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Clinico-Epidemiological Profile of Extra-pulmonary Tuberculosis in a Tertiary Health Care-Center, Ahmedabad, Western India

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Abstract: ***Introduction: Tuberculosis (TB) remains a major global health issue. India being highest TB burden country needs concern. It was found that the percentage of patients with EPTB (Extra pulmonary Tuberculosis) was more in tertiary care centres of India, ranging from 12% to 28.5%. The primary objective of this study was to describe the basic demographic, clinical characteristics and risk factors of Extra pulmonary Tuberculosis in patients, registered at DOTS (Directly Observed Therapy, Short course) centre of tertiary care teaching hospital. Materials and Methods: This is a retrospective, record-based study of patients of EPTB, at Sheth V.S. and C.M. Hospital, Smt. N.H.L Municipal Medical College, Ahmedabad, Gujarat, India, from January 2018 to December 2018. Results: Among 710 cases registered for treatment of all forms of tuberculosis, 540(76.1%) had PTB (Pulmonary Tuberculosis) and 170 (23.9%) had EPTB. The ratio of percentage EPTB: PTB is 1:3.17. Commonest type of EPTB was found in cases of lymph nodes and lymphatic (35.8%), followed by TB in pleural cavity (22.9%). Among different age groups studied, the age group of 20-39 years had the highest proportion of EPTB both in males and females which is the economically productive population of society. Conclusion: The frequency of EPTB in this study was higher (23.9%) with the highest proportion in lymph node (35.8%). The burden of EPTB is more among the productive age group, moreover, being male, young adults and having associated diabetes mellitus were significant risk factors for patient being EPTB positive.***

Keywords: Extra pulmonary Tuberculosis, Lymph node TB, Revised National Tuberculosis Control Programme

1. Introduction

Tuberculosis (TB) remains a major global public health problem with one-third of the world's population being infected with the *Mycobacterium tuberculosis*[1]. Along with HIV and Diabetes Mellitus, it is causing pandemic worldwide. Recently identified TDR (Total drug resistant) tuberculosis is biggest threat for human being. According to WHO, 6.1 million TB cases were reported in 2013, out of which 5.7 million were people newly diagnosed and another 0.4 million were already on treatment. [2].The burden of tuberculosis (TB) in India is the highest accounting for one fifth (21%) of the global incidence.[3].

Tuberculosis infection of any part of body other than lung parenchyma is defined as Extra pulmonary Tuberculosis [EPTB].Diagnosis of EPTB is done as per RNTCP (Revised National Tuberculosis Control Programme, India) guidelines which is based on one culture-positive specimen from the extra-pulmonary site; or histological evidence; or strong clinical evidence consistent with active EPTB disease followed by a medical officer's decision to treat with a full course of anti-TB therapy under DOTS[5].The timely detection and accurate diagnosis of any form of EPTB is necessary for the proper treatment of EPTB[6].Atypical presentation, lack of diagnostic resources for procurement of tissue or fluid for diagnosis from inaccessible sites and a poor yield of conventional diagnostic methods lead to considerable delay in making the diagnosis or diagnosis is even missed. Furthermore guidelines regarding diagnosis of EPTB are not covered by RNTCP but all patients are given treatment as per DOTS regimen. Although there is a rising trend in EPTB in recent decade, still EPTB has never been a priority in the campaigns undertaken by Revised National TB Control Programme (RNTCP) for its control [5,7,8]. The percentage of EPTB cases among all TB cases in developed countries ranges from 12% to 28.5%. In developing countries such as India, the percentage of EPTB cases, is between 15% - 20%, which has increased to more than 50% among the HIV co-infected patients[4,7] suggesting immunity status of host being a major risk factor of EPTB[8].

It was found that the percentage of patients with EPTB was more in tertiary care centers of India, ranging from 30% to 53% [5].This implies that, tertiary care centers such as medical colleges, caters a large and varied type of

population and provides an excellent place for economical and advanced diagnostic facilities for early diagnosis and treatment of EPTB cases, backed up by research facilities. This is much needed, as HIV-TB co-infection, multi-drug-resistant TB, diabetes etc. have made EPTB a major public health threats even in the era of optimally effectiveDOTS [5].

2. Material and Methods

Aim- The aim of study is characterizing EPTB patients with different anatomical site involvement and study of their clinico-epidemiological profile and their associated risk factors.

Study design-This is a retrospective, record-based study of diagnosed patients of EPTB of all age groups.

