

Divergent inflammatory responses in MRSA and MSSA knee PJI

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BACKGROUND & AIM

Staphylococcus aureus is the most common organism causing periprosthetic joint infection (PJI) after total knee replacement worldwide. Both methicillin-resistant (MRSA) and methicillin-sensitive (MSSA) strains are associated with recurrence despite appropriate surgical and antibiotic management. Methicillin resistance is mediated by mecA gene, which encodes an altered penicillin-binding protein (PBP2a) with reduced affinity for β -lactam antibiotics. Reported DAIR failure rates are approximately 42% for MRSA and 40% for MSSA, while two-stage revision failure rates range from 15–30% for MRSA and 7–15% for MSSA. However, comparative data on clinical presentation, inflammatory markers, and mechanisms of failure between MRSA and MSSA PJI remain limited. This study aimed to compare the clinical and inflammatory profiles of MRSA and MSSA knee PJI and explore differences in treatment failure mechanisms.

METHODOLOGY

This retrospective observational study was conducted at a high-volume tertiary arthroplasty center in India and included 70 patients treated between January 2022 and December 2025 with culture-proven Staphylococcus aureus knee PJI following total knee arthroplasty. Patients were categorized into MRSA (n = 40) and MSSA (n = 30) groups. Serum C-reactive protein (CRP) levels and synovial leukocyte counts at presentation were analyzed. Surgical management strategies were reviewed, and treatment failure—defined as recurrence, relapse, or persistence of infection—was assessed.

RESULTS

A total of 70 patients were included (MRSA: 57.1%; MSSA: 42.9%), with male predominance in both groups. The mean CRP was significantly lower in the MRSA group (80.3 mg/L; median 54) compared to the MSSA group (185.6 mg/L; median 173). High CRP levels (>200 mg/L) were more common in MSSA infections (41.3% vs 10%; $\chi^2 = 9.29$, $p = 0.002$). Elevated synovial leukocyte counts (>100,000) were observed in 27.6% of MSSA and 10% of MRSA cases ($p = 0.057$), indicating a trend toward higher inflammatory burden in MSSA. Treatment failure in MSSA occurred after discontinuation of antibiotics, whereas MRSA failures occurred despite ongoing antibiotic therapy.

MRSA vs MSSA — KEY INFLAMMATORY FINDINGS

80.3 mg/L	185.6 mg/L	10%	41.3%	p = 0.002
MRSA mean CRP	MSSA mean CRP	MRSA CRP >200	MSSA CRP >200	CRP comparison

MRSA

n = 40 • 57.1%

Mean CRP: 80.3 mg/L
Median CRP: 54 mg/L

Synovial leukocytes >100,000:
10%

Failure pattern:
Failure despite ongoing antibiotic therapy

MSSA

n = 30 • 42.9%

Mean CRP: 185.6 mg/L
Median CRP: 173 mg/L

Synovial leukocytes >100,000:
27.6%

Failure pattern:
Failure after discontinuation of antibiotics

HIGH CRP >200 mg/L

MRSA: 10%

MSSA: 41.3%

SYNOVIAL WBC >100,000

MRSA: 10%

MSSA: 27.6% • p = 0.057

PROPOSED MECHANISM

Functional agr quorum-sensing system in MSSA → increased toxin production

CONCLUSION & CLINICAL IMPLICATION

MSSA knee PJI demonstrates a higher inflammatory burden compared to MRSA, reflected by elevated CRP levels and synovial leukocyte counts. This may be attributed to a functional agr quorum-sensing system in MSSA, leading to increased toxin production. MSSA failures appear related to inadequate infection clearance, while MRSA failures may reflect persistent infection despite antibiotic therapy. Recognition of organism-specific inflammatory patterns may aid in risk stratification, prognostication, and individualized management of PJI.