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Original Research Article

Study of tuberculosis in HIV positive children in a tertiary care hospital of Odisha

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ABSTRACT

Background: Tuberculosis and HIV have been closely linked since the emergence of AIDS. Worldwide, TB is the most common opportunistic infection affecting HIV seropositive individuals and it remains the most common cause of death in patients with AIDS. HIV infection has contributed to a significant increase in the worldwide incidence of TB. So, an attempt was made in the present study to know the magnitude/extent of tuberculosis, associated clinical patterns, epidemiological factors and outcomes in HIV positive children attending the ART Centre of SCB medical college and hospital, Cuttack.
Methods: A tertiary care hospital based prospective study was carried out in 50 children between 6 months to 14 years of age for a period of 2 years.
Results: Most of the cases were less than 6 years old. TB was more common in male children than in females. Most cases were from rural areas. Majority belong to Class IV (Upper Lower) and Class V(Lower) socio-economic class. Most had Grade II and Grade III malnutrition as per IAP classification. Definite history of contact and recent infection was present in most. Majority (75%) had pulmonary tuberculosis. Pleural variant was predominant in extra-pulmonary form followed by TB lymphadenitis and disseminated forms. 5% had both PTB and EPTB. Most cases were un vaccinated. Common clinical features were fever, cough, FTT, chronic diarrhoea. Disseminated TB was common in unvaccinated group. Recovery pattern was almost similar in vaccinated and unvaccinated groups. Most of the PTB cases were cured of the disease with only 2 deaths in this group whereas the number of deaths, children going LAMA and development of MDR-TB was more in disseminated forms.
Conclusions: Occurrence of TB is high in HIV positive cases. EPTB is common in unvaccinated cases. TB is common in rural and underprivileged children. Drug compliance is poor in disseminated forms. Mortality is high in disseminated forms. Sequele is more in disseminated forms of TB.

Keywords: Co-infection, HIV, Tuberculosis

INTRODUCTION

Tuberculosis (TB) and HIV have been closely linked since the emergence of AIDS. Worldwide, TB is the most common opportunistic infection affecting HIV-seropositive individuals and it remains the most common cause of death in patients with AIDS. HIV infection has contributed to a significant increase in the worldwide incidence of TB. By producing a progressive decline in cell-mediated immunity, HIV alters the pathogenesis of TB, greatly increasing the risk of disease from TB in HIV-coinfected individuals and leading to more frequent extrapulmonary involvement, atypical radiographic

manifestations, and paucibacillary disease, which can impede timely diagnosis. Although HIV-related TB is both treatable and preventable, incidence continues to climb in developing nations wherein HIV infection and TB are endemic and resources are limited. Interactions between HIV and TB medications, overlapping medication toxicities, and immune reconstitution inflammatory syndrome (IRIS) complicate the co-treatment of HIV and TB.[1]

In the recent past, varying levels of drug resistance are also being found in HIV and TB co infected patients. Out of the 12 million prevalent TB cases around 6,50,000 were estimated to be multi drug resistant to at least isoniazid and rifampicin.[2] India has the world's highest burden of TB overall with prevalence of MDR-TB among all patients with TB estimated to be 4.1%. 4500 – 6000 HIV infected persons develop MDR-TB annually in india. Those at highest risk of MDR-TB are cases in whom treatment was a failure, in relapsers in defaulters and contacts of MDR-TB. Drug resistance is rarely seen in the paediatric population due to the paucibacillary nature of the disease and originates mainly in adult contacts who are treatment failures or defaulters. Thus, the main method of resistance in children is primary transmission of the resistant bacilli.[3]

Diagnosis of any form of tuberculosis including DR-TB is more challenging in the presence of HIV disease and together they result higher case fatality rates.

There is also variation in presentation of TB in HIV infected and non-HIV infected patients. Extrapulmonary involvement can be seen in more number of patients with concurrent AIDS and tuberculosis. The risk of extrapulmonary tuberculosis and mycobacteremia increases with advancing immunosuppression. Unique features of AIDS-associated tuberculosis include extra-pulmonary disease, disseminated disease, rapid progression, visceral lymphadenopathy, tissue abscesses, and negative tuberculin skin test. Response to anti-tuberculous therapy is favourable and similar to that of patients without HIV infection, although adverse drug reactions occur more commonly in those with HIV infection. It is unclear whether patients with HIV infection have a higher risk of relapse. Infectious disease consultation is advisable given complex drug-drug interactions and the risk of paradoxical response or immune reconstitution.[4] There is also variation in the mode of presentation in a child than in an adult as children are much more likely to develop extra pulmonary TB as many as 25% approximately compared to only 16% in adults. Children are also more likely to develop severe forms of TB including disseminated TB and TBM. TB co-infection with HIV is common in children. Severe weight loss and cough can be used as a clinical guide to identify HIV infected children at risk of co-infection with TB who will require careful observation further evaluation and intervention.[5]

METHODS

The study was conducted in the ART centre of SCB Medical college, Cuttack during the period from October 2014 to October 2016 to study the magnitude and extent of tuberculosis, associated clinical and epidemiological factors in HIV positive patients.

