ROLE OF HIGH RESOLUTION COMPUTED TOMOGRAPHY CHEST (HRCT) IN SUSPECTED CASES OF PAEDIATRIC TUBERCULOSIS WHERE CHEST X-RAY IS NORMAL

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ABSTRACT

BACKGROUND

Childhood TB contributes to a large proportion (15 - 20%) of all TB patients in developing countries. As per National guidelines on diagnosis and treatment of Paediatric Tuberculosis in India, all efforts should be made to demonstrate bacteriological evidence in the diagnosis of paediatric TB, but difficulty in collection of sputum and due to paucibacillary primary disease in children it becomes difficult. A negative Mantoux and normal chest skiagram cannot rule out TB in a child. Better techniques like HRCT scans have advantages over conventional radiographs in diagnosing tuberculosis in paediatric patients and can detect the disease in patients whose chest radiographs are normal or equivocal.

The aim of this study is to detect pulmonary lesions in suspected cases of childhood tuberculosis, having normal or equivocal findings on chest x-ray and to detect pulmonary lesions in patients with extrapulmonary tuberculosis.

MATERIALS AND METHODS

The present cross-sectional study was conducted over a period of one year from November 2006 to October 2007, in the Department of Paediatrics at Shri Maharaja Gulab Singh Hospital in collaboration with Department of Radiodiagnosis, Govt. Medical College, Jammu, J and K, India. Children between age groups 6 months and 18 years who were admitted in the paediatrics ward or referred from paediatric OPD suspected of tuberculosis and having normal or inconclusive chest x-rays were included in the study.

RESULTS

Out of 34 suspected patients, HRCT findings were suggestive of TB in 28 patients (82.4%). Among them positive Mantoux, gastric lavage smear positive for AFB and lymph node biopsy diagnostic of TB were observed in 16 (57.1%), 3 (10.7%) and 5 (17.8%) respectively. Sputum smear for AFB was not positive in any of these patients. Lymph nodes were present in 26 patients (92.86%). Rim enhancement of lymph nodes, disseminated nodules (Miliary TB), consolidation (parenchymal lesions) and calcification were observed in 10, 2, 6 and 3 patients respectively. 6 out of 34 patients had normal HRCT studies. Overall, sensitivity of HRCT was reported as 100% with comparatively lower specificity.

CONCLUSION

The sensitivity of HRCT chest is quite high, as it provides additional help in improving the diagnostic accuracy as the yield of AFB is low in children and culture results are time consuming.

KEY WORDS

Childhood Tuberculosis, Chest X-Ray, High Resolution Computed Tomography, Lymph Nodes.

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BACKGROUND

Tuberculosis is one of the oldest diseases known to mankind that is caused by bacteria belonging to the Mycobacterium tuberculosis complex¹ and may affect any organ or tissue in the body.² TB has remained a disease of public health importance and is responsible for heavy socioeconomic burden. India accounts for one-fourth of the global TB burden and more than 40% of the population is infected with

Mycobacterium tuberculosis.³ One of the landmark achievement of 2017 is National Strategic Plan (NSP) 2017-25 for TB Elimination. As per the Global TB report 2017, the estimated incidence of TB in India was approximately 28,00,000.⁴ Despite the availability of effective preventive measures and chemotherapy, several factors including poverty, overcrowding, co-existence with HIV, population migration etc. influence the occurrence of new cases and prevalence of TB. Although, childhood tuberculosis (TB) in India is estimated to be approximately 10% of total adult incidence, only 6% of the total cases reported to the Revised National Tuberculosis Control Programme (RNTCP) are children and this proportion has remained constant.⁵ Pulmonary TB remains the most common form of TB, although children suffer more from extrapulmonary forms of TB than all other age groups. However, as most private practitioners do not notify cases to the RNTCP, the overall burden of childhood TB in the country is unknown.

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Demonstration of AFB from any body fluid or tissue is confirmatory of tuberculosis. Such a proof is often lacking in childhood tuberculosis because of difficulty in collection of sputum and due to paucibacillary primary disease in children. However, studies do report that the yield of a positive test in advanced cases may be as high as in adults. Every attempt must be made to bacteriologically prove the diagnosis in every case of suspected tuberculosis.

Sputum smear examination is the primary investigation of choice, if sputum specimen is available from the child. If sputum smear is negative or not available, chest x-ray and Tuberculin Skin Test (TST/Mantoux test) are to be performed. However, a negative Mantoux cannot rule out TB in a child.⁶ Negative chest skiagram also does not exclude tuberculosis, because enlarged subcarinal nodes and even hilar and at times paratracheal nodes are difficult to make out in an initial chest skiagram.⁷

Sputum smear microscopy, often the only diagnostic test available in endemic areas is positive in less than 10 - 15% of children with probable TB. Sputum Culture yields are also low; reported yields in children with probable TB are less than 30 - 40%.^{8,9} In addition to poor bacteriologic yields, the collection of bacteriologic specimens is often problematic. Two to three fasting gastric aspirates collected on consecutive days, usually requiring hospital admission, are routinely performed in young children who cannot cough up phlegm.

