

## Original Research Article

### Treatment outcome of Pulmonary and Extra Pulmonary Tuberculosis patients registered at DOTS centre in a tertiary care hospital, Mysuru, Karnataka, India

#### Abstract:

#### Introduction:

**Aim:** To compare the personal variables, clinical characteristics and treatment outcome of Pulmonary and Extra Pulmonary Tuberculosis (EPTB) patients.

**Settings and Design:** A Retrospective observational study was conducted in Directly Observed Treatment Short term (DOTS) centre of teaching hospital, Mysuru, Karnataka state in India from December 2019 to December 2020.

**Methods and Material:** All newly diagnosed patients were registered and followed up during their course of treatment to assess treatment outcome. Data is collected by using personal variable proforma and clinical characteristic form.

**Results:** Among 197 tuberculosis (TB) patients' 120(60.91%) were suffering with EPTB and the remaining 77(39.08%) have the PTB. Majority 101(51.26%) patients were diagnosed by microbiological confirmation and remaining 96(48.73%) were clinically diagnosed. Even though majority 140 (71.06%) completed the treatment only 10(5.07%) were cured. About 16(8.12%) TB patients have treatment failure and were lost to follow up. The treatment success rate was (0.5%). Confirming the presence of TB by microbiologically and clinically is having influence in diagnosis of EPTB, as well as consumption of alcohol was having statistical significance inferring these clinical characteristics having influence in developing EPTB. Residence of the patient is a risk factor for the treatment outcome as per calculated odds ratio

**Conclusion:** The mean treatment success rate of PTB patients was 80.59% and in EPTB was 73.33%. The treatment success rate was not significantly affected by gender, age and type of TB. .

**Key words:** Tuberculosis, treatment outcome , Clinical characteristics

#### Introduction

More than a quarter of all Tuberculosis (TB) cases are found in India. This equates to around 2.6 million cases out of a total of 10 million worldwide. Nearly 0.44 million individuals have

died in India as a result of this disease<sup>1</sup>. According to the World Health Organization (WHO) report, India has one-third of the world's drug-resistant tuberculosis cases<sup>2</sup>.

The causative organism *Mycobacterium tuberculosis*, which is predominantly airborne, affects the lung causing pulmonary TB. When TB is bacteriologically confirmed or clinically diagnosed in other parts of the body other than the lung such as the abdomen, meninges, genitourinary tract, joints, bones, lymph nodes and skin it is classified as extrapulmonary tuberculosis (EPTB). The prevalence of EPTB among new and relapse TB cases globally in 2016 was 15%. WHO recorded the lowest prevalence (8%) in the WHO Western Pacific Region while the highest (24%) was recorded in the Eastern Mediterranean. The figure for the African Region was 16%<sup>4</sup>.

EPTB has been bacteriologically verified or clinically diagnosed in areas other than the lungs, such as the GI system, meninges, genitourinary tract, joints, bones, lymph nodes, and skin.<sup>5</sup>

EPTB accounts for 15–20 percent of tuberculosis cases in India.<sup>6</sup> TB treatment outcome depends on demographic variable and clinical characteristics of TB patients. Hence, it is critical to compare personal variables, clinical characteristics, and treatment outcomes between PTB and EPTB in order to prevent and manage it.<sup>7</sup>

As a result, this study is to look into the treatment outcomes of PTB and EPTB patients who have been registered at a DOTs centre in a tertiary care hospital in Mysuru, Karnataka, India. The aim of this study is to compare the personal variables, clinical characteristics and treatment outcome of PTB and EPTB.

