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MAPPING THE DEMOGRAPHIC PATTERN AND EVALUATION OF CLINICAL CHARACTERISTICS OF EXTRAPULMONARY TUBERCULOSIS IN JHARKHAND

Medicine

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ABSTRACT

Background: Extrapulmonary Tuberculosis (EPTB) is a major health problem due to significantly high rate of mortality and morbidity. Regional variations have been observed in the Clinico-epidemiological trends. The aim of the present study was mapping the Demographic Pattern and evaluation of clinical characteristics of Extrapulmonary Tuberculosis in Jharkhand.

Methods: The study was conducted in Department of TB & Chest, Rajendra Institute of Medical Sciences (RIMS), Ranchi. Details of samples received at DOTs centre, RIMS were recorded i.e. demographic details, provisional diagnosis (extrapulmonary site) and co-morbidity. Total of 478 extra-pulmonary samples were collected and several tests performed as per institutional protocol including CBNAAT/Gene X-pert test. Data distribution was analysed using appropriate tools.

Results: Rural population (346/478) and males(264/478) showed higher number of cases. Older age group had highest number of cases(139/478) Tuberculous meningitis (TBM) was most common variant(213/478). Comorbidities(HIV/diabetes) were present in 30 cases. 3 CBNAAT positive cases showed Rifampicin resistance.

Conclusion: Understanding regional variations and clinic-epidemiological characteristics can help in better management of EPTB cases. Reasons for a higher number of TBM cases in Jharkhand, is a matter of further research. Developing better immunity and minimizing co-morbidities can help fighting EPTB. CBNAAT/Gene Xpert can help in early diagnosis EPTB and early detection of rifampicin-resistance in EPTB cases.

KEYWORDS

Extrapulmonary Tuberculosis; Rural-urban; Epidemiology

INTRODUCTION-

Tuberculosis(TB) in India is one of the most common chronic communicable disease leading to marked economic burden, DALYs (disability adjusted life years) loss, morbidity and mortality. It is caused by the bacillus Mycobacterium tuberculosis, which is spread when people who are sick with TB expel bacteria into the air; for example, by coughing. It typically affects the lungs (pulmonary TB) but can also affect other sites (extra-pulmonary TB). About a quarter of the world's population is infected with M. tuberculosis and the lifetime risk of developing TB is about 5–10%.[1]

According to World Health Organization (WHO) executive summery 2019, Tuberculosis (TB), Is the leading cause of death from a single infectious agent (ranking above HIV/AIDS). Globally, an estimated 10.0 million (range, 9.0–11.1 million) people fell ill with TB in 2018; There were an estimated 1.45 million TB deaths in 2018. TB affects both sexes in all age groups but the highest burden is in men (aged ≥15 years), who accounted for 57% of all TB cases followed by women (32%) and children (11%) in 2018.[2-3]

Extrapulmonary Tuberculosis (EPTB), although not a public health problem, as it is not contagious, yet it is a major health problem due to significantly high rate of mortality and morbidity in both developed and developing countries.[4] it's frequency varies from place to place, lowest (15.1%) among the Europeans and highest (58.9%) among the Somalians. In Asians the frequency was 44%.[6] In India, EPTB accounts for approximately 15-20% of all types of tuberculosis.[7,8] in few studies it was found that the percentage of patients with EPTB was more in tertiary care centres of India, ranging from 30% to 53%, which indicated better diagnostic facility and peoples' trust over these centres.[9,10]

The two most common comorbidities encountered in India with tuberculosis is Diabetes Mellitus and HIV, As both the disease involves poor immune (lymphocytic) activity the effect of treatment (ATT)is relatively poor if comorbidity is not properly controlled.

India is a large country with people having widely variable socio-economic and cultural backgrounds. There is paucity of data available for the demographic pattern of extra pulmonary tuberculosis in the state of Jharkhand, which covers a heterogeneous geographical and socio-cultural population. Habitat is not just geographical or political boundary lines; especially in Jharkhand, rural habitat is characterised by indigenous people, and further characterised by their traditional use of alcohol and distance from tobacco smoking, despite common tobacco chewing. In contrast urban life style is associated with sedentary life style, presence of metabolic syndrome and city air pollution. These variables identified as associated/risk factors for tuberculous infections[11-12], however these variables may be different for pulmonary and extra-pulmonary variants. There are few studies which suggest that pulmonary tuberculosis is more associated with urban population. Hence we choose to do retrospective chart review of extra pulmonary tuberculosis across rural and urban populations to understand the socio demographic and clinical pattern. Rajendra Institute of Medical Sciences (RIMS), Ranchi which is a premier tertiary centre of Jharkhand receives patients from all corners of Jharkhand on uniform basis. The aim of the present study was mapping the demographic pattern and evaluation of clinical characteristics of extrapulmonary tuberculosis in Jharkhand.

