

# Musculoskeletal manifestations of tuberculosis: An observational study

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## ABSTRACT

**Background:** Data of musculoskeletal manifestations of tuberculosis (TB) are limited to case reports, series, or retrospective studies. Therefore, we conducted this study to create awareness among doctors about musculoskeletal manifestations of TB. **Materials and Methods:** This was a prospective observational study conducted at a referral TB Hospital in North India in September and October 2016. The aim of our study was to study musculoskeletal manifestations of TB. We included patients who had active TB as per the World Health Organization 2010 criteria. Patients with other chronic illnesses were excluded. A detailed history, examination, and appropriate investigations (blood, urine, serological, and radiological) of the 100 consecutive patients fulfilling the inclusion criteria were recorded. **Results:** The mean age of patients was  $32.16 \pm 12.93$  years. Male-to-female ratio was 43:57. The mean duration of disease was  $6.85 \pm 8.83$  months. Of the 100 patients, 60 (60%) had pulmonary TB. The mean duration of antitubercular therapy was  $1.79 \pm 1.34$  months. Fibromyalgia was classified in 21 (21%) patients, polyarthralgia was seen in 9 (9%), Pott's spine in 7 (7%), osteomyelitis in 4 (4%), and scleritis in 2 (2%) patients. Uveitis, tenosynovitis, erythema induratum, subcutaneous abscess, and dactylitis were seen in 1 (1%) patient each. In 21 patients who had fibromyalgia, 11 developed fibromyalgia with the second episode of TB amounting to 60.75% patients. **Conclusion:** This is the first prospective study to look at the musculoskeletal manifestations of TB. Patients with active TB were found to have various rheumatological manifestations.

**Keywords:** Fibromyalgia, osteomyelitis, Poncet's, Pott's spine, rheumatology, Tuberculosis, uveitis

## Introduction

Tuberculosis (TB) infection is a major public health problem around the world. In recent years, there has been a rise in the prevalence of TB in many parts of Europe due to migration of people from countries that are endemic with TB and various socioeconomic factors. The musculoskeletal system is involved in 1%–3% of the cases, and of these only 50% involve the extraspinal bones and soft tissues.

The association of TB and rheumatologic diseases is bidirectional.<sup>[1-3]</sup> In this association, *Mycobacterium tuberculosis* (MTB)

can directly infect the musculoskeletal system. Further, patients with rheumatologic diseases are predisposed to develop TB due to the immunosuppressive state, the disease itself, or drug-induced immunosuppression.

Direct manifestations of TB musculoskeletal involvement include spondylitis, septic arthritis, osteomyelitis, myositis, bursitis, subcutaneous abscesses, or tenosynovitis.<sup>[3]</sup> Immunologic reactions such as reactive arthritis (Poncet's), erythema nodosum, erythema induratum, or secondary amyloidosis may also manifest as a tubercular rheumatism.<sup>[4-7]</sup> In addition, drugs used in the management of TB can also lead to arthropathy or tendinopathy, especially with the use of rifampin or fluoroquinolones,<sup>[8-10]</sup> drug-induced lupus (DILE) by isoniazid or rifampin,<sup>[11,12]</sup> and arthralgias and gout due to pyrazinamide.<sup>[13]</sup> Secondary

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fibromyalgia or chronic pain syndrome may be a manifestation of TB.

These rheumatological or musculoskeletal manifestations may be the presenting symptoms of TB. TB is a common illness in developing country like India, and if not detected at an early stage, it may lead to increased morbidity and mortality. Thus, it is important to have knowledge about these musculoskeletal manifestations for the treating doctors. Data of musculoskeletal manifestations of TB are limited to case reports, series, or retrospective study. To our knowledge, there is no prospective study addressing this issue. Therefore, we conducted this study to create awareness among doctors about musculoskeletal manifestations of TB.

## Materials and Methods

It was a prospective observational study which was conducted at Rajan Babu Tuberculosis Hospital, Kingsway Camp, New Delhi, in the months of September and October 2016. Consecutive patients from outpatient and inpatient department of pulmonology were recruited irrespective of the duration of antitubercular therapy.

We included patients who were a confirmed case of active TB as per World Health Organization 2010 criteria.<sup>[14]</sup> Patients with chronic illness except TB were excluded.

Patients fulfilling the inclusion criteria were recruited for the study. A detailed history, examination, and appropriate investigations (blood, urine, and radiological) of the 100 consecutive patients fulfilling the inclusion criteria were recorded.