## **Materials and Methods**

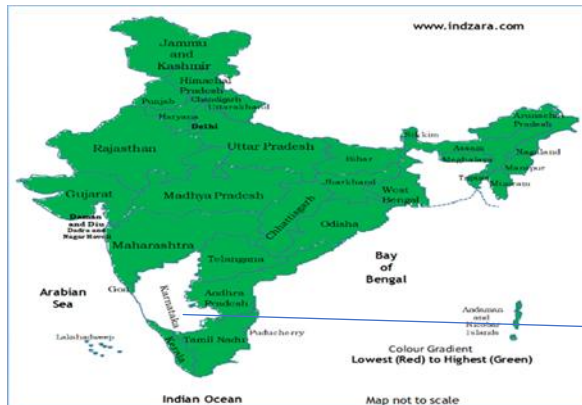
Retrospective case series analyses of TB patients were studied in Tertiary care teaching hospital, Mysuru, Karnataka, India between December 2019 to December 2020. Study included 197 patients who were diagnosed with TB. Data was scrutinized based on personal variables and the clinical characteristics of TB. Only lung parenchyma involvement was considered as Pulmonary TB (PTB). Extra Pulmonary TB (EPTB) was defined as the involvement of organs other than the lung parenchyma, such as the lymph nodes, pleura, abdomen, genitourinary tract, gastrointestinal tract, skin, joints and bones, meninges, and others. Differences in personal variables and clinical characteristics of EPTB and PTB were compared and analysed using the Z test. Odds ratios (ORs) and confidence intervals (CIs)

were calculated to identify factors associated with EPTB compared to PTB related to treatment outcome.

### **Ethical clearance and approvals**

Study was approved by the Ethical Committee of the (ref. JSS/MC/IEC0/605/2018-19, dated:10.05.19).

### **Study area map**



Mysuru, JSS Hospital, Tertiary Care Hospital.

### **Results**

#### **Frequency and percentage distribution of Tuberculosis patients according to their personal variables and clinical characteristics**

In the present study out of 197 TB patient's majority 120 (60.46%) were males, 25(22.84%) of them were in the age group of 30 to 40 years, 174 (81.84%) were married and 141(71.56%) of them were living in nuclear family. Study also shows that 168(85.27%) of TB patients are from urban area and 186 (94.44%) were belong to Hindu religion. 47(23.85%) have Intermediate/ diploma as their education status, 84(42.63%) of them were farmers and 136(69.03%) were from upper lower socioeconomic class

Majority 101(51.26%) of the patients were defined by microbiological confirmation and the remaining 96(48.73%) were clinically diagnosed. In 156 cases (79.18 percent), sputum Ziehl-Neelsen stain (ZN) is used to make the diagnosis, while Cartridge- Based Nucleic Acid Amplification (CBNAAT) is used in 41 cases (20.81 percent). Data also shows majority 181(91.87%) were newly diagnosed and remaining 16(30.96%) were previously treated TB patients .

The study also revealed that 36 (18.27%) were suffering from Diabetes Mellitus. About 38(19.28%) of the TB patients were smokers and 35(17.76%) were known for alcohol taking . Nearly 140 (71.06%) of the patients completed the TB treatment where only 10(5.07%) were cured. Treatment failure and lost to follow up was observed among 16(8.12%) TB patients while treatment success rate in this study was 0.5%.

### Type of TB

Out of 197 TB patients 100 (50.76%) have family history of TB and 120(60.91%) suffering with EPTB and the remaining 77(39.08%) have PTB (Figure 1).