MATERIALS AND METHODS:

The present observational descriptive study was conducted in Department of TB & Chest, Rajendra Institute of Medical Sciences (RIMS), Ranchi between March 2018 & March 2020. All patients who attended RIMS OPD or were admitted here with provisional diagnosis of tuberculosis on the basis of clinical and/or radiological findings with extrapulmonary involvement, were included in this study. Patients who were diagnosed pulmonary tuberculosis with or without

extrapulmonary involvement were excluded from study. Patients of all age group were included in study. All patients sample were received at DOTs centre, RIMS and their details were recorded i.e. name, age, sex, address, provisional diagnosis (extrapulmonary site) , type of sample and enquiry were made about addiction and co-morbidity, especially Diabetes Mellitus and HIV. Those, whose status was unknown, investigated for Diabetes Mellitus and HIV. A total of 1833 patients' specimen was collected out of which 1355 were pulmonary samples and 478 were extra pulmonary sample. All samples were processed as per institutional protocol and cytological and biochemical analysis of the samples were done for diagnosis in the Department Of Biochemistry, Pathology and Microbiology of RIMS, and CBNAAT/Gene X-pert test was done in machine provided by RNTCP programme.

For observational purpose, The patients were divided into Demographic profile like geographical area (Rural & Urban),age group (00-14yrs, 15-29yrs, 30-44yrs, 45-59yrs and above 59yrs), Gender(male and female), , Extrapulmonary Disease with sample type(Pleural effusion-Pleural Fluid, Meningitis-CSF, Lymphadenopathy-aspirate, Koch's abdomen-Ascitic fluid, Psoas abscess- Pus, Endometritis- D&C sample, Arthritis- Synovial fluid etc, Co-morbidity (Diabetic /Non-Diabetic and HIV positive/negative).

Patients whose results were positive on either or both tests (cytological, Biochemical examination and CBNAAT/Gene X-pert test) were declared lab diagnosed and samples negative in both tests were declared negative. However Clinical diagnosis of Tuberculosis was maintained on the basis of clinical and radiological findings as ATT was started as per advice of treating Doctor. Advantage of CBNAAT over routine cytological, Biochemical examination and early detection of Rifampicin resistance were also recorded. For data analysis, MS Excel(2016) and SPSS software version 16 were used. Chi-square test was used to know if differences observed in different groups were statistically significant. Data was described in proportion or percentages. P value of < 0.05 was considered significant.

RESULT:

As per our protocol a total of 1833 patients' specimen were collected out of which 1355 were pulmonary samples (with or without extrapulmonary manifestations) and 478 (35.3%) were extra pulmonary sample. Out of 478 extrapulmonary (EPTB) patients 264(55.2%) were Male and 214(44.8%) were Female. On demographic evaluation larger population 345 (72.2%) were from Rural area and 133 (27.8%) from Urban area. The gender distribution in rural vs urban group were nearly equal (Figure- 1). Out of 345 rural patients, 191(55.4%) were male and 154 (44.6%) were female. In urban patients out of 133 patients 73(54.9%) were male and 60(45.1%) female.

Table-1 shows the age and sex distribution among total of 478 Extrapulmonary Tuberculosis patients. It was observed that the majority of subjects including both sexes were in the elderly age group≥ 60yrs (87 males & 52 females), closely followed by age group 15-29 yrs. which included (64 males & 49 females) and age group 0-14yrs(64 males & 46 females). Lesser number of patients were in the age group of 30-44yrs(24 males & 28 females) and 45 -59yrs (24 males & 28 females). The table shows maximum number of patients involved were from rural area. among all age group and demographic profile male were equal or more than female except rural patients of age group 30-59 yrs. (male 31 and female 40) and urban age group 15-29 yrs. (male 14 and female 20).

