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Original Research Article

Clinical profile of pulmonary tuberculosis and MDR TB in children at tertiary medical institute

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ABSTRACT

Background: India is the country with highest burden of TB. There is paucity of data as far as Pediatric TB is concern. TB in children directly reflects intensity of on-going transmission of TB in a given community. This study was done including indoor cases of Pediatric pulmonary TB in a medical college hospital, a tertiary care institute in the city of Mumbai. The aim and objectives of this study the clinical profile and outcome of Pediatric pulmonary tuberculosis/MDR TB in an indoor setting of a tertiary care center. It was a clinical observational study in a setting of medical college hospital.
Methods: All admitted children with newly diagnosed pulmonary TB were included in study. A detailed clinical analysis was done. Statistical Analysis Association between two qualitative data was assessed by Chi-Square test, Fisher's exact test for all 2 X 2 tables where Chi-Square test was not valid due to small counts. Comparison of quantitative data measured between two outcomes was done using unpaired t-test. PSPP version 0.8.5 was used for statistical analysis.
Results: Total of 41 patients with pulmonary TB were included in the study, making admission rate of 0.7% of total admission. Three out of 41 children had MDRTB making incidence 7% of total TB patients. Severe acute malnutrition was a major risk factor for dissemination of disease and mortality (p value 0.031and 0.0017).
Conclusions: The study estimates 0.7% admission rate and 7% as incidence of MDRTB in indoor patients. Severe malnutrition was found to be risk factor for dissemination of disease [p value 0.031].

Keywords: Children, Pulmonary, MDR TB, Tuberculosis

INTRODUCTION

India is the country with the highest burden of TB. As per the Global TB report 2017 the estimated incidence of TB in India is approximately 28, 00,000 accounting for about a quarter of the world's TB cases.[1] The actual burden of Pediatric TB is not known due to diagnostic difficulties but has been assumed that 10% of total TB load is found in children. First National Drug Resistance Survey results showed the rates of MDR among new TB patients to be 2.84% and that in previously treated to be 11.60 %.[1] Children are mainly infected by adult pulmonary TB source and childhood TB therefore reflects the intensity of the on-going transmission of Mycobacterium tuberculosis within a community.[2] Children can present with TB at any age, but the most common age is between 1 and 4 years. The presence of MDR TB in children directly reflects the burden of adult MDRTB and national TB control program failure in the given community. There is paucity of data in the incidence and outcome of TB &MDR TB in children. Therefore Authors planned to study the clinical profile of pulmonary TB and MDR TB

among the admitted children in a medical college hospital of Mumbai.

METHODS

- To study the clinical profile of pediatric pulmonary tuberculosis/MDR TB in an indoor setting of a tertiary care center.
- To study immediate outcome in terms of survival with or without complications and death.

Type of Study: This was a prospective observational study done in the indoor pediatric setup of a tertiary medical college hospital during June 2014 to May 2015.

Inclusion criteria

Children in the age group of 6 month to 12 years with Pulmonary Tuberculosis admitted in wards.

Exclusion criteria

- Patients admitted with suspicion of pulmonary tuberculosis but later on diagnosed as some other pathology.
- Patients treated on OPD basis
- Patients with relapse or defaulter.
- Patients less than 6 months
- Patients with congenital tuberculosis.

All patients who fulfilled the inclusion criteria were enrolled after informed consent obtained from parents/guardian. After obtaining the institutional ethics committee clearance, the clinical details of patients was recorded in a predesigned proforma. Author used RNTCP and IAP consensus guidelines 2012 for case definitions. All patients were followed up for their outcome at discharge.

Statistical analysis

Qualitative data was represented in form of frequency and percentage. Quantitative data was represented using mean ± S.D and median & IQR (Interquartile range). Association between two qualitative data was assessed by Chi-Square test, Fisher's exact test for all 2 X 2 tables where Chi-Square test was not valid due to small counts. Comparison of quantitative data measured between two outcomes was done using unpaired t-test. PSPP version 0.8.5 was used for statistical analysis. Graphical representation was done in MS Excel 2010.

RESULTS

There were total 41 patients contributing to 0.70% of total indoor admission during study period. The mean age at presentation was 6.26±3.87years .Fifteen patients (36.6%) were in age group of 9 to 12 years with female preponderance (63.4%). More than 60% of patients belong to upper lower and lower socioeconomic class as per modified Kuppuswamy classification.

Eighteen patients gave history of Koch's contact, 3 had measles, 22 (53.6%) received prior antibiotics but none of them were on steroids. Out of 18 Koch's contact patients, 12 had contact with MDR-TB.

