Clinical profile and outcome of abdominal tuberculosis in Indian children

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ABSTRACT

Introduction: Diagnosis of tuberculosis among children poses technical and operational challenges, more so in abdominal tuberculosis (ATB), where the protean clinical manifestations continue to challenge the physicians in its diagnosis and therapy.

Methods: Medical records of 115 patients who were diagnosed with ATB over a period of six years were studied retrospectively. Details of history, physical examination and investigations, treatment and outcome of therapy were evaluated.

Results: The mean age of the patients was 6.4 years. Commonest symptom at presentation was abdominal pain, followed by fever. Nine patients presented with acute abdomen. Mantoux test was positive in 33 percent and accelerated BCG reaction was found in 36.5 percent. Evidence of primary focus was found in 40 percent of chest radiographs. Commonest ultrasonography and computed tomography findings were mesenteric thickening, followed by intra-abdominal lymphadenopathy. Tuberculous infection could be confirmed in 38 patients. The classical plastic variety was the commonest type of ATB found. A complete cure with antituberculous drugs was documented in over 90 percent of the patients

Conclusion: In high prevalence zones, ATB should be considered as a differential diagnosis in children presenting with non-specific constitutional symptoms and abdominal pain. When confirmatory tests are negative or not available, supportive investigations and clinical suspicion should be considered strongly for diagnosis of ATB to avoid delay in treatment. Response to therapy in such conditions indirectly confirms diagnosis. Timely use of laparoscopy and laparotomy may be required for confirmation of diagnosis.

Keywords: abdominal tuberculosis, gastrointestinal infection, *Mycobacterium tuberculosis*, tuberculosis

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INTRODUCTION

The annual incidence of tuberculosis (TB) is nearly eight million, with two million deaths worldwide.[1] The total disease burden in India is enormous and it is estimated that more than 40% of the population is infected. In the paediatric age group, the prevalence is 1–6 per thousand paediatric years.[2] The abdomen remains a major extrapulmonary site for tuberculosis. It may involve the gastrointestinal tract, peritoneum, lymph nodes or solid viscera, and constitutes up to 12% of extrapulmonary TB and 1%–3% of the total TB cases.[3] After the development of specific drugs, gastrointestinal involvement has decreased from a high of 55%–90% to 25% in patients with active pulmonary TB.[4] Yet, the protean clinical manifestations of abdominal tuberculosis (ATB) continue to challenge the physician in its diagnosis and therapy, more so in the paediatric age group where the clinical manifestations may differ from those of the adults. And in most cases, the children's inability to define their problems accurately contribute to this challenge. It is in this group of patients that ATB, due to its indolent course, may present late and hence, delay in its management is likely. The problem is compounded by the restricted availability of specific and sophisticated diagnostic tests in developing countries. In most cases, a working diagnosis has to be made on strong clinical suspicion and on supportive investigational data. In order to assess the adequacy of clinical and investigational data in the diagnosis of ATB, the present study attempts to evaluate the clinical profile, response to treatment and follow-up in a paediatric population in India.

METHODS

All paediatric inpatients diagnosed as having ATB between January 1999 and December 2004 were included in the study. Data was retrieved from the medical records

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section. The diagnosis of ATB was based on: (1) the presence of constitutional symptoms suggestive of TB, (2) the symptoms and signs of gastrointestinal (GI) involvement, along with (3) the presence of at least one direct or indirect evidence of tuberculous infection. Records were reviewed in detail with regard to medical and family history, complete physical examination, routine haematological and biochemical profile, Mantoux test, BCG challenge test in Mantoux negative patients, radiographs of the chest and abdomen, ultrasonography (US) and/or computed tomography (CT) of the abdomen, sputum/gastric aspirate/ascitic fluid examination for acid fast bacilli (AFB), ascitic fluid for adenosine deaminase assay (ADA), fine-needle aspiration cytology (FNAC)/ biopsy from superficial lymph nodes or intra-abdominal mass/lymph nodes, enzyme-linked immunosorbent assay (ELISA) against Antigen 60 of *Mycobacterium* demonstrating IgG, IgA and IgM antibodies, polymerase chain reaction (PCR) and HIV status. The treatment protocol for paediatric patients with ATB in our hospital is chemotherapy with four antituberculous drugs (ATD), i.e. isoniazid (INH), rifampicin, ethumbutol and pyrazinamide for the first two months, and then INH and Rifampicin for the next seven months. In the presence of peritonaeal involvement, oral prednisolone was given for eight weeks and gradually tapered over the following three weeks. All these drugs are available free-of-charge from the hospital pharmacy as a part of our government policy. The details of treatment received, complications developed during the hospital stay, follow-up and response to antituberculous chemotherapy were also reviewed. Data was analysed by statistical software Statistical Package for Social Sciences version 10.0 (SPSS Inc, Chicago, IL, USA).

