

Original Research Article

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Retrospective Analysis of Clinicopathological Characteristics of Osteo-articular Tuberculosis in Different Suspected Samples – A Single Institutional Study of Indian Patients

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ABSTRACT

Osteoarticular (spinal and extra spinal) tuberculosis consist of 1% to 5% of all cases of tuberculosis and 10% to 18% of EPTB. The diagnosis of osteoarticular tuberculosis is often delayed due to insidious onset, lack of constitutional and pulmonary involvement, lack of awareness, or due to lack of characteristic early radiographic findings. The purpose of this analysis is to provide an update on the diagnostic and therapeutic recommendations for osteoarticular TB. In this retrospective study, laboratory and hospital records were collected, evaluated and analyzed for all the patients with suspected osteoarticular TB. Data collection was done during the period of 3 years from 2017 to 2020, from the CBNAAT center, AIIMS Patna with suspected sample for confirmation of TB. Out of 62 suspected patients tested, 9 (14.52%) were detected positive by CB NAAT test for osteoarticular TB. Among these 9 osteo-articular TB cases 4 (44.44%) were Rifampicin sensitive, 4 (44.44%) were Rifampicin resistant and 1 (11.11%) case was indeterminate for Rifampicin. 62 suspects were identified having mean age at the presentation was 33.72 years with age ranges from 4 to 71 years, male to female ratio was 1.8:1 (40:22). The manifestations were articular (arthritis or arthralgia in 54 cases, comprises as 41 were monoarthritis, 9 were oligoarthritis and 4 with polyarthralgia) followed by tenosynovitis (n=13) and tuberculous osteomyelitis (n=3). 2 patients were detected with disseminated TB. Most common clinical symptoms were pain (n=48), followed by swelling of the involved site (n=14). 27 (43.54%) patients presented with fever whereas previous history of TB was shown in 8 patients. 13 (20.96%) patients were associated with concurrent pulmonary TB. 8 (12.9%) patients had lymph node enlargement. A definite diagnosis of osteoarticular TB was made in 9 (14.51%) patients and rest 53 (85.48%) are probable TB patients. Manifestations of osteoarticular TB occurs at any age but in this study most common age group affected were in between 10 to 30 years. Tenosynovitis and/or oligoarthritis may be a presenting manifestation but chronic monoarthritis is the most common presentation. The diagnosis of osteoarticular TB should not be discouraged in the absence of fever. This study makes aware about the burden of osteoarticular tuberculosis cases and higher risk of development of multidrug resistant (MDR) osteoarticular TB. Thus early diagnosis of MDR in osteoarticular TB and start of specific anti-tubercular therapy help into get an earlier and better outcome.

Keywords

Arthritis,
Osteoarticular
Tuberculosis,
CBNAAT, Rifampicin
resistant tuberculosis,
MDR- TB

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Introduction

Tuberculosis (TB) is the leading health problem all over the world till now but in the developing country like in India had highest TB burden accounting for one-fourth (25%) of global TB cases. Global TB report of W.H.O stating that there are estimated 10 million new cases in year 2018⁽¹⁾. India, as a developing country, contributes a major proportion (27%) of the global TB burden with estimated 2.69 million new cases in year 2018^(1, 2).

TB primarily involves the lungs, but extra-pulmonary TB (EPTB) cases also play a major role. EPTB contributes to 15% to 20% of all cases of TB and in India prevalence of EPTB varies from 8.3% to 13.1% in various districts according to cohort analysis by central TB division, Ministry of Health & Family Welfare in 2002^(3, 4).

Osteoarticular (spinal and extra spinal) tuberculosis contributes 1%–5% of all cases of tuberculosis and 10% to 18% of EPTB, where spine being the most common location contributing 50% of osteoarticular TB cases^(5,6,7,8).

TB arthritis usually presents as slowly progressive chronic monoarthritis affecting weight-bearing joints, particularly knee and hip in association with nonspecific constitutional symptoms⁽⁹⁾. The radiological manifestations are characterized by narrowing of joint space, osteoporosis around the joint and peripherally located bone erosion⁽¹⁰⁾. The association between osteoarticular TB and rheumatologic diseases were recognized and this association is vice versa^(10,11). TB can be directly affecting the osteoarticular system, and on the other hand, patients with rheumatic diseases are predisposed to TB infection due to a variety of reasons.

The manifestations of osteoarticular TB can be classified into four groups:

Direct osteoarticular tubercular infection – such as spondylitis, septic arthritis, osteomyelitis, pyomyositis, bursitis, subcutaneous abscesses, and tenosynovitis

TB infections in patients with rheumatic diseases

Drug-induced syndromes – antitubercular treatment (ATT)-induced lupus, tenosynovitis, hyperuricemia, gout, etc.

Reactive phenomenon such as Poncet's disease, erythema nodosum, erythema induratum, and amyloidosis⁽¹²⁾.

