Prevalence of tuberculosis in severe acute malnutrition: a prospective observational study

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Abstract

Background

Tuberculosis (TB) and severe acute malnutrition (SAM) are important causes of morbidity and mortality in children in the developing World. Malnutrition mainly affects cell mediated immunity (CMI) and CMI is the principal host defense against tuberculosis. Hence, there is possibility that children with SAM may have tuberculosis, and often it may be a hidden entity. Further, Children with SAM and TB are 40% more likely to die than children with SAM and without TB. Children with SAM rarely come to health care settings with complaint of under nutrition rather they present for some other illness. For these reasons, this study intends to seek for TB among children with SAM and look into the common presenting complaints.

Methods

All cases of SAM meeting the inclusion criteria were evaluated with mantoux, chest x-ray, gastric aspirate/sputum analysis and gene xpert for diagnosis of TB. Other relevant investigations for diagnosis of TB were also sent as per the clinical scenario. Data was entered and analyzed using Microsoft excel. Descriptive statistics was used for analysis of data.

Result

Total 107 SAM cases were analyzed. The hospital prevalence of wasting and severe wasting was 11.98% and 0.73% respectively. The prevalence of TB in SAM was 4.67%, commonest being pulmonary TB (60%). 40% of TB cases were without any systemic complaints. Only 19.6% of cases presented with nutritional complaint.

Conclusion

This study found that a significant percentage of cases with SAM had TB and hence adds on the importance of screening for TB (pulmonary TB) in every case of SAM irrespective of symptoms.

Background

Tuberculosis (TB) and malnutrition are important causes of morbidity and mortality in children in the developing World [1, 2]. The available literature suggests that the rate of infections are higher in a malnourished children compared to well nourished children [3]. In 2015, an approximately 1 million children developed TB out of which 170,000 died from it [2]. Similarly, an estimated 50 million children suffered from severe wasting worldwide resulting in about 1 million deaths annually which occur mostly in Sub-Saharan Africa and Asia [4, 5]. Malnutrition and tuberculosis together go in a vicious cycle [6, 7].

Severe malnutrition leads to an immunodeficiency state known as NAIDs (Nutritionally Acquired Immune Deficiency) [8]. Malnutrition mainly affects cell mediated immunity (CMI) and CMI is the principal host defense against tuberculosis [9]. The reason is true for many other infectious condition. TB ranks as the second leading cause of death from an infectious disease worldwide, after Human immunodeficiency virus (HIV) [10]. Children with SAM and TB are 40% more likely to die than children with SAM and without TB [11]. Further, children with SAM rarely come to health care settings with complaint of under nutrition rather they present for some other illness, signifying unawareness regarding malnutrition among parents. This leads to the harboring of disease in uncomplicated SAM cases for long duration and presenting to hospital with complications increasing the morbidity and mortality.

The United Nations had adopted the Sustainable Development Goals (SDGs) in 2015 which aimed to end the global TB epidemic by 2030 [12]. Globally, tuberculosis control program has given low priority to childhood Tuberculosis [13]. Despite the strong epidemiological association between malnutrition and TB infection, the burden of TB among severely malnourished children is not well defined. Most of the studies pertaining to this are retrospective. So this study was started with aim to know the prevalence of TB in SAM cases and to know the various presentations of SAM.

Methods

This study was carried out in Department of Pediatrics and Adolescent Medicine, BPKIHS, Dharan for a period of one year from December 2018 to November 2019 after obtaining ethical approval from the Institutional Review Committee (IRC) with aim to know the prevalence of TB in SAM cases and to know the various presentations of SAM. All cases meeting the definition of SAM according to WHO 2013 updated guidelines for SAM were included in the study [14]. World Health Organization (WHO) has defined SAM as a child of age 6–59 months who has any one of the following: 1. Weight for height/length <-3 z score 2. Mid Upper Arm Circumference (MUAC) < 11.5 cm 3. Bilateral pitting edema of nutritional origin [14]. Parents not giving consent and patients who died/left hospital before work up of TB was complete were excluded.

All children in the age group 6 to 59 months were evaluated with detail anthropometry (eg weight, height/length and MUAC). Weight was measured to the least count of 10 gram and height/length and MUAC was measured to the least count of 1 mm following standard method. Nutritional edema was determined by pressing on the dorsum of foot for 10 seconds. These anthropometric values were further interpreted for weight for height/length as per WHO growth chart.