Prolong fever (95.1%) and cough (80.5%) were predominant symptoms, followed by loss of weight or failure to gain weight (46.2%), breathlessness (31.7%), chest pain (19.5%), abdominal pain (12.2%), headache and altered sensorium in one patient.

Seventeen out of 41 (41.5%) had severe acute malnutrition, 10 (24.4%) had moderate acute malnutrition and 10 patients were undernourished. Only four patients had normal nutrition. Twenty eight (68.3%) children had BCG mark, 25 (61%) had pallor, 7 had significant lymphadenopathy and 6 had clubbing.

On respiratory system examination, 24 patients had abnormal respiratory sounds on auscultation, 13 patients had signs of consolidation, 10 had signs of effusion, 7 patients had tachypnea, and 4 had respiratory distress, while 2 patients had signs of pneumothorax. In cardiovascular examination 14 patients had tachycardia, one had cardiomegaly and murmur.

In abdominal examination18 patients had hepato-spleenomegaly, 10 had doughy abdomen, and 6 had ascites. Neurologically two patients had altered sensorium, convulsions, signs of raised intracranial pressure and signs of meningeal irritation. One patient had focal neurological deficit.

Thirty seven patients had raised ESR, Tuberculin test was positive in 23 patients, 09 patient's sputum revealed AFB, and four patients were HIV positive. Out of nine sputum positive cases 3 showed Rifampicin resistance. Thus incidence of MDR TB in this study was found to be 7.31%.

On chest radiology, consolidation was found in 22(53%), hilar lymphadenopathy in 16(39%), pleural effusion in 15, Miliary TB in 8, collapse in 4, cavity in 3 and pneumothorax in 2 patients.

Complications: Among the complications, disseminated TB was most common, observed in 15 patients, 4 patients went into DIC, 2 developed ARDS.

There were 10 out of 17 patients in SAM/Severe Thinness (58.8%), 2 out of 10 in MAM/Thinness (20%), 3 out of 10 in undernourished category (30%) had dissemination. None of the normally nourished children had dissemination. The association between grade of malnutrition and dissemination of disease was found to be statistically significant after pooling of data (p value 0.031).

Table 1: Grade of malnutrition and dissemination.

Grade of malnutrition		Complications-dissemination		Total
		Yes	No	
Severe acute malnutrition/severe thinness	No.	10	7	17
	%	58.80%	41.20%	100.00%
Moderate Acute Malnutrition/Thinness ^	No.	2	8	10
	%	20.00%	80.00%	100.00%
Undernourished ^	No.	3	7	10
	%	30.00%	70.00%	100.00%
Normal ^	No.	0	4	4
	%	0.00%	100.00%	100.00%
Total	No.	15	26	41
	%	36.60%	63.40%	100.00%
Chi-Square tests	Value	Df	p-value	Association is-
Pearson Chi-Square $	7.304	3	0.063	Not significant
Pearson Chi-Square ^	4.661	1	0.031	Significant

Table 2: Association among the cases between grade of malnutrition and outcome.

Grade of malnutrition		Outcome		Total
		Survived without complications	Survived with complications/Died	
Severe Acute Malnutrition/Severe Thinness	No.	3	14	17
	%	17.60%	82.40%	100.00%
Moderate Acute Malnutrition ^ /Thinness	No.	6	4	10
	%	60.00%	40.00%	100.00%
Undernourished ^	No.	8	2	10
	%	80.00%	20.00%	100.00%
Normal ^	No.	4	0	4
	%	100.00%	0.00%	100.00%
Total	No.	21	20	41
	%	51.20%	48.80%	100.00%
Chi-Square tests	Value	df	p-value	Association is-
Pearson Chi-Square $	15.102	3	0.0017	Significant
Pearson Chi-Square ^	10.906	1	0.00096	Significant

None (0%) of the normally nourished children had any complications or death, while 14 (82.4%) among 17 children had complications or death in the severe acute malnutrition group. The association between grade of malnutrition and immediate outcome at discharge was found to be statistically significant (p value 0.0017; p value 0.00096 after pooling of data). The patients without a BCG mark suffered disseminated disease in 46% cases while those having a BCG scar suffered dissemination of disease in 32% cases. However, the association of absent BCG scar and dissemination was not statistically significant.

Clinical profile of MDR TB

Three out of 41 were MDR TB with age of 3, 8 and 11years and 2 were males. All three had persistence of fever and failure to gain weight as common symptoms. They were severely malnourished, anemic and negative for tuberculin test. Two of them were HIV positive. History of Koch's contact was present only in one patient. All three patients had disseminated disease but they survived.