Musculoskeletal manifestations of TB which were looked at in patients are summarized in Table 1.

Diagnosis of Poncet's disease was made clinically by oligo or polyarticular involvement in the presence of TB.<sup>[15,16]</sup> The classification of fibromyalgia was made by American College of Rheumatology 1990<sup>[17]</sup> classification criteria for fibromyalgia.

The patient was classified as gout according to American College of Rheumatology–European League Against Rheumatism 2015 classification criteria for Gout.<sup>[18]</sup>

The patient was classified as DILE in the presence of lupus-like symptoms (commonly fever, musculoskeletal involvement, and serositis) which was temporally related to continuous drug exposure (>1 month) which resolves with cessation of the offending drug and the patient may have positive antinuclear antibody and anti-histone antibodies with negative antibodies to dsDNA.<sup>[19]</sup>

The diagnosis of the rest of musculoskeletal manifestations was clinical, microbiological, radiological, histopathological, joint aspiration, ophthalmological, or serological depending on the manifestation.

## Statistical analysis

Age and duration of disease are represented as mean  $\pm$  standard deviation.

## Results

The prospective study was carried out at Rajan Babu Tuberculosis Hospital. Consecutive patients who presented to the inpatient and outpatient department of respiratory and TB department were recruited. Those patients who fulfilled the inclusion and exclusion criteria were included in the study. The baseline characteristics of the study cohort are shown in Table 2. Many patients were found to have rheumatological manifestations. Table 3 shows rheumatological manifestations in patients with TB.

Rheumatological manifestations such as septic arthritis, DILE, Poncet's arthritis, tendinopathy, amyloidosis, gout, erythema nodosum, and myositis were not seen in any patient.

Fibromyalgia was classified in 21 (21%) patients. Of these 21 patients, 11 patients developed fibromyalgia in patients with second episode of TB amounting to 60.75% patients developing

**Table 1: Musculoskeletal manifestations of tuberculosis**

Spondylitis	Uveitis
Septic arthritis	Tendinopathy
Osteomyelitis	Reactive arthritis
Myositis	Erythema nodosum
Subcutaneous abscesses	Erythema induratum
Tenosynovitis	Amyloidosis
Gout	Drug-induced lupus
Poncet's disease	Fibromyalgia or chronic pain syndrome
Arthralgia	

**Table 2: Baseline characteristic of the study group**

Parameters	n=100
Age in years (mean $\pm$ standard deviation)	32.16 $\pm$ 12.93
Male:females	43:57
Disease duration in months (mean $\pm$ standard deviation)	6.85 $\pm$ 8.83
Tuberculosis type	
Pulmonary	60 (60%)
Pleural	17 (17%)
Abdominal	9 (9%)
Cervical Lymphadenopathy	8 (8%)
Pott's spine	4 (4%)
Others*	2 (2%)
Episode of tuberculosis	
First episode	83 (83%)
Second episode	17 (17%)
ATT category	
Category 1	74 (74%)
Category 2	23 (23%)
Modified ATT	3 (3%)
Duration of ATT in months (mean $\pm$ standard deviation)	1.79 $\pm$ 1.34

ATT, antitubercular therapy; \*Eye tuberculosis (uveitis), breast lump

**Table 3: Rheumatological manifestations in patients with tuberculosis (n=100)**

Parameters	No. of patients (%)
Pott's spine	7 (7%)
Fibromyalgia	21 (21%)
Polyarthralgia	9 (9%)
Scleritis	2 (2%)
Uveitis	1 (1%)
Osteomyelitis	4 (4%)
Tenosynovitis	1(1%)
Erythema induratum	1 (1%)
Subcutaneous abscess	1 (1%)
Dactylitis	1(1%)

fibromyalgia who had second episode of TB. Of these 21 patients of fibromyalgia, 12 were female.

## Discussion

Our study is the first prospective study of its kind to look at rheumatological manifestations in patients with active TB. Fibromyalgia is the second most common rheumatic disease. The prevalence is from 2% to 8% of the population depending on the diagnostic criteria used.<sup>[20]</sup> Fibromyalgia may also occur with other chronic diseases such as osteoarthritis, rheumatoid arthritis, and lupus. Prevalence of fibromyalgia ranges from 10% to 30%<sup>[21]</sup> in patients with chronic rheumatic disorders. TB is a chronic infection. In our patients with active TB, fibromyalgia was seen in 21% of patients with 60.75% with second episode of TB developing fibromyalgia. There has been no study which has evaluated the incidence or prevalence of fibromyalgia in patients with TB.