The difficulty in diagnosis has been compounded by the HIV epidemic, because other HIV associated lung diseases mimic the clinical and radiological picture of TB and the development of anergy has reduced the sensitivity of skin testing for tuberculosis.¹⁰

Better techniques would especially benefit children and infants in whom early diagnosis is imperative for preventing progressive TB. HRCT scans have advantages over conventional radiographs in diagnosing tuberculosis in paediatric patients and can detect the disease in patients whose chest radiographs are normal or equivocal. It demonstrates pulmonary architecture without superimposition of overlying structures and also depicts miliary nodules or bronchogenic nodules in the lung parenchyma, especially in patients with no evidence of nodules on the chest radiograph.^{11,12} It is also helpful in the distinction of active from inactive TB. HRCT finding consistent with presence of active tuberculosis was defined as presence of poorly defined nodules, tree in bud appearance, randomly distributed (Miliary) nodules, cavitations, consolidation, bronchogenic spread and pleural effusion. HRCT is highly valuable in differentiating many diseases that produce similar appearances on chest radiographs without using invasive methods to obtain material for bacteriological examination. Moreover, the delay in obtaining result from sputum culture (6 - 8 weeks) poses a clinical problem. The present study was an attempt to detect pulmonary lesions both in suspected cases of childhood tuberculosis having equivocal findings on chest x-ray and in patients with extrapulmonary tuberculosis.

MATERIALS AND METHODS

The present cross-sectional study was conducted over a period of one year in the Department of Paediatrics at Shri

Maharaja Gulab Singh (SMGS) Hospital in collaboration with Department of Radiodiagnosis, Govt. Medical College, Jammu, J and K. The study included children between the age group of 6 months and 18 years suspected of tuberculosis who were admitted in the Paediatrics department or referred from Paediatric OPD after obtaining informed consent from their parents/guardians. Children with complaints of chronic cough and/or fever, failure to gain weight or unexpected weight loss, recurrent chest infections, short duration of fever and/or cough and fulfilling the inclusion criteria were included in the study. Detailed history regarding symptoms and contact with TB patient was recorded followed by clinical examination. Chest radiographs and tuberculin tests were performed (0.1 mL of 5 TU of PPD with RT 23 and Tween 80 was injected intradermally over the anterior aspect of the forearm and the extent of induration and not erythema was read after 72 hours). Mantoux was considered positive if induration was 10 mm or more.

Inclusion Criteria

1. Suspected case of pulmonary TB/Extrapulmonary TB with normal or inconclusive findings on chest radiography.
2. Positive Mantoux Test.
3. Household contact known to be infected with TB or had taken ATT within past 2 years.
4. Lymphadenopathy.

A strong clinical suspicion in the absence of these symptoms was also considered as sufficient grounds for investigation.

Exclusion Criteria

1. Taking treatment for tuberculosis.
2. Had completed such treatment within the past 2 weeks.
3. Taking prophylaxis for this disease.
4. Patients suspected with CNS Tuberculosis.

HRCT chest of patients were done using the spiral CT scanner (WIPRO GE System). Patients were subjected to HRCT using 1 mm cuts and 10 mm interslice gaps. In the area of interest, inter-slice gaps were reduced. In addition to HRCT, all the patients were also subjected to work up including routine haematological work-up, sputum/gastric lavage smear was done for AFB staining (On three consecutive days, early in the morning), lymph node biopsies and other relevant investigations such as bone marrow aspiration, pleural tap and ascitic tap as and when required.

Statistical Analysis

The results were presented in percentages and proportions. Sensitivity and specificity was calculated. Significance was assessed using Chi-square test.

RESULTS

Maximum children belonged to age group of one to five years. Mean age of patients with probable TB based on HRCT was around 5.6 years (Fig. 1). Overall in the present study, there were more males 20 (58.9%) as compared to females 14 (41.1%) with male-to-female ratio of 1.4: 1 (Table 1). Out of

34 patients who entered the study, HRCT positivity for probable pulmonary TB was observed in 28 patients. The most common complaints among the patients were fever and cough for more than 3 weeks followed by loss of weight/failure to thrive (FTT), loss of appetite, haemoptysis, recurrent chest infections and isolated axillary swellings. (Fig.2). Regarding clinical signs at the time of presentation, maximum patients presented with crepitations and/or wheeze followed by hepatomegaly and splenomegaly (Table-2). Out of 28 patients with probable TB, lymph nodes were detected in 26 patients (92.86%) on HRCT and in 18 patients clinically and among them eight patients were having lymph nodes of more than 1 cm. Rim enhancement of lymph nodes, disseminated nodules (miliary TB), consolidation (parenchymal lesions) and calcification were observed in 10, 2, 6 and 3 patients respectively. The most common site of lymph nodes found on HRCT was subcarinal followed by right hilar and anterior mediastinum (Figure 3).

