

ASSESSMENT OF CLINICAL PROFILE AND TREATMENT OUTCOME OF EXTRA PULMONARY TUBERCULOSIS PATIENTS UNDER RNTCP IN RURAL MEDICAL COLLEGE, SOUTH INDIASiddeswaraswamy P¹, Shubhakara K², Gnanendra D. M³, Mahesh S. Hoolageri⁴, Indushree T⁵**HOW TO CITE THIS ARTICLE:**

Siddeswaraswamy P, Shubhakara K, Gnanendra D. M, Mahesh S. Hoolageri, Indushree T. "Assessment of Clinical Profile and Treatment Outcome of Extra Pulmonary Tuberculosis Patients under RNTCP in Rural Medical College, South India". Journal of Evolution of Medical and Dental Sciences 2014; Vol. 3, Issue 40, September 01; Page: 10174-10182, DOI: 10.14260/jemds/2014/3322

ABSTRACT: BACKGROUND: Few reports exist detailing the clinical profile and treatment outcome of extra pulmonary tuberculosis (EPTB) registered in DOTS centers in a rural medical college. **AIM:** The primary objective of this study was to describe the demographic, clinical profile and treatment outcome of EPTB. **MATERIALS AND METHODS:** A cross sectional study that reviewed the routinely collected data of patients with EPTB registered for treatment under DOTS for the period of 1 November 2010 to 31 September 2013 was carried out at Sri Siddhartha medical college. **RESULTS:** Among 747 cases registered for treatment of all forms of tuberculosis, 406 (54.35%) had EPTB, majority of cases were aged 20 -40 years (193, 47.50%) and males (239, 58.9%) but lymph node and genitourinary TB most commonly affected females. In the present study pleural effusion (35.70%) was most common followed by CNS involvement (19.50%). All patients were treated with the standard RNTCP treatment regimen. The observed treatment outcomes were treatment completion of 82.01%, default of 8.86%, and failure of 0.24% and death 8.86%. Patient treated with category II, HIV-positive patients and diabetic patients had adverse treatment outcomes. **CONCLUSION:** The burden of EPTB is more among the productive age group and in males. Plural TB is most common followed by CNS involvement. A well-defined program specified protocols for the diagnosis and treatment of extra pulmonary tuberculosis cases should be more effectively addressed in RNTCP.

KEY WORDS: EPTB, DOTS, RNTCP, Treatment outcome.

INTRODUCTION: TB can involve any organ system in the body. While pulmonary TB (PTB) is the most common presentation, extra pulmonary TB (EPTB) is also an important clinical problem. The term EPTB is used to describe occurrence of tuberculosis at body sites other than the lung. Extra pulmonary involvement can occur in isolation or along with a pulmonary focus as in the case of patient with disseminated tuberculosis.

Virtually every site of the body can be affected. Isolation of acid fast bacilli (AFB) by specimen smear examination may not be possible in most of the EPTB cases.¹The diagnosis of EPTB, whose confirmation depends on obtaining material for culture is much more difficult and technically more demanding than for PTB. Compared with pulmonary TB, EPTB poses more challenges for diagnosis and monitoring of treatment because it involves relatively less accessible sites.²

The highest priority in TB control programs is the identification and treatment of sputum positive infectious patients. Pulmonary TB is the most important clinical manifestation of this infection, as it is both the most common presentation and practically the only form of the disease that is infectious. TB affecting other sites known as extra-pulmonary TB is rarely smear-positive; it is

ORIGINAL ARTICLE

generally accepted that the contagious potential of this form is negligible and it has, therefore, never been a priority in the campaigns undertaken by national TB control programs.³

The percentage of patients with EPTB in tertiary care centers in India was between 30% and 53%, while the percentage estimated by the national control program in India for HIV-negative adults is between 15% and 20%, whereas the frequency is about 50-70% in patients infected with HIV.^{4, 5}

The Indian branch of Advocacy to Control TB Internationally (ACTION) says the country's TB control program is failing to take sufficient action to diagnose cases of the condition. Diagnosis of EPTB is not covered by RNTCP, and for treatment, these cases are forwarded to the DOTS regimen.⁶ EPTB continues to be a major public health threat even in the era of DOTS.