RESULTS

Of a total of 22,762 paediatric inpatients admitted during the study period, 5,911(25.97%) were found to have TB in at least one organ. ATB was found in 115 children, accounting for 1.95% of total tuberculous admissions. The age of the patients ranged from 1.3 to 12 years [Table I]. The most commonly-affected age group was 6–9 years (38; 33.04%) and the least affected age group was 1–3 years (13; 11.30%). An overall male and Hindu preponderance was seen. On a community-level analysis, the disease was mostly seen in the Bengali community, followed by the migrant Nepalese. The parents were mostly manual labourers, petty businessmen and farmers. The leading symptom at presentation was non-specific abdominal pain. It was vague, non-localised in nature and of indolent course. Only nine patients presented with acute abdominal pain; six with features of acute intestinal obstruction and three with acute peritonitis [Table II]. Mean duration of symptoms before presenting to the hospital was 31.4 ± 10.8 days, and average time for diagnosis and to start ATD after initial presentation was 17 ± 8.7 days.

Majority (103; 89.57%) of the children were malnourished. 14 (12.17%) patients had Grade I protein-energy malnutrition (PEM) according to the Indian

Table I. Clinical profile of patients.

Characteristics	Mean ± standard deviation
Age (years)	6.4 ± 3.2
Male: female	1:0.85
Hindu: Muslim: Christian	1:0.75:0.08
Family size	5.3 ± 2.4
Per capita income of the family (Rs.)	428 ± 50.3
Literacy status of father	
Literate	36 (31.3)
Illiterate	79 (68.7)
Literacy status of mother	
Literate	22 (19.13)
Illiterate	93 (80.87)
History of contact with tuberculosis	
In the family	51 (44.3)
In neighbourhood	24 (20.8)
No history of contact	40 (34.7)
History of BCG vaccination	55 (47.83)
BCG scar mark present	36 (31.30)
Number of patients with PEM	103 (89.57)

Figures in parenthesis are expresed in percentage.

Table II. Symptoms and signs at presentation.

Clinical features	No. of patients (%)
Symptoms	
Abdominal pain	104 (90.43)
Fever	84 (7 3.04
Weight loss	79 (68.70)
Abdominal distension	77 (66.96)
Anorexia	70 (60.87)
Alteration of bowel habits	60 (52.17)
Vomiting	31 (26.96)
Cough	29 (25.22)
Signs	
Distension of abdomen	96 (83.48)
Doughy abdomen	32 (27.83)
Abdominal lump	24 (20.87)
Mixed type (ascites, lump and diffuse peritonitis)	23 (20.00)
Ascites	18 (15.65)
Hepatomegaly	28 (24.35)
Splenomegaly	20 (17.39)
Hepatosplenomegaly	18 (15.65)
Jaundice	11 (9.57)
Pedal oedema	21 (18.26)
Acute abdomen	9 (7.83)

Table III. Investigation profile of patients.

Investigations	Median (range)	No (%)
Haemoglobin (g/dL)	7.46 (4.60–13.20)	-
Total leucocyte count (/mm^3)	13,200 (4,200–15,800)	-
ESR	68 (22–110)	-
Serum albumin (g/dL)	2.62 (1.92–5.86)	-
Positive Mantoux test	-	38/115 (33.04)
Accelerated BCG reaction	-	42/115 (36.52)
Exudative ascitic fluid	-	32/41 (78.05)
CXR suggestive of TB	-	46/115 (40.00)
Multiple air-fluid levels in AXR	-	15/115 (13.04)
Calcification in AXR	-	3/115 (2.61)
US/CT abdomen:		
Mesenteric thickening	-	32/115 (27.83)
Abdominal lymphadenopathy		24/115 (20.87)
Sputum/gastric aspirate for AFB	-	10/108 (9.26)
Mycobacterium tuberculosis grown in culture	-	12/111 (10.81)
Tuberculous granuloma in biopsy	-	22/78 (28.21)
ELISA for tuberculosis	-	17/34 (50.00)
Positive ADA	-	6/7 (85.71)
Positive PCR	-	4/6 (66.67)
ELISA for HIV	-	2/32 (6.25)