Out of 478 patients the most common disease in our study was tuberculous meningitis(TBM) 180 (52.2%) in rural as compared to 33 (24.8%) in urban population, followed by tuberculous pleural effusion 55 (15.9%) in rural and urban 29 (21.8%), then cold abscess from various sites 28 (8.1%) rural and 23 (17.3%) urban. incidence of Tuberculous lymphadenopathy was a fourth 24 (7%) in rural and 12 (9%) in urban population. Patients of Abdominal tuberculosis with Ascites were more common in rural population 20 (5.8%) as compared to 2 (1.5%) in urban population. While Cold abscess was more common in urban23(17%) as compared to rural 28(8,1%) population. Endometrial Tuberculosis and Tuberculous arthritis were more common in urban population(Table-2)

Among comorbidity Diabetes Mellitus and HIV about 30 (6.3%) were detected in the study group. The percentage of Diabetics was more in urban population 9% as compared to 4.1% in rural population. The incidence of HIV infection was found only in rural population 4 (1.2%).

Table-4 shows advantage of performing the CBNAAT/Gene Xpert test. 52(14.1%) out of 367 sample tested 111 were bacteriologically confirmed and 3 cases of Rifampicin Resistance were diagnosed at initial evaluation. The yield of test was better in those samples who tested suggestive of tuberculous infection i.e.22/111(19.8%) as compared to inconclusive samples30/367 (8.2%).

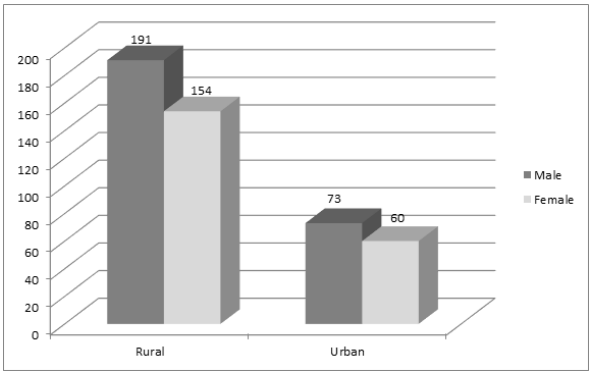

Figure-1 , Gender distribution in Rural vs Urban group

Table-1, Age and Gender distribution of Rural and Urban population

Age group(yrs)	Rural Number (%)			Urban Number (%)			Total Number (%)		Gross total
	Male	Female	Total	Male	Female	Total	Male	Female	
00-14 yrs	50 (26.2%)	37(23.4%)	87(24.9%)	14(19.2%)	9(15.3%)	23(17.4%)	64(24.2%)	46(21.5%)	110(23.0%)
15-29 yrs	50(26.2%)	29(18.8%)	79(22.9%)	14(19.2%)	20(33.9%)	34(25.8%)	64(24.2%)	49(22,9%)	113(23.6%)
30-45 yrs	14(7.3%)	29(18.8%)	43(12.5%)	11(15.1%)	10(16.9%)	21(15.9%)	25(9.5%)	39(18.2%)	64(13.4%)
45-59 yrs	17(8.9%)	21(13.6%)	38(11.0%)	7(9.6%)	7(11.9%)	14(10.6%)	24(9.1%)	28(13.1%)	52(10.9%)
≥ 60 yrs	60(31.4%)	39(25.3%)	99(28.7%)	27(37.0%)	13(22.0%)	40(30.3%)	87(33.0%)	52(23.9%)	139(29.1%)
Total	191	155	346	73	59	132	264	214	478

Table-2, Various anatomical sites of distribution of Extrapulmonary Tuberculosis

Extrapulmonary Diseases	Study group Number (%)		Pearson Chi square test	Degree of freedom	P value
	Rural 345 (72.2%)	Urban 133 (27.8%)			
Pleural Effusion	55 (15.9%)	29 (21.8%)	47.410	7	0.000
Tuberculous meningitis	180 (52.2%)	33 (24.8%)			
Tuberculous lymphadenopathy	24 (7%)	12 (9%)			
Abdominal tuberculosis	20 (5.8%)	2 (1.5%)			
Cold abscess	28 (8.1%)	23 (17.3%)			
Genital tuberculosis	19 (5.5%)	15 (11.3%)			
Tuberculous arthritis	4 (1.2%)	9 (6.8%)			
Others	15 (4.3%)	10 (7.5%)			

Table3- Distribution of comorbidity in demographic group			
Disease	Rural Number (%)	Urban Number (%)	Total Number (%)
Diabetes Mellitus	14 (4.1%)	12 (9%)	26 (5.4%)
HIV	4 (1.2%)	0(0%)	04 (0.8%)
HIV & DM	18 (5.2%)	12 (9%)	30 (6.3%)
None	345	133	478

