



CLINICAL PROFILE OF ADOLESCENT TUBERCULOSIS-A PROSPECTIVE STUDY

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ABSTRACT

Background: Tuberculosis continues to haunt mankind despite its discovery more than a century ago.

The global burden of childhood tuberculosis is under reported due to paucibacillary disease and difficulty in confirming diagnosis.According to 2018 report burden of pediatric tuberculosis is 10 lakh among which 2.2 lakh (22%) is contributed by India .The aim of this study was to assess burden of tuberculosis in adolescent age group,to determine type of tuberculosis among diagnosed cases and to assess the symptomatology and diagnostic modalities.

Methods: A hospital based prospective observational study was conducted on adolescents(10-18 years)diagnosed with tuberculosis from November 2017-18 in tertiary care hospital.The diagnosis of tuberculosis was done based on history,clinical examination and laboratory criteria such as sputum examination,CXR, FNAC CBNAAT, MRI,CECT.

Results:Out of 60 cases,46(76.7%) were adolescents , among which 32 (69.6%) were female. Pulmonary tuberculosis was found in 15 cases(32.6%), extrapulmonary in 31 cases(67.4%). Among extrapulmonary tuberculosis,tubercular lymphadenitis 9(29%) was most common followed by CNS Tuberculosis 6(19.3%) and abdominal tuberculosis 6(19.3%).Fever and cough(90%) were the most common symptom in pulmonary tuberculosis,abdominal pain (75%) in abdominal tuberculosis and headache(100%) in CNS tuberculosis.Sputum CBNAAT was positive in 17 (36.9%), CSF CBNAAT in 6(13%) and FNAC aspirate CBNAAT in 2 cases(4.34%).Diagnosis was made on basis of imaging in 8 cases(17.4%), FNAC findings in 7 cases(15.2%),based on CXR in 6 cases(13%).

Conclusions: Adolescent forms a major burden of pediatric tuberculosis with female preponderance.Extrapulmonary tuberculosis was more common among the total diagnosed cases.Assessment of symptoms aid in opting the appropriate diagnostic method.Availability of CBNAATand other diagnostic modalities enhances diagnostic capacity of pediatric tuberculosis.

KEYWORDS :- Tuberculosis , adolescents , diagnosis.

INTRODUCTION

Tuberculosis haunts mankind since a century and it is the first infectious disease to be declared as global health emergency.(1)The global burden of childhood tuberculosis is under reported due to paucibacillary disease and difficulty in confirming diagnosis.(2) Establishing diagnosis of tuberculosis in children is difficult due to vague symptoms in early stage of the disease , near normal physical examination and pitfalls in the laboratory investigations such as tuberculin test , chest radiograph and sputum smear.(3)According to 2018 report , the global burden of pediatric tuberculosis is 10 lakh out of which 2.2 lakh (22%) is contributed by India .(4) Pediatric tuberculosis accounts to 6% of the total tuberculosis cases notified.(5)Among the total pediatric cases in India 82 % were PTB and 18% EPTB ,out of these 61% were microbiologically confirmed and 39% were clinically diagnosed.(5)In Karnataka 2018 statistics revealed that pediatric cases constituted 5% of the total tuberculosis cases out of which 84% were PTB and 16% were EPTB.64% cases were microbiologically confirmed and the rest 36% were clinically diagnosed.(5)Due to such high burden, children in India are at increased risk of acquiring infection and progressing to disease.Pediatric tuberculosis is a marker for recent transmission of TB..(6) The presentations in childhood tuberculosis and adolescent tuberculosis different from each other. (7)Age specific burden of disease estimation is not done in adolescents as they are either clubbed with pediatric population or with young adults.Also , the signs and

symptoms may be subtle especially in case of extrapulmonary tuberculosis.Hence the aim of this study was to assess burden of tuberculosis in adolescent age group,to determine type of tuberculosis among diagnosed cases and to assess the symptoms and correlate symptomatology with diagnostic modalities.

METHODS

A hospital based prospective observational study was conducted between the period of November 2017 to November 2018 in tertiary care hospital among the children aged 10-18 years of age. All children between 10-18 years(8)proven as cases of TB either by history, clinical or lab parameters , parents / guardians and children willing to give written informed consent and assent respectively , were included in the study. Those children who were already on anti-tubercular therapy and those not willing to give consent/assent were excluded from the study.