Aim of the study was to study of tuberculosis in HIV positive children in a tertiary care hospital of Odisha,

Objectives of the study was to study the magnitude /extent of tuberculosis in HIV positive children in a tertiary care hospital. To study the associated clinical patterns, epidemiological factors and outcome in children. Type of study: Cross sectional hospital based study. Sampling method: Sample size was calculated according to the data regarding magnitude of TB in HIV positive patients according to the studies done in different parts of the world. Materials: The children of 6 months to 14 years attending the ART centre with signs and symptoms of tuberculosis.

Inclusion criteria

All HIV Positive paediatric cases attending the ART centre during October 2014 to October 2016 and willing to participate in the study.

Exclusion criteria

- Not willing to study
- Having other co-morbid conditions

The prospective observational cross-sectional study was conducted in ART centre of SCB Medical college and hospital for a period of 2 years from October 2014 to October 2016

The cases being suspected of having tuberculosis were informed about the study and a written consent was taken from the parents.

On admission, a detailed history of the presenting complaints, duration of illness, recent past history of measles in the child and presence of household contacts of tuberculosis were obtained from the parents or caregiver. The vaccination status of the child was confirmed by the presence or absence of BCG scar, nutritional status of children was assessed and socio-economic status evaluated as per modified kuppuswamy scale. Clinical examination of the child was done and the patient was then subjected to the following investigations. CBC, ESR, RBS, LFT, RFT, Fundoscopy, X-ray chest and spine, Mantoux test, sputum microscopy, gastric aspirate for A.F.B, USG of specific parts (lymphnodes, abdomen), CSF study, CT/MRI of brain and spinal cord, HIV, ELISA, biopsy of lymph nodes, CBNA at study of sputum or gastric aspirate.

Statistical analysis

Statistical analysis was done by statistical software SPSS for windows version 23. P values were calculated using pearson chi-square test. P <0.05 was considered as significant.

RESULTS

The incidence of tuberculosis is more marked in 2-10 years in unvaccinated age group but overall incidence of approx. 55%was observed below 6 years of age (Table 1).

This finding in unvaccinated age group is agreeing with Ramachandran et al and sarma et al.[6-9] Tuberculosis cases were more common in male children (54%) than in female Children (46%) in all age groups as shown in the Table 1).

This is in accordance to a study conducted by YD Mukadi et al conducted in the year 2000.[10]

Table 1: Distribution of cases according to age and sex.

Age group in years	Total no. (%)	Males		Females	
		No. of cases	%	No. of cases	%
1-3	10 (20)	5	50	5	50
4-5	18 (36)	10	55.5	8	44.5
6-10	13 (26)	7	53.8	6	46.2
11-14	9 (18)	5	55.5	4	44.5

Most of the cases approximately 76%were from the rural areas than 24% who belonged to urban or semi urban areas. Similar observations were noted by Mehera et al and Deshmukh et al.[11,12]

Majority of children with tuberculosis belong to class-IV (Upper Lower) and class-V (Lower) (60%) whereas only 10% belong to class-I (Upper) and rest belong to class-II (Upper Middle) and class-III (Lower Middle). Similar observations were also made by Murthy et al, Mehera et al and sheikh et al.[13-15]

Most of the cases belong to poor nutritional status comprising 24%in grade 1 malnutrition,22% In gr. II, 32% in gr. III, and only 6% in gr. IV. However, 16% maintained normal nutritional status as shown in the Table 2. Such low nutritional status association with the disease has been reported by Mathur et al and Raju et al.[16,17]

Table 2: Distribution of cases according to grade of malnutrition according to IAP classification.

Grade of malnutrition	PTB	EPTB/Disseminated	Total
Normal	6	2	8
I	10	2	12
II	8	3	11
III	13	3	16
IV	1	2	3

The pattern of tuberculosis in the present study showed 76% of children had pulmonary tuberculosis, 24% extrapulmonary, among which pleural involvement was seen in 66.6%, lymphnode in 25% and dissemination in 33.3% cases. 6% of children had involvement of both pulmonary and extrapulmonary systems. various studies done with HIV positive children in various parts of the world showed the same findings.Madhi et al showed the pulmonary involvement was 50%.[18] Marais et al showed 86% was pulmonary tuberculosis, 20% extrapulmonary tuberculosis, 6% both pulmonary and extrapulmonary involvement.[19,20] A study conducted in AIIMS, New delhi showed 50% of the HIV positive children were infected with tuberculosis, 34% had miliary or disseminated tuberculosis.[21] According to a study in chennai 20.6% had disseminated Tuberculosis which tallies with our findings of 28%.[22] Jeena et al in the year 2000 had observed the involvement of lymphnode in 27% which is almost similar to our findings.[23]

In our study 6 out of the 8 cases with normal nutrition status developed pulmonary tuberculosis and 32 out of 42 in under-nutrition category developed pulmonary tuberculosis and this finding is statistically insignificant with p value >0.05.

