

G74: What are risk factors for development of Mycobacterial infections?

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Response/Recommendation:

Patients who are immunocompromised, receiving long-term corticosteroid or immunosuppressive therapy, have multiple medical comorbidities, a history of either pulmonary or extrapulmonary tuberculosis, or a history of repeated surgeries are at increased risk of developing Mycobacterial infections.

Strength of recommendation: Moderate

Delegate Vote:

Rationale:

Mycobacterial infections in periprosthetic joint infection (PJI) are rare and occur infrequently [1-4]. The Mycobacterial species associated with PJIs can be classified into two groups. The first is *M. tuberculosis* complex, a pathogen predominantly associated with late-onset chronic PJI [5]. The second group, Nontuberculous Mycobacterial (NTM) infections, is further subdivided into two categories. The first category, rapidly growing Mycobacteria, includes *M. chelonae*, *M. abscessus*, *M. fortuitum*, *M. smegmatis*, and *M. peregrinum*, which are recognized as major pathogens in early-onset PJI. The second category, slow-growing Mycobacteria, comprises species such as *M. avium intracellulare*, *M. kansasii*, and *M. goodii* [6]. As Mycobacterial infections are an uncommon cause of PJI, diagnostic investigations for their identification are not routinely performed. Nevertheless, in culture-negative PJI cases, atypical microorganisms, particularly Mycobacteria should be considered, and proper diagnosis requires submitting a sample for specialized culture [7]. Therefore, a thorough understanding of the risk factors associated with these infections is essential for accurate detection and effective management.

A systematic review was conducted with inclusion criteria restricted to English-language original articles, including case reports, case series, and retrospective or prospective clinical studies on patients with PJI of the hip or knee caused by Mycobacterial infections, specifically those that identified associated risk factors. A comprehensive literature search of the PubMed and Scopus databases retrieved 1,516 abstracts. After the initial screening, 53 studies were selected for full-text review, of which 23 met the eligibility criteria and were included in the final assessment. The total number of patients across the included studies was 85. Of these, 16 studies were case reports, comprising 18 patients [7, 8, 10, 11, 13-24], while the remaining 7 were retrospective studies, involving 67 patients [2, 4, 6, 9, 12, 25, 26] (Table 1).

Patients with compromised immune status are at increased risk of Mycobacterial infection, particularly those with inflammatory joint diseases or autoimmune disorders undergoing chronic corticosteroid therapy or immunosuppressive treatment [4, 8, 16, 19]. Additionally, individuals with several medical comorbidities such as diabetes, peripheral vascular disease, chronic obstructive pulmonary disease, chronic liver disease, cirrhosis, and renal insufficiency are also at elevated risk [20-22]. Hwang et al. [25] reported that 70% of

patients with Mycobacterial PJI in their series following primary total knee arthroplasty (TKA) were classified as American Society of Anesthesiologists (ASA) grade 3 or 4. Furthermore, systemic immunosuppression due to human immunodeficiency virus (HIV) infection is another significant factor predisposing individuals to atypical infectious diseases, including Mycobacterial infection [17, 18, 26].

A prior history of extrapulmonary or pulmonary tuberculosis may be recognized as a risk factor for PJIs caused by *M. tuberculosis*, as these infections may spread hematogenously and reactivate after a quiescent infection, particularly in individuals with compromised immunity [2, 13]. Wang et al. [24] reported a case of a patient with a prior diagnosis of pulmonary tuberculosis one year before developing chronic knee PJI, in which cultures from debridement yielded *M. tuberculosis*. Similarly, Meyssonier et al. [2] documented two cases of tuberculous hip PJI, one in a patient with a history of pulmonary tuberculosis and the other in a patient with bone tuberculosis. A systematic review by Kim et al. [27] demonstrated that 20% of patients with *M. tuberculosis* knee PJI in their evaluation had a history of tuberculosis infection. Moreover, some patients with tuberculous PJI were found to have concurrent disseminated tuberculosis affecting other organs at the time of PJI diagnosis [2].

Surgical factors, particularly multiple procedures on the same joint, may increase the risk of Mycobacterial infection. Cansü et al. [10] reported a case of hip PJI caused by *M. tuberculosis* in a patient with a history of four repeated hip surgeries prior to undergoing THA for the treatment of developmental hip dislocation. They hypothesized that the source of infection was external, with potential modes of inoculation including medical staff members or other patients with tuberculosis. Similarly, Maimaiti et al. [6] demonstrated that, in addition to poor health status, multiple comorbidities, or immunocompromised conditions, multiple surgical interventions are a significant risk factor for Mycobacterial PJIs following total hip and knee arthroplasty.

Table 1 Summarizes the included studies.

Author	Year	Country	Study design	No. of patients	Hip/Knee PJI	Pathogens
Meyssonier et al. [2]	2019	France	Retrospective study	9	Hip	<i>M. tuberculosis</i>
Jitmuang et al. [4]	2017	Thailand	Retrospective study	16	Hip, Knee	<i>M. tuberculosis</i> and Rapid growing Mycobacteria
Maimaiti et	2023	China	Retrospective	7	Hip, Knee	Nontuberculous

al. [6]			study			Mycobacteria
Pring and Eckhoff [7]	1996	USA	Case report	1	Knee	<i>M. Chelonae</i>
Brown et al. [8]	2008	USA	Case report	1	Hip	<i>M. tuberculosis</i> and <i>M. Chelonae</i>
Buser et al. [9]	2019	USA	Case-control study	9	Hip, Knee	<i>M. goodii</i> and <i>M. fortuitum</i>
Cansü et al. [10]	2011	Türkiye	Case report	1	Hip	<i>M. tuberculosis</i>
Cheung and Wilson [11]	2008	Australia	Case report	1	Knee	<i>M. fortuitum</i>
Eid et al. [12]	2007	USA	Retrospective study	8	Hip, Knee	Rapid growing Mycobacteria
Harwin et al. [13]	2013	USA	Case report	1	Knee	<i>M. tuberculosis</i>
Henry et al. [14]	2016	USA	Case report	2	Hip, Knee	Rapid growing Mycobacteria
Kim et al. [15]	2017	South Korea	Case report	2	Knee	Rapid growing Mycobacteria
Malhotra et al. [16]	2017	India	Case report	1	Hip	<i>M. tuberculosis</i>
Marschall et al. [17]	2008	Switzerland	Case report	1	Knee	<i>M. tuberculosis</i>
McLaughlin et al. [18]	1994	USA	Case report	1	Hip	<i>M. avium intracellulare</i>
Porat and Austin [19]	2008	USA	Case report	1	Knee	<i>M. fortuitum</i>
Rodari et al. [20]	2020	Italy	Case report	1	Hip	<i>M. xenopi</i>
Saccante [21]	2006	USA	Case report	1	Knee	<i>M. fortuitum</i>
Dos Santos et al. [22]	2023	Brazil	Case report	1	Knee	<i>M. senegalense</i>
Shanbhag et al. [23]	2007	UK	Case report	1	Hip	<i>M. tuberculosis</i>
Wang et al. [24]	2007	Taiwan	Case report	1	Knee	<i>M. tuberculosis</i>
Hwang et al. [25]	2021	South Korea	Retrospective study	10	Knee	<i>M. tuberculosis</i> and <i>M. Fortuitum</i>
Peng et al. [26]	2022	Taiwan	Retrospective study	8	Hip, Knee	<i>M. abscessus</i> and <i>M. Chelonae</i>

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