

Clinical Profile of Patients with Tuberculous Arthritis Admitted in a Tertiary Hospital in the Philippines

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ABSTRACT

Background. Tuberculous arthritis is a rare extra-pulmonary manifestation of tuberculosis (TB) that can lead to significant disability when left untreated. This study described the clinical profile of patients with TB arthritis admitted in a tertiary hospital in the Philippines.

Methods. We reviewed medical records of 65 patients with TB arthritis admitted in the Philippine General Hospital from 2006 to 2019.

Results. Majority of patients were male (41, 63.0%) and the mean age upon diagnosis was 46.7 ± 1.7 years (20–85). Majority (33, 50.8%) had underlying co-morbidities including hypertension (16, 24.6%), type 2 diabetes mellitus (10, 15.4%), and chronic kidney disease (8, 12.3%). A history of previous TB treatment (10, 15.4%), intake of immunosuppressive drugs (7, 10.8%), and trauma on affected joints (13, 20.0%) were also reported. Majority presented with chronic mono-arthritis (50, 76.9%) involving the knees (27, 41.5%) and hips (21, 32.3%) with a mean duration of symptoms of 20.9 ± 3.9 months. The most frequent initial diagnosis upon admission was septic arthritis (21, 32.3%). Confirmed septic arthritis (10, 15.6%), pulmonary TB (9, 14.3%), and disseminated TB (4, 6.3%) were also observed. Majority were diagnosed based on positive acid-fast bacilli (AFB) smear, polymerase chain reaction (PCR) for *Mycobacterium tuberculosis*, or synovium biopsy (34, 54.0%). Anemia (43, 68.3%) and elevated inflammatory biomarkers (erythrocyte sedimentation rate, ESR [36, 97.3%] and C-reactive protein, CRP [40, 87%]) were also seen in majority of patients. The most common radiographic findings on x-ray were joint space narrowing (42, 84.0%), soft tissue swelling (22, 44.0%), and erosions (21, 42.0%). The mean length of hospital stay was 23.8 ± 2.8 days (2–113). Majority underwent surgical interventions (35, 55.6%) including debridement (28, 80.0%) and arthrotomy (25, 71.4%). All received anti-tuberculosis treatment upon diagnosis.

Conclusion. Majority of patients with TB arthritis in this study were male, with mean age in the 5th decade of life, presenting with mono-arthritis, anemia, elevated inflammatory markers, and radiologic findings of joint narrowing. All patients received medical treatment while more than half underwent surgery. There should be a high index of suspicion for TB arthritis in a patient from an endemic country presenting with chronic mono-arthritis in weight-bearing joints to prevent delay in diagnosis and significant joint destruction and disability.

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INTRODUCTION

Tuberculosis (TB) remains a major public health problem that affected around 10 million people worldwide in 2019. The Philippines is a high TB burden country with one of the highest estimated number of new TB and drug-resistant TB cases worldwide.¹

TB arthritis is an uncommon extrapulmonary manifestation of TB that could lead to significant joint destruction and disability.^{2,3} Diagnosis of TB arthritis is usually delayed due to its indolent nature, lack of systemic or pulmonary involvement, and absence of specific radiographic findings.^{4,5}

Despite the prevalence of TB in the Philippines, there is paucity of data regarding the clinical picture of TB arthritis in the Philippines. Only one cohort of Filipino patients with TB arthritis was described in the literature.⁶ Thus, this study aims to describe the clinical profile of patients with TB arthritis admitted in a tertiary hospital in the Philippines.

METHODS

Study Design and Study Setting

We conducted a medical record review using a descriptive and retrospective design. This study was done at the Philippine General Hospital (PGH), the national university and referral hospital in the Philippines.

Study Population and Case Definition

We included patients 19 years old and above admitted in the PGH from 2006 to 2019 with TB arthritis. TB arthritis was diagnosed based on any of the following: 1) identification of *M. tuberculosis* from affected joint by direct microscopy, culture, or polymerase chain reaction (PCR); 2) evidence of caseating granuloma on synovium biopsy; or 3) clinical diagnosis based on clinical presentation, radiographic findings, and/or response to anti-TB medications.

Sampling Design, Data Collection and Statistical Analysis

Convenience sampling was utilized. Patients were identified retrospectively from the patient census/database of the Division of Rheumatology, Division of Infectious Diseases and the Medical Records Section of PGH. Medical records were reviewed for demographic data, detailed clinical history and physical examination, laboratory investigations performed, and the patient's clinical course. Data were collected on a standard data collection form, computerized and encoded using Microsoft Excel. Statistical analysis was done using STATA version 14 (StataCorp, LP, College Station, TX). Continuous data were presented as mean \pm SD and categorical data as percentages.