Anti-tubercular drug therapy is the mainstay treatment of osteoarticular tuberculosis. Resolution of osteoarticular TB and preservation of the function depends upon the time of starting of anti-tubercular drug therapy. At least 6 to 9 months of anti-tubercular drug therapy is needed for resolution of osteoarticular TB but continued to more duration in case of children's or immunocompromised individuals.

Till now, limited studies have been made for osteoarticular tuberculosis⁽¹³⁾. The present study is for the evaluation of current epidemiology of osteoarticular tuberculosis, especially in this region of the country with respect to age, sex, site of involvement and associated clinical features.

Materials and Methods

Ethical statement

The protocol of this study was approved by Institute Ethics Committee, AIIMS Patna (ref. no. AIIMS/Pat/IEC/2020/439)

Patients

In this retrospective study, laboratory and hospital records were collected and evaluated from for all the patients which comes under inclusion criteria during the period of 3 years from 01-04-2017 to 31-03-2020, and reported to CBNAAT center, AIIMS Patna with suspected sample for bacteriological confirmation of TB. These patients record were evaluated in respect to their age, sex, site of involvement, type of samples for CBNAAT test, associated pulmonary or other extra-pulmonary tuberculosis and associated clinical features.

Inclusion criteria

All the suspected cases of osteoarticular TB (irrespective of their age, gender, caste, religion, socio-economic status, duration and severity of illness), in which sample received for CBNAAT centre at the microbiology department, AIIMS Patna.

Exclusion criteria

All the patients of osteoarticular TB in which sample was not taken for CBNAAT.

Definite diagnosis of osteoarticular TB was done by microbiological confirmation of tubercle bacilli either by AFB staining, CBNAAT, culture or by molecular test.

Probable TB was considered if there was no direct evidence of AFB (either in AFB staining, CBNAAT, culture or molecular test) but histopathological, radiological, clinical and/or serological evidence suggested tubercular infection and the patient responded to empirical anti-tubercular drug therapy.

Statistical analysis

Microsoft Excel sheet (Version 2011) was used to collect and plot the relevant data

(Percentages, ratio or mean). Demographic characteristics were demonstrated by descriptive statistics (frequency and mean) and represented by tables and pie graphs. Categorical variables will be reported as numbers and percentages.

Results and Discussion

A total of 62 suspected samples were collected from different department of AIIMS PATNA during 2017 to 2020. Distribution of samples as follows, 22 from knee aspirate (including synovial fluid), 1 knee synovial tissue, 3 ankle aspirates, 21 hip tissue synovium (including hip joint fluid aspirate), 7 pott's spine biopsy, 6 vertebral aspirate, 1 vertebral disc biopsy and 1 from sternoclavicular joint fluid aspirate. Out of these 62 suspected patients, 9 (14.52%) were CBNAAT positive. Among these 9 CBNAAT confirmed positive cases, 4 (44.44%) were resistant to Rifampicin, 4 (44.44%) were sensitive to Rifampicin and 1 (11.11%) was indeterminate for Rifampicin (Figure 1).

The mean age of the suspected patients was 33.72 years with range from 4 years to 71 years and male to female ratio was 1.8:1 (40:22) (Figure-2 and Figure-3). The manifestations includes articular (arthritis or arthralgia in 54 cases, comprises as 41 were monoarthritis, 9 were oligoarthritis and 4 with polyarthralgia) followed by tenosynovitis (n=13), tuberculous osteomyelitis (n=3) (Table 1). 2 patients were detected with disseminated TB.

Most common clinical symptoms was pain (n=48) followed by swelling of the involved site (n=14). 27 (43.54%) patients presented with fever whereas previous history of TB was shown in 8 patients (Table 2). 13 (20.96%) patients were associated with concurrent pulmonary TB. 8 (12.9%) patients had lymph node enlargement (Table 3). A

definite diagnosis of osteo-articular TB was made in 9 (14.51%) patients and rest 53 (85.48%) are probable TB patients.

Table 1 shows the pattern and number of articular involvement in musculoskeletal tuberculosis Joints involved. Table 2 demonstrates the clinical features of patients

with osteoarticular tuberculosis-Parameter number (%) = Pain (%) 48 (77.42), Swelling (%)14 (22.58), Fever (%) 27 (43.54), Previous TB (%) 8 (12.90), Arthritis (%) 54 (87.09), Tenosynovitis (%) 13 (20.96), Osteomyelitis (%) 3 (4.84), Associated lymphadenopathy (%) 8 (12.90).