Academy of Paediatrics (IAP) classification,[5] 38 (33.04%) had Grade II, 31 (26.96%) had Grade III and 20 (17.39%) had Grade IV PEM. Investigation profile is summarised in Table III. High incidences of anaemia (Hb < 10 g/dL), leucocytosis (total leucocyte count > 11,000/mm^3), raised erythrocyte sedimentation rate (ESR) (> 50 mm in the first hour) and hypoalbuminaemia (serum albumin < 3 g/dL) were observed, in 93.19%, 62.61%, 55.65% and 67.83% of patients, respectively. Evidence of primary focus in chest radiographs was found in 40% of patients. AFB could be demonstrated in ten patients (two from sputum, five from gastric aspirate, two from ascitic fluid and one from lymph node) and 12 patients (six of them already demonstrated AFB) had positive BacTec culture, thus making a total of 16 patients (14%) in whom the bacteria could be isolated. Biopsy specimens showed epithelioid granuloma with central caseous necrosis in 22 patients. ELISA and PCR for TB were positive in 17 out of 34 and four out of six patients, respectively. Adenosine deaminase activity in the ascitic fluid showed high values in six out of seven patients (> 33 u/v), suggestive of tubercular infection. ELISA for HIV was done in 32 children, of which two were positive. Diagnostic laparoscopy was done in seven children with vague abdominal pain. Exploratory laparotomy was done in six patients presenting with acute intestinal obstruction.

The classic plastic variety comprising diffuse peritonitis with thickening of omentum, mesentery and peritonaeal adhesions was the commonest type of ATB found in our study [Table IV]. A total of 104 patients (90.43%) completed nine months of drug therapy. Complete recovery, defined by weight gain, subsidence of symptoms and signs, decrease in ESR and radiological improvement, was documented in 94 children. A marked improvement was seen in the nutritional status at the end of treatment. Only nine were having Grade I PEM. None had Grade II or III PEM. Jaundice and deranged liver function developed in three patients, while persistence of ascites and recurrent abdominal pain was seen in one and two patients, respectively. No mortality was documented.

For statistical analysis, patients were categorised into three groups: Group A or definite cases (n = 38; 33.04%), where in the presence of constitutional symptoms, the diagnosis of ATB was confirmed either bacteriologically by direct demonstration of AFB and/

Table IV. Pathological variety of abdominal tuberculosis.

Type	No. (%)
Classic plastic	26 (22.61)
Nodal	24 (20.87)
Ascitic	18 (15.65)
Mixed	23 (20.00)
Intestinal	21 (18.26)
Hepatic tuberculosis	8 (6.96)
Associated pulmonary tuberculosis	46 (40.00)
Multi-organ tuberculosis	18 (15.65)
Cervical lymphadenopathy	9 (7.83)

or culturing *Mycobacterium tuberculosis* from biological specimens or by histopathological demonstration of epithelioid granuloma with central casaeous necrosis in biopsy specimens. Group B or probable cases (n = 60; 52.17%), where in presence of constitutional symptoms, the diagnosis of ATB was made by the presence of suggestive radiological signs and a good clinical response to antitubercular treatment within three months. The remaining 17 (14.78%) were categorised as Group C or presumed cases, where the diagnosis of ATB was made by presence of constitutional symptoms and other non-specific tests for TB, where antitubercular therapy was started and continued empirically. A comparison between these three groups has been made in Table V. No significant difference was observed in the clinical symptoms, signs and non-specific investigations between the three groups.

