

## Research Article

# A study of culture confirmed cases of extrapulmonary tuberculosis in a tertiary care hospital from Western Maharashtra, India

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**Received:** 02 March 2015

**Revised:** 07 March 2015

**Accepted:** 31 March 2015

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## ABSTRACT

**Background:** The proportion of cases of extrapulmonary tuberculosis (EPTB) has increased in India in recent years. Since the disease can affect virtually all organs, has an atypical clinical presentation, the clinical samples for laboratory diagnosis are sometimes difficult to procure, the confirmation of diagnosis is often delayed. With this background, the present study was undertaken to identify the culture confirmed cases of EPTB from clinically suspected cases, to identify the patient related factors associated with the disease and common sites of involvement in these patients.

**Methods:** The study comprised of 143 patients clinically suspected to have EPTB. Relevant clinical samples were collected from these patients according to the anatomical site involved. Confirmation of diagnosis was done by mycobacterial culture using Lowenstein Jensen (L-J) medium.

**Results:** Out of 143 specimens, 42 (29.37%) were culture positive for mycobacteria (culture confirmed cases). Higher proportion of EPTB was found in females (36.92%) than males (23.08%). Maximum patients of EPTB belonged to the age group of 21-40 years (22 cases out of 57, 38.60%). Out of the 17 HIV positive patients, 6 (35.29%) were culture positive for mycobacteria. Maximum culture positivity was found with pus samples from bone and joint (44.12%) followed by lymph nodes (42.42%).

**Conclusion:** It was found that female sex, younger age (below 40 years) and HIV infection were found to be commonly associated with extrapulmonary tuberculosis. While many studies report TB lymphadenitis as the most common form of EPTB, in our study bone and joint was found to be the commonest site involved in the disease followed by lymph node. Since EPTB has become more common than previously and is difficult to diagnose, it is important to have greater clinical suspicion for the disease and to take appropriate laboratory help for its confirmation.

**Keywords:** Extrapulmonary tuberculosis (EPTB), Tuberculosis (TB), Culture confirmed EPTB, Mycobacteria, HIV

## INTRODUCTION

Tuberculosis remains an important global health problem, causing considerable morbidity and mortality worldwide even after a lot of research and control programs. 1/3<sup>rd</sup> of the world's population is estimated to be latently infected by *M. tuberculosis*.<sup>1</sup> The deadly synergy of HIV and TB

and emergence of multi-drug resistant *M. tuberculosis* (MDR-TB), have further complicated tuberculosis control.<sup>2</sup> Before the emergence of HIV pandemic, more than 85% of tuberculosis cases were limited to lungs. This proportional distribution is substantially different among persons with HIV infection, because extrapulmonary involvement tends to increase in frequency if the immune function is compromised.<sup>2</sup> In

India, the number of newly notified cases of extrapulmonary tuberculosis (EPTB) has increased from 170783 in 2005 to 226965 in the year 2011.<sup>3</sup> In recent times only limited numbers of studies were published on extrapulmonary tuberculosis, most of these were case reports and limited to HIV infected individuals.<sup>2</sup> Though it is estimated that EPTB constitutes 15 to 20 per cent of tuberculosis cases in general practice among HIV-negative adults in India, a higher proportion of EPTB cases have been documented in tertiary care centres.<sup>4</sup>

The definitive diagnosis of EPTB essentially depends on culture of mycobacteria.<sup>5</sup> There is lack of newer diagnostic techniques for tuberculosis in many centers in India. Moreover, the diagnosis of EPTB itself is difficult. The focus of tuberculosis control program has been on pulmonary variety as extrapulmonary tuberculosis is comparatively less common. It has a wide spectrum of clinical presentation depending upon the anatomical site involved, and presents a diagnostic dilemma. Many times, the tuberculosis etiology is not even suspected and it may not even figure in the list of probable diagnosis.<sup>6</sup> Since the disease can affect virtually all organs, has an atypical clinical presentation, the clinical samples for laboratory diagnosis are sometimes difficult to procure, the microbiological confirmation of diagnosis is often delayed.<sup>4</sup> With this background, the present study was carried out to identify the culture confirmed cases of EPTB from clinically suspected cases, to identify the commonly associated patient related factors with the disease and common sites of involvement in these patients.

