

## Extra-Spinal Osteoarticular Tuberculosis: A Retrospective Analysis of 103 Cases

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**ABSTRACT:** Introduction. Many studies in the literature deals with epidemiology, diagnosis and management of spinal tuberculosis but there is scant amount of such data for extraspinal osteoarticular TB. Material and methods. Demographic patient data like age, sex, bone and joint involved, side involved, duration of symptoms was noted. All suspected cases of extra-spinal musculoskeletal TB with positive acid-fast bacilli (AFB) staining or positive cartridge based nucleic acid amplification test (CBNAAT) or histopathological evidence of granulomatous infection and minimum 1 year follow up after completion of 12-month ATT were included in the study. Outcome evaluation was done on the basis of residual pain, range of motion of joint along with deformity of the affected part, if any. Results. A total of 103 patients (55 males, 48 females) were analyzed. The mean duration of treatment was 14.2±2.8 months. The mean age of the patients at presentation was 30.5±18.5 years. The most common site affected was the ankle joint followed by hip and knee. 95 cases (92.2%) were diagnosed by histopathological examination of synovial tissue or material obtained from core biopsy. 90 cases (87.3%) were treated conservatively on oral drugs only while 13 cases (12.7%) were treated operatively. Outcome after completion of ATT were graded as good in 46 (46.9%), fair and poor each in 26 patients (26.5%). Conclusion. Extraspinal osteoarticular TB can be managed effectively by 12-month ATT if diagnosed early. Some cases with advanced arthritis can be salvaged with implant arthroplasty or arthrodesis under cover of ATT.

**KEYWORDS:** Tuberculosis, extraspinal, histopathological, cartridge based nucleic acid amplification test

### Introduction

Developing countries contribute to around 95% of total tuberculosis (TB) case load worldwide [1]. India being a developing country and second most populous in the world has a large number of TB patients with a reported 24% global prevalence and 20% global TB mortality [1]. Due to poor socioeconomic conditions, rapid population growth, illiteracy and inadequate treatment, the number of TB cases in India continue to rise.

After pulmonary TB, the next most common system involved is musculoskeletal. Musculoskeletal TB comprise 2% of all and 11% of extra-pulmonary cases [2]. In musculoskeletal system, spine and extra-spinal sites are involved equally [3]. Extra spinal involvement may be in the form of peripheral arthritis or synovitis, osteomyelitis, tenosynovitis or bursitis [3]. The primary sites from which skeletal system is secondarily affected are usually lung, kidney, lymph nodes or viscera. Many cases of extra-spinal TB present late to clinicians resulting in advanced joint destruction and increasing morbidity. Diagnosis may also be delayed due to paucibacillary presentation, indolent course, non-specific imaging signs and occasionally, absence of adequate tissue for histopathology. Although in endemic areas, diagnosis can be

made by clinico-radiological correlation, histopathological confirmation is mandatory before starting treatment. If diagnosed early, and started on effective anti-tubercular therapy (ATT), complete healing is possible in 90-94% of cases [4]. Delayed or ineffective treatment can be detrimental to the joint and debilitating to the patient [1].

Many studies in the literature deals with epidemiology, diagnosis and management of spinal tuberculosis but there is scant amount of such data for extraspinal osteoarticular TB [3,5]. Such data is helpful in determining favored sites of involvement, common clinical features, age group, diagnostic difficulties and management dilemmas like duration of chemotherapy and need & extent of surgery. Such data is also helpful in determining natural course of disease and explaining prognosis. Keeping these facts in mind we decided to retrospectively analyse all the patients diagnosed as extraspinal skeletal TB which may help to further our knowledge on diagnosis, management and prognosis of this common clinical entity in the developing world.