In general, the true prevalence of EPTB is grossly underreported.⁷ Recent studies suggested that sites of EPTB may vary according to geographic location, population and host factors, also literature on various forms of EPTB is scant and this lack of evidence is of particular concern in case of treatment guidelines.

With this background we conducted the present study to describe the basic demography, clinical presentations and treatment outcome of extra pulmonary TB.

MATERIALS AND METHODS: A cross sectional analytical study that reviewed routinely collected data from TB register of DOTS center at Sri Siddhartha Medical College, Agalakote, Tumkur, Karnataka, India from 1 November 2010 to 31 September 2013. All patients meeting our inclusion criteria during our study period were included in the study. The data collected was entered in Microsoft excel 2007 and analyzed using Epi Info 3.5.3. Descriptive statistics and Chi square test was used to test the association between variables of interest.

Source of information and definitions: The sources of information were the TB register.

In all the cases of EPTB, sputum examinations and chest radiographs were used to investigate the involvement of lung parenchyma.

The diagnosis of EPTB was based on the following Criteria:

(i) Suggestive clinical features, (ii) Positive microbiological or histopathological evidence of Mycobacterium tuberculosis from an extra pulmonary site, (iii) Radiological changes consistent with extra pulmonary TB followed by the decision of the treating MO to treat with a full course of anti-TB therapy⁸ and (iv) A satisfactory response to anti tuberculosis therapy.⁹

Extra pulmonary TB is defined as TB of any organ other than the lungs, such as the pleura (TB pleurisy), peripheral lymph nodes, intestines, genitourinary tract, skin, joints and bones, meninges of the brain, eye etc.

Investigations used for Diagnosis:

1. Fine needle aspiration cytology (FNAC) for lymph node.
2. FNAC and histopathology for skin, genitourinary and breast tuberculosis.
3. X-ray for bone tuberculosis.
4. Synovial biopsy for joint tuberculosis.
5. Cerebrospinal fluid CSF cytology and biochemistry for tubercular meningitis.
6. Computed tomography (CT) or magnetic resonance imaging (MRI) of brain.

7. MRI of spine.
8. Chest X ray.
9. Pleural fluid study for tubercular pleural effusion.
10. Ascitic fluid study for tubercular peritonitis.
11. RBS, HIV.

Methods of data Collection: The institutional ethical committee clearance was taken before the study. At the first step, all the records pertaining to extra pulmonary TB cases registered from November 2010 to December 2012 and followed up to September 2013 were separated and analyzed.

Inclusion Criteria:

- All new cases of EPTB put on DOTS between 1st November 2010 and 31st December 2012 and followed the patients for treatment outcome up to September 2013.
- Patients of age >15 years.

Exclusion Criteria:

- A patient diagnosed with both pulmonary and extra pulmonary TB
- Patients transferred in or transferred out during the study period.
- The patients who had completed their treatment at the time of start of study.

All the 406 subjects who fulfilled the inclusion criteria were included in the study.

The data was entered into a structured proforma. Study variables included: demographic (age, sex), clinical (site of extra pulmonary TB (EPTB)) and category of EPTB (new cases or retreatment cases) and treatment outcome. Treatment outcome of patients was evaluated in accordance with World Health Organization recommendation and classified as: treatment completed, default, treatment failure, death or other.

RESULTS: Among 747 cases registered for treatment of all forms of tuberculosis, 406 (54.35%) had EPTB.

