

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:

Context: Extrapulmonary tuberculosis (EPTB) constitutes 15–20% of tuberculosis cases in India. Earlier studies have evaluated treatment outcomes of TB with little information on comparison of outcomes of Pulmonary and EPTB.

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

Settings and Design: A Prospective observational study was conducted in DOTS centre of teaching hospital, Mysuru, Karnataka 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 TB patients' 120(60.91%) suffering with EPTB and remaining 77(39.08%) have 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. Among 16(8.12%) TB patients have treatment failure and were lost to follow up. Treatment success rate is (0.5%). Confirming the presence of TB by microbiologically and clinically is having influence in diagnosis of EPTB, as well as consumption of alcohol is having influence in developing EPTB. Residence of the patient is a risk factor for the treatment outcome.

Conclusion: TB treatment outcome can be enhanced by improved supervision, improved counselling activities and implementation of default tracing and home visit by health worker.

Key words: Tuberculosis, Pulmonary, Extrapulmonary, Outcome

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 disease¹. According to the World Health Organization (WHO), India has one-third of the world's drug-resistant tuberculosis cases².

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)³. The prevalence of EPTB among new and relapse TB cases globally in 2016 was 15%. The lowest prevalence (8%) was recorded in the WHO Western Pacific Region while the highest (24%) was recorded in the Eastern Mediterranean. The figure for the African Region was 16%⁴.

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.⁵

EPTB was found in 15% of new and relapsed TB patients worldwide in 2016. EPTB accounts for 15–20 percent of tuberculosis cases in India.⁶

It is critical to compare personal variables, clinical characteristics, and treatment outcomes between PTB and EPTB in order to prevent and manage it.⁷

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.

Method and Methodology

Retrospective case series analyses of TB patients were studied in Tertiary care teaching hospital, Mysuru, Karnataka, India between December 2019 to December 2020. The aim of this study was to compare the personal variables, clinical characteristics and treatment outcome of Pulmonary and EPTB. 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.

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

Result and Discussion

Data collected is analysed and presented in the following headings.

1. 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

The present study shows that out of 197 TB patients 100 (50.76%) have family history of TB and 120(60.91%) suffering with EPTB and remaining 77(39.08%) have PTB. Majority 101(51.26%) patients were defined by microbiological confirmation and remaining 96(48.73%) were clinically diagnosed. Sputum ZN is the method of diagnosis in 156(79.18%) and remaining 41(20.81%) diagnosis is confirmed by CBNAAT. 181(91.87%) were newly diagnosed TB patients, 12(6.09%) were transferred in cases and 4(2.03%) were recurrent cases. (and 16 (30.96%) were previously treated.

Study also reveals that majority were 161(81.72%) not suffering from Diabetes Mellitus and all (100%) have nonreactive HIV status. Only 38(19.28%) of TB patients were smokers and 35(17.76%) were known alcoholics and majority 140 (71.06%) completed the treatment where only 10(5.07%) were cured. Among 16(8.12%) TB patients have treatment failure and were lost to follow up. Treatment success rate is (0.5%)