### Materials and methods

It was a retrospective clinical study conducted at a tertiary care national teaching hospital situated in northern India from March 2014 to December 2017. Electronic patient records, files and radiological investigations of

all the diagnosed cases of extra-spinal musculoskeletal TB were analyzed after obtaining proper ethical clearance from institution review board. Demographic patient data like age, sex, bone and joint involved, side involved, duration of symptoms was noted. Patient's socioeconomic data such as economic status, and place of residence (hills or plains) was also recorded. Patients staying at an altitude of 1000 metres and above were classified to be from hilly region [6]. Clearance from the institutional ethical clearance board was obtained for this study. All suspected cases of extra-spinal musculoskeletal TB with positive acid-fast bacilli (AFB) staining or positive cartridge based nucleic acid amplification test (CBNAAT) or histopathological evidence of granulomatous infection and minimum 1 year follow up after completion of 12 month ATT were included in the study. Patients suffering from underlying immunocompromised state like HIV, AIDS, chemotherapy and radiotherapy for unrelated malignancies and concomitant spinal tuberculosis and rheumatological diseases were excluded.

All the patients with clinical suspicion of extraspinal musculoskeletal TB were subjected to hematological tests ESR, CRP, and complete and differential leucocyte counts. Plain AP and lateral radiographs of the involved joint and extremity as well as chest x-ray was also obtained. Tuberculin skin sensitivity testing was done in all the patients under 14 years of age. Cases with suspicion of clinical effusion were aspirated and sent for CBNAAT, AFB staining, Gram staining and culture sensitivity. Cases in which joint fluid wasn't aspirable mini-incisional open biopsy of the synovium was undertaken and sent for same tests along with histopathological examination. Core biopsy was taken in cases in which there was frank extraarticular bony involvement. Cases with subtle clinical and x-ray findings but with raised ESR/CRP were further investigated by contrast enhanced MRI. Final diagnosis of tuberculosis was based upon either positive CBNAAT or AFB stain or histopathological evidence of granulomatous infection. No attempt was made to differentiate between typical and atypical mycobacteria. After definite diagnosis, 4 drug oral ATT was started according to modified Revised National Tuberculosis Control Program (RNTCP) regimen [5]. Two months of intensive therapy with isoniazid (5mg/kg), rifampin (10mg/kg), pyrazinamide (25mg/kg) and

ethambutol (15mg/kg) is instituted followed by 10 months of 3 drug therapy with isoniazid, rifampin and ethambutol. After completion of intensive phase, patient was assessed clinicoradiologically and by blood parameters like ESR, CRP, CBC and liver function test (LFT). Further follow up was done at 3 monthly intervals till 12 months. After 12 months ATT was stopped if clinical symptoms have subsided and blood parameters have been normalized. In those cases, in whom clinical symptoms were still persisting and blood parameters were abnormal, MRI was done and further 6 months of three drug ATT was continued and opinion of infectious disease specialist was taken to rule out MDR TB or atypical mycobacteria. Outcome evaluation was done on the basis of residual pain, range of motion of joint along with deformity of the affected part, if any (Table 1).

**Table 1. Parameters used for outcome assessment and its interpretation**

Parameters
1. Residual pain
2. Reduced ROM of neighbouring joints
3. Deformity
Interpretation
Good-none of parameters present
Fair-any one parameter present
Poor-more than one parameter present

Descriptive statistical analysis of the collected data was done and presented in the form of charts and tables. Continuous variables are presented as mean±SD and categorical variables are presented as absolute numbers and percentages.

## Results

**Table 2. Table showing age distribution of patients with increased incidence in younger age group**

Age	0-18 years	18-45 years	>45 years
n (%)	28 (27.2%)	53 (51.5%)	22 (21.3%)

A total of 103 patients (55 males, 48 females) fulfilling the inclusion criteria were analysed starting from March 2014 to December 2017. Five patients were lost to follow up, so 98 patients were available for final analysis. The mean duration of treatment was 14.2±2.8 months (12-24months). The mean age of the patients at presentation was 30.5±18.5 years (4-76 years) (Table 2).