Demographic, disease characteristics and treatment outcomes: Majority of 'EPTB patients' were aged 21–40 years (193, 47.50%) shows significant differences ($p < 0.05$) (Table 1), predominantly males ($n = 239$, 58.90%) constituting a significant difference ($p < 0.01$) with male: female ratio of 1.4:1 but lymph node and genitourinary TB most commonly affected females (Table 2).

Plural involvement (145, 35.70%) is the commonest site of EPTB followed by CNS involvement (79, 19.50%) and lymph node TB (73, 18%) (Table 3). HIV status was known, 29 (7.15%) were HIV-reactive, History of diabetes also known 71 (17.5%) were diabetic.

All patients were treated with the standard RNTCP treatment regimen, 395 (97.3%), and 11 (2.7%) cases received Category-I and Category-II respectively. Successful treatment outcome completed were observed in ($n = 323$, 82.07%) of cases. Default of 8.86%, failure of 0.24% and death 8.86% were also observed.

ORIGINAL ARTICLE

Association of demographic and clinical characteristics with treatment Outcomes: Successful treatment outcome, treatment completed were more in females (86.82%) than males (78.66%), aged 21-40 years (90.67%), in lymph node TB (87.67%) and in patients with category I treatment regimen (82.53%). Treatment after default was common in age group of 41-60 (14.87%), in males (10.04 %) compared to females (7.18%). Death was common in >61 years age group (37.25%) and in males (10.87%). Patient treated with category II, HIV-positive patients and diabetic patients had adverse treatment outcomes (Table 4, 5).

DISCUSSION: The study was done to know the demographic and clinical profile and treatment outcome of EPTB patients in this single center experience, wherein mainly patients from the rural area seek medical care. Among 747 cases registered for treatment of all forms of tuberculosis, 406 (54.35%) had EPTB more than pulmonary TB, Comparison of the number of PTB and EPTB cases in India by various studies has shown a higher incidence of EPTB cases in tertiary centers and medical college hospitals ^{6,10,11}. EPTB cases need more investigations and invasive procedures for definitive diagnosis and hence are reported more in tertiary centers under the program.

The majority of cases (193, 47.50 %) belonged to the age group of 21–40 years, who are young and working individuals, highlighting the socio-economic burden of extra pulmonary tuberculosis. Similar reports of higher incidence of EPTB in younger individuals are reported by other studies as well^{10, 11, 12}. In our study male to female ratio was about 1.4:1 which is similar to the study done by S Rama Prakash et al⁶ but lymph node and genitourinary TB was more common in females, similar to study done by Sunil Kumar Raina et al.¹³

The difference in the occurrence of EPTB by site between males and females is statistically significant in this study. The above two facts show the difference in the occurrence of various types of EPTB cases in different age groups and sexes and the predilection to involve one site over the other depending on the host factors as well.

Different studies show different pattern of EPTB site involvement. Some studies show pleural TB to be the most common type of EPTB whereas in other studies lymph nodes were found to involved most frequently. In the present study, pleural TB was found to be the most common type of EPTB followed by CNS and lymph node involvement this is similar to study done in Pereira, Colombia.¹⁴ Sunil Kumar Raina et al¹³ found that pleural TB is most frequent form of EPTB (61.64%) followed by lymph node (23.2%) and abdominal (9.3%).

In our study 97.29% cases were treated with category I regimen and only 2.71% cases were treated with category II, It is notable that the observed treatment outcome of category I regimen with a treatment completion of 82.01%, default of 8.86%, and failure of 0.24% and death of 8.86% was worse than that reported for the country under the past and the present RNTCP,¹ i.e., treatment completed 91%, default 6.4% and died 2% but our study results are similar to study done by Thushar KS et al¹⁵ shows treatment completion was achieved in 84.2% of EPTB patients.

Treatment outcome, treatment completion was more in the age group of 21-40 years (90.67%), in the females (86.82%) than males (78.66%) and lymph node TB (87.67%). EPTB patients treated with category II regimen had adverse treatment outcome, treatment completion of (63.63%) and treatment after default rate of (36.37%). Treatment after default was more common in the age group of 41-60(14.87%) and in males (10.04%) and those treated with category II regimen, strengthening the services for this vulnerable group improves the treatment outcome.