Ethical Considerations

The study was approved by the University of the Philippines Manila Research Ethics Board (UPMREB 2016-190-01) last March 18, 2020.

RESULTS

Baseline Characteristics

We included 65 adult patients with TB arthritis admitted in the PGH from 2006 to 2019 in the study. Majority were

Table 1. Baseline characteristics of the study population (N = 65)

Baseline Characteristics	n (%)
Age [Mean \pm SD (Range)], years	46.6 \pm 1.7 (20–85)
20–29	8 (12.3)
30–39	14 (21.5)
40–49	13 (20.0)
50–59	18 (27.7)
60 and older	12 (18.5)
Male	41 (63.0)
Previous TB treatment	10 (15.4)
Trauma on affected joint/s	13 (20.0)
Immunosuppressive therapy	7 (10.8)
Co-morbidities	33 (50.8)
Hypertension	16 (24.6)
Type 2 diabetes mellitus	10 (15.4)
Chronic kidney disease	8 (12.3)
Gouty arthritis	5 (7.7)
Bronchial asthma	4 (6.2)
Malignancy	3 (4.6)
Systemic lupus erythematosus	2 (3.1)
Cardiovascular disease	1 (1.5)
Rheumatoid arthritis	1 (1.5)
Dermatomyositis with scleroderma overlap	1 (1.5)
HIV	1 (1.5)

male (63.0%) and the mean age upon diagnosis was 46.6 \pm 1.7 years. A history of previous TB treatment (15.4%), intake of immunosuppressive drugs (10.8%), trauma on affected joints (20.0%) and co-morbid conditions (50.8%) were reported. The most commonly reported co-morbid conditions were hypertension (24.6%), type 2 diabetes mellitus (15.4%), and chronic kidney disease (12.3%). Rheumatologic disorders, including gouty arthritis (7.7%), SLE (3.1%), rheumatoid arthritis (1.5%) and dermatomyositis with scleroderma (1.5%), were also reported (Table 1).

Clinical Presentation

Majority of the patients presented with chronic monoarthritis (76.9%) with a mean duration of symptoms of 20.9 \pm 3.9 months (Range: 0.25–180). The most commonly involved joints were the knees (41.5%) and the hips (32.3%). The most common local symptoms were limitation in range of motion (ROM) (98.4%) and soft tissue swelling (46.2%). Systemic symptoms, such as fever (21.5%), weight loss (15.4%), and malaise (6.2%), were less commonly observed. The most common initial diagnosis upon admission was septic arthritis (32.3%). However, only 10 patients (15.6%) had confirmed septic arthritis. Nine patients (14.3%) also had concomitant PTB while four had disseminated TB (6.3%).

More than half (53.9%) of the TB arthritis diagnosis was confirmed bacteriologically with a positive AFB smear on synovial fluid/tissue/aspirate (33.3%), biopsy result showing chronic granulomatous inflammation with Langhans type giant cells (14.3%), or a positive PCR for *M. tuberculosis* (12.7%); the rest (46.0%) were diagnosed clinically. Anemia, predominantly normocytic, normochromic, was a

Table 2. Clinical and diagnostic profile of patients with TB arthritis (N = 65)

Profile	n (%)
Clinical presentation	
Chronic mono-arthritis	50 (76.9)
Acute mono-arthritis	7 (10.8)
Chronic oligo-arthritis	4 (6.2)
Acute oligo-arthritis	3 (4.6)
Chronic polyarthritis	1 (1.5)
Duration of symptoms, in months [Mean ± SD (Range)]	20.9 ± 3.9 (0.25 - 180)
Chronicity	
Acute (≤ 6 weeks)	10 (15.4)
Chronic (> 6 weeks)	55 (84.6)
Number of joints involved	
Mono-arthritis (1)	57 (87.7)
Oligo-arthritis (2 - 3)	7 (10.8)
Polyarthritis (≥ 4)	1 (1.5)
Joint Involvement	
Knee	27 (41.5)
Hip	21 (32.3)
Ankle	12 (18.5)
Wrist	6 (9.2)
Elbow	2 (3.1)
Shoulder	2 (3.1)
Proximal interphalangeal joint	2 (3.1)
Associated symptoms	
Limitation in ROM	64 (98.4)
Soft tissue swelling	30 (46.2)
Draining sinus/Abscess	17 (26.2)
Fever	14 (21.5)
Weight loss	10 (15.4)
Malaise	4 (6.2)
Initial diagnosis	
Septic arthritis	21 (32.3)
TB arthritis	10 (15.4)
Avascular necrosis	7 (10.8)
Chronic osteomyelitis	6 (9.2)
Soft tissue mass	6 (9.2)
Gouty arthritis	5 (7.7)
Osteoarthritis	3 (4.6)
Bursitis	1 (1.5)
Charcot foot	1 (1.5)
Bone cancer	1 (1.5)
Deep space infection	1 (1.5)
Post traumatic arthritis	1 (1.5)
Rheumatoid arthritis	1 (1.5)
SLE arthritis	1 (1.5)