Outcome

Three out of 41 patients did not survive making mortality rate of 7%. Two patients had ARDS and one had disseminated disease with DIC. They all were malnourished (2 SAM, 1MAM), anemic (Hb - 7.8, 6.2, 4.8 gm%), one had positive TT and all were sputum and HIV negative. BCG mark was present in two. History of Koch's contact was present in only one patient.

DISCUSSION

Tuberculosis even today, remains a major health problem among children in the world, especially in India. Authentic information about the extent and magnitude of tuberculosis is scant. The extent of childhood tuberculosis problem is a reflection of infectious pool of adult smear positive cases in the community. Of the total 5822 patients admitted during the study period, forty one patients had clinical and laboratory evidence of pulmonary tuberculosis, accounting for 0.7% (41/5822) of the total pediatric admissions at this referral center. In another study conducted in Nepal, by Shrestha et al[2], of the total 3152 pediatric admissions over a period of 3 years, 60 children were diagnosed with one or the other forms of tuberculosis with the overall percentage of all forms of tuberculosis admitted being 1.96%. In a recent study by Landge & Singhal, 49 children were investigated for PUO, 12 children diagnosed to have TB with 2 of MDR and 01 of XDR TB.[3]

Study by Shah and Chilkar showed 6.8% of drug resistant TB among 500 children with TB.[4]

Mean age in this study was 6.26 years, the youngest being 6 months and the oldest 12 years of age. Similar mean age was reported by Shah and Chilkar.[4] In the study by Shrestha et al, the mean age was 7.4 years. In another study by Salazar et al, among children suffering from Pulmonary TB in Peru, the mean age was 6.8 years .[5]In this study author found similar age distribution and mean age which highlights the prevalence of pulmonary tuberculosis in the younger age group. The probable reasons for this may be factors such as low resistance of the host, increased prevalence of malnutrition and close contact with the infected adults.

In this study, females (63.4%) outnumbered males (36.6%). In a retrospective study carried out by Mazta et al, where a ten year data was analyzed outlining the demographic profile of childhood TB, a similar sex distribution was found, with 64.5% females and 35.5% males when including all forms of tuberculosis, and 71.7% females and 28.3% males in the pulmonary TB category.[6] However in a study conducted in Bellary, by Nagaraj K between 2006 to 2008, overall prevalence was more in boys than girls.[7] A study conducted by VK Arora et al, showed that female children were more susceptible to tuberculosis.[8] This study was in conformance with majority of the studies where female preponderance was found. One of the reasons for this may be because the privileged and male dominated society usually delays the medical treatment for girls. Females are ignored in a society like India especially in rural areas thus leading to malnutrition and various infections like tuberculosis.

We found fever to be the most common symptom on presentation, found in 95.1% cases. This was followed by prolonged cough more than 2 weeks in 80.5%, and loss of weight in 34.1%.Studies done by K Nagaraj and Shrestha et al, found similar observations. The natural history of disease illustrates that progression to disease is indicated by the onset of persistent, non-remitting symptoms, referred to as the breakpoint of clinical significance, whereas the complete absence of symptoms usually indicates good organism containment.[9]

In this study, only 18 of the 41 patients (43.9%) had a contact with an open sputum positive tuberculosis patient in the family. In the study by Shrestha et al, among 60 cases, in 20 (33.3%) of the respondents, history of exposure to TB from immediate family member was elicited. Study by Schaaf et al, in South Africa in culture confirmed childhood tuberculosis revealed 49.5% had contact history this may be due to social stigma attached to the disease, due to which true history may not be revealed.[10] In densely populated city of Mumbai, it may not be possible to pinpoint contacts to be only of familial origin. People in slum areas have poor knowledge about nature of TB and all the family members are usually sleeping in a common room leading to overcrowding and more chances of transmission of tuberculosis in these children. This study however closely agrees with the percentage having positive contact history with other studies.

Author found that only 4(9.8%) among the 41 patients in this study had a normal nutrition status with the rest (90.2%) suffering from malnutrition of varying extents. Among 37 malnourished patients 17 (41.5%) suffered from severe form of malnutrition while 10 each had moderate and under-nutrition. The study by Shrestha et al, found malnutrition in 33.3% of their study group. However it doesn't specify the distribution of grades of malnutrition.

BCG mark was present in 28 patients (68.3%) and was absent in 13 patients (31.7%). In the study by Shrestha et al, BCG mark was seen in 86.6% patients. They found that absent BCG vaccination was significantly associated with disseminated TB ($p<0.05$). In this study, author found that more proportion of patients having absence of BCG mark developed dissemination (46.2%, compared to 32.1% having BCG mark), however this difference was not statistically significant (p value 0.386).

