**ABSTRACT**

Tuberculous (TB) arthritis accounts for 1-3 percent of all the tuberculosis cases globally. Extra-pulmonary TB affects most commonly the spine followed by hips and knees. The diagnosis of knee Tuberculosis can be challenging especially in patients with no obvious pulmonary disease or discharging sinuses. The medical management of osteoarticular tuberculosis is usually augmented by various surgical interventions for ideal outcomes. The role of surgery is both diagnostic, and reconstructive.

The diagnosis has however improved markedly with newer diagnostic modalities but for joint tuberculosis the histopathologic examination of the synovium with demonstration of caseating granulomas is the gold standard.

The development of better diagnostic and therapeutic methods for TB arthritis have improved the outcomes despite resurgence in TB cases globally due to the association with Acquired Immunosuppression Syndrome (AIDS). As the strategies for the diagnosis improve the management of TB arthritis should as well be aimed at better functional outcomes. For osteoarticular tuberculosis the ultimate aim of treatment should be to restore joint function and mobility with minimal disability.

**Keywords**

Tuberculosis, Diagnosis, Surgical management options.

**Introduction**

Tuberculosis is an ancient disease and spinal TB has been in existence for over 5000 years with the first known description of tuberculosis being written by Sanskrit between 1500 and 7000 BC. By the beginning of the twentieth century TB was a major cause of death in the western society with treatment being confined to the sanatorium and a mortality of 60% recorded at 6 years post discharge. However that dropped between 1950s and the 1970s with discovery of effective at TB medications. Mycobacterium tuberculosis is the primary causative agent though Mycobacterium Africanum and Mycobacterium Bovis are known to cause similar infections. On histology Mycobacterium tuberculosis is thin, rod like and non capsulated.

The osteoarticular tuberculosis commonly affects the large weight bearing joints of the hip, knee and ankles but rarely the non weight bearing joints such as elbow and wrists [1-5]. Hip TB accounts for 10-15% of osteoarticular tuberculosis [1,3,5]. The disease usually begins from the synovium and spreads to the peri-articular regions causing marginal erosions and destruction [6].

TB of the joints in most cases is haemotogenous in spread with a primary focus in the lungs or lymphoid tissues but rarely from direct adjacent spread to the synovium as in Poncets arthritis. Poncets disease refers to a nondestructive polyarthritis seen during the active phase of TB infection and is rarely of surgical interest. However TB arthritis is usually monoarticular with a positive synovial biopsy for mycobacterium TB being the most diagnostic finding [7,8,9-12].

Osteoarticular disease presents with minimal constitutional symptoms leading to delays in diagnosis and occasionally missed diagnosis [13-16]. A delay in diagnosis results in a delay in the
treatment and hence significant joint destruction follows that may require advanced surgical reconstructive procedures [17,18]. This study therefore reviewed the current trends in diagnosis and surgical management options.

Methodology
I initially performed a MEDLINE (National Library of Medicine, Bethesda, Maryland, USA) search using the key words “Diagnosis and Surgical management tuberculosis arthritis”. Articles that were not published in the English language, manuscripts without an abstract (which were assumed to not be original), and opinion articles were excluded from the review. After selecting 131 articles, the relevant information was extracted and classified according to TB arthritis diagnosis, TB arthritis management. The searches were performed in July 2108 and December 2018.

Diagnostic Challenges
The diagnosis of arthritis due to TB is a challenge and yet a correct diagnosis is essential in preservation of the articular cartilage and joint space. Early diagnosis, specific and adequate medical treatment can be rewarding for maintaining good joint function. The diagnosis of TB monoarticular arthritis is often delayed due to lack of clinical suspicion, insidious nature of onset, lack of characteristic early radiographic findings and often lack of constitutional [15-18].

A high index of suspicion is necessary, especially in the context of persistent monoarthritis in a susceptible host. There is usually a long delay in diagnosis, partly due to the fact that it can mimic other diseases due to its varied clinical presentation and radiographic appearance [10,12]. In immunocompromised patients, the elderly, children or patients on long-term treatment with corticosteroid and/or immunosuppressive agents microbiological or histological tests for TB remain the gold standard for the diagnosis of TB.