frequent finding (68.3%). Elevated inflammatory markers, such as ESR (36/37, 97.3%) and CRP (40/46, 87.0%), were also documented in majority of patients. The most common radiographic findings on x-ray were joint space narrowing (42, 84.0%), soft tissue swelling (22, 44.0%), and erosions (21, 42.0%). Nine patients each had different MRI findings namely: 1) bright signals, irregular cortical defects, subluxation and narrowing; 2) progressive erosive changes; 3) cystic focus, osteomyelitis, tenosynovitis, anterolateral fluid collection; 4) synovial thickening; 5) avascular necrosis; 6) synovitis; 7) cortical destruction; 8) abnormal marrow signal; and 9) non-specific findings. Two patients underwent bone scan which showed increased activity on the affected

Profile	n (%)
Confirmed septic arthritis (n = 64)	10 (15.6)
Concomitant PTB (n = 63)	9 (14.3)
Concomitant disseminated TB (n = 63)	4 (6.3)
Diagnosis of TB arthritis (n = 63)	
Clinical	29 (46.0)
Bacteriologically-confirmed	34 (53.9)
Acid-fast bacilli positive	21 (33.3)
Biopsy-confirmed	9 (14.3)
MTB detected by PCR	8 (12.7)
Laboratory findings	
Anemia (n = 63)	43 (68.3)
Elevated WBC (n = 63)	12 (19.05)
Elevated ESR (n = 37)	36 (97.3)
Mean ESR ± SD (Range)	54.7 ± 5.9 (12 - 144)
Elevated CRP (n = 46)	40 (87.0)
Radiographic findings (n = 50)	
Joint space narrowing	42 (84.0)
Soft tissue swelling	22 (44.0)
Erosions	21 (42.0)
Lytic lesions	17 (34.0)
Osteopenia	11 (22.0)
Sclerosis	10 (20.0)
Sequestrum	2 (4.0)

TB, tuberculosis; ROM, Range of motion; ESR, Erythrocyte sedimentation rate; CRP, C-reactive protein

areas. Computed tomography (CT) scan was also done in one patient revealing multiple osseous lytic lesions and bony defects (Table 2).

Clinical course

The mean length of hospital stay of patients admitted for TB arthritis was 23.8 ± 2.8 days (2–113). Surgical intervention was performed in majority of patients (55.6%). The most common surgical procedures performed were debridement (80%) and arthrotomy (71.4%). All patients received standard anti-TB therapy during admission. Three patients (4.8%) developed mild adverse drug event (cutaneous rash) upon administration of anti-TB medications. No mortality was reported among patients admitted for TB arthritis (Table 3).

Table 3. Clinical course of patients with TB arthritis (N = 65)

Clinical Course	n (%)
Length of hospital stay, days [Mean ± SD (Range)]	23.8 ± 2.8 (2 - 113)
Surgical intervention (n = 35)	
Debridement	28 (80.0)
Arthrotomy	25 (71.4)
Synovectomy	9 (25.7)
Arthroplasty	9 (25.7)
Osteotomy	2 (5.7)
Incision and drainage	1 (2.9)
Sequestrectomy	1 (2.9)
Received anti-tuberculous medications (n = 63)	
Developed ADE	3 (4.8)

DISCUSSION

Similar to previous studies done in Thailand, Taiwan, and the United States, TB arthritis was commonly observed among the older population^{2,3,7,8}, male sex³, and those with underlying rheumatologic disease and immunocompromised conditions.⁷⁻⁹ The mean duration between onset of symptoms and consult was almost 21 months compared to the Thailand cohort that reported a mean duration of 25.4 months.³ The delay in the diagnosis may be attributed to the chronic and indolent nature of the disease and/or our patient's poor health-seeking behavior; this is comparable to previous literature showing long duration between symptom onset and diagnosis.^{2,3} Other pertinent information on the patient's clinical history such as intake of immunosuppressive therapy, history of trauma in affected joint/s, and previous TB treatment should also be sought since they may predispose a patient to TB.