**Table 3. Depiction of the sites involved along with its clinical presentation**

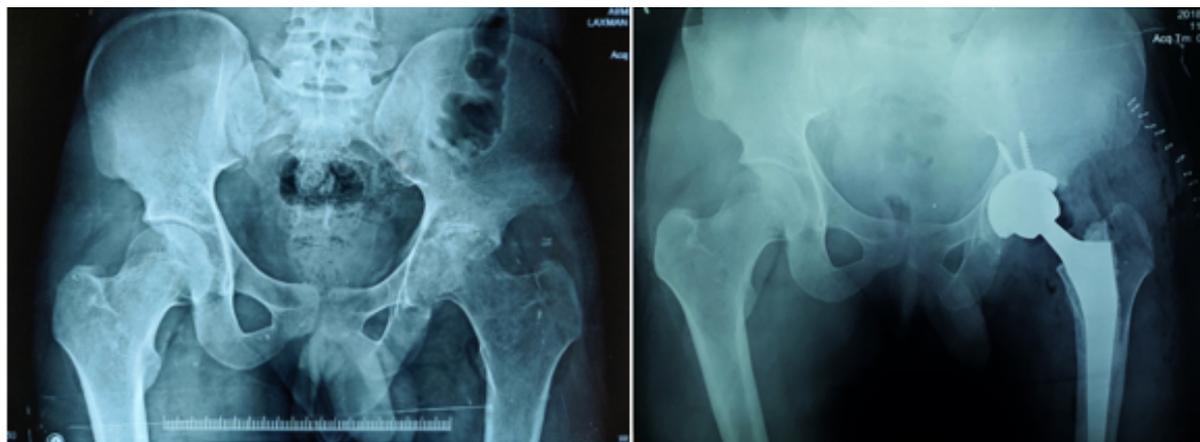
Sites	Numbers (%)	Clinical Presentation
Ankle	26 (25.2%)	Pain (n=11), Synovitis (n=9), Arthritis (n=6)
Hip	21 (20.4%)	Arthritis (n=9), Pain (n=7), Synovitis (n=3), limp (n=2)
Knee	20 (19.4%)	Pain (n=7), Synovitis (n=5), triple deformity (n=5), Chronic and recurrent swelling (n=3)
Wrist	15 (14.6%)	Synovitis (n=7), Pain (n=4), Arthritis (n=4)
Elbow	6 (5.8%)	Swelling (n=5), Discharging sinus (n=1)
Osteomyelitis	6 (5.8%)	Discharging sinus (n=4), swelling (n=2)
Shoulder	4 (3.9%)	Recurrent swelling (n=3), arthritis (n=1)
Dactylitis	2 (1.9%)	Chronic swelling with pain (n=2)
Foot	2 (1.9%)	Swelling (n=2)
Sternum	1 (1%)	Pain (n=1)

The most common site affected was the ankle joint (n=26) followed by hip (n=21) and knee (n=20) (Table 3). The most common symptoms noted were pain, swelling and restricted motion of the involved joint with the mean duration from start of symptoms to presentation in hospital being 6.75±3.2 months. Majority of patients (n=73, 70.9%) were residents of hilly altitude more than 1000 metres. Also, majority of the patients (n=83, 80.5%) belonged to lower socioeconomic status [6]. 95 cases (92.2%) were

diagnosed by histopathological examination of synovial tissue or material obtained from core biopsy. In 28 cases (27.2%), positive results of CBNAAT from the aspirated joint fluid was noted. 90 cases (87.3%) were treated conservatively on oral drugs only while 13 cases (12.7%) were treated operatively. Of the 13 cases managed operatively there were 6 cases of tubercular hip involvement who underwent total hip arthroplasty (Table 4) (Fig.1).

**Table 4. Showing surgical intervention in the patients with the duration of ATT at which surgery was performed**

Joints	Numbers	Surgery Performed	Timing of surgery with respect to ATT
TB Hip Arthritis	6	Total hip arthroplasty	4 months (n=4), 8 months (n=2)
Triple Deformity of Knee	5	Knee Arthrodesis	3 months (n=3), 6 months (n=2)
Wrist TB Arthritis	2	Wrist Arthrodesis	10 months (n=2)



**Fig.1. Radiographs showing advanced arthritis of left hip joint which was diagnosed as tuberculosis by core biopsy from proximal femur which was treated by total hip arthroplasty under the cover of ATT after 4 months duration of therapy**

In 5 patients with tubercular arthritis of knee joint, radical debridement and arthrodesis using ring external fixator was done. In 2 patients with wrist involvement and destruction of multiple carpals wrist arthrodesis was done. Six patients were noncompliant to drug therapy and modified and prolonged regime was started in

consultation with infectious disease consultant. 20 patients had complications associated with chemotherapy (Table 5). Outcome after completion of ATT were graded as good in 46 (46.9%), fair and poor each in 26 patients (26.5%).