METHODOLOGY

The study was conducted on children admitted in Department of Pediatrics , Bangalore Medical College and Research Institute ,on the basis of inclusion and exclusion criteria.The adolescents were further categorized into early adolescence(10-14 years) , middle adolescence(15-17 years).Late adolescence (18-21 years) was not part of our study as the cutoff of admission under pediatrics was less than 18 years.(9)The demographic details of the patient,presenting

complaints, history of contact were collected. Clinical examination and investigations necessary for diagnosis were performed. Presumptive pediatric tuberculosis was taken as any child with history of persistent fever and/or cough for more than 2 weeks, loss of weight/no weight gain and/or history of contact with infectious tuberculosis cases. Contact was defined as a child in close contact with any form of infectious tuberculosis. Montoux test was performed using 0.1 ml of 2TU PPD RT23, injected on the ventral forearm and results interpreted between 48-72 hours. Induration more than 10 mm in any child is considered positive, and induration more than 5 mm in an immunodeficient child is considered positive. (10) 2 sputum or induced sputum samples were subjected to microscopy and CBNAAT. In suspected abdominal tuberculosis, ultrasound abdomen/contrast enhanced computed tomography/ascetic fluid analysis was performed based on the clinical presentation. Lymph node aspirate/biopsy was performed in suspected tubercular lymphadenitis and subjected to microscopy and cartridge based nucleic acid amplification. In case of suspected central nervous system tuberculosis, imaging was performed along with cerebrospinal fluid analysis. Diagnosis was made based on presenting complaints, clinical findings and supportive laboratory findings such as Montoux test, sputum examination, chest X-ray, fine needle aspiration cytology (FNAC), magnetic resonance imaging (MRI), contrast enhanced computed tomography (CECT) and cartridge based nucleic acid amplification test (CBNAAT). The statistics were computed in Microsoft Excel, SPSS version 22 and analysed. The descriptive statistics were expressed in frequencies and percentages.

RESULTS

Total of 60 children were enrolled in the study out of which 46 were adolescents (76.6%), and the rest 14 (23%) were less than 10 years of age. (FIGURE 1, TABLE 1).

FIGURE 1:

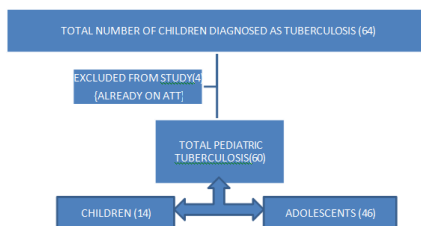


TABLE 1:

AGE GROUP	MALE	FEMALE	TOTAL
<10 YEARS	3	11	14
10-14 YEARS (Early Adolescence)	7	14	21
14-17 YEARS (Middle Adolescence)	7	18	25
18-21 YEARS (Late Adolescence-not included)	0	0	0
TOTAL	17	43	60

The adolescents were further divided into early adolescence-21 cases (45.6%) and middle adolescence-25 cases (54.34%). Genderwise comparison showed that females outnumbered the males, comprising 32 (69.6%) of the total cases, whereas males were only 14 (30.4%). 14 females (30.4%) and 7 (15.2%) males constituted the early adolescence group whereas the middle adolescence group comprised of 18 females (39.1%) and 7 males (15.2%).

Extrapulmonary tuberculosis were more compared to pulmonary tuberculosis. (TABLE 2) Extrapulmonary tuberculosis was found in 21 (45.6%) children and pulmonary

