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PROTEIN ENERGY MALNUTRITION

Pediatrics

Dr. Pardeep Kumar Patidar Resident Medical Officer, Department of Paediatrics, M.G.M. Medical College & M.Y. Hospital, Indore (M.P.)

Dr. Nilesh Jain* Associate Professor, Department of Paediatrics, M.G.M. Medical College & M.Y. Hospital, Indore (M.P.) *Corresponding Author

ABSTRACT

Background: Protein energy malnutrition a major public health problem in children under 5 years causing nearly 50 lakh deaths annually. Malnutrition affects the cell mediated immunity, a principal host defence against tuberculosis. Diagnosis of tuberculosis in these children is a challenge and with inadequate availability of good sputum specimen.

Objectives: To diagnose tuberculosis in children age less than 5 years with severe acute malnutrition using CBNAAT and also correlation between positive cases (diagnosed by Gene Xpert) and their past BCG vaccination and HIV status.

Material & methods: Study carried out on 106 children of age 1 to 5 years with severe acute malnutrition from June 2017 to September 2018. CBNAAT and Gene Xpert done for diagnosing tuberculosis. HIV testing was done at ICTC. Study done with prior approval of Institutional Ethics committee. Being a government hospital, there was no financial burden on the patient's legally acceptable representatives.

Results: 53.77% children were females. 91.5% had received BCG vaccination. No HIV case was seen. Presumptive tuberculosis was seen in 13 cases (12.3%). Significant association was seen between cough >2 weeks and chest X-ray; fever >2 weeks and chest X-ray; history of contact with chest X-ray; TST and CBNAAT; BCG scar mark and chest X-ray and chest X-ray and CBNAAT ($p<0.05$).

Conclusion: CBNAAT has not proved very effective in diagnosing tuberculosis, hence we recommend this to be used as a confirmatory diagnostic tool.

KEYWORDS

CBNAAT, Severe acute malnutrition, tuberculosis, Gene Xpert, BCG vaccination

INTRODUCTION

Protein energy malnutrition is a major public health problem in under 5 children,[1] causing adverse effects later in life , affecting health, intellect, scholastic achievements, productivity and earning ability. According to the Government of India, severe acute malnutrition is defined as "very low weight for height/length (Z score below 3 SD of the median WHO child growth standards) or by visible severe wasting or by the presence of nutritional edema.[2]

Estimates show that nearly 65% of children under age of 5 years suffer from varying degree of malnutrition. Severe acute malnutrition (SAM) affects nearly 6.4% of children under 5 years in our country.[2] Every year more than 50 lakh children die as a result of malnutrition, while the risk of death due to SAM is 9 times more than a well-nourished child. Infections and deficiency of micronutrients increase mortality in children with SAM.[3]

Children presenting with clinical features of infection , metabolic disorder, severe edema , decreased appetite are classified as 'complicated' and need admission for treatment, while children with SAM who are clinically well, alert and having normal appetite, are classified as 'uncomplicated' and can be treated on community basis. Severe malnutrition leads to nutritionally acquired immune deficiency (NAIDs).[2]

Malnutrition affects the cell mediated immunity (CMI) which is a principal host defence against tuberculosis.[4] Tuberculosis combined with severe malnutrition becomes more lethal than malnutrition alone.[5] According to the National Tuberculosis Institute, Bengaluru there are nearly 1.9 million cases of primary infection each year in children under the age of 5 years.

Diagnosis of pulmonary tuberculosis in children is challenging as it is largely based on clinical, radiological findings and medical history.[6,7] Bacteriological confirmation becomes difficult due to unavailability of good sputum specimens from children, inadequate clinical sample volume and paucibacilary nature of biological samples and also unavailability of simple diagnostic tests with high sensitivity.[8,9]

While Culture which is the gold standard test for diagnosis of tuberculosis takes nearly 4-8 weeks and is not cost effective, becomes unaffordable at a resource-limited settings. The polymerase chain reaction based diagnostic test have a large varying sensitivity and specificity.[10]

Various meta-analysis have shown that cartridge based nucleic acid amplification test (CBNAAT) / Xpert MTB / RIF to have high specificity with varying sensitivity in different types of specimens for diagnosis of tuberculosis.[11,12,13]

Another major infection HIV has an additional effect on tuberculosis. HIV has been found to increase the risk of having tuberculosis. The clinical presentation of pulmonary tuberculosis overlaps with other opportunistic pulmonary infection and HIV related illnesses and may therefore, be overdiagnosed. Most of the children are perinatally infected with HIV and later on with tuberculosis. Tuberculosis in such children is detected at a later age, as before these children are detected with tuberculosis, they succumb to other respiratory diseases.