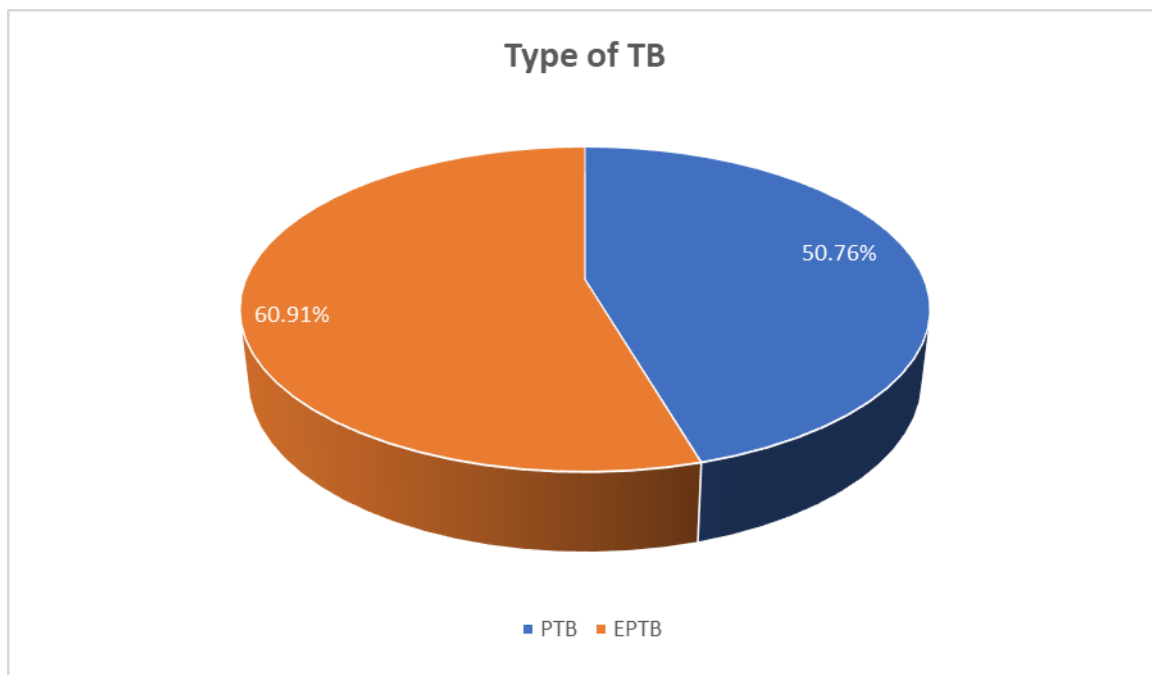


Fig.1: Type of TB

### Type of EPTB

Data presented in table 1 shows that out of 120 EPTB patients' majority were suffering with pleural effusion (46.66%). 25.83% of them were manifested with lymphadenopathy of cervical, supraclavicular, submandibular, axillary and femoral. In lymphadenopathy most of them 23(19.16%) had cervical lymph node involvement. Ocular TB was found among 7(5.83%), Miliary TB among 3(%), urogenital TB among 2(1.66%). Out of 7 (5.83%) abdominal TB cases Intestinal TB was 6(5%) and one (0.83%) patient had peritoneal involvement. Data also revealed that 4(3.33%) were suffering with Nervous system TB which includes meningeal involvement 3(2.5%) and Potts spine among. One (0.83%) patient had vocal cord TB. One (0.83%) more patient was suffering with skin TB.

Table 1: Distribution based on type of EPTB cases

n=120

<b>Involved area</b>	<b>Frequency</b>	<b>%</b>
<b>Lymph nodes</b>	<b>31</b>	<b>25.83</b>
Cervical	23	19.16
Submandibular	3	2.5
Supraclavicular	3	2.5
Axilla	1	0.83
Femoral	1	0.83
<b>Nervous system</b>	<b>4</b>	<b>3.33</b>
Potts spine	1	0.83
Meninges	3	2.5
<b>Vocal cord TB</b>	<b>1</b>	<b>0.83</b>
<b>Ocular</b>	<b>7</b>	<b>5.83</b>
<b>Pleural</b>	<b>64</b>	<b>53.33</b>
<b>Abdominal</b>	<b>7</b>	<b>5.83</b>
Intestine	6	5
Peritoneum	1	0.83
<b>Urogenital</b>	<b>2</b>	<b>1.66</b>
Renal TB	1	0.83
Epididymitis	1	0.83
<b>Skin TB</b>	<b>1</b>	<b>0.83</b>

<b>Miliary TB</b>	<b>3</b>	<b>2.5</b>
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### **Difference in PTB and EPTB patients with their selected personal variables and clinical characteristics**

Data shows that 15(12.5%) in PTB and 30(25%) in EPTB were in the age group of 31-40 years and the calculated Z value is -2.3674 and p value is 0.0177, inferring that in EPTB patients age was not an influencing factor for developing EPTB than PTB patients.