Similar to previous studies, chronic monoarthritis was the most common presentation.^{2,3,6,9} However, acute arthritis was also observed in some patients especially among those aged 50 and above and those with concomitant rheumatologic diseases (SLE and septic arthritis) consistent with other studies.^{2,3} Our study observed fewer polyarticular involvement compared to Thailand where 30% showed polyarticular involvement. We only had 1 patient with polyarticular involvement and this patient had disseminated TB.³ We also observed fewer oligoarticular involvement compared to a previous study in the Philippines.⁶

The most commonly observed local symptoms were limitation in ROM and soft tissue swelling. However, abscess and sinus tract formation were also seen especially among those presenting with chronic arthritis. On the other hand, systemic symptoms, such as fever, weight loss, and night sweats, were not commonly reported compared to a study in Netherlands, where systemic symptoms were frequently observed.¹⁰

Compatible with previous literature, our study also showed that the weight-bearing joints, such as knees and hips, were most commonly involved in TB arthritis.^{2,3,6,10,11} This is also similar to the previous cohort of Filipino patients with TB arthritis where monoarthritis of the knees was predominant.⁶ However, we have also observed TB arthritis in less typical areas such as the small joints of the hands, elbow, and shoulder.

Septic arthritis was the most common initial diagnosis upon consult; however, we only observed bacteriologically-confirmed septic arthritis on top of TB arthritis in 10 patients. Since both TB arthritis and septic arthritis can present acutely, every attempt to determine the etiology of the inflamed joint should be made. However, the low rate of positivity of synovial fluid and/or tissue for acid-fast staining remains a challenge.^{4,7} Although a synovial fluid aspirate or tissue is easier to collect than synovium biopsy, histopathologic evidence of TB still remains the gold standard

in the diagnosis of TB arthritis. Nucleic acid amplification test for TB may also be done to confirm the diagnosis.

Ancillary studies such as CBC and inflammatory markers may also be useful. Our study showed that majority of patients had normocytic, normochromic anemia and elevated ESR and CRP. This reflects the ongoing inflammation occurring in the joints. Despite a previous report in Thailand where blood eosinophilia was present in more than half of the population, only one patient in our study showed elevated blood eosinophil level. Imaging of the affected joint/s should also be done promptly in all patients. Radiographic findings on x-ray commonly seen were joint space narrowing, soft tissue swelling, and erosions consistent with previous literature.^{12,13} However, these radiographic findings are non-specific and may also occur in other inflammatory arthritis.

When diagnostic tests yield negative results, the diagnosis of TB arthritis can still be made with a detailed history taking, physical examination, and laboratory tests/radiographic imaging. In this study, majority of those with clinically diagnosed TB arthritis also presented with chronic mono-arthritis predominantly affecting the knees and the hips. All presented with limitation in ROM while systemic symptoms were less frequent. Anemia, elevated inflammatory markers, and typical radiographic findings were also observed. Interestingly, all patients diagnosed with disseminated TB arthritis in the study had clinically diagnosed TB arthritis. Thus, the presence of an inflamed joint, in the background of TB affecting other organ system/s, makes TB arthritis the most likely diagnosis.

Due to the indolent nature of this disease, majority of our patients already presented with significant joint damage on admission requiring prompt surgical intervention such as debridement, arthrotomy, synovectomy, and arthroplasty; this is in comparison with a previous study done in the Philippines where only 6% underwent surgical intervention.⁶ Hospital stay was also prolonged, with an average of 24 days, likely from the delayed diagnosis and initiation of treatment.

CONCLUSION

This is the largest cohort of TB arthritis patients described in the Philippines. TB arthritis commonly presents with chronic mono-arthritis involving the knees and the hips associated with local symptoms of inflammation. Anemia and elevated inflammatory markers were commonly present while radiographic findings mostly revealed non-specific joint space narrowing and erosions.

There should be a high index of suspicion for TB arthritis in any inflamed joint among patients living in endemic countries such as the Philippines. Early recognition may lead to prompt treatment with anti-tuberculosis medications and/or surgical interventions for patients already presenting with significant joint destruction.

Statement of Authorship

All authors participated in the data collection and analysis, and approved the final version submitted.

Author Disclosure

All authors declared no conflicts of interest.

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