Study area-The study was conducted in Sheth V.S. and Sheth C.M. Hospital, Smt. N.H.L Municipal Medical College, Ahmedabad a tertiary care centre in Western India. So patients from nearby villages and adjoining districts were referred for diagnosis and treatment.

Study period- Data for this study has been obtained from 1st January 2018 to 31stDecember 2018.

Study population- The population includes all patients attending various OPD of Hospital who were suspected for extra pulmonary tuberculosis infection during the study period. This study includes total of 710 patients diagnosed for TB clinically, pathologically and radiologically as tuberculosis in our institute, out of which 170 were diagnosed as extra-pulmonary tuberculosis.

Source of information - For this study data has been obtained from Patient Record Sheets of Hospital, Lab register, treatment Cards or Referral Registers of RNTCP and utilized for analysis.

Inclusion criteria

1) All patients suspected of tuberculosis attending OPD of various departments of our institute.
2) EPTB - a patient with active tuberculosis of any part of body other than lung parenchyma.

Exclusion criteria

1) Patients with PTB
2) Patients of EPTB with PTB.

The study was conducted after obtaining institutional ethical clearance from institutional ethical committee. The study includes all patients coming to various OPD during the study period with suspected TB. The diagnosis of Pulmonary and Extra pulmonary Tuberculosis cases were established, following the RNTCP programme guidelines, which required one culture positive specimen from an extra-pulmonary site or histological evidence or strong clinical evidence consistent with active EPTB followed by concerned Medical Officer's decision to treat with a full course of anti-TB therapy. Whenever needed, investigative procedures such as X-Ray, FNAC, Pleural fluid aspiration, ultrasonography, computed tomography, MRI were performed for diagnosis and specimen collection. The specimen was then subjected to a culture or histopathology for evidence of TB. After diagnosis of EPTB, patients were registered at DOTS Centre, whereas patients belonging to other villages or districts were referred to DOTS centres of their respective area.

At the first step, all the records pertaining to EPTB cases diagnosed during the study period were collected and analyzed. Total 170 cases diagnosed as EPTB were included in the study. Clinical and epidemiologic characteristics of the patients were abstracted from laboratory records, medical files and were categorized as: age in years, gender, urban or rural, comorbidities.
In addition, patients with EPTB were grouped into 7 categories, based on site of involvement-

1) Pleural cavity,
2) Peripheral Lymphatic and Lymph Nodes,
3) Genitourinary,
4) Bone and Joint,
5) Abdomen,
6) Skin and muscles,
7) Others -miliary, ocular, breast, CNS etc.

3. Results

Table 1 depicts that out of 710 cases of tuberculosis, 510 (76.1%) were diagnosed as PTB group, 170 (23.9%) were diagnosed as EPTB -which were included in the study. The ratio of percentage EPTB: PTB was 1:3.17.

Table 2 shows that women and men each accounted for approximated half of the cases. Out of 170 EPTB patients, 52.3% were males. Male to female ratio was 1.09:1. Among the 5 age groups studied, the age group of 20-39 years had the highest proportion of EPTB (42.2%) both in males and females which is the economically productive population of society. Next most affected was 40-60 years age group (31.5%). Pediatric age group had 6.2% contribution. The lowest proportion (3.5%) was observed in the geriatric age group (.>60 years old). In this study out of 170 cases of EPTB, 109 of them reside in urban areas (64.3%) whereas 61 cases (35.7 %) came from rural areas.

Table 3 shows that maximum number of cases belongs to lymph nodes and lymphatic (35.8%), pleural cavity is second most common site with 22.9%. Rest of the cases were found in decreasing order in abdomen 12.3%, bones and joints 10.0%, skin and muscles 5.9% .Ocular and miliary tuberculosis were having minimal incidence. In this study, pleural, bone and joints, skin and muscles, meningeal, military and ocular TB appeared to be more commonly observed among the male patients while lymph nodes, genitourinary and breast TB cases were predominant among females. Abdominal tuberculosis was found in equal proportions in both males and female population.

Table 4 shows that involvement of pleural cavity (9.4%) and lymph nodes (14.1%) were the commonest manifestation among the 20-39 years age group. In the youngest age group (< 9 years), lymph node TB was the most frequently observed.

Table 5 shows that 32 cases (18.8%) out of 170 had diabetes mellitus. All the patients were of age 40 years and above. 9 cases (5.3%) had chronic obstructive lung disease. 28(14.7%) cases had associated HIV infection. 6 patients had coexistent carcinoma.