Multiple sites of involvement were present in 22 patients (78.57%). Isolated subcarinal lymphadenopathy was observed in 5 patients (17.86%) only.

Among patients with HRCT findings probable of Tuberculosis (n= 28), positive Mantoux, gastric lavage smear positive for AFB and lymph node biopsy diagnostic of TB were observed in 16 (57.1%), 3 (10.7%) and 5 (17.8%) respectively. Sputum smear for AFB was not positive in any of these patients. Among patients with normal HRCT study, positive Mantoux was observed in two patients (33.33%), while none of these patients showed positive gastric lavage/sputum smear for AFB or lymph node diagnostic of TB.

Among patients with probable TB based on HRCT, history of contact was present in 21 (75%) patients and among patients with normal HRCT; history of contact was present in only 2 patients (33.3%). The findings were statistically significant, $p < 0.05$. Majority, i.e. 18 (64.3%) of probable TB patients based on HRCT findings were suffering from Protein Energy Malnutrition (PEM), out of them 4 children were suffering from grade IV malnutrition. Among patients with normal HRCT, malnutrition was found in 3 patients only.

Out of 34 patients, TB was confirmed in 8 patients (Gastric Lavage Smear positive for AFB in 3 patients and lymph node biopsy diagnostic of TB in 5 patients). All these patients had pulmonary lesions detected on HRCT scan. Sensitivity of HRCT in relation to other investigations like Mantoux test, gastric lavage and lymph node biopsy came out to be 100%, while specificity was comparatively low. Since no patient with probable TB on HRCT had sputum smear positive for AFB, so sensitivity in this case was 0%. Specificity in relation to combined gastric lavage smear positive for AFB and lymph node biopsy diagnostic of TB (confirmatory tests) was 23% and sensitivity was 100%.

Figure 1. Age Wise distribution of Patients

Age	Total (n=34)		Probable TB based on HRCT(n=28)	
	Male	Female	Male	Female
6 months - 1 year	4	2	3	1
1 - 5 years	10	4	10	4
5 - 10 years	4	4	2	2
10 - 18 years	2	4	2	4
Total	20	14	17	11

Table 1. Sex Wise distribution of Children

Figure 2. Presentation of Symptoms in patients with Normal HRCT and probable TB based on HRCT

Signs		Total Patients	Probable TB Based on HRCT (n=28)
Crepitations and or Wheeze		24 (70.6%)	19(67.9%)
Hepatomegaly and/or splenomegaly		22 (64.7%)	17(60.7%)
Lymphadenopathy	Axillary	13 (38.2%)	8 (28.6%)
	Cervical	11 (32.4%)	6 (21.4%)
	Generalised	5 (14.7%)	4 (14.3%)

Table 2. Clinical Signs observed in Patients

	Size of Lymph Nodes					
	< 0.5 cm		0.5 – 1 cm		> 1 cm	
	Normal HRCT	Probable TB based on HRCT	Normal HRCT	Probable TB based on HRCT	Normal HRCT	Probable TB based on HRCT
Axillary	5	2	2	2	6	4
Cervical	3	2	6	2	2	2
Generalised	0	1	1	1	4	2
Total	8	5	9	5	12	8

Table 3. Distribution of Lymph Nodes as per Size

Investigation	Normal HRCT n=6	Patients with Probable TB on HRCT n=28
Positive Mantoux	2	16
Gastric lavage smear for AFB	0	3
Sputum smear for AFB	0	0
LN biopsy diagnostic of TB	0	5
ESR	2	13
Leucocytes	2	20
Anaemia	6	28

Table 4. Lab Investigations of Children

Figure 3. Distribution of Patients according to Site of Lymph Nodes

	Investigation	Sensitivity	Specificity
HRCT	Positive Mantoux	100%	33.3%
	Gastric lavage smear for AFB	100%	19.4%
	Sputum smear for AFB	0	17.6%
	Lymph node biopsy diagnostic of TB	100%	26.1%
	ESR	100%	28.6%
	Combined gastric lavage smear for AFB and lymph node biopsy diagnostic of TB	100%	23%

Table 5. Sensitivity and Specificity of HRCT in relation to Other Investigations

DISCUSSION

In the present study, majority (58.8%) of patients were < 5 years of age and mean age was 5.42 years, which corroborated with study done by Kim WS et al¹³ in which 52% patients were < 5 years and mean age was 6 years. Male preponderance (M: F= 1.42: 1) observed in present study is in concordance with the studies done by various authors.^{13,14} The reason may be more parental care and concern for male children.