tuberculosis in 15 (32.6%) children. There were 10 (21.7%) cases of disseminated tuberculosis. Among pulmonary tuberculosis, upper lobe involvement was found in 5 cases (33.3%), cavitary lesions in 4 cases (26.6%), middle lobe involvement in 3 cases (20%), miliary mottling in 2 cases (13.3%), lung collapse in 2 cases (13.3%) and lower lobe involvement in 1 case (6.6%). Among extrapulmonary tuberculosis, majority were tubercular lymphadenitis in 9 cases (42.8%), whereas tuberculosis of central nervous system and abdominal tuberculosis comprised 6 cases (28.6%) each. Among the 6 cases of abdominal tuberculosis, peritoneal involvement was found in 2 cases (33.3%), ileocecal involvement in 3 cases (50%). Meningeal involvement was found in 2 cases (33.3%) of CNS tuberculosis, parenchymal involvement in 3 cases (50%) and basal exudates in 1 case (16%). The cases of disseminated tuberculosis were analysed and found that 4 children (40%) had Pulmonary tuberculosis along with abdominal tuberculosis, 4 children (40%) had Pulmonary tuberculosis along with Central nervous system tuberculosis, 2 children (20%) had miliary tuberculosis along with Central nervous system tuberculosis.

TABLE 2:

TYPE	NUMBER OF CASES	PERCENTAGE
Pulmonary tuberculosis	15	32.6
Disseminated tuberculosis	10	21.7
Lymph node tuberculosis	9	13
Abdominal tuberculosis	6	13
Central nervous system	6	19.5
Total	46	100

Among the children with pulmonary TB, fever and cough were the most common complaint in 14 cases (90%), loss of weight in 5 cases (32.3%), chest pain in 4 cases (26.6%), loss of appetite and hemoptysis in 1 case each (6.6%). Among the children diagnosed as abdominal TB, abdominal pain was the most common presenting complaint in 5 cases (75%), vomiting in 3 cases (50%), fever in 3 cases (50%), abdominal distension in 2 cases (33%), weight loss and loss of appetite in 2 cases (33%). The children diagnosed with CNS TB manifested with headache in 6 cases (100%), vomiting in 5 cases (83%), fever and altered sensorium in 4 cases (66.6%), convulsions in 2 cases (33%) and weight loss in 2 cases (33%). (TABLE 3)

TABLE 3

SYMPTOMS	NUMBER OF CASES	PERCENTAGE
Fever	17	36.9
Cough	14	30.4
Weight loss	9	19.5
Vomiting	8	17.3
Headache	6	13
Abdominal pain	5	10.8
Chest pain	4	8.7
Altered sensorium	4	8.7
Loss of appetite	3	6.5
Convulsions	2	4.3
Abdominal distension	2	4.3
Hemoptysis	1	2.2

The durations of symptoms at the time of presentation were analysed and it was found that fever more than 2 weeks was present in all 15 cases(100%) of the pulmonary tuberculosis ,whereas cough more than was present in 11 cases(73 %).Abdominal pain >1 month duration was the presenting complaint in 5 cases(90%) of abdominal tuberculosis.Only 3 cases(50%) of central nervous system tuberculosis presented with headache >15 days, suggesting most had acute presentation.

Only 7 cases(15.2%) out of the total diagnosed cases had a history of contact with tuberculosis.

Among total cases of TB, 25 patients(54.3%) had a positive Montaux test. The BMI of the 25 Montaux positive patients were analysed and found that 24(96%) had normal BMI. Of the 21 patients who showed a negative Montaux test ,14(67%) had BMI less than 3 standard deviation.(TABLE 4)

TABLE 4

	BMI > (-3SD)	BMI <(-3SD)	Total
Montaux positive	24	1	25
Montaux negative	7	14	21
Total	31	15	46

Among the cases diagnosed, 8 were based on clinicoradiological findings,7(15.2%) were based on FNAC findings, 5(10.8%)were by CT and 3(6.5%) were by MRI.Among 46 sputum samples examined 17 were positive (36.9%). 13 samples of CSF were subjected to CBNAAT out of which 6 were positive (46.15%).Out of the 9 samples of FNAC aspirate subjected to CBNAAT, 2 were positive(22.2%).Sputum microscopy was positive in 7 cases (15.2%). (TABLE 5).Among the total proven cases of pulmonary tuberculosis, including those with disseminated tuberculosis(23), smear microscopy was positive in 30.4% whereas CBNAAT was positive in 73.9%.