ORIGINAL ARTICLE

During this era of growing HIV epidemic, EPTB becomes more important as chances of developing EPTB in immuno-compromised patients are higher than their immuno competent counterparts.¹⁶In our study 7.5 % were HIV reactive with poor treatment outcome, treatment completed (72%), death(20%) and treatment after default (8%), Ades et al¹⁷ study shows similar results in HIV reactive patients. Diabetic patients had poor treatment outcome, with the treatment completed (67.60%), death (21.92%), needs further studies to know the association of treatment outcome of EPTB with diabetes.

Treatment of EPTB was effective to some extent. This provides support to the argument that EPTB can and should be more effectively addressed in the revised national TB control programme to reduce the adverse outcome. Currently, the focus is on the more infectious smear-positive pulmonary TB; however, as DOTS continues to expand, it has become clear that the ultimate control of TB cannot be achieved simply through treating only pulmonary cases.

Limitations of the Study: Being a study on a small sample size and in a tertiary care centre, the true prevalence of EPTB in general population is not reflected in this study. The data was collected primarily from TB register. So there is a probability of record bias.

CONCLUSION: The burden of EPTB is more among the productive age group and in males but lymph node and genitourinary TB most commonly affected females. This highlights the importance of strengthening the services for this vulnerable group. Plural effusion is the most common form of EPTB followed by CNS involvement and lymph node tuberculosis. Higher reporting of EPTB cases in tertiary centers necessitates the need for ongoing medical education for doctors and DOTS providers. A well-defined program specified protocols for the diagnosis and treatment of extra pulmonary tuberculosis cases should be more effectively addressed in RNTCP.

REFERENCES:

1. Wares F, Balasubramanian R, Mohan A, Sharma SK. Extra pulmonary tuberculosis: Management and control In: Tuberculosis control in India, . New Delhi: Elsevier; 2005, p 95-114.
2. Gonzalez OY, Adams G, Teeter LD, Bui TT, Musser JM, Graviss EA. Extra-pulmonary manifestations in a large metropolitan area with a low incidence of tuberculosis. *Int J Tuberc Lung Dis.* 2003 Dec; 7(12):1178-85.
3. World Health Organization. Tuberculosis programme: Framework for effective tuberculosis control. Geneva, Switzerland: WHO; 1994. p. 179.
4. Sharma SK, Mohan A. Extra pulmonary tuberculosis. *Indian J Med Res.* 2004; 120: 316–53.
5. Ozvaran MK, Baran R, Tor M, Dilek I, Demiryontar D, Arinc et al. Extra pulmonary tuberculosis in non-human immunodeficiency virus-infected adults in an endemic region. *Ann Thorac Med* 2007 Jul; 2 (3):118-21.
6. Prakasha SR, Suresh G, D'sa IP, Shetty SS, Kumar SG. Mapping the pattern and trends of extra pulmonary tuberculosis, *J Glob Infect Dis.* 2013 Apr; 5 (2): 54-9.
7. Zhang X, Andersen AB, Lillebaek T, Kamper-Jørgensen Z, Thomsen et al. Effect of sex, age, and race on the clinical presentation of tuberculosis: a 15-year population-based study. *Am J Trop Med Hyg.* 2011 Aug; 85 (2):285-90.