In PTB 16(7.79%) and in EPTB 38(31.66%) patients were having Graduation/Profession as their educational qualification. The calculated z value is -4.2426 and p-value is <0.0001, hence, there is significant association between graduation/professional education with PTB and EPTB patients.

The calculated Z value for microbiologically confirmed cases is 2.9772 which is statistically significant where p value is 0.0028. Inferring that case definition will influence the PTB and EPTB patients (Table 2).

Table:2 Difference in PTB and EPTB with their selected personal variables and clinical characteristics ( n=77+120=197)

<b>Personal variables and clinical characteristics</b>		<b>PTB</b>	<b>EPTB</b>	<b>Z value</b>	<b>P value</b>
<b>Gender</b>	Male	51(66.23%)	69(57.5%)	1.3079	0.1902
	Female	26(33.76%)	51(24.28%)	1.5583	0.1187
<b>Age in years</b>	20-30	17(22.07%)	25(20.83%)	0.1721	0.865
	31-40	15(12.5%)	30(25%)	- 2.3674	0.0177
	41-50	10(12.98%)	16(13.33%)	0	1
	51-60	18(23.37%)	25(20.83%)	0.3414	0.7278
	61-70	11(44.28%)	20(16.66%)	4.1467	<0.000

					1
	71-80	4(5.19%)	4(1.90%)	0	1
	81-90	2(2.59%)	0	1.7452	0.0801
<b>Marital status</b>	Married	68(88.31%)	106(88.33%)	0	1
	Unmarried	9(11.68%)	14(11.66%)	0	1
<b>Type of family</b>	Nuclear	55(71.42%)	86(71.66%)	- 0.1566	0.8728
	Joint	22(28.57%)	34(28.33%)	0.1566	0.8728
<b>Residence</b>	Urban	67(87.01%)	101(84.16%)	0.6025	0.5485
	Sub urban	7(9.09%)	11(9.16%)	0	1
	Rural	3(3.89%)	8(10.38%)	- 1.6628	0.0969
<b>Religion</b>	Hindu	74(96.10%)	112(93.33%)	0.9305	0.3523
	Muslim	2(2.59%)	7(5.83%)	- 1.0233	0.3077
	Christian	1(1.29%)	1(0.83%)	0	1
<b>Education</b>	Illiterate	5(6.49%)	10(8.33%)	- 0.5543	0.5823
	Primary/middle school	19(24.67%)	30(25%)	0	1
	High School	19(24.67%)	18(15%)	1.7678	0.0767
	Intermediate/ diploma	18(23.37%)	24(20%)	0.5164	0.603
	Graduation/Profess	16(7.79%)	38(31.66%)	-	<0.000

	ion			4.2426	1
<b>Occupation</b>	Home maker /Unemployed	2(2.59%)	6(7.79%)	- 1.5508	0.1211
	Student	2(2.59%)	2(1.66%)	0.4529	0.6527
	Coolie worker	5(6.49%)	3(2.5%)	1.7055	0.0872
	Farmer	35(45.45%)	49(40.83%)	0.0571	0.5686
	Clerical worker	12(15.58%)	18(15%)	0.1954	0.8414
	Professional/ Technical	21(27.27%)	42(35%)	- 1.2231	0.2224
	Upper middle	0	1(0.83%)	- 1.0025	0.3173
	Lower middle	14(18.18%)	23(19.16%)	- 0.1821	0.8571
	Upper Lower	56(72.72%)	80(66.66%)	0.9258	0.3523
	Lower	7(9.09%)	16(13.33%)	-0.904	0.3681
<b>Family history of TB</b>	Yes	37(48.05%)	63(52.5%)	- 0.5657	0.5686
	No	40(51.94%)	57(47.5%)	0.7071	0.4777
<b>Case Definition</b>	Microbiologically confirmed	49(63.63%)	52(43.33%)	2.9772	0.0028
	Clinically diagnosed	28(14.21%)	68(56.66%)	- 6.3542	<0.000 1
<b>Type of patient</b>	New	72(93.50%)	109(90.83%)	0.5213	0.603
	Transferred in	4(5.19%)	8(6.66%)	-	0.5485