Raised ESR was found in 90.2% of this study population. In a study by Al-Marri MR et al, of 144 childhood TB patients, 68 (47%) had an ESR documented at the time of diagnosis.[11] Culture positive and symptomatic children had significantly higher ESR values than culture negative and asymptomatic children, respectively, at the time of diagnosis in their study.

Author found 9 (21.9%) of the 12 patients (Koch's contact) tested, to have a positive test on nucleic acid amplification, and 3 showing presence of rifampicin resistance these patients were in the high risk group of MDR TB and were isolated and initiated on treatment as per guidelines for the same. All the above children were

transferred to the regional TB isolation center. In the study by Shrestha et al, on all forms of tuberculosis, AFB could be demonstrated in 5 out of 60 (8.33%) cases.[2]

In the study by Panigatti et al, acid fast bacilli (AFB) were isolated in 13 (14 %) children in various fluid/histological specimens.[12] In a Study conducted by S.K Kabra in AIIMS among tuberculosis patients without conducting culture, AFB could be isolated in 11% and was more common in lymph node tuberculosis.

Poor yield of AFB in tuberculosis in children may be due to paucibacillary nature of illness and inability of young children to give appropriate sputum samples. Bacteriological yield among children admitted in hospitals has been reported to vary from 15 to 35% in gastric lavage specimens.[13]

Three out of four cases (75%) having cavitatory lesions had a close contact with an adult sputum positive patient in this study. In a study by Vijayasekaran D et al, 85% of children having pulmonary cavitatory tuberculosis had definite history of contact with an adult with tuberculosis. this study findings are similar to above studies.[14]

There was mortality in 3 (7.3%) patients in this study during the course of hospital stay. In the study by Shrestha et al, mortality rate on follow up was 6.67% for all forms of tuberculosis.[2] Follow up studies done by Cherry Lyn et al, even in culture positive cases revealed 13.4% mortality.[15]

The fact that the majority of transmission in children less than 3 years of age occurs in the household, while they are also the group at highest risk of progressing to disease following primary infection with M. tuberculosis, emphasizes the particular importance of active contact tracing and the provision of preventive chemotherapy in high-risk children. Active tracing and screening of high-risk household contacts will also allow diseased children to be diagnosed earlier, lessening advanced disease.[16]

In malnourished children there is a higher risk of a localized lesion to become progressive or generalized disseminated tuberculosis, because of poor immune response to infection. Studies have shown malnutrition adversely affects the host's defense mechanism by suppressing cell mediated response to the infection.[17]

Shrestha et al, observed that malnourished children had more extra pulmonary tuberculosis (p=0.05) and there were more malnourished children who had disseminated TB which was statistically significant.[2] In this study maximum percentage of dissemination was seen in the severely malnourished group (58.8%). Study by Shah and Chilkar reported 10 out of total 500 TB children [2%] to have dissiminated TB.[4]

On comparing the grade of malnutrition and its association with dissemination (Table 1), it was found to be statistically significant (p value 0.031 after applying continuity correction and pooling of data). Further, SAM as a grade of nutrition when individually assessed for its association with disseminated disease (Table 1), the association was found to be statistically significant (p value 0.013; 0.031 after continuity correction).

On assessment of outcome in this study population, we found that none of the children with normal nutrition status had any morbidity in form of complications or mortality at the end of their course of hospital stay. The outcome worsened in terms of percentage affliction with complications or death as we progressed from relatively mild to more severe forms of malnutrition (Table 2). Authors found the above association between various grades of malnutrition and the immediate outcome at time of discharge to be statistically significant (p value 0.0017; p value 0.00096 after pooling of data).

In a study by Drobac et al, on risk factors for in-hospital mortality among children with tuberculosis, a 25 year data was analyzed and it was found that underweight status was associated with mortality in univariable but not multivariable analysis. However it was observed that malnutrition as a risk factor for mortality could not be ruled out. Malnutrition affects genetic expression and immune function that predisposes children to tuberculosis progression, and the resulting disease and inflammatory response further worsens the nutritional state.[18]

Negative reaction to TST is highly predictive of death among children with active TB and that a negative TST result may be a proxy for the impaired immune function resulting from malnutrition.[19] In this study, of the 17 SAM patients, TST was negative in 12 (70.6%), and among those twelve having a negative TST, ten had complications or death, accounting for 83.3%.

CONCLUSION

It must be emphasized that this hospital-based study probably represents a biased population of sicker children, but author believe it should provide a good overview of children with pulmonary TB who present to referral hospitals in TB endemic settings. Though this study covers all incoming patients to this tertiary center, due to presence of other referral centers in the area, it may not fully reflect disease prevalence thus necessitate the need for a community based study to derive a holistic picture.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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