Clinical Presentation
Tubercular arthritis is characteristically monoarticular in presentation and commonly affects the spine and weight-bearing joints such as the knee, hip, and ankle [1,18]. It commonly presents with chronic joint pain, progressive deformity, and stiffness with limitation of joint movements.

The most common presenting symptom is local joint pain and swelling followed by restriction of joint movement. There is wasting of the regional muscle groups, while stiffness and deformity follow much later. Less commonly, a painless cold abscess can be the initial clinical presentation especially in the hip joint. Multiple joint involvement is seen in 5-30% cases of tubercular arthritis, but less than 50% of individuals with tubercular arthritis have active pulmonary TB at the time of diagnosis [18].

Joints swelling and evidence of effusion, periarticular abscess and chronic sinus formation occur at varying times in TB arthritis. Systemic symptoms of fever, weight loss, and night sweat may not be present during active TB arthritis.

Clinically, TB arthritis has been classified into 5 stages as follow [19-21]. Stage I or the synovitis stage presents with soft tissue swelling, no bony lesion, localized osteoporosis, and outcome after medical treatment is excellent.

Stage II is early arthritis with marginal erosions (one or more erosions or lytic lesion in the bone; discrete diminution of joints space). Muscle wasting becomes apparent and there is multidirectional restriction of joint movement. The outcome of medical treatment is good with mild stiffness as the residual effect.

Stage III is advanced arthritis with subperichondral cysts and plain X rays reveal a significant reduction of joint space. The medical and surgical outcome is fair with notable loss of motion if no reconstructive surgery is done.

Stage IV is more advanced arthritis with joint destruction and gross restriction of movements at the joint after treatment. In cases of the hip joint this stage may be associated with subluxation or joint dislocation. The patients at this stage will benefit from reconstructive procedures in addition to TB chemotherapy.

Stage V is a fully ankylosed joint with no joint movements at all. The best outcome is achieved by total joint replacement of the knee or hip for restoration of normal joint mobility.

Diagnostic Techniques
Microscopy
Basic microscopy and culture is an established test for the diagnosis and follow up of pulmonary TB. A confirmation of acid fast bacillus (AFB) from any body fluid especially sputum or other body tissues is the traditional gold standard for the diagnosis of tuberculosis. However, several studies have reported a low positivity on bacteriology at approximately 33% even for primary disease states, hence the necessity for better diagnostic tests. This is more difficult in TB affecting the knee and hip joints where microscopy of the synovial fluid is rarely positive. Therefore, every attempt must be made to bacteriologically prove the diagnosis in each case of suspected articul tuberculosis by other tests. Whatever method a clinician uses its imperative to collect at least two or preferably three samples.

A Ziehl-Neelsen stain can reveal AFB only if the sample collected contains greater than 10,000 bacilli per mL. Different culture methods, such as Lowenstein-Jensen medium, radiometric (Bactec 12B liquid medium), and non-radiometric (Bactec MGIT 960 system), can be used for confirming diagnosis in the paucibacillary state. The newer bacteriology methods are capable of providing faster results in doubtful cases. Mycobacterial culture is of significance in patients suspected to have drug resistance or relapse of previously treated disease [15].

Tuberculin Skin Test (TST)
Traditionally the Mantoux test has been the recommended standard tuberculin skin test [TST] for diagnosis. It is performed and analysed by rising of a wheal of approximately 6 mm after
an intra-dermal injection [22]. The test result is read 48-72 hours after an injection using a ballpoint or palpatory methods to read the induration. A previous Bacillus Calmette-Guérin (BCG) vaccine has an influence on the PPD reaction depending on the intervals between BCG vaccination and TST or the age at initial vaccination [22]. A repeat is recommended if there is no induration and the wheals presents after the stipulated time for reading. In case of a repeat test it’s best performed on the opposite arm.

**Interferon Gamma Release Assays (IGRAs)**

In addition to the Tuberculin Skin Test, which is known to be of lower sensitivity and specificity, blood-based assays are useful in non specific cases. These are T-cell assays, which are based on the stimulation of host blood cells by M. tuberculosis-specific antigens and usually measured, based on the production of gamma interferon. The T-cell assays have been found to be more specific than the TST though unable to distinguish between active disease and latent tuberculosis infection [23,24]. Therefore, the interpretation of the results remains dependent on the clinical presentation and other diagnostic findings. T-SPOT, Quantiferon-TB and TST are of great diagnostic values for chronic inflammatory arthritis.

