Original Article

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Spectrum of Pulmonary and Extra-Pulmonary Tuberculosis: A Retrospective Study from Northeast India

Internal Medicine Section

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ABSTRACT

Introduction: Tuberculosis (TB) remains a global health problem with India having the highest burden. The commonest site of TB is the lungs (85%), the remaining 15% being clubbed as extra-pulmonary TB (EPTB). The diagnosis of TB poses a number of challenges which becomes more pronounced in resource limited settings.

Aim: To ascertain the demographic characteristics, clinical spectrum and methods of diagnosis of TB in a tertiary care centre having limited culture based facilities.

Materials and Methods: Hospital-based retrospective study in TB patients registered for treatment in a DOTS centre attached to a tertiary care teaching hospital in Northeast India, from January 2013 to December 2014. Data was collected from the TB registers and patient record sheets of the DOTS centre. All TB patients registered under DOTS centre were included in the study while patients found to have alternative diagnosis leading to discontinuation of anti-tubercular therapy were excluded.

Results: There were 1344 participants with a male to female ratio of 1.15:1. Most of the patients (30.95%) were in the age group 21-30 years followed by 31-40 years (18.82%), with a mean and median age of 32.78±15.64 and 30 years respectively. Majority of patients had EPTB (57.22%). Majority of the patients with TB (83.22% of EPTB and 77.21% of PTB) were in the newly detected category. Among EPTB cases, pleural effusion was commonest (30.04%), followed by lymphadenitis (24.58%), abdominal TB (13.91%) and central nervous system TB (12.35%). Sputum for AFB was the commonest mode of diagnosis (29.91%) followed by body fluid analysis (25.30%), Fine Needle Aspiration (FNA) cytology (17.78%) radio-imaging techniques (15.57%) and DNA PCR (1.12%). Overall, acid fast bacilli could be demonstrated in 38.76% of the cases. Sputum was the commonest sample positive for AFB (77.16%), followed FNA specimens from lymph nodes (19.39%). Molecular methods (DNA PCR) were used for the diagnosis in only 1.12% of cases.

Conclusion: Our study showed a high burden of TB with a very high proportion with EPTB. AFB demonstration, supplemented by ancillary investigations formed the cornerstone of TB diagnosis. Considering the very high EPTB prevalence, there is need for advanced diagnostic facilities for better diagnostic yield.

Keywords: Clinical profile, Resource limited settings, TB patients

INTRODUCTION

Tuberculosis (TB) remains a global health problem with an estimated 8.6 million people developing TB in 2012 and a mortality of 1.3 million globally [1]. India contributes to the highest burden of TB in the world with 40% of the Indian population being infected with TB [1]. Pulmonary TB (85%) contributes to the majority of the TB cases while extra-pulmonary TB (EPTB) comprises the rest 15 % of the cases [2].

There are a number of challenges in the diagnosis of TB. Although chest X-ray is very useful it lacks specificity and can be normal even when the disease is present [3]. Conventional sputum smear microscopy with Ziehl-Neelsen (ZN) staining, which is the widely used tool in resource limited settings, is highly specific, but has a variable sensitivity (20%–80%) [4]. Fluorescence microscopy, though more sensitive than ZN staining, has limited availability [5]. Mycobacterial culture on solid media, though considered the gold standard for tuberculosis diagnosis, has limitations for the long time of 4-8 weeks taken, thus causing a delay in appropriate diagnosis [6]. Liquid culture has the advantages of a shorter time required and its ability to perform drug susceptibility testing; it requires a well-equipped laboratory, besides its increased tendency for contamination [4]. More advanced diagnostic methods, including nucleic acid amplification tests, line probe assay and Xpert MTB/RIF are highly sensitive and specific but are not readily available and expensive in areas of resource constraints [4]. In addition to the overall limitation of diagnostics in resource limited settings, cases of EPTB further suffers due to lack of a clear consensus on algorithms for diagnosis [7]. Moreover, because of its potentially non-contagious nature EPTB has never been a priority in the

national TB control program campaigns [8].

In this background this study was undertaken to ascertain the basic demographic characteristics, clinical spectrum and methods of diagnosis of pulmonary and EPTB in patients registered for TB treatment in a tertiary care centre having limited culture based facilities for the diagnosis of TB.

MATERIALS AND METHODS

This hospital-based retrospective study was conducted, during the time period of January 2013 to December 2014 in patients with TB registered for treatment in a DOTS centre attached to North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences, Shillong, a tertiary care teaching hospital in Northeast India. Data was collected from the TB registers and patient record sheets of the DOTS centre.

Inclusion Criteria: All patients registered under DOTS centre with the diagnosis of TB.

Exclusion Criteria: Patients having alternative diagnosis leading to discontinuation of Anti-Tubercular Therapy (ATT) during the course of treatment.

At the first step, all the records pertaining to Pulmonary Tuberculosis (PTB) and EPTB cases registered with DOTS centre from 1st January 2013 till 31st December 2014 were separated and analysed. The data was entered into a structured proforma. Study variables included demographic characteristics (age and sex) of the patients, clinical parameters comprising of type and site of TB, methods of diagnosis and classification into various treatment categories.