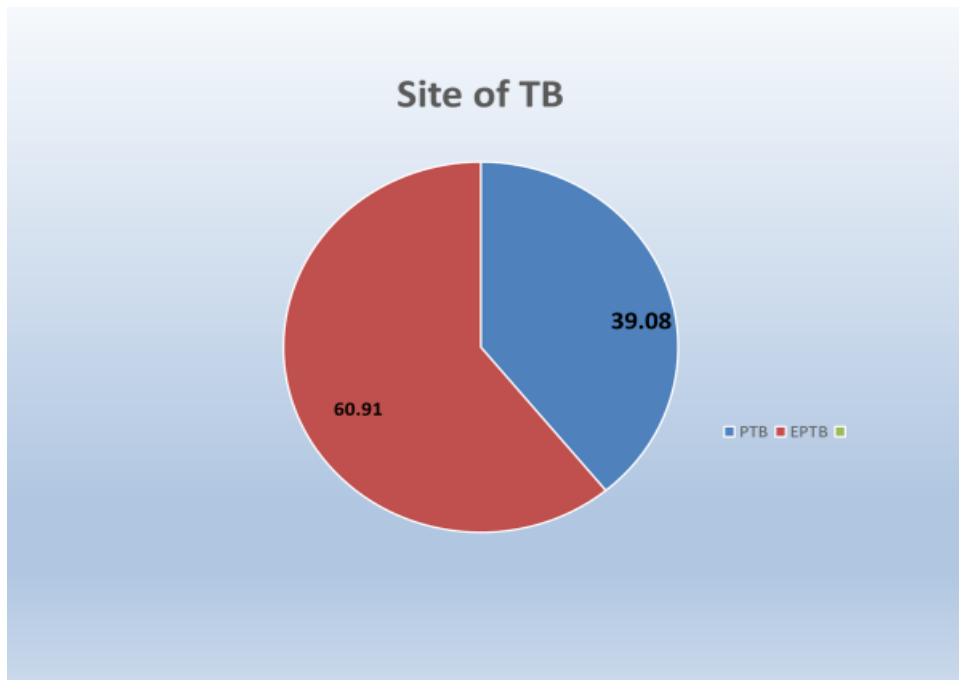


Fig.1: Distribution based on site of TB

Table1: Distribution based on type of EPTB cases

n=120

| Involved area | Frequency | % |
|-----------------------|-----------|--------------|
| Lymph nodes | 31 | 25.83 |
| Cervical | 23 | 19.16 |
| Submandibular | 3 | 2.5 |
| Supraclavicular | 3 | 2.5 |
| Axilla | 1 | 0.83 |
| Femoral | 1 | 0.83 |
| Nervous system | 4 | 3.33 |
| Potts spine | 1 | 0.83 |
| Meninges | 3 | 2.5 |
| Vocal cord TB | 1 | 0.83 |
| Ocular | 7 | 5.83 |

| | | |
|-------------------|-----------|--------------|
| Pleural | 64 | 53.33 |
| Abdominal | 7 | 5.83 |
| Intestine | 6 | 5 |
| Peritoneum | 1 | 0.83 |
| Urogenital | 2 | 1.66 |
| Renal TB | 1 | 0.83 |
| Epididymitis | 1 | 0.83 |
| Skin TB | 1 | 0.83 |
| Miliary TB | 3 | 2.5 |

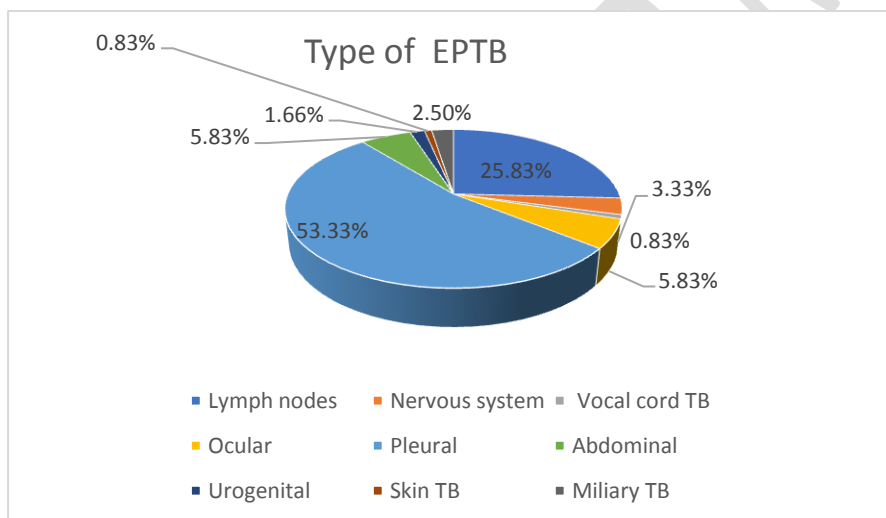


Fig.2: Distribution based on type of EPTB cases

Data shows that out of 120 EPTB patients pleural effusion (46.66%) is the most frequent type of 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.