				0.5955	
	Recurrent	1(1.29%)	3(2.5%)	-	0.5619
				0.5817	
<b>Method of diagnosis</b>	ZN	64(83.11%)	92(76.66%)	1.0607	0.2891
	CBNAAT	13(16.88%)	28(23.33%)	-	0.2891
				1.0607	
<b>Treatment regimen</b>	New	70(90.90%)	111(92.5%)	0.2536	0.8025
	Previously treated	7(9.09%)	9(7.5%)	0.5213	0.603
<b>Known case of Diabetes</b>	Yes	11(14.28%)	25(12.69%)	0.2069	0.8336
	No	66(85.71%)	95(48.22%)	5.7144	<0.0001
<b>Smoking</b>	Yes	16(20.77%)	22(18.33%)	0.5354	0.5892
	No	61(79.22%)	98(81.66%)	-	0.5892
				0.5354	
<b>Alcoholism</b>	Yes	19(24.67%)	16(13.33%)	2.163	0.0307
	No	58(75.32%)	104(86.66%)	-2.163	0.0307
<b>Outcome</b>	Treatment completed	56(72.72%)	84(70%)	0.4699	0.6383
	Cured	6(7.79%)	4(3.33%)	1.5508	0.1211
	Treatment failed	4(5.19%)	12(10%)	-	0.1802
				1.3423	
	Died	8(10.38%)	6(5%)	1.3423	0.1802
	Lost to follow up	3(3.89%)	13(10.83%)	-	0.0601
				1.8792	

	Treatment success	62(80.59%)	88(73.33%)	1.3442	0.1802
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### Treatment outcome among PTB and EPTB

Out of 77 PTB patients 62(80.59%) of them has completed the TB treatment and remaining 15(19.48%) has not completed the TB treatment. Out of 120 EPTB patients 88(73.33%) has completed the TB treatment and remaining 32(26.66%) has not completed the treatment (Figure 2).

