Original Article

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Determination of Sites Involved, HIV Co–Infection & Utility of Diagnostic Modalities in EPTB

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ABSTRACT

Background: Tuberculosis remains a major global public health problem and an on-going epidemic. Though the chief objectives of the Revised National Tuberculosis Control Programme (RNTCP) in detecting and curing the infectious pulmonary cases is well taken, there has been a steady rise in the number of Extra Pulmonary Tuberculosis (EPTB) cases as documented in several studies. EPTB which usually constitutes around 15%-20% of the total TB cases is now being increasingly reported due to a combination of better diagnostic facilities, and the HIV pandemic. Though several studies have shown increasing prevalence of EPTB, only few studies are available, especially in the Indian scenario, that study the pattern and risk factors. Hence, this retrospective observational study was undertaken to determine the sites of the involvement, HIV co-infection and usefulness of various diagnostic modalities in EPTB affecting patients attending a medical college DOTS clinic.

Material and Methods: One hundred ten EPTB patients referred to the DOTS clinics of the TB & Chest department from the period Dec 2010– Mar 2012 were included in the study. The diagnosis of EPTB was established by combined clinical, microbiological, histopathological &/or imaging modalities. Their medical records were assessed to determine the age distribution, gender and anatomical sites of involvement. The presence of co-morbid conditions like smoking history, alcoholism, diabetic and HIV status were noted. BCG status and Mantoux test readings were recorded. The different diagnostic tests used in confirming EPTB at different sites were recorded. Chest x-ray was analysed for all patients to assess coexisting pulmonary involvement. All patients were followed to assess the outcome of treatment.

Results: The mean age of patients was 34.4. The male to female ratio was 58:52 showing a slight male predominance. The most common site of involvement was lymph node followed by pleural effusion and abdominal TB. The prevalence of lymph node TB was noted to be higher in female patients as compared to other sites of EPTB. Mantoux test was positive in 57 (51.8%) patients. HIV co-infection was noted in only 3 (2.7%) patients. Concomitant pulmonary involvement was seen in 19 (17.3%) patients.

Conclusions: Lymph node was the most common site involvement showing a significant female preponderance followed by pleural effusion and abdominal TB. The rates of HIV co-infection and diabetes mellitus were 2.7% and 20% respectively. The most useful diagnostic modality was tissue sampling followed by imaging. Mantoux test is not unequivocal for the diagnosis of EPTB.

Key words: Extra–Pulmonary Tuberculosis, DOTS clinic, TB Lymphadenopathy, HIV co-infection, Mantoux test

INTRODUCTION

Tuberculosis is the leading cause of death and morbidity worldwide with approximately 9.4 million incident cases and 1.3 million deaths annually [1-3,4]. The WHO has identified the high burden TB countries that are collectively responsible for 80% of the total cases. India has the largest number of TB cases in the world accounting for nearly 1/5th of the global burden. Though the newly diagnosed sputum-positive pulmonary TB patients are the chief target population in national TB programmes, the trend of EPTB has shown changes in many areas [4,5,6,7]. EPTB which usually accounts for about 15%–20% of the total TB cases, is now being increasingly reported due to the rise in the HIV pandemic [6,7] and better diagnostic facilities. Recent studies have suggested that the sites of EPTB may vary according to geographic location and population [2,3,8,7]. The clinical manifestations of TB are variable and depend on a number of factors that are related to the microbe, host and environment. Our understanding of the role of host related factors responsible for the occurrence of TB at extra–pulmonary sites is limited in that few Indian studies are available to date. Since the manifestations of EPTB maybe non-specific and tissue diagnosis may not be possible in all cases, the utility of diagnostic modalities like Mantoux, ESR, Serology and PCR have been assessed in several studies [1,2,8]. Hence, this retrospective observational study was undertaken to determine the sites of involvement, HIV co-infection and usefulness of various diagnostic modalities in EPTB affecting patients attending a medical college DOTS clinic.

MATERIAL AND METHODS

Study Setting: The DOTS clinic in the Department of TB & Chest of a Medical College Hospital catering to predominant rural population.

Data Collection: The medical records of 110 EPTB patients referred to the DOTS clinic from the period Dec 2010 to March 2012 were analysed. Their medical records were assessed to determine the age and gender distribution and anatomical sites of involvement. A diagnosis of EPTB was confirmed by microbiological, biochemical, histopathological evidence and/or imaging modalities and strong clinical evidences consistent with active EPTB followed by a decision to treat with full course of anti-tuberculous treatment. The different diagnostic modalities as mentioned above were recorded. The presence of comorbid conditions like DM, HIV co-infection, chronic alcoholism and smoking were recorded. A reading of more than 10mm induration using 5TU after 48 hours was taken as a positive Mantoux test result. BCG status was noted. Chest X-rays of the above patients were assessed to determine concurrent pulmonary involvement. All 110 patients were followed-up and the outcome of the treatment assessed.