ORIGINAL ARTICLE

8. Ministry of health and family welfare; Govt of India. Revised National Tuberculosis Control Programme. 2004:5-7.
9. Sharma SK, Lawaniya S, Lal H, Singh UB, Sinha PK. DOTS centre at a tertiary care teaching hospital: Lessons learned and future directions. Indian J Chest Dis Allied Sci. 2004; 46: 251-6.
10. Arora VK, Gupta R. Trends of extra-pulmonary tuberculosis under Revised National Tuberculosis Control Programme: A study from South Delhi. Indian J Tuberc. 2006; 53:77-83.
11. Chennaveerappa PK, Siddharam SM, Halesha BR, Vittal BG, Jayashree N. Treatment outcome of tuberculosis patients registered at dots centre in a teaching hospital, South India. Int J Biol Med Res. 2011; 2: 487-9.
12. Patel AK, Patel T, Patel KR, Clinical profile of patients with extra pulmonary tuberculosis in Gujarat Int J Res Med. 2014; 3(1); 65-67
13. Vishav C, SK Raina, AK Bharadwaj et al.: Clinico-Epidemiological Profile of Extra Pulmonary Tuberculosis: A Report from a High Prevalence State of Northern India. Public Health Research 2012; 2 (6): 185-189
14. Arciniegas W, Orjuela DL. Extrapulmonary tuberculosis: a review of 102 cases in Pereira, Colombia. Biomedica 2006; 26 (1): 71-80
15. Tushar KS, Amitabha S, Sonali S et al a Follow-up Study on the Performance, Outcome and present status of patients treated Under 'RNTCP' in a slum area of Kolkata. IOSR Journal of Dental and Medical Sciences 2013; 6(3):63-67
16. Jones BE, Young SM, Antoniskis D, Davidson PT, Kramer F, Barnes PF. Relationship of the manifestations of tuberculosis to CD4 cell counts in patients with human immunodeficiency virus infection. Am Rev Respir Dis 1993; 148: 1292-7.
17. Ade S, Harries AD, Tre'buq A, Ade G, Agodokpessi G, et al. National Profile and Treatment Outcomes of Patients with Extra pulmonary Tuberculosis in Be'nin. PLoS ONE 2014 9(4): e95603.

Age group	Abdomen (%)	Bone (%)	Genitourinary (%)	Lymph (%)	CNS (%)	Others (%)	Pleura (%)	Total number of EPTB (%)
<20	5(7.35)	0(0)	1(14.28)	8(10.95)	15(18.98)	1(16.66)	11(7.58)	41(10.10)
21-40	32(47.05)	12(42.85)	4(57.14)	47(64.38)	36(45.56)	3(50)	59(40.68)	193(47.50)
41-60	21(30.88)	11(39.28)	2(28.58)	16(21.91)	19(24.05)	1(16.66)	51(35.17)	121(29.80)
>60	10(14.70)	5(17.85)	0(0)	2(2.74)	9(11.39)	1(16.66)	24(16.55)	51(22.70)
TOTAL	68	28	7	73	79	6	145	406

Table 1: Age wise distribution of EPTB

Chi square value: 31.37 p value: 0.02

ORIGINAL ARTICLE

Gender	Abdomen (%)	Bone (%)	Genitourinary (%)	Lymph (%)	CNS (%)	Others (%)	Pleura (%)	TOTAL (%)
Female	28(41.17)	12(42.85)	4(57.15)	50(68.50)	25(31.65)	2(33.33)	46(31.72)	167(41.10)
Male	40(58.83)	16(57.15)	3(42.85)	23(31.50)	54(68.35)	4(66.67)	99(68.28)	239(58.90)
TOTAL	68	28	7	73	79	6	145	406

Table 2: Gender wise distribution of EPTB patients

Chi square value: 31.73 p value: 0.001

Site of EPTB	Number (%)
Lymph node	73 (18.00)
Pleura	145 (35.70)
Abdomen	68 (16.70)
CNS	79 (19.50)
Bone	28 (6.90)
GU	7 (1.70)
Others	6 (1.50)
Investigation	
FNAC	80 (19.70)
Pleural fluid analysis	145 (35.70)
Ascitic fluid analysis	68 (16.70)
CSF Analysis	77 (19.00)
Biopsy	06 (1.40)
CT scan	02 (0.50)
Montoux test	03 (0.70)
MRI	15 (3.70)
X ray	10 (10.10)