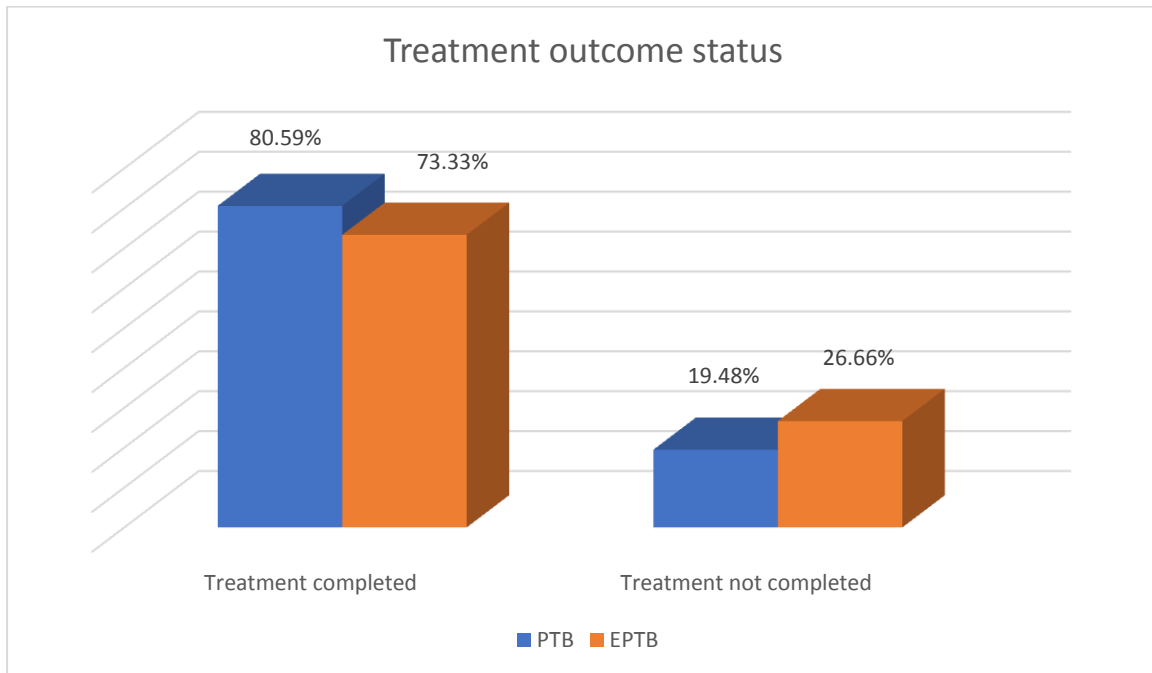


Figure 2: Distribution of treatment outcome among PTB and EPTB

It is evident in the figure 3 that out of 77 PTB patients 72(93.50%) were survivors and remaining 8(4.06%) of them died due to PTB. Among 120 EPTB patients 117(97.45%) were survivors and remaining 3(2.05%) of them died due to complication of EPTB (Figure 4).

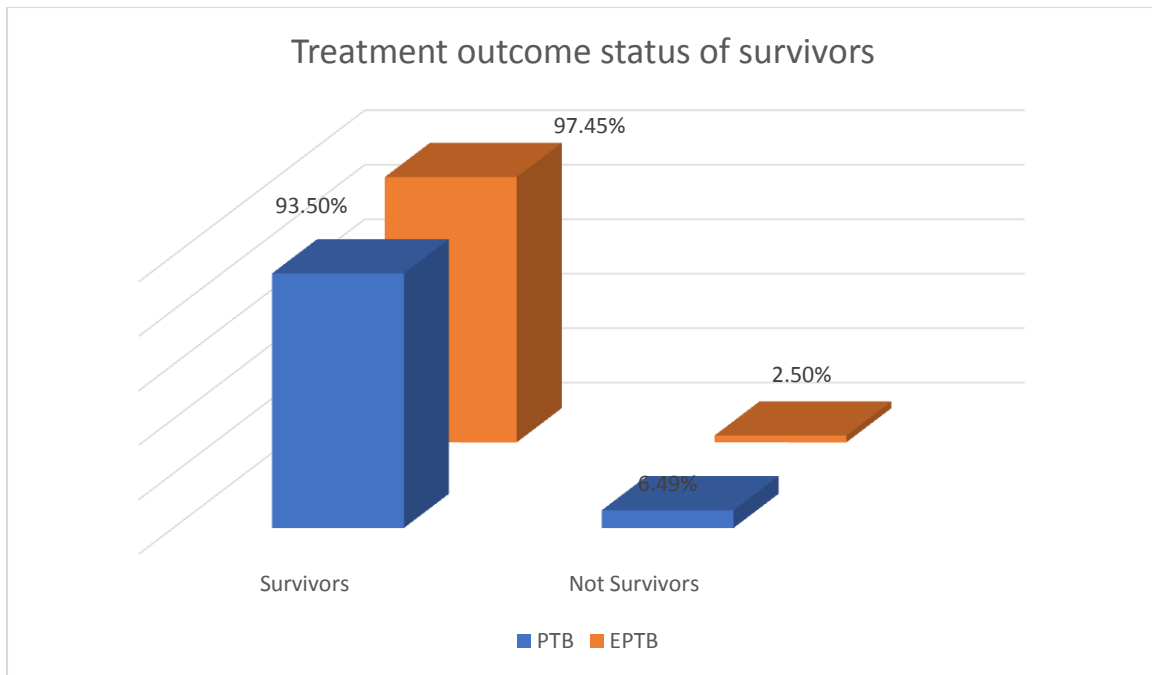


Figure 3: Distribution of treatment outcome among PTB and EPTB

**Comparison between the treatment outcome of TB patients and their selected personal variables and clinical characteristics**