With a higher incidence of mortality in severe acute malnourished children and tuberculosis adding to this burden, we carried out the present study to diagnose tuberculosis in children of less than 5 years with severe acute malnutrition using CBNAAT technique. Also, correlation between positive cases of tuberculosis diagnosed using Gene Xpert and their BCG vaccination and HIV status was seen.

MATERIAL AND METHODS

The present cross-sectional study was carried out at Chacha Nehru Bal Chikitsalaya Nutritional Rehabilitation Centre, Indore from June 2017 to September 2018. A total of 106 children with severe acute malnutrition of age between 1year to 5 years, admitted in our institution were included who were tested for tuberculosis using CBNAAT by gastric lavage. Children whose LAR gave negative consent for participation in the study were excluded. The study was approved by the Institutional Ethics Committee.

Severe acute malnutrition was defined as WHO as W/H or W/L < -3SD or MUAC < 11.5 cm or bipedal edema. Children underwent routine hematological investigations and Chest X-ray, TST, Gastric lavage CBNAAT investigations. Their BCG status was ascertained.

Chest X-ray which was suggestive of hilar or mediastinal lymphadenopathy or chronic fibrocavitory shadows was considered as pulmonary tuberculosis. A positive TST conveyed that the child is infected with MTb either recently or in the past.

Procedure for performing CBNAAT/Gene Xpert for diagnosing Tuberculosis:

The child was kept for fasting for about 6 hours (in the night) and

appropriate sized nasogastric tube was passed. Early morning aspirate sample was collected. Aspirate was drawn from the stomach and then further washed with 15-30 ml normal saline. The contents so recovered were immediately transferred to the laboratory for analysis.

Procedure for HIV testing:
The blood sample was sent to ICTC (National Guidelines for HIV testing by NACO). Enzyme Linked Immunosorbent Assays (ELISAs), rapid tests and Western Blot (WBs) are the commonly used tests for the diagnosis of HIV antibodies.

Based on the symptomatology and results of the investigations, children were classified as (a) presumptive pulmonary tuberculosis; (b) bacteriologically confirmed case and (c) clinically diagnosed case according to RNTCP guidelines.

The data was initially collected in the customized proforma and then transferred to Microsoft Excel for analysis. Statistical software was used for calculating the P values. Association between non-parametric variables was done using Pearson Chi-square test. A P value of < 0.05 was taken as statistically significant.

Being a government run medical college with hospital, there was no financial burden on the parents of these children. All the investigations were done free of cost. This study was not funded by any organization or institution. All the study related expenses were borne by the investigator himself.

RESULTS

Of the 106 severely malnourished children, there were 49 (46.23%) males and 57 (53.77%) females showing a female preponderance in the study. 95.2% children had MUAC $\leq$ 115 mm and 1.8% children had bilateral pedal edema. HIV positivity was not seen in any of the children. 91.5% children had already received BCG vaccination.

Of the 106 patients, based on the signs and symptoms 8 (7.54%) had cough > 2 week, while 13 (12.26%) had fever >2 weeks. Tuberculosis contact was reported in 5 (4.71%) patients and TST was positive in 9 (8.4%) patients. Only 1 (0.94%) patient had history of contact as well as positive TST.

Pulmonary tuberculosis was found to be positive on chest X-ray in 12 (11.32%) patients and on CBNAAT in 4 (3.77%) patients. There was a statistically significant association between chest x-ray results; CBNAAT and presumptive tuberculosis ($p<0.05$). [Table 1]

The association between ATT taken and presumptive tuberculosis was found to be significant ($p<0.05$).

The association between fever > 2weeks and CBNAAT findings was found to be significant ($p<0.05$). [Table 2] Of the 14 presumptive tuberculosis cases, 13 had received ATT while 1 patient with fever > 2 weeks responded well to the antibiotics, hence ATT not given. Hence, presumptive tuberculosis was seen in 13 cases. [Table 3]

The association between cough > 2weeks and chest X-ray findings was found to be significant ($p<0.05$), suggestive of presence of tuberculosis. Similarly association between fever > 2 weeks and chest X-ray was found to be statistically significant ($p<0.05$). Significant association was seen between history of contact and chest X-ray findings ($p<0.05$).

Association between TST and CBNAAT was found to be statistically significant ($p<0.05$).

