</sup> There are many reasons for missing the diagnosis of tuberculosis in SAM children, of these important reasons were paucibacillary nature, difficulty in getting high-quality specimens,

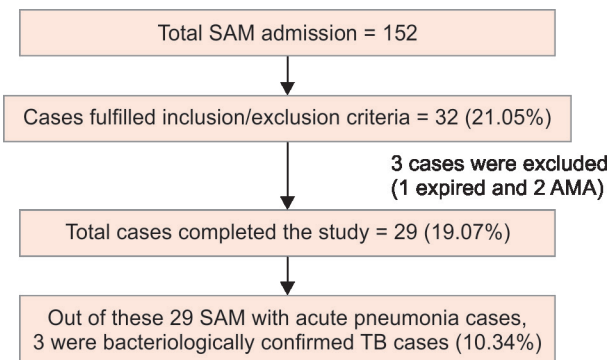
**Table 1:** Baseline characteristics of SAM children (n = 29)

Age	<12 months	13
	13–60 months	16
Sex	Male	14
	Female	15
Residence	Urban	7
	Rural	22
Socioeconomic status	Lower	15
	Upper lower	7
	Lower middle	6
	Upper middle	1
Contact with TB	Present	2
	Absent	27
Immunization	Fully immunized	17
	Partially immunized	7
	Unimmunized	5
Clinical s/o	Fever	28
	Cough	27
Chest X-ray	Consolidation	10
	Collapse with consolidation	2
	Perihilar prominence	1
	Normal	16

**Table 2:** Clinical features of confirmed TB cases (n = 3)

Characteristics	Case 1	Case 2	Case 3
Age	19 months	5 months	1.5 months
Sex	Male	Male	Male
Residence	Rural	Urban	Rural
SES	Lower SES	Upper lower SES	Lower SES
Fever	12 days	13 days	12 days
Contact TB history	Present	Absent	Present
Immunization	Fully immunized	Not immunized	Not immunized
HIV	Negative	Negative	Negative
Mantoux	15 mm induration	14 mm induration	Negative
CXR	Rt mid and lower zone consolidation	B/L hilar prominence with increased density L>R	B/L perihilar haziness f/s/o bronchopneumonia
Smear for AFB	Negative	Negative	Positive
Gene Xpert	Positive	Positive	Positive

**Flowchart 1:** Enrolled cases



the increased presence of extrapulmonary disease, lack of standard case definition.

In our study, prevalence of TB in SAM children with acute pneumonia was 10.3%. Similar observation were made by other studies.<sup>23</sup> However, Veeraraja et al. showed that the prevalence of PTB in SAM children irrespective of the presentation was 22%. All three children with TB in our study were from low SES, and all were males. All the three cases had prolonged fever (>12 days) and respiratory distress. The cough was present in only two cases, and all three had bilateral crepitations and Ronchi and their chest X-ray revealed consolidation features.

Pulmonary coinfection were common in SAM children as SAM itself is an immunocompromised condition (like HIV) wherein, they have reduced the ability to clear the microorganisms and reduced mucosal immunity. Hence, disease progress might be more severe and potentially might present with features of acute pneumonia.<sup>24</sup> In general, the younger age group, especially infants were more commonly affected. The reason for having more cases during infancy in our study was probably due to decreased phagocytic function, reduced microbial killing, poor response of T-cells.<sup>25,26</sup>

Family history of contact with tuberculosis and a positive Mantoux test was a significant risk factor in our study. The observation of the strong association of childhood PTB with a history of contact with TB source case is very important. Children under 5, especially under 1 year of age, who come in contact with TB source case usually have 50% chances to develop TB and 95% of the cases develop TB within 1 year of the exposure.<sup>27</sup>

Mantoux test often negative in SAM children due to the poor inflammatory response. Positive Mantoux test in SAM children increases the chances of having TB, more so if associated with abnormal (patchy/or lobar consolidation) chest radiography.

All 29 children's gastric lavage was sent for both smear and Xpert MTB/RIF. AFB was detected in three children with Xpert MTB/RIF and only one with smear. All three were rifampicin sensitive. Similar findings were highlighted by Chisti et al.<sup>9</sup> As per WHO, for gastric lavage or aspirate sensitivity varied from 40–100%. WHO recommended that Xpert MTB/RIF may be used rather than conventional microscopy and culture as the initial diagnostic test in all children suspected of having TB.<sup>28</sup>

Limitations of our study were smaller sample size, and the gold standard test for TB that is culture for *M. tuberculosis* was not done.

To conclude pulmonary tuberculosis should be considered in children with severe acute malnutrition presenting as acute pneumonia. Family history of contact with tuberculosis and positive Mantoux test was significant risk factors. Xpert MTB/RIF was found superior in isolating TB bacilli as compared to smear for AFB.

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