Ethics: Ethical clearance for the study was taken from the Institutional Ethical Committee.

STATISTICAL ANALYSIS

The results were tabulated and graphically represented using Microsoft Office for Windows 2008. Statistical Analyses which included descriptive statistics was done using Statistical Package for Social Survey (SPSS) for Windows version 17.0.

RESULTS

A total of 1344 cases were included in the study of which 718 (53.42%) were males with a male to female ratio of 1.15:1.The age group most commonly affected was 21-30 years (30.95%) followed by 31-40 years (18.82%) and 11-20 years (17.34%). The age of the patients ranged from 1 year to 85 years with a mean age of 32.78±15.64 years. The mean age for the males was 34.63± 15.93 years while that for females was 30.20±15.00 years. Median age for males, females and the entire study population was 30 years. The age and sex distributions of the study subjects are depicted in [Table/Fig-1].

0Majority of patients had EPTB (57.22%) compared to PTB (42.78%). The categorisation of both forms of tuberculosis into new cases, relapse, defaulters and others are illustrated in [Table/Fig-2].

Age (yrs)	Male (%)	Female (%)	Total (%)
0-10	62(4.61)	34(2.53)	96(7.14)
11-20	95(7.07)	138(10.27)	233(17.34)
21-30	198(14.73)	218(16.22)	416((30.95)
31-40	148(11.01)	105(7.81)	253(18.82)
41-50	97(7.22)	59(4.39)	156(11.61)
51-60	64(4.76)	51(3.79)	115(8.55)
61-70	35(2.60)	8(0.60)	43(3.20)
71-80	16(1.19)	11(0.82)	27(2.01)
>80	3(0.22)	2(0.15)	5(0.37)

[Table/Fig-1]: Age and sex distribution of patients with tuberculosis.

The spectrum of EPTB was wide [Table/Fig-3], with pleural effusion being the commonest (30.04%), followed by lymphadenitis (24.58%), abdominal TB (13.91%) and central nervous system TB (12.35%).

Sputum for AFB was the commonest mode of diagnosis in 29.91% of the total patients. Fluid analysis for biochemical and physical analysis established the diagnosis in 25.30%

Category of cases	Type of tuberculosis	
	Pulmonary n (%)	Extra-pulmonary n (%)
New	444(33.04)	640(47.62)
Relapse	65(4.84)	1(0.07%)
Defaulter	19(1.41)	-
Treatment failure	12(0.89)	-
Others	35(2.60)	128(9.52)
Total	575(42.78)	769(57.22)

[Table/Fig-2]: Various treatment categories of TB patients.

Site of EPTB	N (%)
Pleural effusion	231(30.04)
Lymphadenitis	189(24.58)
Abdominal	107(13.91)
Central nervous system tuberculosis (Meningitis/Tuberculoma)	95(12.35)
Disseminated	47(6.11)
Genitourinary	34(4.42)
Skeletal	29(3.77)
Milliary	12(1.56)
Pericardial Effusion	11(1.43)
Skin	10(1.30)
Laryngeal	4(0.52)
Total	769(100)

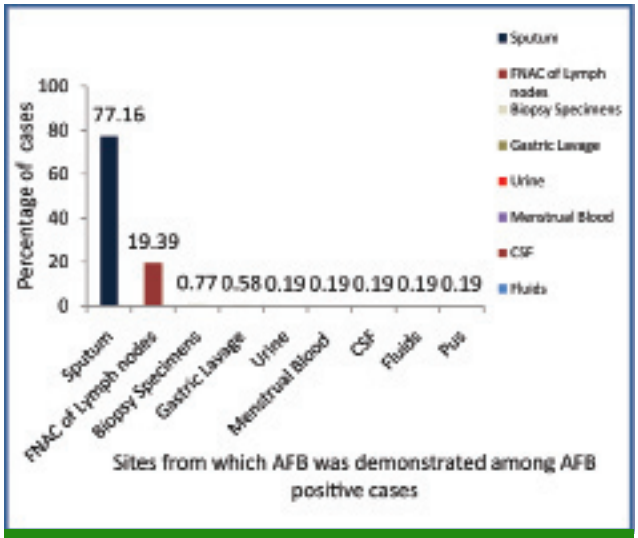
[Table/Fig-3]: Types of Extra-Pulmonary Tuberculosis (EPTB).

of the cases. Fine needle aspiration cytology was used to diagnose 17.78% of the cases with radio-imaging techniques (chest X-ray, Computed tomography, Magnetic resonance imaging, and ultrasonography) established the diagnosis in 15.77% of the cases. Cerebrospinal fluid analysis aided in the diagnosis of 6.77% of the cases. Molecular methods including DNA PCR for *Mycobacterium tuberculosis* was used for diagnosis in only 1.12% of the cases [Table/Fig-4].