**Polymerase Chain Reaction (PCR) Testing**

Polymerase chain reaction (PCR) testing has revolutionized the diagnosis of TB due to the rapid turn round time and the increased sensitivity with the ability to diagnose minimal bacterial loads. Nucleic acid amplification PCR tests though useful have the draw back of inability to differentiate between a living bacilli and dead bacilli. Thus, these tests continue to give positive results even after successful treatment. The PCR tests are positive in 95% to 100% of culture positive cases and in 50% to 60% of culture negative cases [25,26]. Positive results on PCR have been reported in a patient with negative synovial and joint fluid cultures after Total Knee Replacement.

**Synovial Fluid Examination and Synovial Biopsy**

Joint fluid aspiration from the affected joint for standard/routine investigation and TB culture is recommended when possible for at-risk patients, even where previous cultures have been negative. Synovial fluid culture is positive in approximately 20-40% of sampled cases [27].

Synovial fluid aspirate in TB is usually nonhaemorrhagic and turbid with moderate elevation of white blood cell, and specifically the polymorphonuclear leukocytes. PCR analysis in synovial fluid, tissue samples, bone marrow aspirate, and peripheral blood is faster and more specific though less sensitive [27].

The gold standard test for the diagnosis of tubercular arthritis is a synovial biopsy, with positive results being reported in 80% of cases [12]. The diagnosis is usually confirmed microscopically by presence caseating granulomas, lymphocytes, and giant cells with caseation. For synovial biopsies it’s important to take multiple specimens for a good yield even in cases with a culture negative result.

**Plain Radiography and Imaging**

Bone and joint changes become evident after 3 to 5 months of disease progression. The classical chemister triad of TB arthritis is juxta articular osteoporosis, peripheral osseous erosion and gradual narrowing of the joint space [7,10]. In contrast to the other forms of arthritis, the joints space is relatively preserved in early TB arthritis hence creating a delay in the diagnosis.

Computerized tomography (CT) and Magnetic Resonance Imaging (MRI) are useful adjuncts to plain radiography [23,24]. The MRI defines the soft tissue destruction well, while CT scan defines the bony changes better. The CT Scans may help to demonstrate kissing sequestra, which are wedge shaped necrotic foci on the sides of an affected joint. The MRI features of tubercular arthritis include synovitis, effusion, central and peripheral erosions, chronic pannus, abscess, bone erosions, and hypointense synovium [27]. MRI is the investigation of choice to demonstrate both the extent and severity of capsular, cartilage and subchondral bone damage [9]. An MRI can be nonspecific in early disease but is known to evaluate the extent of the lesions better than X-rays (Figures 1 & 2).

**Surgical Treatment Options**

**Tissue Biopsy, Joint drainage and Arthrolysis**

The initial role of surgery is both diagnostic, and later therapeutic [28-32]. Initially a biopsy is done to provide samples for synovial fluid analysis and synovial tissue for histo-pathologic evaluation. The surgical procedures performed are open or arthroscopic debridement, incision and drainage of abscess, and synovectomy [32-42]. The preference is to initially perform an arthroscopy since its minimally invasive and leave the open procedures for the definite reconstructive procedures. Arthroscopy can also be used to release adhesion in the joint and to perform a biopsy, which can aid in diagnosis of other synovial disorders such as pillonodular synovitis that may mimic osteoarticular tuberculosis.

**Splints and Traction**

After the biopsy splints may be used to relieve acute symptoms and to prevent contracture or deformity formation [41]. Traction is useful in the early stages especially for hip TB. Skeletal Traction is preferred and it serves to relieve muscle spasms, prevent deformity...
and subluxation, and maintains the joint space. Surgical procedures should be restricted to joints with severe cartilage destruction, joint deformity, large abscesses, multiple drug resistance or atypical mycobacteria [17,29].