Pott's spine is a common form of extrapulmonary TB. Around half the cases of skeletal TB are Pott's spine. In total, 1%–2% of total TB cases are attributable to Pott's disease.<sup>[22]</sup> In our cohort, Pott's spine was seen in 7% of patients with 2% having only Pott's spine and the remaining 5% having pulmonary TB with Pott's spine.

Polyarthralgia was observed in 9 (9%) of our study cohort. Arthralgia can be caused by antitubercular drugs as isoniazid<sup>[23]</sup> and pyrazinamide.<sup>[23]</sup> All our patients who developed polyarthralgia were on isoniazid or pyrazinamide.

Osteomyelitis was seen in 4 (4%) patients. Tubercular osteomyelitis occurs in 1%–2% of all cases of TB and 10% of all cases of extrapulmonary TB.<sup>[24]</sup>

Scleritis was seen in 2 (2%) of our patients. Donahue<sup>[25]</sup> found 1.4% ocular TB in 10,000 patients with primary pulmonary TB in the United States. In a study recently reported at Srilanka,<sup>[26]</sup> of the total of 2130 patients with TB, ocular TB was diagnosed in 23 patients among whom episcleritis and inflammatory scleral nodule were observed in 1 patient each.

Uveitis, dactylitis, tenosynovitis, subcutaneous abscess, and erythema induratum were seen in 1 (1%) each in patients with active TB.

However, a recent study from Japan by Wakabayashi et al.<sup>[27]</sup> showed an increasing frequency of tuberculous uveitis. Of 189 referred uveitis cases, 6.9% were found to have tuberculous uveitis. According to a study by Mercanti *et al.*,<sup>[28]</sup> 7% of patients with uveitis in Italy had presumed tuberculous etiology. In India, where pulmonary TB is endemic, TB was the etiology of uveitis in 5.6%<sup>[16]</sup>–10.1%.<sup>[29]</sup>

Dactylitis was seen in 1 (1%) of our patient. As shown in studies, 7% of children with pulmonary TB may develop dactylitis.

In our study cohort, tubercular tenosynovitis was seen in 1 (1%) patient. Our patient developed tenosynovitis of the extensor tendons of right wrist.

Subcutaneous abscess and erythema induratum were seen in 1 (1%) patient, who developed breast abscess. The overall incidence of cutaneous TB among all forms of TB is approximately 1%–2%. The nodules are usually seen around the ankles.<sup>[30]</sup>

Limitation of our study: It was a single-center study with relatively small number of subjects. Patients with extrapulmonary TB were quite less when compared with pulmonary TB.

## Conclusion

This is the first prospective study to look at musculoskeletal manifestations of TB. Patients with active TB were found to have secondary fibromyalgia (21%) and polyarthralgia (9%). Other manifestations that were seen were Pott's spine, dactylitis, scleritis, uveitis, tenosynovitis, erythema induratum, and subcutaneous abscess.

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## Conflicts of interest

There are no conflicts of interest.

## References

1. Rothschild BM, Martin LD, Lev G, Bercovier H, Bar-Gal GK, Greenblatt C, *et al.* Mycobacterium tuberculosis complex DNA from an extinct bison dated 17,000 years before the present. *Clin Infect Dis* 2001;33:305-11.
2. Santos AL, Roberts CA. A picture of tuberculosis in young Portuguese people in the early 20<sup>th</sup> century: A multidisciplinary study of the skeletal and historical evidence. *Am J Phys Anthropol* 2001;115:38-49.
3. Kramer N, Rosenstein ED. Rheumatologic manifestations of tuberculosis. *Bull Rheum Dis* 1997;46:5-8.
4. Southwood T, Gaston JSH. The molecular basis of Poncet's