2. Comparison between PTB and EPTB patients with their selected personal variables and clinical characteristics

Table:2 Comparison between PTB and EPTB with their selected personal variables and clinical characteristics. n=77+120=197

| Personal variables and clinical characteristics | | PTB | EPTB | Z value | P value |
|--|-----------|------------|-------------|----------------|----------------|
| Gender | Male | 51(66.23%) | 69(57.5%) | 1.3079 | 0.1902 |
| | Female | 26(33.76%) | 51(24.28%) | 1.5583 | 0.1187 |
| Age in years | 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 |
| Marital status | Married | 68(88.31%) | 106(88.33%) | 0 | 1 |
| | Unmarried | 9(11.68%) | 14(11.66%) | 0 | 1 |
| Type of family | Nuclear | 55(71.42%) | 86(71.66%) | - 0.1566 | 0.8728 |
| | Joint | 22(28.57%) | 34(28.33%) | 0.1566 | 0.8728 |
| Residence | 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%) | - | 0.0969 |
| | | | | 1.6628 | |
| Religion | Hindu | 74(96.10%) | 112(93.33%) | 0.9305 | 0.3523 |
| | Muslim | 2(2.59%) | 7(5.83%) | - | 0.3077 |
| | | | | 1.0233 | |
| | Christian | 1(1.29%) | 1(0.83%) | 0 | 1 |
| Education | Illiterate | 5(6.49%) | 10(8.33%) | - | 0.5823 |
| | | | | 0.5543 | |
| | 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/Profession | 16(7.79%) | 38(31.66%) | - | <0.000 |
| | | | | 4.2426 | 1 |
| Occupation | Home maker /Unemployed | 2(2.59%) | 6(7.79%) | - | 0.1211 |
| | | | | 1.5508 | |
| | 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%) | - | 0.2224 |
| | | | | 1.2231 | |

| | | | | | |
|-----------------------------|-----------------------------|------------|-------------|-------------|-------------|
| | 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 |
| Family history of TB | Yes | 37(48.05%) | 63(52.5%) | - 0.5657 | 0.5686 |
| | No | 40(51.94%) | 57(47.5%) | 0.7071 | 0.4777 |
| Case Definition | 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 |
| Type of patient | New | 72(93.50%) | 109(90.83%) | 0.5213 | 0.603 |
| | Transferred in | 4(5.19%) | 8(6.66%) | - 0.5955 | 0.5485 |
| | Recurrent | 1(1.29%) | 3(2.5%) | - 0.5817 | 0.5619 |
| Method of diagnosis | ZN | 64(83.11%) | 92(76.66%) | 1.0607 | 0.2891 |
| | CBNAAT | 13(16.88%) | 28(23.33%) | - 1.0607 | 0.2891 |
| Treatment regimen | New | 70(90.90%) | 111(92.5%) | 0.2536 | 0.8025 |
| | Previously treated | 7(9.09%) | 9(7.5%) | 0.5213 | 0.603 |
| Known case of | Yes | 11(14.28%) | 25(12.69%) | 0.2069 | 0.8336 |

| | | | | | |
|-------------------|---------------------|------------|-------------|---------|---------|
| Diabetes | No | 66(85.71%) | 95(48.22%) | 5.7144 | <0.0001 |
| Smoking | Yes | 16(20.77%) | 22(18.33%) | 0.5354 | 0.5892 |
| | No | 61(79.22%) | 98(81.66%) | -0.5354 | 0.5892 |
| Alcoholism | Yes | 19(24.67%) | 16(13.33%) | 2.163 | 0.0307 |
| | No | 58(75.32%) | 104(86.66%) | -2.163 | 0.0307 |
| Outcome | 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%) | -1.3423 | 0.1802 |
| | Died | 8(10.38%) | 6(5%) | 1.3423 | 0.1802 |
| | Lost to follow up | 3(3.89%) | 13(10.83%) | -1.8792 | 0.0601 |
| | Treatment success | 62(80.59%) | 88(73.33%) | 1.3442 | 0.1802 |

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.