Odds ratio was used to determine the association between the treatment outcome of TB patients and their selected personal variables and clinical characteristics. It is evident from the study that residence of the patient is an influencing factor for the treatment outcome as the odd ratio is  $<1$  (2.53) and  $<1$  (1, 6.4) with confidence interval 95%. Hence patients residing in urban area have 2% more treatment completion rate than the patients residing in rural area. Other selected personal variables and clinical characteristics where not influencing the treatment outcome.

**Table:3** Comparison between PTB and EPTB with their selected personal variables and clinical characteristics.  
N=197

<b>Sl.No</b>	<b>Personal variables and clinical Characteristics</b>	<b>Odds ratio</b>	<b>Confidence Interval</b>
1	Gender	0.75	(0.33, 1.69)
2	Marital status	0.5	(0.11, 2.24)
3	Place of residence	2.53	(1, 6.4)
4	Type of family	0.9	(0.38, 2.16)
5	Religion	1.36	(0.42, 4.36)
6	Socio economic status	1.23	(0.44, 3.46)
7	Family history of TB	1.04	(0.48, 2.26)
8	Site of TB	0.81	(0.37, 1.78)
9	Type of case	1.06	(0.49, 2.31)

11	Known case of Diabetes	0.69	(0.27, 1.76)
12	Smoking	2.39	(0.68, 8.33)
13	Alcohol	0.38	(0.05, 2.98)
14	Method of diagnosis	0.73	(0.26, 2.04)

## Discussion

Aim of the study was to compare the personal variables, clinical characteristics and treatment outcome of PTB and EPTB patients in tertiary care Hospital , Mysuru, Karnataka,India. Total number of patients recruited were 197 among them 156(73.6%) were males, 128(60.38%) of the patients had rural residence and 84(39.62%) were from urban setting. Majority 120(60.91%) of TB patients were by EPTB and remaining 77(39.08%) were diagnosed as PTB. Similar findings were found in a study which revealed that globally ,the notification rates decreased over time, rates in males became higher than those of females for all ages over 15. Present notification rates of both sexes combined in many developing countries are similar to those of industrialized countries in the middle of the century, although the sex and age pattern is similar to that in industrialized countries at present, with men's disease rates exceeding women's after the age of 15.7 Gender differences observed in the study confirm the findings of previous studies in both developing 9,10 and developed countries 11,12.This may be a consequence of gender differences in both exposures to TB infection and prevalence of susceptibility risk factors (e.g., smoking) 9. In this study also the main reasons for gender differences was susceptible risk factors like smoking, consumption of alcohol and inadequate intake of balanced diet.

The majority of PTB patients 40(51.94%) did not have family history of TB on the other hand majority of EPTB patients 63(52.5%) were having family history of TB in their family. The main risk factor for EPTB relative to PTB that we identified was being younger than 25

years. This is consistent with studies from the USA <sup>13</sup> and in Western Europe <sup>14</sup> which have reported that younger age was an independent risk factor for EPTB due to the high rate of immigration. Other studies from the USA<sup>15</sup> and Turkey<sup>16</sup>, have reported that age was not associated with EPTB. These inconsistencies could be due to differences in prevalence of host-related factors or important co-exposures.

