A Profile of Bacteriologically Confirmed Pulmonary Tuberculosis in Children

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ABSTRACT

Objective: *To describe the clinical profile of children with bacteriologically confirmed tuberculosis.* ***Study Design:*** *A multicentric study was conducted in three hospitals in Chennai city between July 1995 and December 1997. Children aged 6 months to 12 years with signs and symptoms suggestive of tuberculosis were investigated further. Clinical examination, chest radiograph, tuberculin skin test with 1 TU PPD and, sputum or gastric lavage for mycobacterial smear and culture were done for all and, lymph node biopsy when necessary.* ***Results:*** *A total of 2652 children were registered and tuberculosis was bacteriologically confirmed in 201. Predominant symptoms were history of an insidious illness (49%), fever and cough (47%), loss of weight (41%) and a visible glandular swelling (49%). Respiratory signs were few and 62% were undernourished. Over half the patients with confirmed TB had normal chest X-ray. Abnormal X-ray findings included parenchymal opacities in 47% and hilar or mediastinal lymphadenopathy in 26%. The prevalence of isoniazid resistance was 12.6% and MDR TB 4%.* ***Conclusions:*** *Children with tuberculosis present with fever and cough of insidious onset. Lymphadenopathy is a common feature even in children with pulmonary TB. A significant proportion of children have normal chest X-rays despite positive gastric aspirate cultures. Drug resistance rates in children mirror the pattern seen in adults in this geographic area.*

Key words: *Bacteriologic diagnosis, Clinical features, Drug Resistance, M . Tuberculosis, Pediatric TB.*

INTRODUCTION

The diagnosis of tuberculosis (TB) in children is often based on clinical suspicion, in the absence of definite bacteriologic proof(1). In most situations, bacteriologic confirmation is not possible because of the paucibacillary nature of the disease and difficulty in collecting sputum specimens from young children.

In an attempt to devise simple and reliable clinical diagnostic criteria for tuberculosis in children, the Tuberculosis Research Centre undertook a multicentric study in the city of Chennai. Of the 2652 children referred for investigations, tuberculosis was confirmed in 201. This paper describes the clinical and radiographic features of children with bacteriologically confirmed pulmonary tuberculosis.

METHODS

Children in the age group 6 months to 12 years attending the outpatient department of the following

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hospitals were included in this study.

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Children attending the hospital with cough or fever for more than two weeks, recurrent respiratory infections (more than 6 episodes in 3 months), and failure to thrive or unexplained loss of weight were referred for the study. Detailed history including all symptoms and a history of contact with TB was recorded. Clinical examination was done and weight recorded. Nutrition status was graded according to the IAP classification. Informed consent was obtained from a parent of all children who participated in the study. The study protocol was approved by the Institutional Ethics Committee of the Tuberculosis Research Centre.

A chest *X*-ray PA was taken for all children and a lymph node biopsy was performed in those who had significantly enlarged superficial (cervical or axillary) lymph nodes. Mantoux test was done with 1 TU PPD RT23 with Tween 80 and the size of induration recorded after 48-72 hours by trained readers. Sputum specimens were collected wherever possible in cooperative children. Gastric lavage was performed as an out patient procedure by trained field investigators on two consecutive days, early in the morning on an empty stomach.

Gastric lavage specimens were collected in sterile bottles with Vancomycin (10mg/L) to reduce contamination rates by aerobic spore bearers(2), processed by the modified Petroff's method(3) and cultured using standard techniques(4,5). Lymph node samples were divided into two: one part was sent in formalin for histopathological examination and the other transported aseptically in selective Kirschner's liquid medium for culture. All liquid medium cultures were incubated for up to six weeks, centrifuged and the deposit inoculated into 2 slopes of LJ medium. Species identification was done by a battery of biochemical tests and isolates of tubercle bacilli were tested for susceptibility to isoniazid and rifampicin by the indirect method(6). Resistance to the two drugs were defined thus; MIC of greater than 1.0mg/L or MIC of 1.0mg/L on two occasions for isoniazid and an MIC of 128 mg/L or more in the case of rifampicin.

Children were followed up at 1,2,3,6,9 and 12 months from the time of intake. Anti-tuberculosis treatment (ATT) was started when the treating physician felt it was indicated on clinical and/or radiographic grounds or when a gastric lavage culture was reported as positive. Most patients received short course ATT (2EHRZ/4HR or 2HRZ/4 HR).

Radiographs were read by a radiologist and two pediatricians (SS, AMR) independently and a consensus reading taken, to reduce bias due to inter-observer variation.

RESULTS

In all, 2652 children were referred from the various outpatient clinics for investigations for suspected pulmonary TB. Among these, 201 cases were diagnosed to have tuberculosis on either bacteriologic or histopathological basis (7.6%). There were 100 males and 101 females and 34% were <5 years of age. Of the 201 children, 175 were positive by smear and/or culture from sputum, gastric lavage and/or lymph nodes (bacteriologic group). The nine children with positive smear alone had >10 bacilli and so have to be considered as positive. 26 children had tuberculosis diagnosed by lymph node histopathology, though they had been referred for respiratory symptoms.

***Table* I** shows the prevalence of various symptoms and signs at the time of diagnosis of tuberculosis, in children diagnosed bacteriologically or histopathologically, respectively. Chest *X*-rays were available for subsequent reading and of good quality in 148 children. Of these, in 84 (56%) the *X*-rays were read as normal by the radiologist and pediatricians. Of the abnormalities identified, the commonest was parenchymal opacity in 47% of cases followed by hilar or mediastinal lymphadenitis alone in 15%. In 30% of the cases, the hilum was reported to be prominent or minor fissure opacification was observed, without any other definite lesion. Cavitation was observed in only 1 child.