4. Discussion

The prevalence of Extra Pulmonary Tuberculosis (EPTB) is increasing over the last several years globally. Risk of EPTB is determined by the degree of exposure to the pathogen and host immune factors like HIV, diabetes, malignancy, malnutrition, chronic renal disease, liver disease, post organ transplant etc [4,7]. Identification of the risk factors that predispose to EPTB would allow for targeted strategies to prevent active tuberculosis infection and hence decrease the prevalence of EPTB.

As per RNTCP, the prevalence of EPTB in was 15%-20% [4], but in our study it was 23.9%,which is more than the RNTCP statistics. This increase in prevalence is due to availability of advanced diagnostic facilities at low cost in medical college settings and tertiary care referral centre [5]. In this study, the ratio of percentage of EPTB: PTB is 1:3.17 which is similar to other studies and national statistics. [9,10].

In this study 64.3% patients were belong to urban areas and only 35.7% belong to rural areas, whereas in other countries like Ethiopia, majority were rural dwellers (67.4%)[11]. This may emphasize the fact that awareness, diagnosis and reporting of EPTB is still lacking in rural areas.

Globally, women were found to be more at risk of developing EPTB [12,13,14]. In contrast, in this study, the male: female ratio was found 1.09:1. Prevalence of EPTB was found to be higher in male than female (52.3% Vs 47.7%). Male preponderance has also been found in various other studies from India and other countries like Ethiopia, Nigeria, Turkey etc. [5,11,14,15]. The failure to detect an increased association between female sex and EPTB in our study could be due social stigma associated with TB which hinders female population especially those belonging to rural areas, to seek medical assistance from DOTS centre in developing countries [16,17]. Small sample size may be another possibility.

Although EPTB cases were found in all age groups but majority of cases (42.4%) belonged to the age group of 20-39 years, which constitutes of young adult and working individuals. This is the reproductive and working group in both males and females and is economically productive population. This highlights the socioeconomic burden of EPTB on Indian economy also. Similar reports of high prevalence of EPTB among economically and sexually productive age groups, especially in endemic countries, was reported globally by various studies from India, Ethiopia, Pakistan, San Francisco, Saudi Arabia, USA, Nepal etc. [5,11,13,18,19,20,21]. Our study shows that young adult is itself an independent risk factor for EPTB. The possible explanation of this may be because of reactivation and spread of TB from primary infection from the lungs to extra-pulmonary sites, delayed diagnosis of primary tuberculosis because of lack of time and decreased immunity to due life style changes and improper nutrition.

Globally, lymph node TB continues to be the most common form of EPTB, of which cervical group of lymph nodes is most commonly affected[5,11,20,22].In our study also we found similar pattern, lymph node tuberculosis being the most common site in which majority of cases were of cervical lymph nodes. Similar pattern of distribution was found in studies from Ethiopia, Canada, Turkey, Nepal and other Indian studies [11, 21, 23, 24, 25]. Second most common site of involvement of EPTB was pleural cavity (23.03%). Rest of the EPTB cases distributed in decreasing order of sites were abdomen, bones and joints, skin and muscles and genitourinary tuberculosis, which is similar to studies from India and world [23,24,25,26]. The national pattern of distribution of EPTB sites, as per RNTCP statistics reports a similar pattern as this studies lymph node 47%, pleural cavity 30%, abdomen 10%, bones and joints 8% TB, CNS 2% and 3% others)[27].

The difference in the occurrence of EPTB by site in different age groups and sexes shows the difference in predilection to involve one site over the other depending on the host factors such as immunity status. In our study most common sites involved in EPTB cases in the age groups 20-39 years was lymph node and pleural cavity (58.7%) as seen in other studies also [5,6]. Tubercular lymphadenitis is more frequent in female whereas tubercular pleural effusion is more common in male. Such demographic and social factors contributing to the development of EPTB were identified by previous reports as well [5,7,15,21,22,25,26].

A number of environmental and social modifiable risk factors make people more susceptible to tuberculosis infections by decreasing their immunity, the modification of which at the population level could have significant impact on the incidence of TB. The most important risk factor globally is HIV infection where extra-pulmonary involvement can be seen in more than 50% of patients with concurrent HIV and TB infection [4,7].

The cumulative effect of other risk factors such as smoking, malnutrition and alcohol consumption increases the prevalence of both tuberculosis and diabetes [30,31]. Diabetes increases the risk of developing TB approximately three times, as it produces an immune-compromised state and pleural effusion is the most common site of EPTB involvement [4]. The prevalence of EPTB with diabetes is 18.8% in our study, which is similar to the prevalence in different studies (5.4%-12.8%) [31,32]. So, routine screening of TB patients for DM can be helpful for early diagnosis and hence improve EPTB treatment outcomes.