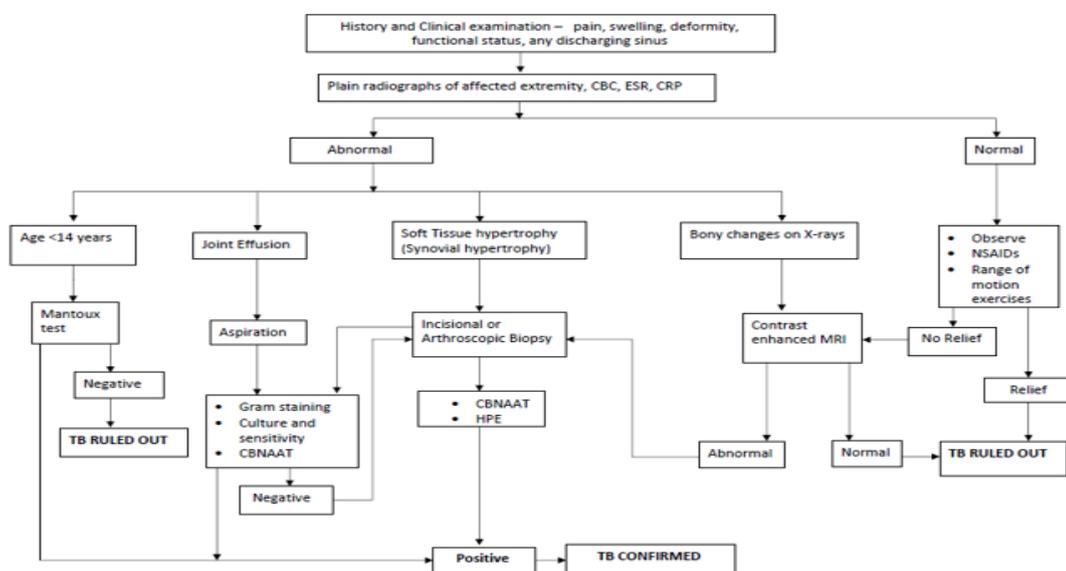
**Table 5. Complications noted during the course of ATT and its management**

Complications	Numbers	Management
ATT induced hepatitis	17	Modified ATT (Streptomycin, Isoniazid, Ethambutol, Levofloxacin) till LFT normalizes, followed by routine ATT
Rifampicin resistance	2 (ankle TB)	Modified regime [Levofloxacin, Kanamycin, Ethambutol, Cycloserine, Ethionamide, Pyrazinamide (intensive)+Levofloxacin, Ethambutol, Cycloserine, Ethionamide (continuation)]
Isoniazid induced psychosis	1	Isoniazid stopped, antipsychotics
Concurrent pulmonary TB	1	ATT

**Discussion**

Tuberculosis is still a public health concern in developing countries of Asia and Africa associated with significant morbidity. In the present study, majority of patients (51.5%) were young in the age group 18-45. There was nearly equal distribution among the two sexes. Chandir et al in a study from Pakistan found more prevalence of the disease among the females which was attributed to the poor nutritional status and poor access to healthcare in a male dominated society [7]. The most common symptom was pain and swelling of the affected part in our study which was also noted by other studies from developing countries [8]. The most common site of involvement in was ankle followed by hip and knee. Other studies in literature have shown hip joint to be the most common site of involvement [9]. The increased frequency of ankle involvement in our study may be attributed to the fact that many a times, ankle pain and swelling is diagnosed as sprain or minor injuries but strong suspicion of TB many

a times lead to diagnosis of tubercular arthritis. There were 8 cases of tubercular osteomyelitis, 2 involving metacarpals, 2 of metatarsals, 3 of the diaphysis of femur and 1 of the shaft of the humerus. All of these were successfully treated conservatively with good functional outcome. Delay between start of symptoms and presentation to hospital was found to be 6.7±3.2 months (range 5-14 months). Other studies have also shown this duration to be 5 to 12 months [5,8]. The reason for the delay maybe subacute onset of symptoms, ignorance and poor socioeconomic status of the patients. One important finding of the study is that 70.9% of the patients hailed from higher altitude of Himalayan region. The reason for the same maybe lack of hygiene, illiteracy, overcrowding and difficult access to healthcare facilities. The government agencies and non-governmental organizations in these geographical regions may find this data useful in increasing public awareness of the social issues involved and providing better healthcare services.