DISCUSSION

North Bengal Medical College is a major referral centre for five districts (Darjeeling, Jalpaiguri, Coochbehar, Maldah and West Dinajpur) of North Bengal, India. Moreover, it also caters to patients from adjoining states like Bihar, Sikkim and Assam, and even neighbouring countries like Nepal, Bhutan and Bangladesh. The population is mixed; mostly migrant Nepalese, the Bengalis and those who are native to the region, the tribal population. This results in a considerable amount of paediatric patients being presented to the college due to the sheer numbers of the mixed population. ATB accounted for 1.95% of total TB admissions in the present study, which is in the same range as some previous studies (0.22-3.6%).[6-7] The mean age of presentation in our study (6.4 years) was slightly younger than the reported common age group (6–11 years).[8,9] Since ATB spreads through close contact, a positive family history is very likely in most cases, especially in the paediatric patients, who are highly susceptible to this infection.[10,11] This possibility is supported in our findings of positive history in close family contacts in 65% of the cases. Delay does occur in seeking medical advice, due to the indolent course of ATB and poor awareness among the parents and primary healthcare providers. It may range from one month to six years.[12-14] Mean delay in the present study was less (49 days). Non-specific abdominal pain, a common symptom,[10,15,16] was the most common presenting complaint in the present study, though abdominal distension, ascites and anorexia have also been reported as the common presenting symptoms in some series.[11-17] Routine laboratory investigations are non-specific and do not confirm diagnosis. One study has reported high ESR in 60% and positive Mantoux test in 24% of cases.[18] In areas where TB is highly endemic, positive Mantoux test neither confirms nor excludes the diagnosis. Prevalence of associated pulmonary TB in our series (40%) is comparable to findings from previous reports (19-58%).[8,10,19]

It has been observed that radiographical features of paediatric ATB may frequently mimic other conditions.[20] Calcified lymph nodes, granuloma of spleen, liver and pancreas, dilated and thickened bowel loops, dilatation of terminal ileum and ascites are the common findings in radiographs and US. The combination of mesenteric thickening of 15 mm or more with mesenteric lymphadenopathy are prominent US findings in ATB.[21-23] The common CT findings of ATB are peritonaeal thickening, abdominal lymphadenopathy and thickened bowel wall,[18] which is in accordance with the present series. The similarity of radiological features between the adult and paediatric patients with ATB indicates that such features are common in both age groups, and their presence in children may be taken in favour of the diagnosis of ATB. Ascitic fluid ADA has been considered to be a useful screening test in children with ATB.[24,25] Though it was highly positive, we could not do it routinely due to its high cost.

Out of 115 children, TB could only be confirmed in 38 (33.04%) children (16 were bacteria-positive and 22 were confirmed on histopathology). Majority (52.17%) of the patients were diagnosed by suggestive radiological examinations and clinical improvement within three months of starting antituberculous therapy. In 14.78%, the treatment was even empirical and diagnosis was based on the suggestive history, clinical examination and presence of indirect evidence(s) of TB. Even on statistical analysis, we did not find any significant difference between these three groups in the clinical presentation and non-specific investigations. Other studies have also faced similar difficulties in the microbiological confirmation of the disease; most of them relied on histopathological diagnosis.[23,26,27] Thus, we find that in the majority of cases, the diagnosis of

Table V. Investigation profile of patients.

Parameters	Confirmed TB (n = 38)	Probable TB (n = 60)	Presumed TB (n = 17)
Symptoms			
Abdominal pain	34 (89.47)	55 (91.67)	15 (88.23)
Fever	28 (73.68)	44 (73.33)	12 (70.59)
Weight loss	28 (73.68)	39 (68.33)	12 (70.59)
Abdominal distension	26 (68.42)	38 (63.33)	11 (64.70)
Anorexia	24 (63.16)	36 (60.00)	10 (58.82)
Altered bowel habits	20 (52.63)	31 (51.67)	9 (52.94)
Vomiting	10 (26.31)	17 (28.33)	4 (23.53)
Cough	9 (23.68)	16 (26.67)	4 (23.53)
Signs			
Abdominal distension	32 (84.21)	50 (83.33)	14 (82.35)
Doughy abdomen	10 (26.31)	17 (28.33)	5 (29.41)
Abdominal lump	8 (21.05)	12 (20.00)	4 (23.53)
Ascites	7 (18.42)	13 (21.67)	3 (17.65)
Hepatomegaly	10 (26.32)	14 (23.33)	4 (23.53)
Splenomegaly	7 (18.42)	10 (16.67)	3 (17.65)
Hepatosplenomegaly	6 (15.79)	9 (15.00)	3 (17.65)
Jaundice	4 (10.53)	5 (8.33)	2 (11.76)
Pedal oedema	7 (18.42)	11 (18.33)	3 (17.65)
Investigations			
Haemoglobin (g/dL)#	7.12 (4.60–12.50)	7.58 (5.10–13.20)	7.79 (4.70–13.00)
Total leukocyte count (/mm^3)#	13,340 (4,800–14,900)	13,110 (4,200–15,240)	13,200 (4,640–15,800)
ESR#	64 (24–98)	70 (22–108)	70 (26–110)
Serum albumin (g/dL)#	2.70 (2.00–5.86)	2.61 (1.92–5.66)	2.73 (2.22–5.86)
Positive Mantoux test	12 (31.58)	20 (33.33)	6 (35.29)
Accelerated BCG reaction	14 (36.84)	23 (38.33)	5 (33.33)