RESULTS

Out of the 110 cases, the male to female ratio was 58:52. The mean age of presentation was 34 years. Majority (N=55) of patients belonged to the age group 24 to 48. The age and gender distribution of the patients is shown in [Table/Fig-1].

The most common site of involvement was the lymph nodes (43%, 47 cases) followed by pleural effusion (28%, 31 cases) and abdominal tuberculosis (12%, 13 cases). Within lymph nodes, the sites of involvement were cervical (33), axillary (5), mediastinal (4), submandibular (3), inguinal (2). Matted lymph nodes were observed in 12 patients and sinuses in 2 patients. Cold abscesses were seen in 3 patients. Disseminated TB involving two or more of these anatomical sites were noted in 3 patients. PUO as a presenting manifestation was noted in 3 patients (all abdominal TB). The details of the distribution of the anatomical sites of involvement and the various diagnostic methods are given in [Table/Fig-2].

BCG scar was seen in 96 patients (87.2%). The Mantoux test was positive in 57 (51.8%) of confirmed EPTB patients. [Table/Fig-3] shows the Mantoux test positivity in relation to the anatomical site of involvement.

Age Group (years)	No. of Males	No. of Females	Total	Percentage
0 – 12	2	0	2	1.8 %
12 – 24	17	15	32	29.1 %
24 – 36	16	15	31	28.2 %
36 – 48	14	8	22	20.0 %
48 – 60	7	8	15	13.6 %
Greater than 60	2	6	8	7.3 %
Total	**58**	**52**	**110**	

[Table/Fig-1]: Age and Gender Distribution

Site	No. of Males	No. of Females	Total	Diagnosis Based On				
				H	I	M	B	C
Lymph nodes	15	32	47	45	2	-	-	-
Pleural effusion	23	8	31	-	-	-	31	-
Abdomen	8	5	13	3	5	-	5	-
Bone & Joint	6	2	8	2	4	1	-	1
Genito Urinary	3	3	6	1	1	-	-	4
Breast	-	3	3	3	-	-	-	-
CNS	1	-	1	-	-	-	1	-
Skin	-	1	1	1	-	-	-	-
Total			110	55	12	1	37	5

[Table/Fig-2]: Site and Diagnostic Method.
(H-Histopathology, I-Imaging, M-Microbiological, B-Biochemical, C-Clinical)

Site	Mantoux Test Positivity	Total	% of Mantoux Test Positivity by site
Lymph nodes	29	47	61.7 %
Pleural effusion	13	31	41.9 %
Abdomen	5	13	38.4 %
Bone & Joint	3	8	37.5 %
Genito Urinary	4	6	66.6 %
Breast	2	3	66.6 %
CNS	-	1	0 %
Skin	1	1	100%
Total	57	110	51.8 %

[Table/Fig-3]: Rate of Mantoux Test Positivity in relation to site of involvement

Comorbid conditions like DM were seen in 22 patients (20%), chronic alcoholism observed in 32 patients (29%) and 37 patients (33.6%) were chronic smokers. HIV co-infection was detected in 3 patients (2.7%). Two of them had pleural effusion and the third had cervical adenopathy whose FNAC showed extensive necrosis with abundant AFB.

All the 110 patients irrespective of whether they had symptoms like cough/wheeze underwent X-ray Chest. Coexisting pulmonary involvement as assessed by chest X-ray was seen in 19 (17.3%) patients.

Follow-up of the 110 EPTB cases analysed showed that 107 completed the treatment while 2 patients had a relapse and 1 patient defaulted on the treatment.

DISCUSSION

EPTB can occur in isolation or along with a pulmonary focus or can involve multiple sites as in disseminated disease. In immune competent individuals, it constitutes about 15% to 20% of the total cases, but can rise upto 50% in HIV infected patients [9,10,11]. EPTB still continues to pose several challenges in many areas. Since the presentation of EPTB maybe atypical and its symptoms and signs are non-specific, the foremost challenge is in its diagnosis followed by the identification of specific host-related risk factors that favour its presence and location.

Several studies [4,8,12] have reported increasing prevalence rates of EPTB and assessed host risk factors and diagnostic tests for EPTB. Since Indian studies are limited in this regard, this retrospective observational study was undertaken to determine the sites of involvement, HIV co–infection and usefulness of various diagnostic modalities in EPTB affecting patients attending to a medical college DOTS clinic.