Table.1 Pattern and number of articular involvement in osteoarticular tuberculosis

Joints involved	Total	Monoarthritis	Oligoarthritis	Polyarthritis
Knee	19	15 (78.94%)	3 (15.78%)	1 (5.26%)
Hip	17	11 (64.70%)	4 (23.53%)	2 (11.76%)
Spine	14	11 (78.57%)	2 (14.29%)	1 (7.14%)
Ankle	3	3 (100%)		
Sternoclavicular	1	1 (100%)		

Table.2 Clinical features of patients with osteoarticular tuberculosis

Parameter	Number	Percentage (%)
Pain (%)	48	77.42
Swelling (%)	14	22.58
Fever (%)	27	43.54
Previous TB (%)	8	12.90
Arthritis (%)	54	87.09
Tenosynovitis (%)	13	20.96
Osteomyelitis (%)	3	4.84
Associated lymphadenopathy (%)	8	12.90

Table.3 Comparison of demographic and clinical features of osteoarticular tuberculosis

	Present study	Prasad <i>al.</i> ⁽¹⁴⁾	<i>et</i>	Muangchan <i>al.</i> ⁽¹⁵⁾	<i>et</i>	Huang <i>al.</i> ⁽¹⁶⁾	<i>et</i>
Total number of patients (musculoskeletal TB)	62	51		99		51	
Mean age (years)	33.72	33.4		50.9		58.9	
Male:female	1.8:1	1.1:1		08:1		2.18:1	
Spinal involvement (%)	22.58	None		66.7		None	
Associated pulmonary lesion (%)	20.96	3.9		30.3		51	
Associated lymph node involvement (%)	12.90	23.5		-		-	
Constitutional symptoms (fever, weight loss) (%)	43.54	17.6		38.4		8	
Comorbidities	No	No		Yes		Yes	

Fig.1 CB-NAAT result

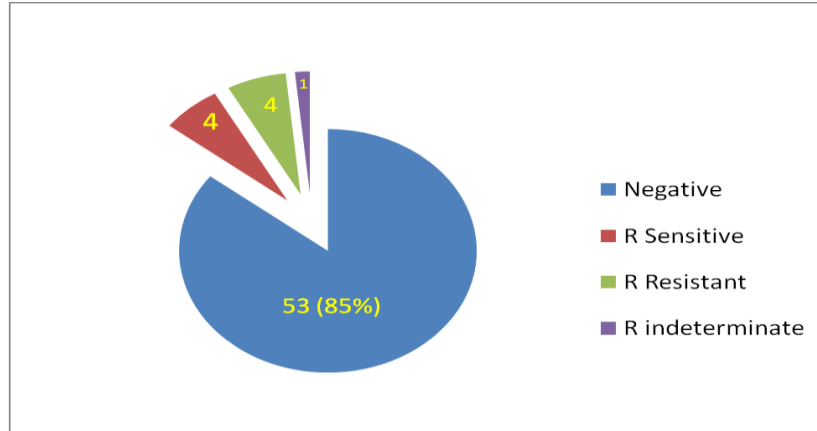


Fig2 Age-wise distribution of the lesions

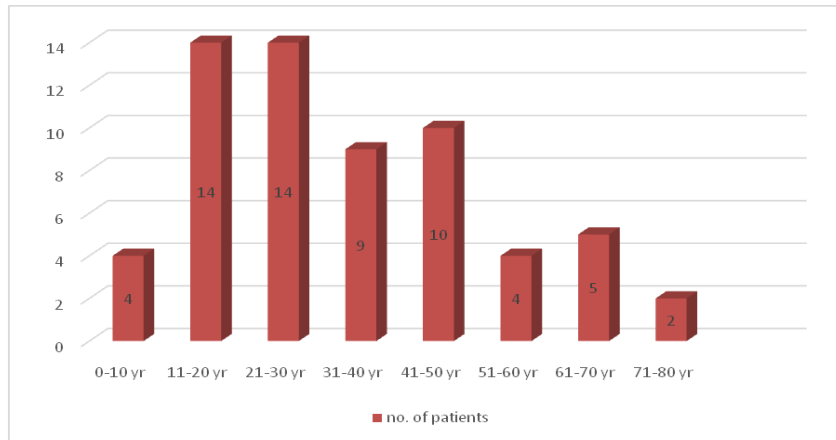
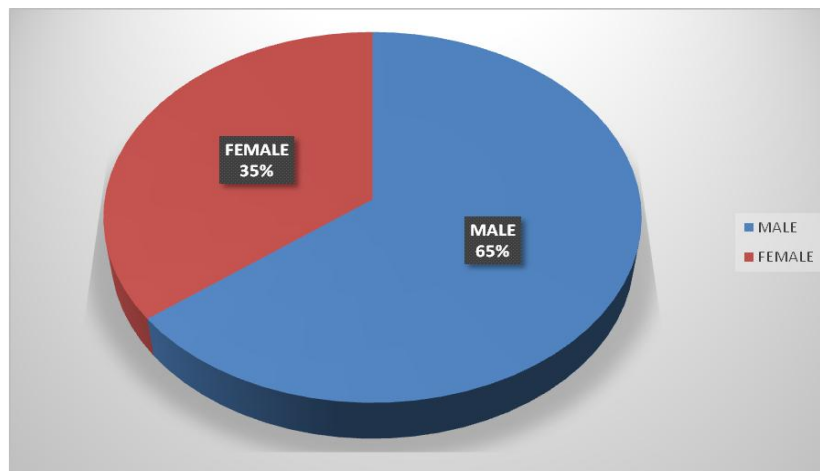