Table 3: Cases according to nutritional status.

Nutritional status	PTB	EPTD/Diss.	Total
Normal	6	2	8
Undernutrition	32	10	42

The distribution of cases according to various predisposing factors revealed that there was a definite history of contact with tuberculosis in 42% of cases (Table 4) and this finding of increased incidence of pulmonary tuberculosis in children with contact history is statistically significant with p value <0.05. Similarly,

history of contact was noted in 42% and 53% of cases by sheik et al and shah et al respectively.[24,25]

Table 4. Association of the predisposing factors of the cases.

Factors	No. of cases	%
Contact history	21	42
History of recent infection	24	48
No history	5	10

Table 5: Association of history of contact with PTB and EPTB.

Contact history	PTB	EPTB	Total
Present	17	4	21
Absent	21	8	29
Total	38	12	50

Besides history of contact there were preceeding illnesses like measles and whooping cough also in them and this is also statistically significant with $p<0.05$. Since the children are already immune-compromised there is a likeliness of increased occurrence of the disease and the same observation was noticed in various study conducted by Bhakoo et al, Magotra et al, and shah et al.[26,27]

Table 6: Association of history of recent infection with PTB and EPTB.

History of recent infection	PTB	EPTB	Total
Present	20	4	24
Absent	18	8	26
Total	38	12	50

In considering the BCG status in various types of tuberculosis as evidenced by the presence of BCG scar, it was observed that out of the 50 cases, 40 (80%) were un immunised and 10 (20%) were immunised.

The higher incidence of miliary and disseminated forms in unvaccinated age groups and pulmonary Tb in vaccinated age group is statistically significant with $p<0.05$ and this is in accordance to the study conducted by Chandra et al, udani et al which proved that BCG provides partial protection against tuberculosis.[28,29]

Table 7: Cases according to the immunisation status.

Immunisation status	PTB	EPTB/ Disseminated	Total
Immunised	9	1	10
Unimmunised	29	11	40

There were varied signs and symptoms with various forms of tuberculosis.

Most frequent presenting complaint was fever (88%), cough (76%), failure to thrive in 70% of cases, loss of appetite in 48% cases, chronic diarrhoea in 66% cases, generalised lymphadenopathy in 58% cases and altered sensorium in 10% cases.

Table 8: Symptoms of the studied cases.

Symptoms	No. of cases	%
Fever	44	88
Cough	38	76
Failure to thrive	35	70
Chronic diarrhoea	33	66
Generalised lymphadenopathy	29	58
Loss of appetite	24	48
Altered sensorium	5	10

In our study 37 cases (34 from pulmonary Tb category and 3 from extrapulmonary and disseminated Tb category) were compliant to therapy and 13 cases (4 from pulmonary Tb category and 9 from extrapulmonary Tb category) were non-compliant to therapy and it has been observed that the pulmonary Tb cases were more compliant to therapy than the disseminated forms of extrapulmonary Tb and the difference is statistically significant ($p<0.05$).

Table 9: Compliance to treatment of the studied cases.

Compliance to T/T	PTB	EPTB
Compliant	34	3
Non-compliant	4	9
Total	38	12

Compliance to treatment was divided into complete treatment, defaulter and those who did not follow up. those who completed treatment were grouped under compliant group and defaulter plus those who did not follow up were grouped under non-compliant group.

defaulters were put into re- treatment for tuberculosis after which they were cured off the disease. There was development of arthralgia in 80% cases, neuropathy in 74% cases, headache in 35% cases, vomiting in 50% cases, rash in 24% cases, nephropathy in 10% cases and hepatitis in 4% cases.

Table 10: Complications during therapy of the studied cases.

Complication	No. of cases	%
Arthralgia	40	80
Neuropathy	37	74
Headache	35	70
Vomitting	25	50
Rash	12	24
Nephropathy	5	10
Hepatitis	2	4

Course after drug induced hepatitis was such that among the two patients who developed hepatitis one child

improved and the other failed to improve, developed other complications too and died.

36 cases with pulmonary Tb and 1 with extrapulmonary Tb were cured of the disease and 2 cases with pulmonary Tb and 11 with extrapulmonary Tb were not cured of the disease. The cure rate was higher in pulmonary Tb group as compared to disseminated forms of extra pulmonary Tb with p value <0.05.