## METHODS

This study was an open label prospective study carried out in compliance with the protocol in the microbiology department of a medical college & tertiary care hospital in Western Maharashtra, India, after approval from the institutional ethics committee, from January 2012 to November 2014.

143 patients in all age groups and both sexes, irrespective of their HIV status, who were strongly suspected to have extrapulmonary tuberculosis, were included in the study. Relevant clinical samples were collected from these patients such as urine, lymph node aspirates, biopsies, surgically resected tissues, pus samples, cerebrospinal fluid (CSF), other fluids like pleural, ascitic or synovial fluids and stool. Aseptically collected specimens like fluids (CSF, pleural, pericardial, synovial, ascitic fluids, and aspirated pus) were processed directly without digestion & decontamination whereas contaminated specimens like urine, stool etc. were decontaminated by appropriate decontamination procedures before smear and culture.<sup>7,8</sup>

Direct smears of all samples were examined for Acid Fast Bacilli (AFB) after staining with Ziehl Neelsen (Z-N) method. Culture was done using Lowenstein Jensen (L-J)

medium. Cultures were examined for mycobacterial growth and pigment production every day for the 1<sup>st</sup> week (for rapidly growing mycobacteria) and later at weekly intervals for a minimum of 10 weeks. The cultures showing any type of growth were examined for presence of acid fast bacilli by preparing direct smears from the colonies and Z-N staining. Patients whose culture were tested positive for AFB were considered as culture confirmed cases of EPTB; however the possibility of EPTB could not be totally ruled out in culture negative cases.

## RESULTS

Different clinical samples were received from 143 patients (78 males and 65 females). Out of these patients, 42 (29.37%) were culture confirmed cases of EPTB (18 males and 24 females). Maximum number of patients included in the study belonged to the age group between 21- 40 years (57 patients). Moreover, maximum number of culture confirmed cases of EPTB (22 cases, 38.60%) were also observed in the same age group.

Out of total 143 patients, 17 were HIV positive, 82 were HIV negative and in the remaining 44 patients, HIV status was not known. Of these 17 HIV positive patients, 6 (35.29%) were culture positive for EPTB.

Out of 143 patients, 22 patients had previous history of pulmonary tuberculosis of which, 6 (27.27%) were culture confirmed cases of EPTB. Table 1 shows the distribution of patients according to different characteristics such as sex, age groups, HIV status and past history of pulmonary tuberculosis and their culture positivity rates.

**Table 1: Distribution of patients according to sex, age group, HIV status & past history of pulmonary tuberculosis and their mycobacterial culture positivity rates.**

Characteristic	Subgroup	Total No. of patients (143)	Culture confirmed cases (42)
Sex	Male	78	18 (23.08%)
	Female	65	24 (36.92%)
Age group (years)	0-20	21	07 (33.33%)
	21-40	57	22 (38.60%)
	41-60	48	10 (20.83%)
	>60	17	03 (17.65%)
HIV status	Positive	17	06 (35.29%)
	Negative	82	23 (28.05%)
	Status not known	44	13 (29.54%)
Past H/O PTB	Yes	22	06 (27.27%)
	No	121	36 (29.75%)

Different samples which were received included pus samples from bone & joints (34), pus from abscesses

(25), fluids such as pleural (12), pericardial (1), ascitic fluids (6), cerebrospinal fluid (CSF) (4), aspirates from lymph nodes (33), tissues samples (7), stool samples (5) and urine (16). Out of 34 pus samples from bone & joint, 15 were positive for mycobacterial culture (44.11%, maximum culture positivity). For lymph node aspirates, the culture positivity rate was 42.42%, with 14 samples being culture positive out of 33. The rates of isolation of mycobacteria from various clinical specimens are shown in Table 2.

**Table 2: Mycobacterial culture positivity in different clinical samples from suspected cases of EPTB.**

Specimen	No. of samples received (143)	Culture positive (42)	Positivity rate (%)
Pus from bone & joint	34	15	44.12
Lymph node aspirates	33	14	42.42
Pus from abscesses	25	06	24
Pleural fluid	12	02	16.67
Pericardial fluid	01	00	00
Ascitic fluid	06	01	16.67
CSF	04	00	00
Tissues	07	01	14.28
Urine	16	03	18.75
Stool	05	00	00