Elderly, alcoholics, malnourished, HIV-infected, tobacco smoking and those with underlying COPD appears to be significant risk factors especially for relapse in already treated PTB cases [33]. COPD was found in 9 patients (5.3%) EPTB occurs 9 to 22 times more frequently in cancer patients than in the general population due to their immune-compromised state which is the result of the underlying malignancy and its treatment [34].

Our study had several limitations. The main limitation of the study is that the being a retrospective, hospital-based study, the findings cannot be generalized to the community, but it gives valuable information regarding trend of EPTB cases in Ahmedabad, Gujarat and Western region of India with the associated risk factors. Although associated HIV infection is known risk factors for increasing EPTB infection, HIV status was not known in substantial number of EPTB cases..

5. Conclusion

In conclusion, our study expands the knowledge regarding the epidemiology of EPTB and enhances understanding of the relative contribution of host related factors to its pathogenesis. The frequency of EPTB in this study was higher with the highest proportion in lymph node. Young adults between age 20-39 yrs, and associated diabetes mellitus were significant risk factors for patient being EPTB positive. Based on the above conclusions the following recommendations are suggested:

1) Newer diagnostic tests like molecular characterization, PCR etc. which are sensitive and specific and easy to use for early detection and confirmation of diagnosis of EPTB, should be made available through government programmes in rural resource-poor settings.
2) Large scale, community based studies and well-defined programme-specified protocols for education and prevention of EPTB are needed for decreasing its burden as it is a curable disease.
3) Young adult males of 20-39 yrs. is the target population even in rural areas, who should be examined and investigated thoroughly to rule out EPTB, so that burden of EPTB cases on society decreases and hence improve the nation's economy.

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7. Declaration

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Tables

Table 1: Pattern of Distribution of tubercular patients in study population

Type of TB	Number of cases	
PTB	540	76.1%
EPTB	170	23.9%
Total	710	100%

Table 2: Demographic characteristics of EPTB cases

Age Group (In Years)	Sex distribution				Total (%)	
	Male (%)		Female (%)			
0-9 Years	06	3.2%	05	3.0%	11	6.2%
10-19 Years	17	10.2%	11	6.4%	28	16.6%
20-39 Years	35	20.5%	37	21.7%	72	42.2%
40-60 Years	29	17.3%	24	14.2%	53	31.5%
>60 Years	2	1.1%	04	2.4%	6	3.5%
Total	89	52.3%	81	47.7%	170	100%

Table 3: Frequency distribution of different Sites of EPTB

S. No.	Site of EPTB	Total No. of Cases (%)
1	Lymph Nodes and Peripheral lymphatics	61(35.8%)
2	Pleural Cavity	39(22.9%)
3	Genitourinary	8(4.7%)
4	Bones and Joints	17(10.0%)
5	Abdomen	21(12.3%)
6	Skin and Muscles	10(5.9%)
7	Others*	14(8.4%)

*Others: CNS, Miliary, Ocular, Breast, etc.

Table 4: Clinico-epidemiological trends- Age, Sex and Site specific distribution of EPTB

S No	Site of EPTB	Age Group (In years)																	
		0-9 yrs.			10-19yrs			20-39yrs			40-60 yrs.			>60 yrs.			TOTAL		
		M	F	T	M	F	T	M	F	T	M	F	T	M	F	T	M	F	T
01	Pleural	0	0	0	3	4	7	10	6	16	8	3	11	4	1	5	25	14	39
02	Lymphatics	3	12	15	3	5	8	5	19	24	4	3	7	2	5	7	17	44	61
03	Genito-urinary	0	0	0	0	0	0	4	2	6	0	2	2	0	0	0	04	04	08
04	Bones & Joints	1	0	1	2	0	2	5	3	8	4	2	6	0	0	0	12	05	17
05	Abdomen	0	2	2	1	1	2	6	5	11	3	2	5	1	0	1	11	10	21
06	Skin & Muscles	0	0	0	3	3	6	4	1	5	1	0	1	0	0	0	08	02	10
07	Others	0	0	0	1	0	1	5	1	6	4	1	5	2	0	2	12	02	14
	Total	4	14	18	13	13	26	39	37	76	24	13	37	9	6	15	89	81	170

Table 5: Associated Risk Factors in EPTB Cases

Risk Factor	Cases (%)
Diabetes	32 (18.8%)
Carcinoma	6 (3.5%)
COPD	9 (5.3%)
HIV	28(14.7%)