Table 3: Different sites of EPTB and investigations used for diagnosis

ORIGINAL ARTICLE

Characteristic	Treatment outcome				Chi square value	p value
	Treatment completed (%)	Death (%)	Treatment after default (%)	Failure (%)		
Age group						
<20	37(90.24)	2(4.87)	2(4.87)	0(0)	76.8	0.001
21-40	175(90.67)	7(3.62)	11(5.69)	0(0)		
41-60	95 (78.51)	8 (6.61)	18(14.87)	0(0)		
>61	26 (50.98)	19 (37.25)	5 (9.80)	1(1.96)		
Sex						
Female	145(86.82)	10(5.98)	12(7.18)	0(0)	5.05	0.17
Male	188(78.66)	26(10.87)	24(10.04)	1(0.41)		
Religion						
Hindu	308(82.35)	33(8.82)	33(8.82)	0(0)	11.77	0.008
Muslim	25(78.12)	3(9.37)	3(9.37)	1(3.12)		
Site of EPTB						
Abdominal	52(76.47)	7(10.29)	9(13.23)	0(0)	15.14	0.65
Bone	23(82.14)	1(3.57)	4(14.28)	0(0)		
Genito urinary	6(85.71)	0(0)	1(14.28)	0(0)		
Lymph	64(87.67)	2(2.73)	7(9.58)	0(0)		
Central nervous system	63(79.74)	11(13.92)	5(6.32)	0(0)		
Others	5(83.33)	0(0)	1(16.66)	0(0)		
Plural	120(82.75)	15(10.34)	9(6.20)	1(0.68)		
HIV						
Non-Reactive	312(82.75)	31(8.22)	33(8.75)	1(0.26)	4.05	0.25
Reactive	18(72)	5(20)	2(8)	0(0)		
DIABETES						
Non-diabetic	285(85.07)	21(6.26)	28(8.35)	1(0.29)	17.53	0.001
Diabetic	48(67.60)	15(21.12)	8(11.26)	0(0)		

Table 4: Association between various characteristic and treatment outcome

CATEGORY OF TREATMENT	Treatment completed (%)	Death (%)	Treatment after default (%)	Treatment after failure (%)	TOTAL
Category I	326(82.53)	36(9.11)	32(8.10)	1(0.25)	395(97.29)
Category II	7(63.63)	0(0)	4(36.37)	0(0)	11(2.71)
TOTAL	333 (82.01)	36(8.86)	36(8.86)	1(0.24)	406

Table 5: Association between category of treatment and Treatment outcome of EPTB patients

Chi square value: 11.13 p value: 0.01

AUTHORS:

1. Siddeswaraswamy P.
2. Shubhakara K.
3. Gnanendra D. M.
4. Mahesh S. Hoolageri
5. Indushree T.

PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of General Medicine, Sri Siddhartha Medical College, Agalakote, Tumkur, Karnataka, India.
2. Assistant Professor, Department of General Medicine, Sri Siddhartha Medical College, Agalakote, Tumkur, Karnataka, India.
3. Assistant Professor, Department of General Medicine, Sri Siddhartha Medical College, Agalakote, Tumkur, Karnataka, India.
4. Assistant Professor, Department of Community Medicine, Sri Siddhartha Medical College, Agalakote, Tumkur, Karnataka, India.

5. Resident, Department of General Medicine, Sri Siddhartha Medical College, Agalakote, Tumkur, Karnataka, India.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Siddeswaraswamy P,
Assistant Professor,
Department of General Medicine,
Sri Siddhartha Medical College,
Agalakote, Tumkur, Karnataka, India.
Email: swamyp26@gmail.com

Date of Submission: 18/08/2014.

Date of Peer Review: 19/08/2014.

Date of Acceptance: 26/08/2014.

Date of Publishing: 01/09/2014.