

# Comparative Analysis of Synovial Fluid and Periprosthetic Tissue Using Bacterial Metagenomic Next-Generation Sequencing and Culture in the Diagnosis of Periprosthetic Joint Infection

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**Introduction:** Accurate pathogen identification in periprosthetic joint infection (PJI) is essential for targeted antimicrobial therapy. Conventional culture techniques frequently yield false-negative results, particularly in patients with prior antibiotic exposure. Bacterial metagenomic next-generation sequencing (mNGS) offers culture-independent pathogen detection, but its diagnostic performance and clinical relevance in PJI remain uncertain. This study evaluates the diagnostic utility of mNGS compared with conventional culture in patients with suspected PJI.

## Methods

This prospective observational study was conducted at a tertiary care centre in South India and included 20 adult patients with clinically suspected PJI. Synovial fluid and periprosthetic tissue samples were obtained and analysed using Gram staining, aerobic and anaerobic cultures, and bacterial mNGS. Culture was considered the reference standard. A sample was classified as mNGS-positive if at least one organism exceeded a predefined reporting threshold. Concordance was assessed at both sample and organism levels. Associations between culture–mNGS concordance and inflammatory markers, including erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and synovial total cell count (TC), were analysed. Statistical analysis was performed using R software, with  $p < 0.05$  considered significant.

**Results:** Conventional culture identified pathogens in 12 of 20 samples (60%), while mNGS detected organisms in 17 of 20 samples (85%), including 7 of 8 culture-negative cases (87.5%). Overall concordance between culture and mNGS for positive or negative status was observed in 11 of 20 samples (55%). Using culture as the reference, mNGS demonstrated a sensitivity of 83.3% and a specificity of 12.5%. Among samples positive by both methods, organism-level concordance was observed in 10 of 11 cases (approximately 90%). Elevated synovial total cell count was significantly associated with concordant culture–mNGS results, whereas ESR and CRP showed no significant association. Organisms detected by both culture and mNGS demonstrated higher relative abundance compared with those detected only by mNGS, although this difference was not statistically significant.

**Conclusions:** Bacterial mNGS demonstrates high analytical sensitivity for pathogen detection in periprosthetic joint infection, particularly in culture-negative but clinically suspected cases. However, detection of low-abundance organisms of uncertain clinical significance limits its standalone diagnostic value. Concordance with conventional culture is greatest in cases with elevated synovial total cell counts, suggesting optimal performance in highly inflamed joints. Careful clinical interpretation and standardized reporting thresholds are essential before routine adoption of mNGS in PJI diagnostic algorithms.