All cases meeting the inclusion criteria were evaluated for TB with mantoux, sputum/gastric aspirate smear and gene xpert, chest x-ray. Other tests to diagnose tuberculosis were sent as per the decision of treating physician based on clinical scenario like CSF analysis, CT/MRI, FNAC, fluid Adenosine deaminase (ADA).

Mantoux test was done using 1 U of purified protein derivative (PPD) with an insulin syringe. PPD was injected intra dermally on the ventral surface of forearm. The reading was done at 48 hours and

induration greater than 5 mm was considered positive. If reading at 48 hours was negative then reading was repeated at 72 hours.

Two early morning samples of **sputum/gastric aspirate** taken 24 hours apart were sent for microscopic examination for Acid Fast Bacillus (AFB). Gene xpert was also performed from the sample. Sputum production was induced by nebulization with hypertonic saline (3% NaCl) for 15 minutes. Gastric aspiration was done after an overnight fasting of at least 4 hours. **Chest x-ray** was done and when required opinion from radiologist experienced in reading pediatric x-ray was taken. Values of ADA > 60 IU/L for pleural fluid and values > 10 IU/l for CSF was considered positive [15].

Cases were managed as per the WHO protocol for the management of SAM [14] and other clinical condition were managed as per hospital protocol.

Diagnosis of TB was categorized as bacteriologically confirmed if acid fast bacillus (AFB) was demonstrated or gene xpert was positive and clinically diagnosed based on overall clinical scenario, supportive investigations and response to standard treatment.

Data was entered and analyzed using Microsoft excel. Descriptive statistics was used for representation of data.

Results

Total of 14,756(Male:7976, Female:6780) children of the age group 6 to 59 months were evaluated with detailed anthropometry. Out of which 1768 had acute malnutrition (wasting): 1659(Male:487, Female:390) had moderate acute malnutrition (MAM) and 109(M:67, F:42) had SAM, showing the hospital prevalence of MAM and SAM to be 11.98% and 0.73% respectively. Two cases of SAM died before TB work up and hence were excluded from the study. Finally, 107 samples were available for further analysis. Male to female ratio among 107 sample was 1.55. The median age was 22 months (IQR: 13–37 months). Average MUAC was 11.44 cm. Moderate and severe stunting was present respectively in 19 and 25% of SAM cases respectively.

Total 5 cases of tuberculosis were diagnosed, the prevalence being 4.67%. The characteristic of cases with TB has been described in **table** below. Pulmonary TB was present in 60% cases of TB. 40% of TB cases were bacteriologically confirmed. 80% of the TB cases were male. Military TB was diagnosed in a child with known case of HIV. 2 cases (40% of TB cases) had no any pulmonary complaint but on work up were diagnosed to have pulmonary TB; out of these 2 cases 1 case (the 14 months female child) had contact history of TB.

Table: Characteristics of children with tuberculosis

Age (months)	Sex	Type	Diagnosis	Presenting complaint
24	male	pulmonary	clinical	Fever and cough
14	female	pulmonary	bacteriological	Not gaining weight
49	male	pulmonary	clinical	Not gaining weight
59	male	Disseminated (pulmonary + abdominal)	clinical	Fever, cough and vomiting
24	male	miliary	bacteriological	Fever and cough

Only 19.6% of cases presented with complaints related to nutrition and physical growth like not gaining weight. 80.4% presented with other complaints and not nutritional (34.6%: respiratory infection, 10.3%: gastroenteritis, 9.3%: neurological complaint, 6.5%: each for renal and cardiovascular related, 2.8%: blood related like anemia and 10.3%: other complaints). No mortality was recorded among enrolled cases during the hospital stay.

Discussion

We found that 11.98% and 0.73% of children between 6–59 months had MAM and SAM respectively. Out of 107 SAM cases 4.67% had TB, pulmonary TB being the most common (60%). 40% of the TB cases were diagnosed to have pulmonary TB but had no respiratory complaint and over 80% of SAM cases presented for non-nutritional complaint. This shows that under nutrition is still prevalent in low income countries and TB is quite prevalent in severely malnourished children. These children are harboring TB without obvious sign and symptoms except for under nutrition. Further, parents are neglecting under nutrition as a serious problem.