In this study, only 16(20.77%) in PTB and 22(18.33%) in EPTB were smokers. This raises the possibility that the age and sex differences between PTB cases and EPTB cases could be a result of confounding by smoking. However, after adjusting for potential confounding factors (including smoking) by logistic regression analysis, younger age and female gender remained strongly associated with EPTB. Therefore, after primary infection in the lungs the probability of reactivation at an extra-pulmonary site may be higher at younger age. It would be useful to confirm the association of age and gender with EPTB in other high-burden countries. 8

In this study, smoking was not associated with treatment outcome. Contradictory to this finding another study reported smoking as a risk factor for TB infection and for pulmonary TB disease<sup>17</sup>. Another report has suggested that smoking is associated with relapse of TB and smokers are less likely to have isolated extrapulmonary TB <sup>18</sup>. Another study showed that past history of TB was associated with PTB, but it was as a result of reactivation (relapse) or reinfection was not confirmed<sup>19</sup>. However, evidence suggests that in high-burden countries reinfection is more common than relapse <sup>20</sup>.

Other studies have reported an association between diabetes mellitus and treatment outcome <sup>22,23</sup>. However, study from Turkey<sup>16</sup> examined the association of diabetes, use of immunosuppressive drugs/steroids and past history of TB with EPTB has no association with any of these factors. A study from the UK <sup>23</sup> reported that use of immunosuppressive drugs/steroids and co-morbid conditions were associated with PTB. Therefore it is important to periodically screen the patients with chronic conditions like diabetes, those on immunosuppressive drugs/steroids for occurrence of tuberculosis.

In the present study majority 120(60.91%) of TB patients were infected by EPTB and remaining 77(39.08%) were diagnosed as PTB. A recent study from a large tertiary hospital in south India reported that EPTB showed an increasing trend among HIV infected patients. But in our study all PTB and EPTB patients HIV status was non reactive.

In the present study out of 120 EPTB patients pleural effusion (46.66%) is the most frequent type of EPTB. Of the EPTB, 25.83% of them were having lymphadenopathy of cervical, supraclavicular, submandibular, axillary and femoral. In lymph node involvement majority 23(19.16%) had cervical lymph node involvement. Another study conducted in India also showed the commonest sites of EPTB were lymph node (34.4%) and pleural effusion (25.2%) followed by abdominal (12.8%) and central nervous system (CNS) (9.4%).<sup>24</sup> Another study conducted in Karnataka revealed Extra-pulmonary cases accounted for 30.5% of total TB cases. Among 224 cases of extra-pulmonary TB studied, 136 (60.7%) were males and 88 (39.3%) were females. Most common site of extra-pulmonary tuberculosis was pleura (29.9%) followed by meninges (22.5%), abdomen (19.6%) and lymph node (10.7%) tuberculosis.<sup>26</sup>

Out of 77 PTB patients 62(80.59%) of them has completed the TB treatment. while out of 120 EPTB patients 88(73.33%) has completed the TB treatment. Patient tracking system followed in DOTS centre and Mobile Based Counselling and regular reminders sent by the investigator was the reason for treatment completion. In remaining patients reason for not completing the treatment was as a complication of the illness death occurred among them.

Out of 77 PTB patients 72(93.50%) were survivors and remaining 8(4.06%) of them died due to PTB. Among 120 EPTB patients 117(97.45%) were survivors and remaining 3(2.05%) of them died due to complication of EPTB. A study conducted in Uzbekistan reported overall, 83% of patients were successfully treated, 6% died, 6% were lost-to-follow-up, 3% failed treatment and 2% transferred out<sup>25</sup>. Other study conducted in Karnataka showed 82.2% completed treatment, 7.5% were defaulted, 9.9% died and 0.4% treatment failure. The mostcommon reason for default was irregular treatment (29.5%) followed by alcohol abuse (23.5%).<sup>26</sup>

### **Conclusion:**

The mean treatment success rate of PTB patients was 80.59% and in EPTB was 73.33%. The treatment success rate was not not significantly affected by gender, age and type of TB. However, Based on this finding it is recommended to implement frequent supportive supervision during the course of treatment, strengthen referral linkage among facilities, and conduct further research to find out the reasons for the observed difference among PTB and EPTB patients.

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