Table 11: Outcomes of treatment.

Outcome	PTB	EPTB	Total
Cured	36	1	37
Not cured	2	11	13

The initial CD 4 count of the studied cases was less than 100 in 8% cases, between 100 to 200 in 22% cases and between 200 to 500 in 70% cases.This showed almost 100 percent HIV affected patients who developed tuberculosis of any form had CD 4 count less than 500.

There was complete recovery in pulmonary tuberculosis in both vaccinated and unvaccinated groups. Almost all cases of tuberculosis in vaccinated groups recovered and around 30% cases in the non-vaccinated groups had sequele, 11% cases died and 12% cases could not be followed up during the study period. The incidence of MDR-Tb was only 1% in consistence with the studies by Asch et al and Spellmann et al who said MDR-Tb is not more common among children infected with HIV.[40,41]

DISCUSSION

The present study consisted of 50 HIV positive children suffering from different patterns of tuberculosis who were taken for analysis. The work was conducted in the ART Centre of SCB Medical college and hospital, Cuttack.

The higher incidence of tuberculosis in 2-10 years unvaccinated age group is due to the facts that children in this age group are more in close contacts with open cases of tuberculosis in the family without having protective immunity.

Tuberculosis was more common in male children than female Children in all age groups. This can be explained by the fact that more care and attention is taken to bring the male children to hospital during their illness.

Most of the cases were from rural areas. Since, cases coming from rural areas outnumbered those coming from urban areas it is concluded that facilities were not adequate in rural areas for which case detection was delayed and cases became critical needing hospitalisation. Lack of awareness among poor and illiterate is also a contributing factor in rural areas. Majority of children with tuberculosis belonged to lower socio-economic status. Since most of the cases belonged to rural areas, it seems that their socio-economic status might have contributed to the disease as it is a well-known fact that tuberculosis is a disease of the poor and under-privileged.

Most of the cases belong to poor nutritional. Such low nutritional status association with the disease has been reported by Mathur et al and Raju et al.[16,17] Shah et al reported PEM Grade III in 65.31% to 76% in cases of tuberculosis which does not support our study in which only 32% of cases belong to Grade III malnutrition.[25] In our study 6 out of the 8 cases with normal nutrition status developed pulmonary tuberculosis and 32 out of 42 in undernutrition category developed pulmonary tuberculosis and this finding is statistically insignificant with p value >0.05 and this is because all are HIV positive cases and malnutrition has no direct impact on tuberculosis in our case.

The distribution of cases according to various predisposing factors revealed that there was a definite history of contact with tuberculosis in 42% of cases and this finding of increased incidence of pulmonary tuberculosis in children with contact history. This is because for acquiring tuberculosis contact is one of the predisposing factors for the spread of the disease to young children by infected adults either in their own house or in their neighbourhood. Starke et al has clearly stated that children usually get the disease from adult patients of tuberculosis in immediate house members or neighbours.[42] Besides history of contact there were preceeding illnesses like measles and whooping cough also in them. Since the children are already immune-compromised there is a likeliness of increased occurrence of the disease.

In considering the BCG status in various types of tuberculosis as evidenced by the presence of BCG scar, it was observed that most were un-immunised. Comparing tuberculous lesions in vaccinated and un vaccinated groups showed much higher incidence of miliary or disseminated tuberculosis in unvaccinated age groups as compared to pulmonary tuberculosis in immunised children and it is well known that immunisation with BCG does not prevent the development of Pulmonary Tb but it has role in preventing the disseminated forms of the disease.

It has been observed that the pulmonary Tb cases were more compliant to therapy than the disseminated forms of extrapulmonary Tb. This may be due to relative better clinical conditions and single system involvement in pulmonary Tb cases as compared to disseminated forms of tuberculosis.

There was development of various complications. The cases were then given various symptomatic, prophylactic and drug withdrawal and gradual re introduction treatment accordingly. This development of complication may be due to the disease process itself or may be due to

the drugs used in the treatment process. The cure rate was higher in pulmonary Tb group as compared to disseminated forms of extra pulmonary Tb due to better compliance and clinically better conditions in pulmonary Tb cases as compared to their sick counterparts in disseminated Tb.

CONCLUSION

Occurrence of tuberculosis is high in HIV positive cases. Extra pulmonary forms of Tuberculosis are more common in unvaccinated children. Tuberculosis is more common in rural and under privileged children. Drug compliance is poor in extra pulmonary forms of tuberculosis. Mortality is higher in HIV positive children with extra pulmonary and disseminated forms of tuberculosis. Sequele was more in children with disseminated forms of tuberculosis.

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