Age and Gender

The age distribution of the 110 patients in our study showed clustering of cases in the 12–24 and 24 to 36 age groups which is the most productive group. Extremes of age were comparatively less affected. Similar studies [2,8,12] done on EPTB showed that it was common at younger age groups (less than 25 years). Our study showed no major gender differences with both males and females being affected across the age groups. Though the incidence of pulmonary TB reported in several studies [8,12,13] showed a definite male preponderance and EPTB showed female predominance [2,8,13], no significant gender differences was noted in our study. But within the sites of involvement, lymph nodes showed a significant female preponderance and pleural effusion showed a significant male preponderance.

Anatomical Site of Involvement

Our study showed the most common site of involvement was lymph nodes followed by pleural effusion and abdominal TB. We have noted a significant number of abdominal TB diagnosed in this population which may need further analysis to study the probable risk factors in this group. Similar studies in India as well as other countries also show that lymph nodes are the most common site of involvement [1,2,8,12]. Some studies though showed a predominance of genito urinary and skin TB [3,8,12]. One study [8] showed a high number of abdominal TB as the second most common site (14.8%). Hence, the sites of anatomical involvement may vary with geographic, race and other characteristics though lymph node seems to be the most common across studies.

Mantoux as a Diagnostic Test for EPTB

Mantoux was assessed as an adjunctive diagnostic test for EPTB as in several situations, the diagnosis of EPTB posed difficulty in various areas. Sometimes, tissue samples for HPE are not possible and the clinical scenario may point to a host of other differential diagnosis. Despite many limitations and the non–specific nature of the Mantoux test, it is still used in the diagnostic workup of EPTB and paediatric TB as an adjunctive tool. Whether Mantoux is sufficiently sensitive and specific for the diagnosis of

active EPTB is debatable and data for and against its use are available [1,8,12]. Also, Mantoux test does not give unequivocal results in EPTB as reported in studies [8,12]. Anergy testing in Mantoux negative patients irrespective of their HIV status is not recommended routinely as per latest CDC guidelines [14]. In our study of the confirmed 110 EPTB cases, Mantoux was positive in 57 patients (51.8%). The sensitivity and specificity of Mantoux in various studies have been reported between 47%–86% [1,12,15]. Hence the Mantoux test cannot be used as confirmative evidence of EPTB.

HIV Co-infection in EPTB

As compared to immuno-competent individuals, the percentage of EPTB in HIV infected individuals is relatively high [9,10]. Documentation of EPTB in HIV is important because it constitutes an AIDS defining illness. EPTB occurs frequently and much earlier than other opportunistic infections in patients dually infected with HIV and TB. In our study, only 3 patients showed concomitant HIV infection. 2 cases were pleural effusion and the last was a case of lymphadenitis whose FNAC showed extensive necrosis with plenty of AFB's. In all 3 patients, Mantoux test showed no induration and there was no concomitant pulmonary involvement. HIV TB co-infection is not as highly associated in Asian patients as it is with Africans [10,16]. The HIV co-infection in EPTB has varied between 0.4%–20.1% and is steadily on the rise in India [6,11,17]. Sub–Saharan African rates for HIV co-infection vary from 24%–67% [16]. Mortality is also higher in EPTB co-infected with HIV. Studies have shown that in HIV patients the most common form of EPTB is still lymph node [10,18,19,20].

Pulmonary Involvement in EPTB

EPTB can occur in isolation or as a disseminated form with or without pulmonary involvement. Patients with EPTB diseases are not usually infectious unless they have concomitant pulmonary or non-pulmonary disease located in their oral cavity/larynx. All EPTB patients should be considered potential pulmonary TB suspects unless coexisting pulmonary involvement is excluded. Several studies have shown that patients with concomitant pulmonary and extra-pulmonary infections were more likely to die within 6 months of diagnosis [9,11]. In our study concurrent X–ray lesions were detected in 19 cases. Studies have reported the prevalence of pulmonary involvement from 20% to 50% in EPTB [21,22,23]. Some studies have also shown sputum positivity by culture even in the presence of a normal chest X–ray [22,23]. Hence all EPTB cases should be screened with a chest X–ray and if needed sputum for AFB culture.

CONCLUSIONS

Lymph node was the most common site involved showing a significant female preponderance followed by pleural effusion and abdominal TB. The rates of HIV co–infection and diabetes mellitus were 2.7% and 20% respectively. The most useful diagnostic modality was tissue sampling followed by imaging. Mantoux test is not unequivocal for the diagnosis of EPTB.

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