Table-4. Result of CBNAAT/Gene Xpert in Extrapulmonary Samples

	CBNAAT – Result	Frequency	Percent
Cytological and Biochemical test conclusive of tuberculosis	Negative	89	80.2
	Positive & Sensitive to Rifampicin	21	18.9
	Positive & Resistant to Rifampicin	1	0.9
	Total	111	100.0
Cytological and Biochemical test inconclusive of tuberculosis	Negative	337	91.8
	Positive & Sensitive	27	7.4
	Positive & Resistant	2	0.5
	Positive Indeterminant	1	0.3
	Total	367	100.0

DISCUSSION

Extrapulmonary tuberculosis (EPTB) still poses important diagnostic and management challenges in India. The first and basic information that might help in early and specific diagnosis would be to understand the local demographic pattern and clinical trends. The current study was done to know the demographic pattern and clinical characteristics of various EPTB patients in our tertiary care centre, where patients from all over Jharkhand state come to seek medical care. Firstly the study population (n=478) was divided into rural vs urban population and it was observed that majority of population were from rural background. Males were slightly more affected. A study from Lucknow (Gaur *et al*) showed a significantly higher prevalence in females and a slightly higher number of cases in rural group[13]. This might be attributed to lower awareness & healthcare facilities in rural areas.

Results of age-wise distribution showed that maximum cases of EPTB were in the two age extremes (ie ≤14 yrs and ≥60 yrs) in the rural group, whereas in the urban group maximum cases were in ≥ 60 yrs and 15-29 yrs. Compared to the Lucknow study (Gaur *et al*), maximum cases belonged to the 31-40 yr age(41.7%). Another study from Goa (Velingker *et al*) showed highest prevalence in mid-age group 30-50yrs (47.35%).[14] Similar study by Prakasha *et al* from Mangalore also showed higher prevalence of EPTB in mid-age group.[9] In our study higher prevalence in the older age group can be because of decreasing immunity with older age especially in the tribal and rural areas. Understanding the local clinicepidemiolgical trends can help in Effective and timely clinical decision-making and lead to positive improvements in patient's health outcome.

Before clinical profiling, all cases of EPTB were categorised into two distinct groups rural and urban, as the socioeconomic and other risk factors may be different in both backgrounds. The most common extrapulmonary disease in both groups was Tuberculous meningitis(TBM), followed by pleural effusion. In the rural group the cases of Tuberculous meningitis were significantly higher compared to other anatomical sites($p<0.01$). We compared our findings to four other recent regional studies in india which can possibly represent data from different parts of India. In the Mangalore study (Prakasha *et al)* Pleural effusion was most frequent in males whereas lymph node involvement was most coon in females.[9] The findings were similar to Gaur *et al in* Lucknow and Velingeker *et al* from Goa. [13,14] Rao *et al* from Bhubaneshwar and Rai *et al* from Garhwal, Uttarkhand found that lymph nodes were most common anatomical site for extrapulmonary involvement.[15,16] In this regard, findings in Jharkhand were different from other regional studies. Why tuberculous meningitis is more common in Jharkhand can be a matter of further research.

HIV and diabetes mellitus are the most important risk factor influencing EPTB. The current study revealed only 5.4% had diabetes and 0.4% had HIV in total. Diabetes was more common in urban population. Velingeker *et al* from Goa found that 9.34% of the cases of EPTB were immunocompromised with HIV and 9.55% had diabetes mellitus. [14] Gaur *et al* study showed Diabetes was present in 16.7% of the EPTB patients and HIV was present in 8%.[13] So, it simply can be concluded that any immunocompromising conditions may pose an increased risk of EPTB.

Although the sensitivity of CBNAAT/Gene Xpert is relatively less in extrapulmonary specimen, still performing this test on a selected number of samples yielded very important information. On initial evaluation 3 samples were found to be refampicin resistant in our study. Some other studies have also suggested that CBNAAT may have an promising role in diagnosing EPTB cases.[17] In addition, it can help in rapid & early detection of rifampicin-resistant M. tuberculosis strains.

CONCLUSION

Diagnosis and management of extrapulmonary tuberculosis is still a challenge in India. Regional variations have been observed in the demographic pattern and clinical characteristics of EPTB. The rural population of Jharkhand has a higher prevalence of EPTB, whereas older and male population is at increased risk. Tuberculous meningitis (TBM) has a higher prevalence compared to other anatomical sites of EPTB. Besides, Jharkhand state showed a higher rate of TBM compared to other regional studies in India. Diabetic and HIV positive individuals are at increased risk of developing EPTB. CBNAAT/Gene Xpert may have a promising role in early diagnosis EPTB. In addition, it can help in rapid & early detection of rifampicin-resistance in EPTB cases.

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