**Fig.2. Flowchart depicting approach to a patient of suspected extraspinal musculoskeletal tuberculosis**

A pre-defined algorithm for the management of all cases of extra-spinal TB was followed (Fig.2).

A high index of suspicion is required in any case complaining of pain, discomfort or restricted range of motion in the joint in the endemic areas.

As part of initial work up, x-rays of the involved joint and extremity, chest x-ray and biochemical tests such as CBC, ESR and CRP should be done.

Cases having clinically evident effusion or synovitis should be aspirated and sent for gram staining, AFB staining, bacterial culture and sensitivity and CBNAAT. Cases having positive CBNAAT should be started on ATT.

Those cases with negative CBNAAT report should undergo confirmation of diagnosis by synovial or core biopsy.

Our study showed CBNAAT positivity in 28 cases. Some cases exhibit no radiological clues with persistent symptoms after few days of anti-inflammatory drug therapy.

Such cases should undergo MRI of the involved joint or extremity to look for synovitis/periosteal changes/osseous edema.

This further helps in pointing out the site for biopsy.

76 patients in this study had undergone MRI as an adjunct and we feel that although the cost is prohibitive but it is an important tool in initial diagnosis and further follow up.

The gold standard of diagnosis of TB is histopathological examination showing caseating granulomas along with giant cells [9].

92.2% of our cases showed the above-mentioned findings on biopsy. The mainstay of treatment in TB is appropriate ATT.

Complete resolution of infection with return of function of the extremity maybe expected with adequate ATT.

72 of the 98 patients in our study had complete eradication of infection as evident by biochemical and/or MRI evaluation after 12 months of ATT.

46 of these had good results. 26 patients had poor results and it may be due to delay in presentation to hospital when advanced arthritic changes have already set in. ATT was continued for a minimum of 12 months in our patients.

Literature suggests ATT for a minimum of 12-18 months with increased duration in children, concomitant connective tissue disorders and in immunocompromised [4,10].

Studies have also shown 7-9 month regimen containing rifampicin are as effective as

12-18 month regimen without containing rifampicin [3,11].

We recommend, based on our experience 12 months of ATT for all these cases. In those cases, not responding favorably to 12-month ATT alternatives such as atypical mycobacteria or noncompliance to therapy should be kept in mind.

13 patients in our group underwent definitive treatment for tubercular arthritis during the course of ATT. The procedures performed were total hip arthroplasty (THA) (6), knee arthrodesis (5) and wrist arthrodesis (2). Studies have shown that definitive procedures performed under appropriate ATT cover coupled with extensive debridement of the diseased synovium are safe [12,13,14].

A few studies reporting THA in active TB have been published [15,16].

We performed 6 THA in cases of advanced hip arthritis without any added complication or reactivation of disease at minimum 1-year follow up. Same principles of THA surgery can be applied to knee and wrist arthrodesis.

Like all retrospective clinical studies, this study has some limitation. There was no uniformity in the site of involvement. It may be possible that disease behaves differently according to the site of involvement. Larger series concentrating on specific joint are required to further address the issues in diagnosis, requirement of surgery and duration of ATT.

No attempt was made to differentiate typical from atypical mycobacteria. Differentiating this is important to prevent unnecessary and inappropriate in some cases.

Our minimum follow-up was 1 year, so studies with longer follow up is desirable.

## Conclusion

Extraspinal osteoarticular TB can be managed effectively by 12-month ATT if diagnosed early.

Some cases with advanced arthritis can be salvaged with implant arthroplasty or arthrodesis under cover of ATT.

## Abbreviations used

TB Tuberculosis

ATT Anti tubercular therapy

AFB Acid fast bacilli

CBNAAT Cartridge based nucleic acid amplification test.

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