TABEL 5

INVESTIGATIONS	SAMPLES SUBJECTED	POSITIVE CASES	PERCENT AGE
Montaux test	46	25	54.34
Sputum CBNAAT	46	17	36.9
Chest Xray	46	8	17.4
Sputum microscopy	46	7	15.2
FNAC microscopy	9	7	77.7
CSF CBNAAT	12	6	50
CECT	9	5	55.5
MRI	10	3	30
FNAC aspirate CBNAAT	9	2	22.2

Among total TB cases 20 cases (43.4%) were associated with anemia and 15 cases (32.6%) were associated with malnutrition among which 8 were females (53.3%) and 7 males(46.6%).

All the cases in our study belonged to upper lower socioeconomic class.

DISCUSSION

The presentation of adolescent tuberculosis is different from that of children and adults. The exact national or international figure for adolescent tuberculosis is not known as adolescents are either clubbed with children or with adults.In adolescents, most pulmonary tuberculosis are adult type both clinically and radiologically thus being more bacilliferous and intum more infectious.(11,12) Hence this study aimed at analysing the burden of adolescent tuberculosis , their gender

distribution, the type of tuberculosis among the diagnosed cases and the investigation tools used.

Our study was a prospective study and included 60 cases between the age group of 10-18 years of age , out of which 46 (76.6%) were found to be adolescents.54.3% belonged to middle adolescence group ,implying higher occurrence in this age. There is increase in incidence of tuberculosis in adolescent age group, reasons for which are poorly understood.One hypothesis is that psychological and behavioural variables associated with adolescence may increase risk of developing tuberculosis ,though no such statistical significance has been studied.(13)The major portion among the adolescents diagnosed with tuberculosis was constituted by females in our study , amounting to 69.6% cases.In a retrospective study conducted by Jayasree Poroo et al(14) in 2015 on 67 children between the age of 13-19 years, adolescents constituted 40.2% cases, out of which 55% were females. The study conducted by Shyam L Kaushik et al(15) over 4 years involving 477 children in the age group of 10-19 years, found 50.5 % female preponderance.Andrea T Cruz et al(16) conducted a retrospective study on 145 children between 12-18 years at Children's Tuberculosis Clinic, Houston and found equal distribution between male and female.A retrospective study conducted by Loi`c de Pontual et al(17)among 52 children between 12-18 years , found females in 52% cases and males in 48% cases ,indicating slight female preponderance.

The most common type of tuberculosis in our study was extrapulmonary , constituting 45.6% of the total cases. Disseminated tuberculosis constituted 21.7% of the total diagnosed cases. Extrapulmonary tuberculosis was higher in study conducted by Jayasree Poroo et al, where it was found in 52% of the total diagnosed cases.Pulmonary tuberculosis was found more in studies conducted by Shyam L Kaushik et al, Andrea T Cruz et al and Loi`c de Pontual et al accounting for 51.8% , 78.6% and 52% respectively. TB lymphadenitis cases were the maximum among extrapulmonary tuberculosis , accounting for 42.8% cases , followed by equal occurrence of central nervous system tuberculosis and abdominal tuberculosis(28.6%).The most common extrapulmonary tuberculosis in the study conducted by Shyam L Kaushik et al was pleural effusion (25.7%) , whereas it was lymph node tuberculosis in the study conducted by Andrea T Cruz et al.

All cases of lymph node tuberculosis presented as either unilateral or bilateral neck swellings. Fever and cough(90%) were the most common presenting complaint in pulmonary tuberculosis followed by weight loss. Abdominal tuberculosis cases presented as abdominal pain(75%) as the most common presenting complaints followed by vomiting(50%),fever(50%),weight loss and loss of appetite(33%). All cases of CNS tuberculosis presented with headache(100%) followed by vomiting(83%) , fever(66.6%) , altered sensorium(66.6%) and convulsions(33%) as the other presenting complaints.In a study conducted by Anuradha G et al , cough was the most common presenting complaint followed by sputum production and fever in cases of pulmonary tuberculosis , lymphadenopathy was the major presenting complaint in extrapulmonary tuberculosis.(18).Andrea T Cruz et al in their study found that fever was the most common symptom(63%) , followed by cough (60%) and weight loss (30%).Fever followed by weight loss and cough were the most common symptoms in the study conducted by Loi`c de Pontual et al .Fever of more than 2 weeks was present in all cases, whereas cough more than 2 weeks was present only in 73% cases of pulmonary tuberculosis.Abdominal tuberculosis presented with more chronicity as abdominal pain of more than 1 month duration was the major presenting complaint in 90% cases.CNS tuberculosis mainly had an acute presentation as fever more

than 15 days was found in only 50 % cases and the rest were acute symptoms of 3-5 weeks duration. The progression of infection to disease can be subtle in adolescents, especially in case of extrapulmonary tuberculosis. (19,20). This could be the reason for delayed seeking of medical attention. Hence it is important to have a high index of suspicion, especially in cases of extrapulmonary tuberculosis.