## DISCUSSION

The present study was an open label prospective study carried out in a tertiary care hospital from January 2012 to November 2014. The study included 143 patients who were clinically suspected to have extrapulmonary tuberculosis. Different clinical specimens were received from these patients according to the anatomical site involved in the disease. Out of these 143 specimens, 42 (29.37%) were culture positive for mycobacteria (culture confirmed cases of EPTB). The proportional distribution of culture confirmed EPTB cases was varied, especially with age and sex of the patients. Out of the 143 patients included in the study, 78 were males and 65 were females. Out of 78 male patients, 18 were culture positive for mycobacteria (23.08%) whereas out of 65 females, 24 were culture positive (36.92%). We found more culture confirmed cases of EPTB in female population as compared to males. Similar findings were reported in two different studies carried out by Zhenhua Y et al.<sup>2</sup> and Lowieke AM et al.<sup>9</sup> where higher proportion of EPTB was found in females than males.

In our study it was found that the disease was more common in younger age group. Out of the 57 patients from the age group of 21-40 years included in the study, 22 were confirmed cases of EPTB (38.60%). In 21 patients who were less than 20 years of age, EPTB was confirmed in 7 cases (33.33%). Some other studies,<sup>2,10</sup>

have also reported similar finding, where higher proportion of EPTB cases was observed in younger patients.

HIV infected persons are at increased risk for primary or reactivation tuberculosis and for second episodes of tuberculosis from exogenous reinfection.<sup>4</sup> In the era before the HIV pandemic, and in studies involving immunocompetent adults, it has been observed that EPTB constituted about 15 to 20 per cent of all cases of tuberculosis. In HIV positive patients, EPTB accounts for more than 50 per cent of all cases of TB.<sup>4</sup> Out of 143 patients included in our study, HIV status was known for 99 patients; 17 patients being HIV positive and 82 being negative. Comparison of the proportion of patients with extrapulmonary tuberculosis between HIV positive and HIV negative cases was limited to the 99 patients whose HIV status was known. Out of 17 HIV positive patients, 6 were having EPTB (35.29%) whereas out of 82 HIV negative patients, 23 were having EPTB (28.05%). The proportion of culture confirmed EPTB cases was higher in case of HIV positive individuals. Similar observation was reported in the study carried out by Zhenhua Y et al.<sup>2</sup> where EPTB was found more commonly in HIV positive patients than HIV negative.

Out of 22 patients who gave positive past history of pulmonary tuberculosis, 6 patients (27.27%) had EPTB. Of the 121 patients who did not give such history, 36 patients (29.75%) had EPTB. The proportion of EPTB cases was not found to be higher in patients with previous history of pulmonary tuberculosis.

In the present study, bone and joint was found to be the commonest site affected by tuberculosis followed by lymph nodes. Out of the 34 specimens from bone and joint, 15 (44.12%) were mycobacterial culture positive. For lymph nodes the culture positivity was 42.42%, with 14 samples being culture positive out of 33. Similar finding has been reported in other studies<sup>2</sup> where bone and joint was the commonest site affected in EPTB while some authors<sup>4</sup> report TB lymphadenitis as the most common form of EPTB.

## CONCLUSION

In this study, it was found that female sex, younger age (below 40 years) and HIV infection were commonly associated with extrapulmonary tuberculosis. While many studies report TB lymphadenitis as the most common form of EPTB, in our study bone and joint was found as the commonest site involved in the disease followed by lymph node. Since the disease has become more common than previously and is difficult to diagnose, it is important to have greater clinical suspicion for extrapulmonary tuberculosis and to take appropriate laboratory help for its confirmation. As the disease seems to have a greater association with delayed reactivation of latent infection,<sup>11,12</sup> the measures for prevention and treatment

of latent TB infection in the goal of tuberculosis control needs to be reinforced.

## ACKNOWLEDGEMENTS

The authors are thankful to the faculties of department of microbiology, Ashwini rural medical college, Kumbhari, Solapur (Maharashtra), India, for their cooperation and support for this study. The authors also acknowledge the immense help received from the scholars whose articles are cited and included in references of this manuscript.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the institutional ethics committee*

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DOI: 10.5455/2320-6012.ijrms20150509

**Cite this article as:** Nakate PC, Kashetty VA, Ghatole MP. A study of culture confirmed cases of extra-pulmonary tuberculosis in a tertiary care hospital from Western Maharashtra, India. Int J Res Med Sci 2015;3:1077-80.