Fig.3 Male: Female ratio



India being an endemic country for TB, osteoarticular TB comprises major part of (10%–18%) of EPTB, and their common symptoms may mimic other inflammatory arthritis. In this retrospective analysis, finding summarized as – osteoarticular TB affects patients of all age groups (children to elderly), chronic monoarthritis remains the most common clinical presentation (66.13% of cases), oligoarthritis was observed in 14.52% cases followed by tenosynovitis (20.96% of cases). Constitutional symptom like a fever and pain was observed in 43.54% and 77.42% of the cases respectively. Active pulmonary TB was observed in 13(20.96%) cases in this study.

These findings are consistent to the previous study conducted by Prasad *et al.*,⁽¹⁴⁾ Muangchan *et al.*,⁽¹⁵⁾ and Huang *et al.*⁽¹⁶⁾. The mean age at presentation in this study was 33.72 years, which is comparable to study conducted by Prasad *et al.*,⁽¹⁴⁾ (i.e 33.4), but study conducted by Muangchan *et al.*,⁽¹⁵⁾ and Huang *et al.*,⁽¹⁶⁾ shows mean age at presentation were in higher age group *i.e* 50.9 years and 58.9 years respectively. A study by Solagberu BA *et al.*,⁽¹⁷⁾ in Nigeria also showed that osteoarticular TB most prevalent during 20 to 30 years of age (mean age: 27.3 years); a similar study by Jabalameli M *et al.*,⁽¹⁸⁾ from Iran reported that 10 to 20 years of age group were most commonly affected, but study by Houshian *et al.*,⁽¹⁹⁾ in Denmark found that the most common patients were of more than 60 years of age. The reason for this discrepancy may be either due to endemicity, referral bias or different ethnic, and local environmental factors that predispose to musculoskeletal TB.

In osteoarticular TB, we have observed knee as the most common joint involved followed by hip and ankle and this finding was comparable with the study conducted by Kramer *et al.*,⁽¹¹⁾ and Garrido *et al.*,⁽²⁰⁾ which

findings were ‘Osteoarticular TB with single joint involvement was mostly weight-bearing joints and especially knee and hip joints were affected the most’.

Oligoarticular involvement has been reported in <10% of the cases and pain and swelling of the affected joints were the predominant presenting complaints in the study conducted by Franco-Paredes *et al.*,⁽¹²⁾ and Al-Saleh Set *al.*,⁽²¹⁾ were comparable to the study.

A study from Thailand by Muangchan *et al.*,⁽¹⁵⁾ found that in patients which have compromised conditions for infections (such as having diabetes, fracture, on systemic corticosteroids or immunosuppressive drugs etc.) have more chance to develop extra spinal osteoarticular TB.

In the study bacteriological diagnosis of osteoarticular TB (by CBNAAT and AFB stain) has been made in 9 (14.51%) patients which were comparable to study conducted by Rai DK *et al.*,⁽⁸⁾ in which 18% and 11.4% of EPTB patients showed bacteriological and CBNAAT positive respectively.

Out of 9 bacteriological diagnosed osteoarticular TB, 4 (44.44%) were Rifampicin resistance but the study conducted by Singh RP *et al.*,⁽²²⁾ shows nearly 20% patients were Rifampicin resistance among all CBNAAT positive patients. This differences may be due to local environmental factors, demographic factors and/or due to other factors such as in the study conducted by Singh RP *et al.*,⁽²²⁾ included all TB cases (i.e. pulmonary TB and EPTB) where as in this study only osteo-articular TB had considered.

In conclusion this present study, we would like to emphasize that osteoarticular manifestations of TB can be associated with any age group. Although, the most common presentation is chronic monoarthritis and

oligoarticular involvement, with or without tenosynovitis is also not uncommon. Primary musculoskeletal involvement in the absence of systemic symptoms may delay the diagnosis. Careful search for lymphadenopathy and/or past, family history or history of contact may provide clues for the diagnosis. Thus, the importance of the newer diagnostic techniques in diagnosing osteoarticular TB becomes relevant like CB-NAAT test, multiplex PCR utilizing two target genes specific for *M. tuberculosis*. Routine availability of these kinds of newer diagnostic tests will help the clinicians in diagnosing osteoarticular TB quickly and confidently start on the ATT for efficient and early cure.

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