In a retrospective study done by Munthali T et al in Zambia over a period of four years among 9540 under-five children with SAM, the prevalence of TB was 1.58% of which 25% were bacteriologically confirmed cases [11]. Our study was prospective study with relatively small sample size but the findings were similar: prevalence of TB being 4.67% of which 40% were bacteriologically confirmed. Similarly in a retrospective cohort study involving 269 (age: 0–6 years) severely malnourished children by Payghan BS et al in India the prevalence of pulmonary tuberculosis was 5.6%, out of them 86.6% were females and only 5.2% of TB cases were bacteriologically confirmed [16]. The prevalence of TB was similar to our study. Male preponderance for TB in our study could be because of increased proportion of male in our study compared to the above study where female was the predominant gender. The difference in bacteriologically confirmed cases could be because of difference in obtaining sample which has not been explained in the compared study and because of small size of TB cases in both study. In a observational pilot study conducted in tertiary hospital; Delhi, India by Kumar P et al among 76 children with SAM the prevalence of tuberculosis was 9.3% and pulmonary tuberculosis (57%) being the predominant one similar to our study [17]. Similarly in a review by Chisti MJ et al, they quoted three studies from Gambia,

Ethopia and Thailand showing the overall prevalence of bacteriologically confirmed TB in children with SAM to be 21% [18]. The low prevalence of both TB and bacteriologically confirmed TB in our study could be because the difference in type of sample (lung aspirate and induced sputum in compared study vs gastric aspirate and induced sputum in ours).

In a prospective study done by Jena P et al among 190 SAM patients, fever (71%), vomiting (51%), loose stool (46.8%), cough (46.3%) were the common presenting complaints signifying respiratory and gastroenteritis as common presenting complaint similar to our study [19]. The same study found that poor appetite/weight loss was the presenting complaint only in 31% of SAM cases similar to our study (19.6%). In a retrospective study done by Derseh B et al [20] among 413 children, common comorbidities reported were pneumonia(54.8%), gastroenteritis(41.8%) and in a descriptive study by Baskaran VM et al [21] among 200 SAM cases the common comorbidities were acute gastroenteritis (57.5%), pneumonia (44.5%) and anemia (27%). These findings were similar to our study.

Our study had various limitations like relatively small sample size, bronchoalveolar lavage was not performed which is better for diagnosing tuberculosis than gastric aspirate and other modalities to diagnose TB like mycobacterium growth indicator tube (MGIT), culture were not performed because of unavailability.

Conclusion

TB is common among children with SAM. These children might not have typical manifestations of TB except for under nutrition. So screening for TB should be made compulsory in every case of SAM irrespective of symptoms. Further, children usually don’t come to hospital for under nutrition rather they remain in the community till they have other comorbidity, so it would be prudent to search for TB among cases of SAM at community level as well. This will especially becomes important in post CoViD world where malnutrition is definite to rise.

Abbreviations

ADA
Adenosine Deaminase
AFB
Acid Fast Bacillus
CMI
Cell Mediated Immunity
CNS
Central Nervous System
CSF
Cerebrospinal Fluid
CT Scan

Computerized Tomographic Scan
GA
Gastric Aspirate
HIV
Human immunodeficiency virus
IQR
Interquartile Range
LN
Lymph Node
MAM
Moderate acute malnutrition
MRI
Magnetic Resonance Imaging
MUAC
Mid upper arm circumference
NaCl
Sodium chloride
NAID
Nutritionally Acquired Immune Deficiency
PPD
Purified Protein Derivative
SAM
Severe Acute Malnutrition
SDGs
Sustainable Development Goals
TB
Tuberculosis
WHO
World Health Organization

Declarations

Ethical clearance

Ethical clearance was obtained from Institutional Review Committee (IRC).

IRC: 1256/018

Consent: Informed assent was taken from Parents. Confidentiality of data was maintained.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Authors' contributions:

Dr. Jitendra Thakur: concept and design, drafting the article, data collection, final approval of the article

Dr. Ranjana Thakur, Prof. Dr. Nisha Keshary Bhatta, and Dr. Shankar Prasad Yadav: design, drafting the article, data analysis of article

Prof. Dr. Rupa Singh, Prof. Dr. Basudha Khanal and Dr. Narayan Raj Bhattarai: design and drafting of article

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