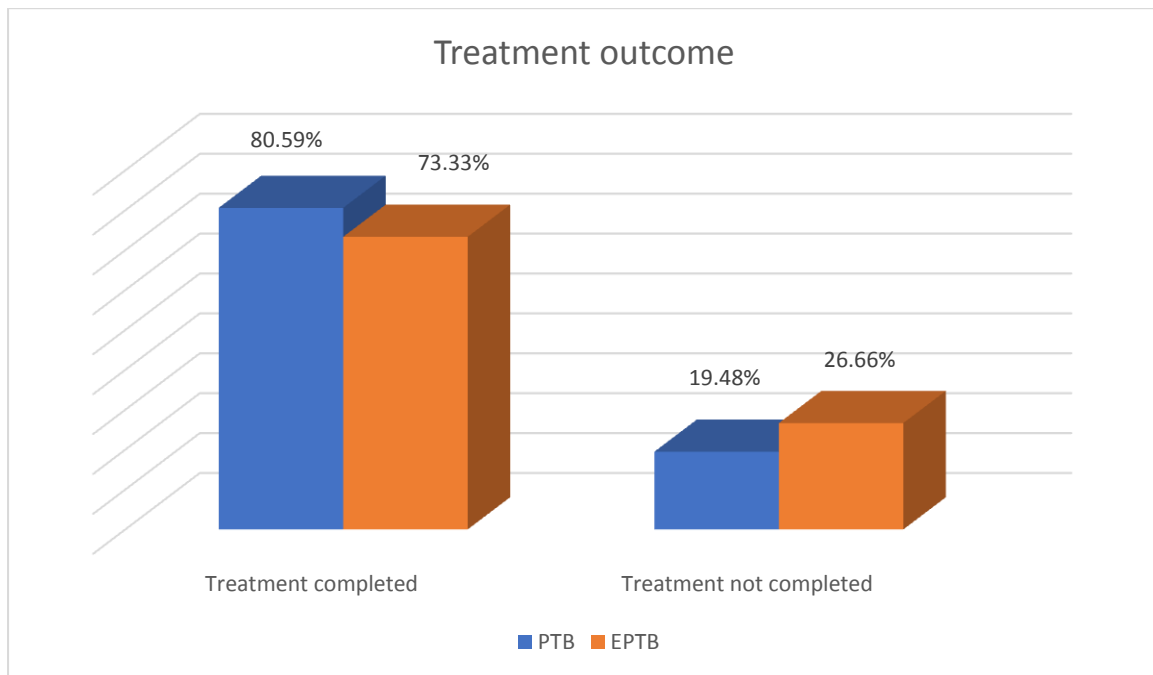


Figure 3: distribution treatment outcome among PTB and EPTB

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.