**Arthrodesis**

Arthrodesis in a functional position was traditionally used for pain control and to eliminate infection. The drawback has always been the functional limitation and loss of joint function that follows. Historically arthrodesis was popular for tubercular arthritis of the hip in poor resource settings.

**Joint Replacement Surgery**

Prior to attempts at joint replacement excision arthroplasty was useful as it allowed for disease control by excision of all the infected tissues. Though highly successful the excision arthroplasty results in limb shortening and chronic instability of the affected joint. Excision arthroplasty is mainly done for the hip joint with active infection and replacement surgery is reserved for severely damaged joints.

With the advent of modern artificial joint replacement successful treatment with excellent functional outcomes has been reported in patients with TB arthritis of the hip and knee joint [14]. It can be done when the diagnosis is made early and the patient treated with systemic chemotherapy but it’s also useful in case of postoperative incidental diagnosis.

While most orthopaedic surgeons would be reluctant to treat tuberculosis of the major joints with replacement procedures due to the risk of reactivation and implant infection, there is compelling evidence to the contrary. Its important to note that mycobacterium tuberculosis has specific biologic behavior that distinguishes it from most pyogenic infections and hence its response to implanted orthopaedic materials also differs significantly. Firstly the mycobacterium is known to reproduce slowly while producing minimal adhesion molecules, slime and occasionally becomes dormant. Secondly TB Bacilli forms a biofilm that differs from other pyogenic organisms and which according to Ha et al TB bacilli rarely or don’t adhere to the metal surfaces [43]. This is however in contrast to the findings of a study by Ma et al that described biofilm formation by M tuberculosis on the surface of cobalt-chromium-molybdenum alloy or titanium alloy [44]. Various studies have confirmed the difference in replication and biofilm formation on implants in TB infections as compared to other bacterial infections [44]. Further to this M tuberculosis is known to divide once in 15-20 hours, which is a much slower rate than Staphylococcus Aureus that divides every 20 min. Therefore TKR can be safely done in joints with active TB if the patient is properly treated with anti TB treatment pre operatively and postoperatively with good outcomes compared to the alternatives. In a prospective study of 15 patients (16 knees) who had TKR done and divided into two groups [45] Su reported good outcomes with long term follow up. These findings make total hip and total knee replacement surgeries (Figures 4 & 5) a better option in functional outcome as compared to the joint destructive procedures.

**Role of TB chemotherapy in surgically treated patients**

The mainstay treatment of tuberculosis arthritis is appropriate anti- TB drug therapy. Early institution of antimicrobial therapy can result in near-complete resolution and preservation of function. In TB arthritis without pulmonary involvement, the risk of transmission to contact persons is minimal and thus constitutes little threat to public health. Antimicrobial therapy in general should be of at least 12-18 months [38-42] depending on the presentation. The basic principles that underlie the treatment of pulmonary tuberculosis also apply to extrapulmonary forms of the disease including the knee and hip [4-6]. Some randomized
controlled trials, suggests the 6 to 9 months regimens (2 months of isoniazid (INH) and rifampicin (RIF), pyrazinamide (PZA), and ethambutol (EMB) followed by 4-7 months of INH and RIF is recommended as initial therapy unless the organisms are known or strongly suspected of being resistant to the first-line drugs. If PZA cannot be used in the initial phase, the continuation phase must be increased to 7 months, as describe for pulmonary tuberculosis. Several studies have examined treatment of bone and joint tuberculosis and have shown that 6-9-month regimens containing RIF can achieve excellent disease control.

**Conclusion**

Synovial biopsy by arthroscopy or open techniques provides the best diagnostic yield for histopathologic evaluation. Surgery plays a critical role in the management of monoarticular TB arthritis and should always be considered and offered as an option when restoration of joint function is the ultimate goal. Further its critical role in the management of monoarticular TB arthritis and should always be considered and offered as an option when restoration of joint function is the ultimate goal. Further its