- disease? *Br J Rheumatol* 1990;29:491.
5. Chowdhary V, Aggarwal A, Misra R. Multifocal tuberculous dactylitis in an adult. *J Clin Rheumatol* 2001;8:35-7.
  6. El-Hennawy AS, Goldstein M, Nicastri A. Renal amyloidosis secondary to tuberculosis of cecum. *Nephron* 2002;92:708-10.
  7. Khaliq Y, Zhanel GG. Fluoroquinolone-associated tendinopathy: A critical review of the literature. *Clin Infect Dis* 2003;36:1404-10.
  8. Lipsky BA, Baker CA. Fluoroquinolone toxicity profiles: A review focusing on newer agents. *Clin Infect Dis* 1999;28:352-64.
  9. Siegal FP, Eilbott D, Burger H, Gehan K, Davidson B, Kaell AT, *et al.* Dose-limiting toxicity of rifabutin in AIDS-related complex: Syndrome of arthralgia/arthritis. *AIDS* 1990;4:433-41.
  10. Berning SE, Iseman M. Rifamycin-induced lupus syndrome. *Lancet* 1997;349:1521-2.
  11. Shakoor N, Michalska M, Harris CA, Block JA. Drug-induced systemic lupus erythematosus associated with etanercept therapy. *Lancet* 2002;359:579-80.
  12. Scott JT. Drug induced gout. *Baillieres Clin Rheumatol* 1991;5:39-60.
  13. Sanchez-Albisua I, Vidal ML, Joya-Verde G, del Castillo F, de Jose MI, Garcia-Hortelano J. Tolerance of pyrazinamide in short course chemotherapy for pulmonary tuberculosis in children. *Pediatr Infect Dis J* 1997;16:760-3.
  14. World Health Organization. Treatment of Tuberculosis: Guidelines. 4<sup>th</sup> ed. WHO/HTM/TB/2009.420. Geneva: World Health Organization; 2010.
  15. Abdulaziz S, Almoallim H, Ibrahim A, Samannodi M, Shabrawishi M, Meeralam Y, *et al.* Poncet's disease (reactive arthritis associated with tuberculosis): Retrospective case series and review of literature. *Clin Rheumatol* 2012;31:1521-8.
  16. Garg S, Malaviya AN, Kapoor S, Rawat R, Agarwal D, Sharma A. Acute inflammatory ankle arthritis in northern India - Lofgren's syndrome or Poncet's disease? *J Assoc Physicians India* 2011;59:87-90.
  17. Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL, *et al.* The American College of Rheumatology 1990 criteria for the classification of fibromyalgia. *1990;33:160-72.*
  18. Neogi T, Jansen TL, Dalbeth N, Fransen J, Schumacher HR, Berendsen D, *et al.* 2015 Gout classification criteria: An American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Ann Rheum Dis* 2015;74:1789-98.
  19. Sarzi-Puttini P, Atzeni F, Capsoni F, Lubrano E, Doria A. Drug-induced lupus erythematosus. *Autoimmunity* 2005;38:507-18.
  20. Vincent A, Lahr BD, Wolfe F, Clauw DJ, Whipple MO, Oh TH, *et al.* Prevalence of fibromyalgia: A population-based study in Olmsted County, Minnesota, utilizing the Rochester Epidemiology Project. *Arthritis Care Res (Hoboken)* 2013;65:786-92.
  21. Phillips K, Clauw DJ. Central pain mechanisms in the rheumatic diseases: Future directions. *Arthritis Rheum* 2013;65:291-302.
  22. Beek LA, van der Werf MJ, Richter C, Borgdorff MW. Extrapulmonary tuberculosis by nationality, The Netherlands, 1993-2001. *Emerg Infect Dis* 2006;12:1375-82.
  23. Gholami K, Kamali E, Hajiabdolbagh MI, Shalviri G. Evaluation of anti-tuberculosis induced adverse reactions in hospitalized patients. *Pharm Pract* 2006;4:134-8.
  24. Rieder HL, Snider Jr DE, Cauthen GM. Extrapulmonary tuberculosis in the United States. *Am Rev Respir Dis* 1990;141:347-51.
  25. Donahue HC. Ophthalmologic experience in a tuberculosis sanatorium. *Am J Ophthalmol* 1967;64:742-8.
  26. Yasaratne BMGD, Madegedara D, Senanayake NS, Senaratne T. A case series of symptomatic ocular tuberculosis and the response to anti-tubercular therapy. *Ceylon Med J* 2010;55:1.
  27. Wakabayashi T, Morimura Y, Miyamoto Y, Okada AA. Changing pattern of intraocular inflammatory disease in Japan. *Ocul Immunol Inflamm* 2003;11:277-86.
  28. Mercanti A, Parolini B, Bonora A, Lequaglie Q, Tomazzoli L. Epidemiology of endogenous uveitis in north-eastern Italy: Analysis of 655 new cases. *Acta Ophthalmol Scand* 2001;79:64-8.
  29. Salimpour R, Salimpour P. Picture of the month. Tuberculous dactylitis. *Arch Pediatr Adolesc Med* 1997;151:851-2.
  30. Kuramoto Y, Aiba S, Tagami H. Erythema induratum of bazin as a type of tuberculid. *J Am Acad Dermatol* 1990;22:612-6.