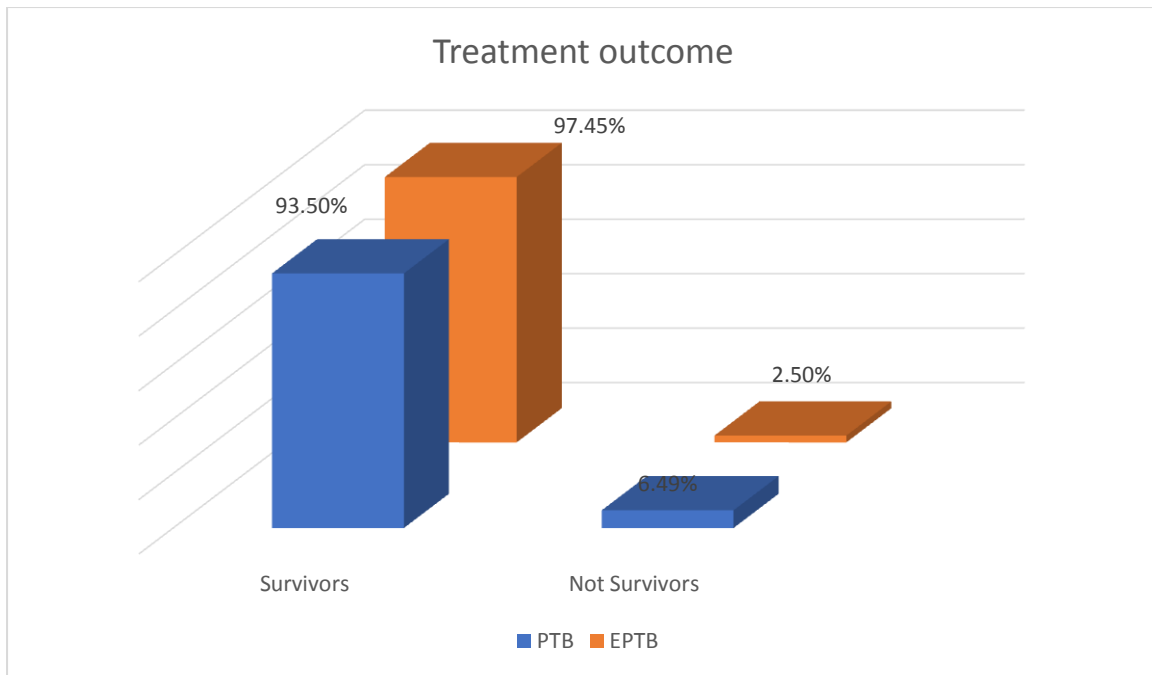


Figure 4: Distribution of treatment outcome among PTB and EPTB

It is evident in the figure 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.

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

To determine the association between the treatment outcome of TB patients and their selected personal variables and clinical characteristics odd ratio was calculated.

Table:3 Association between the treatment outcome of TB patients and their selected personal variables and clinical characteristics
n=197

| Sl.No | Personal variables and clinical Characteristics | Odds ratio | Confidence Interval |
|-------|---|------------|---------------------|
| 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) |

It is evident from the study that residence of the patient is influencing factor for the treatment outcome as the odd ratio is <1 (2.53) with confidence interval <1 (1, 6.4). 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 were not influencing the treatment outcome.

Discussion

Total number of patients recruited was 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 our

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.

The majority of PTB patients 40(51.94%) did not have family history of TB and EPTB majority of patients 63(52.5%) were having family history of TB. The other main risk factor for EPTB relative to PTB that we identified was being younger than 25 years. This is consistent with studies from the USA¹³ and Europe¹⁴ which have reported that younger age was an independent risk factor for EPTB. Other studies from the USA¹⁵ and Turkey¹⁶, 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 our 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 our study, smoking was not associated with treatment outcome. Contradictory to this finding another study which reported that smoking is a risk factor for TB infection and for pulmonary TB disease¹⁷. Another report has suggested that smoking is associated with relapse of TB and smokers are less likely to have isolated extrapulmonary TB¹⁸. We also found that past history of TB was associated with PTB, although we could not identify if this was as a result of reactivation (relapse) or reinfection¹⁹. However, evidence suggests that in high-burden countries reinfection is more common than relapse²⁰.

Our results are consistent with other studies that have reported an association between diabetes mellitus and treatment outcome^{22,23}. However, study from Turkey¹⁶ examined the association of diabetes, use of immunosuppressive drugs/steroids and past history of TB with EPTB but found no association with any of these factors. A study from the UK²³ 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 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 patients¹⁴. 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. 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%).²⁴ 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.²⁶

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.

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 out²⁵. Other study conducted in Karnataka showed 82.2% completed treatment, 7.5% were defaulted, 9.9% died and 0.4% treatment failure. The most common reason for default was irregular treatment (29.5%) followed by alcohol abuse (23.5%).²⁶

Conclusion:

The mean treatment success rate of PTB patients was 80.59% and in EPTB was 73.33%) it was 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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