Prolonged fever and/or prolonged cough were the most common presenting complaints in the present study observed in 70.6% and 61.8% respectively, which were similar to the observations made by Leung et al.¹⁵ In the present study 18 patients (52.9%) had positive Mantoux, out of which 16 had positive HRCT findings, while 2 patients had normal HRCT and this was not statistically significant (p value > 0.05). Tuberculin tests are unreliable in children, especially in endemic areas.^{16,17} Study done by Schaaf HS et al¹⁸ showed that only 41% of children with confirmed TB had positive Mantoux. The low sensitivity is attributed to anergy in children less than 2 years of age and because the reaction lags behind the radiological findings.^{18,19}

In the present study, gastric lavage smear positive for AFB was seen in 8.8% of total patients. According to study done by American Thoracic Society and the Centres for Disease Control and Prevention, the sensitivity of acid fast stain for gastric contents is usually below 10%.²⁰ Gastric aspirates have low sensitivity for mycobacterium tuberculosis, because it cannot survive acid environment and because of the low organism burden in gastric fluid.²¹ Hence, the diagnosis often relies heavily on imaging and a combination of clinical and laboratory findings.²² In current study, the most common site of lymph nodes found on HRCT was subcarinal (32%) followed by right hilar and anterior mediastinum (19%). There are contradictory reports on the incidence of lymphadenopathy in children with pulmonary TB as demonstrated by different imaging methods. Following studies reported an incidence of 90 - 98% for mediastinal and hilar lymphadenopathy in children with Pulmonary TB using radiographs alone.^{23,24,25}

Delacourt et al compared the findings of radiographs and CT showing that up to 60% of children with normal radiographs had lymphadenopathy on CT.²⁶ In the same study, the authors report that 75% of children with TB anywhere in the body had a normal chest radiograph. An apparently normal chest radiograph therefore cannot exclude pulmonary TB infection in children.

Mediastinal lymphadenopathy with or without parenchymal abnormality is a radiologic hallmark of primary tuberculosis in childhood.^{27,28,29} In the present study with negative or inconclusive chest radiography, HRCT showed mediastinal lymphadenopathy and hilar lymphadenopathy in 75.58% and 38.23% of patients respectively. The most frequent HRCT finding in the present study was the enlarged subcarinal lymph nodes as also depicted in the study by Andronikou et al.¹⁴

The present study reported that HRCT scans delineated lymphadenopathy in 26 and miliary TB in 2 out of 34 patients. Therefore, HRCT scans can be helpful in diagnosing tuberculosis when findings of chest radiographs are normal or inconclusive. This conclusion is in concordance with study done by Katakura et al (1999)³⁰ done on 5 children, in whom

CT scan revealed abnormal changes including primary complexes, although chest radiographs were normal.

In our study calcification was present in 8.8% which is comparable with study done by Kim WS and Moon et al,¹³ where it was reported that calcification is helpful, but is present in only 15 - 21% of pulmonary TB patients. Harisinghani M et al³¹ and Gulati M et al in their studies reported 55.85% presence of rim-enhancing nodes. However, in the present study, rim enhancement was observed in 29.4% only. The pickup rate of HRCT in detecting lesions in suspected cases of TB with normal chest radiographs was found to be 82% in our study. While in patients of TB confirmed by smear positivity for AFB in gastric lavage/ lymph node biopsy, HRCT showed positive findings in all with 100% sensitivity.

High sensitivity of HRCT suggests it is good screening test in correctly identifying the patients with symptoms suggestive of TB who had equivocal/ non-suggestive chest x-ray findings. However, lower specificity in relation to other diagnostic tests suggest that its discriminatory power to exclude patients without disease, i.e. true negatives is low. Hence, it fares poorly as a confirmatory test. Bacteriological confirmation remains the gold standard.

Utility of HRCT in our settings and in the present study lies in the fact that in areas with high burden of TB and limited time constraints, we cannot afford to miss even a single case of TB or delay the timely initiation of treatment as other investigations like sputum smear examination, AFB culture, Mantoux test, Gastric lavage, lymph node biopsy either are more time consuming or have poor yield in cases of Paediatric TB.

Study Limitations

Follow-up of probable TB patients (based on HRCT findings) could not be done to know the response with ATT, as our setting being government tertiary care centre caters to large population from both near and remote areas and following them was difficult due to time and resource constraints.

CONCLUSION

HRCT is a very useful imaging study in children with suspected TB with normal or inconclusive chest radiographs. The sensitivity of HRCT chest is quite high, as it provides additional help in improving the diagnostic accuracy as the yield of AFB is low in children and culture results are time consuming.

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