**References**

1. Malaviya AN, Kotwal PP. Arthritis associated with tuberculosis. Best Pract Res Clin Rheumatol. 2003; 17: 319-343.
2. Ellis ME, el-Ramahi KM, el-Dalaan AN. Tuberculosis of peripheral joints: a dilemma in diagnosis. Tuber Lung Dis. 1993; 74: 399-404.
3. WHO Report. Global tuberculosis control. Epidemiology, strategy, financing. Geneva: World Health Organization. 2011.
4. Peto HM, Pratt RH, Harrington TA, et al. Epidemiology of extrapolmonary tuberculosis in the United States, 1993-2006. Clin Infect Dis. 2009; 49: 1350-1357.
5. Mateo L, Ruiz Manzano J, Olivé A, et al. Ostearticular tuberculosis. Study of 53 cases. Med Clin (Barc). 2007; 129: 506-509.
6. Tuberk, Tuli SM. General principles of osteoarticular tuberculosis. Clin Orthop Relat Res. 2002; 11-19.
7. Leibe H, Köhler H, Kessler P. Osteoarticular tuberculosis. Review - current status of diagnosis and therapy. Zentralbl Chir. 1982; 107: 322-342.
8. Magnusen A, Dinneen A, Ramesh P. Osteoarticular tuberculosis: increasing incidence of a difficult clinical diagnosis. Br J Gen Pract. 2013; 63: 385-386.
9. Samuel S, Boopalan PR, Alexander M, et al. Tuberculosis of and around the ankle. J Foot Ankle Surg. 2010; 50: 466-472.
10. Harisinghani MG, McLeod TC, Shepard JA, et al. Tuberculosis from head to toe. Radiographics. 2000; 20: 449-470.
11. Scanzello CR, Goldring SR. The role of synovitis in osteoarthritis pathogenesis. Bone. 2012; 51: 249-257.
12. Sequeira W, Co H, Block JA. Osteoarticular tuberculosis: current diagnosis and treatment. Am J Ther. 2000; 7: 393-398.
13. Furia JP, Box GG, Linttm PH. Tuberculous arthritis of the knee presenting as a meniscal tear. Am J Orthop (Belle Mead NJ). 1996; 25: 138-142.
14. Al-Shaikh R, Goodman SB. Delayed-onset Mycobacterium tuberculosis infection with staphylococcal superinfection after total knee replacement. Am J Orthop (Belle Mead NJ). 2003; 32: 302-305.
15. Abdelwahab IF, Bianchi S, Martinoli C, et al. Atypical extraspinal musculoskeletal tuberculosis in immunocompetent patients: part II, tuberculous myositis, tuberculous bursitis, and tuberculous tenosynovites. Can Assoc Radiol J. 2006; 278-286.
16. Abdulaziz S, Almoailim H, Ibrahim A, et al. Poncet's disease (reactive arthritis associated with tuberculosis): retrospective case series and review of literature. Clin Rheumatol. 2012; 31: 1521-1528.
17. Netval M, Hudec T, Hach J. Our experience with total knee arthroplasty following tuberculous arthritis (1980-2005). Acta Chir Orthop Traumatol Cech. 2007; 74: 111-113.
18. ChenskiÄ EP, Omirova KT, SuleÄmanov BSh. Characteristics of osteoarticular tuberculosis patient contingents in Kazakhstan and the ways for their detection. Probl Tuberk. 1980: 6-8.
19. Sandher DS, Al-Jibury M, Paton RW, et al. Bone and joint tuberculosis: cases in Blackburn between 1988 and 2005. J Bone Joint Surg Br. 2007; 89: 1379-1381.
20. Spiegel DA, Singh GK, Banskota AK. Tuberculosis of the musculoskeletal system. Tech Orthop. 2005; 20: 167-178.
21. Koskinen S. Musculoskeletal tuberculosis: are you ready to diagnose it? Acta Radiol. 2011; 52: 591.
22. Sun L, Yan HM, Hu YH, et al. IFN-Î3 release assay: a diagnostic assistance tool of tuberculin skin test in pediatric tuberculosis in China. Chin Med J (Engl). 2010; 123: 2786-2791.
23. Arend SM, Thijsen SF, Leyten EM, et al. Comparison of two interferon-gamma assays and tuberculin skin test for tracing tuberculosis contacts. Am J Respir Crit Care Med. 2007; 175: 618-627.