7 cases (15.2%) out of the total diagnosed cases had a history of contact with tuberculosis in our study. In the study conducted by Andrea T Cruz et al, contacts were identified in 24% of cases, and 52% were identified in study conducted by Loïc de Pontual et al. The low proportion of contacts in our study could be explained due to the fact that most of the cases were from distinct parts of Karnataka and India, and contact tracing could not be done beyond the immediate family contacts.

Montaux was positive among 54.34 % of the total diagnosed cases in our study. 96% of the children with positive Montaux test had normal BMI, whereas 67% of the children with negative montaux test had BMI less than 3 standard deviation (severe thinness), thus indicating that children with good nutrition status showed a good immune response. Study conducted by Loïc de Pontual et al had 82.6% montaux positivity, 54.6% in study by Shyam L Kaushik et al and only 7% in a study conducted by Andrea T Cruz et al. Low BMI has been shown to increase the susceptibility to tuberculosis, due to the decreased immune response. Very few studies have stressed upon the importance of nutrition on Montaux, especially in children, though few studies on adults (21,22) have been found. Our study could be one of the first in adolescents, to highlight the role of nutrition on Montaux interpretation.

Bacteriological diagnosis was done by smear microscopy and CBNAAT in our study. Diagnosis was made on the basis of CBNAAT in maximum cases, sputum CBNAAT in 36.9%, CSF CBNAAT in 13% and FNAC aspirate CBNAAT in 4.3% cases. Sputum microscopy was positive in 7 (15.2%) cases, whereas sputum CBNAAT was positive in 17 (36.9%) cases. This could be due to the fact that microscopy can detect bacteria when present in concentration of 10000 per ml whereas CBNAAT can detect as low as 10 bacilli. (23) Bacteriological confirmation was done either by microscopy, rapid diagnostic tests or by culture in few other studies where it showed positivity in 46 % cases in study by Shyam L Kaushik et al, 53.8% in Jayasree Poroo et al, 43% in Andrea T Cruz et al and 61.5% in Loïc de Pontual et al.

Chest Xray helped in the diagnosis of 6 cases. Upper lobe involvement was the most common followed by cavitory lesions. The other findings observed were middle lobe involvement, collapse and military mottling. Infiltration and consolidation were found as the Xray findings in 42.4% of the cases in the study conducted by Shyam L Kaushik et al. Similarly infiltrates, followed by lymphadenopathy were the most common radiological finding in the study by Andrea T Cruz et al. The other cases were diagnosed on the basis of FNAC microscopy in 7 cases and by imaging in 8 cases.

No cases were found to be HIV infected in our study. The study conducted by Shyam L Kaushik et al and Loïc de Pontual et al had 2.9% and 13% HIV positive cases respectively.

CONCLUSION :

Adolescent forms a major burden of pediatric tuberculosis with female preponderance. Fever, cough and weight loss were the most common symptoms in all types of tuberculosis. Despite this, the presentation is late mostly because the symptoms are neglected. Extrapulmonary tuberculosis was more common among the total diagnosed cases. Montaux positivity in those with normal BMI indicates

the importance of nutrition and immune status. As most adolescent cases are bacilliferous, microbiological diagnosis is possible in most cases. Availability of CBNAAT further aids in diagnosis of these cases. The other diagnostic modalities in conjunction with history, microscopy and CBNAAT enhances diagnostic capacity of pediatric tuberculosis. This emphasizes the need for comprehensive evaluation of symptoms, examination and relevant investigations, especially in the absence of a gold standard diagnostic test.

DECLARATIONS

Funding: None

Conflict of interest: None declared

Ethical approval: Approved

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