Association between BCG scar mark and chest X-ray findings was found to be statistically significant ($p<0.05$). [Table 4]

Significant association was seen between chest X-ray and CBNAAT results ($p<0.05$). [Table 5]

DISCUSSION

Chakravorty et al[14] reported an incidence of pediatric tuberculosis in 54.3% and study done by **Narain et al**[15] reported it to be 38.98% in children age less than 4 years. The disease usually presents within 1 year of infection and dissemination is higher in younger age group. The disease in young children reflects recent infection, rather than secondary reactivation, the pediatric disease burden provides a measure of current transmission within the community.[16]

Payghan et al[17] reported a higher prevalence of tuberculosis in age group 3-6 years (6.5%) in comparison to 4.9% in the age group 0-3 years.

Singh et al[18] in their study reported an incidence of pulmonary tuberculosis in 22.1% patients and HIV infection in 2.9%. **Mittal et al**[19] and **Dwivedi et al**[20] reported incidence of tuberculosis to be higher in females in comparison to the males, which is comparable to our results. In contrast, study done by **Pathak et al**[21] reported a higher incidence in males.

Study done by **Hossain et al**[22] showed that 9% of severely acute malnourished children were suffering from presumptive pulmonary tuberculosis. **Kumar et al**[18] reported a slightly lower incidence of pediatric tuberculosis among severely acute malnourished children. Our results are much higher than those reported by above authors.
LaCourse et al[23] reported positive findings on chest X-ray in 16% patients, while **Payghan et al**[17] reported it to be 5.6%. Our results were higher than Payghan et al, while it was slightly lower than that reported by LaCourse et al.

Payghan et al[17] reported 5.2% tuberculosis positive cases on the basis of sputum or gastric aspirate, while study done in **Bihar**[21] reported it to be less than 1% by sputum microscopy. Results are varying, but being a confirmatory test, efforts should be made to detect AFB in various samples from the body.

Diagnosis of tuberculosis in severely acute malnourished children is difficult. A study from **Ghana**[24] confirmed tuberculosis in 9.35% severely acute malnourished children on the basis of clinical features, history of contact and laboratory investigations.

In other studies, Gene Xpert was positive in 8-23% among the tuberculosis suspects with a sensitivity between 57-79% in comparison to the culture.[25] While low positivity reported in our study underestimates the true prevalence of pulmonary tuberculosis in this age group.

uddin Siddiqui et al[26] reported an incidence of tuberculosis to be 66% with household contact and said that tuberculosis in children was mainly due to failure of tuberculosis control in the adults.

Report showed that no protective effect of BCG vaccination in pulmonary tuberculosis[27] which is similar to our results. No association was found between CBNAAT and BCG vaccination in past,[28] which is similar to other studies.

CONCLUSION

Detection of tuberculosis in severely acute malnourished children is a difficult task. CBNAAT has not proved very effective in diagnosis of tuberculosis. Hence, use of CBNAAT alone as a screening tool is not recommended. It should be used as a confirmatory diagnostic test. We could not find any significant association between Gene Xpert and past vaccination with BCG.

Table 1: Association between Chest X-ray result and Presumptive Tuberculosis

Chest X-ray		Presumptive Tuberculosis		Total
		Negative	Positive	
Absent	Count	92	2	94
	Percentage	100.0%	14.3%	88.7%
Present	Count	0	12	12
	Percentage	0.0%	85.7%	11.3%
Total	Count	92	14	106
	Percentage	100.0%	100.0%	100.0%

Pearson Chi-square value = 88.925, df=1, P value = 0.001, Significant

Table 2: Association between CBNAAT result and Presumptive Tuberculosis

CBNAAT Result		Presumptive Tuberculosis		Total
		Negative	Positive	
Absent	Count	92	10	102
	Percentage	100.0%	71.4%	96.2%

Present	Count	0	4	4
	Percentage	0.0%	28.6%	3.8%
Total	Count	92	14	106
	Percentage	100.0%	100.0%	100.0%

Pearson Chi-square value = 27.317, df=1, P value = 0.0001, Significant

Table 3: Association between ATT given and Presumptive Tuberculosis

ATT Taken		Presumptive Tuberculosis		Total
		Negative	Positive	
Absent	Count	92	1	93
	Percentage	100.0%	7.1%	87.7%
Present	Count	0	13	13
	Percentage	0.0%	92.9%	12.3%
Total	Count	92	14	106
	Percentage	100.0%	100.0%	100.0%

Pearson Chi-square value = 97.370, df=1, P value = 0.0001, Significant

Table 4: Association between BCGSMARK and Chest X-ray result

BCGSMARK		Chest X-ray Result		Total
		Negative	Positive	
Absent	Count	6	3	9
	Percentage	6.4%	25.0%	8.5%
Present	Count	88	9	97
	Percentage	93.6%	75.0%	91.5%
Total	Count	92	14	106
	Percentage	100.0%	100.0%	100.0%

Pearson Chi-square value = 4.747, df=1, P value = 0.029, Significant

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