Methods of diagnosis	n (%)
Sputum for acid fast bacilli	402(29.91)
Fluid analysis	340(25.30)
Fine needle aspiration cytology	239(17.78)
Radiological analysis	212(15.77)
Cerebrospinal fluid analysis	91(6.77)
Biopsy	36(2.68)
Gastric lavage	3(0.22)
Urine	1(0.07)
Menstrual blood	1(0.07)
Pus	1(0.07)
Clinical	3(0.22)
Molecular analysis (DNA PCR for *M.tuberculosis*)	15(1.12)

[Table/Fig-4]: Methods used to diagnose tuberculosis.

Demonstration of Acid Fast Bacilli (AFB) by ZN staining in various specimens including sputum, body fluids, fine needle aspirates and biopsies was positive in 521(38.76%) of 1344 cases. Sputum was the commonest sample which was positive for AFB being positive in 402 (77.16%) of the cases. Fine needle aspiration specimens from lymph nodes were positive for AFB in 101 cases (19.39%) of the cases. The site specific positivity for AFB is shown in [Table/Fig-5].



[Table/Fig-5]: Sites from which AFB was demonstrated in AFB positive cases.

DISCUSSION

Our study showed TB to be more common in males (M: F=1.15:1). Previous literature also shows similar distribution patterns between the two sexes with a comparatively higher prevalence in males [9]. The age distribution in our study showed that both forms of TB (PTB and EPTB) are more common in the younger patients, with maximum number of the cases belonging to the age group 21-30 years, with a mean age of 32.78±15.58 years. Our findings are similar to those reported earlier in other studies which have concluded that the commonest age group affecting tuberculosis is in the reproductive period of 20-39 years [10,11].

In our study we found that EPTB was commoner than PTB (57.22% vs. 42.78%). This is in contrast to other studies, which have shown a higher prevalence of PTB in comparison to EPTB, the latter comprising of 10-20% of all TB cases [12,13]. A possible reason for this may be the fact that ours being a tertiary care referral institute it was more probable that EPTB cases which are more difficult to diagnose in peripheral hospitals had higher referral rates thus leading to a referral bias. A previous study from Turkey reported a high prevalence of EPTB at 45.1% which was in line with the high prevalence in our study [2]. Over the years there has been documentation of an increasing trend of EPTB in studies reported from various parts of India [14,15]. In both the forms of the TB in our study, the newly detected cases that were initiated on Category 1 anti-tubercular therapy formed a majority. This was in concordance with a previous study which reported 64.77% of the total cases being newly detected cases [14].

The distribution of patients with EPTB was wide with pleural effusion being the commonest (30.04%), followed by tubercular lymphadenitis, abdominal tuberculosis and central nervous system tuberculosis. Previous studies from India have also reported similar findings with tubercular lymphadenitis and pleural effusion being the two most common forms of EPTB [14,16]. A study from the United States had reported lymph node involvement as the commonest site in the body [13]. In this study, we found that 6.11% of EPTB patients had multi-organ involvements which were designated as disseminated tuberculosis. During the primary infection of TB, bacteria can spread to all organs in the body therefore leading to multiple organ involvement in cases of EPTB.

Demonstration of acid fast bacilli by Ziehl-Neelsen staining in various specimens was positive in 38.76% of the overall cases. In cases of PTB sputum was positive for acid fast bacilli

being positive in 77.16% of the cases, whereas in Fine needle aspiration specimens the positivity was only 19.39% of the cases. The detection of AFB in fine needle aspiration smears depends upon multiple factors like presence of granulomas, necrosis along with the pH and PO2 of the lesions [17]. There is an inverse relationship between the presence of granuloma and AFB due to which there may be a quantitative threshold value for granulomas below which AFB are found in the smears [18]. Previous studies have shown the sensitivity of Ziehl-Neelsen staining for sputum samples in the range of 55.55% while it was only 9.9 % for cases of EPTB [18].

In our study conventional methods like sputum examination for acid fast bacilli by Ziehl-Neelsen staining aided by body fluid analysis and radio-imaging formed the cornerstones of diagnosis of tuberculosis. Molecular methods, including DNA-PCR for *Mycobacterium tuberculosis*, and other high end diagnostic tests were used for diagnosis in a very small fraction of the cases. In spite of newer diagnostic facilities, the microbiological diagnosis of TB in resource limited settings still depends primarily on the direct visualisation of the bacilli. In a resource limited setting like ours with lack of facilities for molecular diagnosis and culture of *Mycobacterium tuberculosis*, appropriate clinical diagnosis, supplemented by sputum microscopy, FNA, tissue biopsy together with ancillary radiological and biochemical investigations forms the backbone in the diagnosis of various forms of pulmonary and EPTB.

LIMITATION

Being a hospital based retrospective study our study does not reflect the actual burden and spectrum of tuberculosis prevalent in the community which is a limitation of the study.

CONCLUSION

Our study showed a high burden of TB with a very high proportion having EPTB. In the absence of facilities for molecular diagnosis and mycobacterial culture, AFB demonstration, supplemented by ancillary investigations formed the cornerstone of TB diagnosis. Considering the very high EPTB prevalence, there is need for advanced diagnostic facilities for better diagnostic yield.

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