24. Efthimiou P, Sood S. Quantiferon TB Gold Test: the new standard for screening of latent tuberculosis in patients with rheumatoid arthritis? Ann Rheum Dis. 2007; 66: 276.
25. Kim JH, Kim YJ, Ki CS, et al. Evaluation of Cobas Taqman MTB PCR for detection of Mycobacterium tuberculosis. J Clin Microbiol. 2011; 49: 173-176.
26. Veretts D, Kazakos C, Tilkeridis C, et al. Polymerase chain reaction for the detection of Mycobacterium tuberculosis in synovial fluid, tissue samples, bone marrow aspirate and peripheral blood. Acta Orthop Belg. 2003; 69: 396-399.
27. Popescu E, Munteanu E, Zeligsohn M. Results of bacteriological examinations in lymph-node and osteoarticular tuberculosis. Rev Ig Bacteriol Virusol Parazitol Epidemiol. 1980; 29: 191-192.
28. Sawlani V, Chandra T, Mishra RN, et al. MRI features of tuberculosis of peripheral joints. Clin Radiol. 2003; 58: 755-762.
29. Besser MI. Total knee replacement in unsuspected tuberculosis of the joint. Br Med J. 1980; 280: 1434.
30. Varango G, Bamba I, Kodo M, et al. Osteonecrosis of the hip in sickle-cell disease associated with tuberculosis arthritis. A review of 15 cases. Int Orthop. 1998; 22: 384-389.
31. Moon MS, Kim SS, Lee SR, et al. Tuberculosis of hip in...
children: A retrospective analysis. Indian J Orthop. 2012; 46: 191-199.
32. Walker GF. Failure of early recognition of skeletal tuberculosis. Br Med J. 1968; 1: 682-683.
33. Hsiao CH, Cheng A, Huang YT, et al. Clinical and pathological characteristics of mycobacterial tenosynovitis and arthritis. Infection. 2013; 41: 457-464.
34. Foocharoen C, Nanagara R, Foocharoen T, et al. Clinical features of tuberculous septic arthritis in Khon Kaen, Thailand: a 10-year retrospective study. Southeast Asian J Trop Med Public Health. 2010; 41: 1438-1446.
35. Höpfner S, Becker-Gaab C, Hahn K. Chronic pain in the mid-foot area. Osteoarticular tuberculosis of the tarsal bones. Radiologe. 2000; 40: 1183-1185.
36. Al-Qattan MM, Al-Namla A, Al-Thunayan A, et al. Tuberculosis of the hand. J Hand Surg Am. 2011; 36: 1413-1421.
37. Dlimi F, Bellarbi S, Mahfoud M, et al. Tuberculosis of the hand and wrist: different aspects of 30 cases. Chir Main. 2011; 30: 198-204.
38. Tsuduki E, Kawada H, Takeda Y, et al. A case of multiple bone and joint tuberculosis which had been misdiagnosed as the rheumatoid arthritis and treated with prednisolone for eleven months. Kekkaku. 2002; 77: 361-366.
39. Chocarro Martínez A, García García I, González López A. Arthritis tuberculosis. An Med Interna. 2005; 22: 255-256.
40. Chawla KP, Pandit AA, Jaiswal PK, et al. Osteoarticular tuberculosis with involvement of multiple sites (a case report). J Postgrad Med. 1990; 36: 171-172.
41. Krama SB, Lee SHS, Abramson SB. Non vertebral infections of musculoskeletal tuberculosis. In: Rom WN, Garay SM (eds.) Tuberculosis. (2nd edn), Lippincott, William & Wilkins. 2004; 577-591.
42. Lesić AR, Pesut DP, Marković-Denić L, et al. The challenge of osteoarticular tuberculosis in the twenty-first century: a 15-year population-based study. Int J Tuberc Lung Dis. 2010; 14: 1181-1186.
43. Ha KY, Chang YG. Adherence and biofilm formation of S.Epidermidis, M tuberculosis on various spine implants, Spine (Phila Pa 1976), 2005; 30: 38-43.
44. Ma J, Li GQ, Cao L. Adhesive ability of Mycobacterium tuberculosis onto the surface of different joint prosthesis materials. Chin J Tissue Eng Res. 2012; 16: 8807-8812.
45. Su JY, Huang TL, Lin SY. Total knee arthroplasty in tuberculous arthritis, CORR. 1996; 323: 181-187.