Figures in parenthesis indicate percentage; # Values are expressed as median and range

ATB has to depend only on indirect evidences. In children with the relevant history, laparoscopy has been found to be a very rewarding investigation.[28] This was further confirmed by the high success rate in histopathological diagnosis on the tissues retrieved for biopsy during laparoscopy in the present series.

In children with ATB, surgery, in an emergency or elective setting, increases the chances of a obtaining specimen for histopathological confirmation. However, it may not be 100% confirmatory, as in some occasions, the biopsy may show non-specific features. Use of ATD prior to surgery is debated, as most emergency surgeries precede medical therapy. Moreover, in an already-stenosed gut, a trial of ATD does not improve the stricture, and following medical therapy, the biopsy is non-confirmatory in a good percentage of cases due to microbiological clearance. The healing granuloma mostly shows non-specific histology. On the other hand, in the non-intestinal variety of ATB, response to ATD is remarkable and is worth a trial as soon as diagnosed. The role of laparoscopy has been promising in procuring tissue for histopathological diagnosis. It has brought down the rate of unnecessary laparotomies in children and with experience its role may also be extended to therapeutic purposes (stricturoplasty, adhesiolysis).

In areas with a low prevalence of ATB, tissue or microbiological diagnosis is highly justified prior to commencement of therapy. The same is theoretically true for areas with high prevalence. However, in places where the disease is very common and confirmatory investigations are inadequately available, the treatment may be initiated, based on strong clinical diagnosis and supportive investigations. In such situations, it is the response to therapy which indirectly proves the diagnosis. Classical four-drug chemotherapy was used in all children in the present study and a favourable outcome was observed in those who completed the full course. Some studies have used three-drug regime (INH, rifampicin and pyrazinamide), with good results.[11,29] All children showed rapid catch-up growth after start of the antituberculous chemotherapy. On completion, the number of PEM patients had reduced from 103 to nine. Complications were minimal, commonest being jaundice, which probably was drug-induced. Viral

markers for hepatitis were negative in all of them.

Young children form a separate group altogether. They are not mini-adults. They have inadequate self-care and on most occasions, they are unable to define their complaints adequately. Compared to adults, they are more susceptible to PEM, especially in the lower rungs of the socioeconomic strata. This decreases general immunity and in the presence of overcrowding, they become more susceptible to tuberculous infection. Though much has been investigated about the adult ATB, few studies have focused on ATB in children. The clinicians tend to believe that ATB in both age groups have similar presentations. Therefore, most physicians may actually diagnose ATB in children based on the clinical features of the disease in adults. Hence, the main aim of the present study was to establish the clinical, radiological and laboratory features of childhood ATB, and the outcome of treatment of ATB in the paediatric population.

In conclusion, the results of this study show that the clinical features, investigations and treatment of childhood ATB are quite similar to that of the adult disease. It should be strongly considered in children in the 5–10 year age group presenting with vague abdominal pain, weight loss, low-grade fever and abdominal distension combined with PEM and anaemia, who hail from the low economic strata, have a large family with overcrowding, and with strong history of contact to others with ATB. Acute abdomen is rare. The parents are usually illiterate and are mostly manual labourers. Histological diagnosis is confirmatory. However, in the absence of specific investigations, diagnosis may depend on supportive laboratory and radiological investigations. Early treatment decreases morbidity. In India, where the incidence of childhood TB is very high and confirmatory investigation facilities are not uniformly available across the country or not always affordable, a trial of ATD is a worthwhile treatment in paediatric cases which have a high index of suspicion of ATB.

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