TABLE I PREVALENCE OF SYMPTOMS AND SIGNS AMONG CONFIRMED TB CASES

Description	Bacteriologic (n = 175)	Histopathologic (n = 26)	Total (%) (n = 201)
Fever > 2 weeks alone	35	3	38 (19)
Persistent cough > 2 weeks alone	43	2	45(22)
Fever and cough	92	3	95(47)
Recurrent respiratory infections	48	6	54(27)
Fever and recurrent respiration infections	37	5	42(21)
Visible gland	74	24	98(49)
Loss of weight	73	10	83(41)
Insidious illness	83	15	98(49)
Contact with TB	40	5	45(22)
Mantoux positive (≥ 10mm)	136	22	158(79)
Respiratory signs	64	4	68(35)
Glandular enlargement	68	23	91(47)
Hepatomegaly	39	5	44(23)
Grade 3, 4 malnutrition	99	20	119(62)

Drug susceptibility results were available for 175 children. The overall prevalence of INH resistance was 12.6% and MDRTB was 4%, while 87.4% of the isolates were susceptible to all first line drugs.

DISCUSSION

It is rare to find studies with culture confirmation of TB, as tuberculosis in children is usually paucibacillary in nature and sputum specimens are difficult to obtain(7,8). In the present study we were able to confirm TB by smear and/or culture of sputum or gastric aspirate or histopathologic evidence in 7.6% of children investigated. Gastric lavage has higher yield for *M.tuberculosis* than bronchoalveolar lavage in children with pulmonary tuberculosis(9,10) and this has been successfully done as an outpatient procedure(11,12). Vancomycin was added to the sterile culture bottles which reduces contamination and increases yield(5).

Our finding of isoniazid resistance in 12.6% and MDRTB in 4% of cases is cause for concern as it indicates the occurrence of significant drug-resistant TB, particularly MDRTB in children. Drug resistance rates in adults in this geographic area are also in this range(13). Because children with TB are infected in the community and progress from infection to disease more rapidly than adults, the patterns of drug resistance in children may serve as an early marker of patterns present in the wider community. Our study provides data about drug resistant tuberculosis in children, for the first time from India. A study from Peru reported resistance to isoniazid in 18% and MDRTB in 2% of children with pulmonary tuberculosis(14), similar to adult rates in Peru(15).

Irregular or prolonged fever appears to be a more important symptom than cough in children, unlike in adults where cough is the commonest presenting symptom. Only 79% of children had a positive Mantoux test reaction of >10mm. The tuberculin test, which indicates prior infection with *M. tuberculosis*, is used as evidence of disease in almost all scoring systems for the diagnosis of TB in children but may be negative for a variety of reasons(16). Another important finding of this study is that almost 50% of children with suspected pulmonary tuberculosis had visibly enlarged cervical lymph nodes. In twenty six of the 201 (12.9%) children, the diagnosis was based on histopathologic or bacteriologic evidence of TB in the gland biopsy, in the absence of gastric lavage/sputum positivity. This indicates that superficial lymph node biopsy is a useful procedure to diagnose TB in children.

WHAT IS ALREADY KNOWN?

- Childhood tuberculosis is a paucibacillary disease, diagnosis is clinical and supported by chest radiography, tuberculin test and/or histopathology of lymph node.

WHAT THIS STUDY ADDS?

- Half of the bacteriologically/histopathologically proven 204 children with tuberculosis had normal chest radiograph. Multidrug resistance was observed in 4% children.

Further, over half of the children with confirmed TB had normal chest radiographs, higher than previous reports of 5 to 10%(17,18). In a subset of 9 children in whom CT scans were performed, 8 of them were found to have parenchymal / nodal lesions that were not visible on *X*-ray chest(19). Children who are screened following recent exposure/ infection may have a positive culture in the absence of symptoms(20). A French study of thoracic CT in 15 children with tuberculous infection found enlarged mediastinal lymph nodes in 60%(21). Schaaf, *et al.*(1) have suggested that the finding of a positive gastric aspirate culture for *M. tuberculosis* despite normal findings on chest radiography is indicative of the presence of actively multiplying organisms and recent infection and is deserving of supervised multidrug therapy. Tuberculosis in children is known to be a continuum between infection and disease and our study provides further evidence that the distinction between them may not be as clearcut as previously thought.

The present study provides data that is representative of a patient population attending outpatient pediatric clinics of tertiary urban hospitals. The strengths of the study are its multicentric nature, comprehensive investigations including mycobacterial culture and drug susceptibility testing and the large number of children screened. Limitations include differences in referral patterns at the various hospitals and lack of data on outcomes after treatment completion.

Our findings have implications for policy and practice of TB diagnosis and treatment in children. The value of findings like contact history, tuberculin skin test reaction and recurrent respiratory infections need to be reconsidered when developing scoring systems – prolonged fever/respiratory symptoms and enlarged superficial lymph nodes (that can be biopsied) appear to be better indicators of disease. Chest radiography is a relatively insensitive tool apart from its known limitations of poor specificity and high inter-observer variability. Drug resistance including MDRTB could be potential problems if the rates in adults are not controlled immediately. In this setting, the current recommendation of a 4-drug intensive phase for most forms of pulmonary TB in children under the RNTCP is appropriate(22). Further research is required to develop a sensitive and specific diagnostic algorithm for pulmonary TB as well as monitor patterns and prevalence of drug resistance in the community.

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