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Pathogen-Specific Variation in Routine Serum and Synovial Inflammatory Markers in Periprosthetic Joint Infection: Implications for Diagnostic Thresholds

SUJEESH SEBASTIAN¹, VERONIKA ACHATZ^{1,2}, ANNA ÖLLINGER¹, CHRISTOPH ZEHETMAYER¹, SEBASTIAN SIMON¹, JOHANNA KAUTSCHITZ¹, JOCHEN G. HOFSTÄTTER^{1,3}

¹MICHAEL OGON LABORATORY FOR ORTHOPAEDIC RESEARCH, ORTHOPAEDIC HOSPITAL VIENNA-SPEISING, VIENNA, AUSTRIA; ²DEPARTMENT OF ORTHOPAEDICS AND TRAUMATOLOGY, MEDICAL UNIVERSITY OF VIENNA, AUSTRIA; ³SECOND DEPARTMENT, ORTHOPAEDIC HOSPITAL VIENNA-SPEISING, VIENNA, AUSTRIA

Introduction

Although the diagnostic performance of routine biomarkers for periprosthetic joint infection (PJI) varies by infecting pathogen, existing evidence is largely limited to a small number of pathogen groups, with limited data available for anaerobes, fungi, and polymicrobial infections.

In this single-center study across ten microbiological categories, we aimed to characterize organism-specific patterns of serum and synovial biomarkers and to evaluate pathogen-specific differences in the proportion of cases exceeding current European Bone and Joint Infection Society (EBJIS) diagnostic thresholds.

Method

This retrospective study analyzed 754 culture-confirmed revision hip and knee arthroplasties performed for chronic PJI between 2008 and 2024, defined according to EBJIS criteria. Synovial WBC, PMN%, and serum CRP were recorded. Patients were stratified into ten microbiological categories: *Staphylococcus aureus*, *S. epidermidis*, other coagulase-negative staphylococci (CoNS), Streptococci, Enterococci, Gram-negative bacilli, anaerobes, other Gram-positive bacteria, fungi, and polymicrobial. Mean biomarker levels were compared across groups using one-way ANOVA with post hoc testing. Pathogen-specific proportions exceeding EBJIS cutoffs (WBC ≥ 3000 cells/ μ L, PMN% ≥ 80 and CRP ≥ 10 mg/L) were assessed using chi-square tests.

Results

Synovial and serum biomarkers differed significantly across all ten organism groups (WBC, CRP: both $p < 0.001$; PMN%: $p = 0.006$).

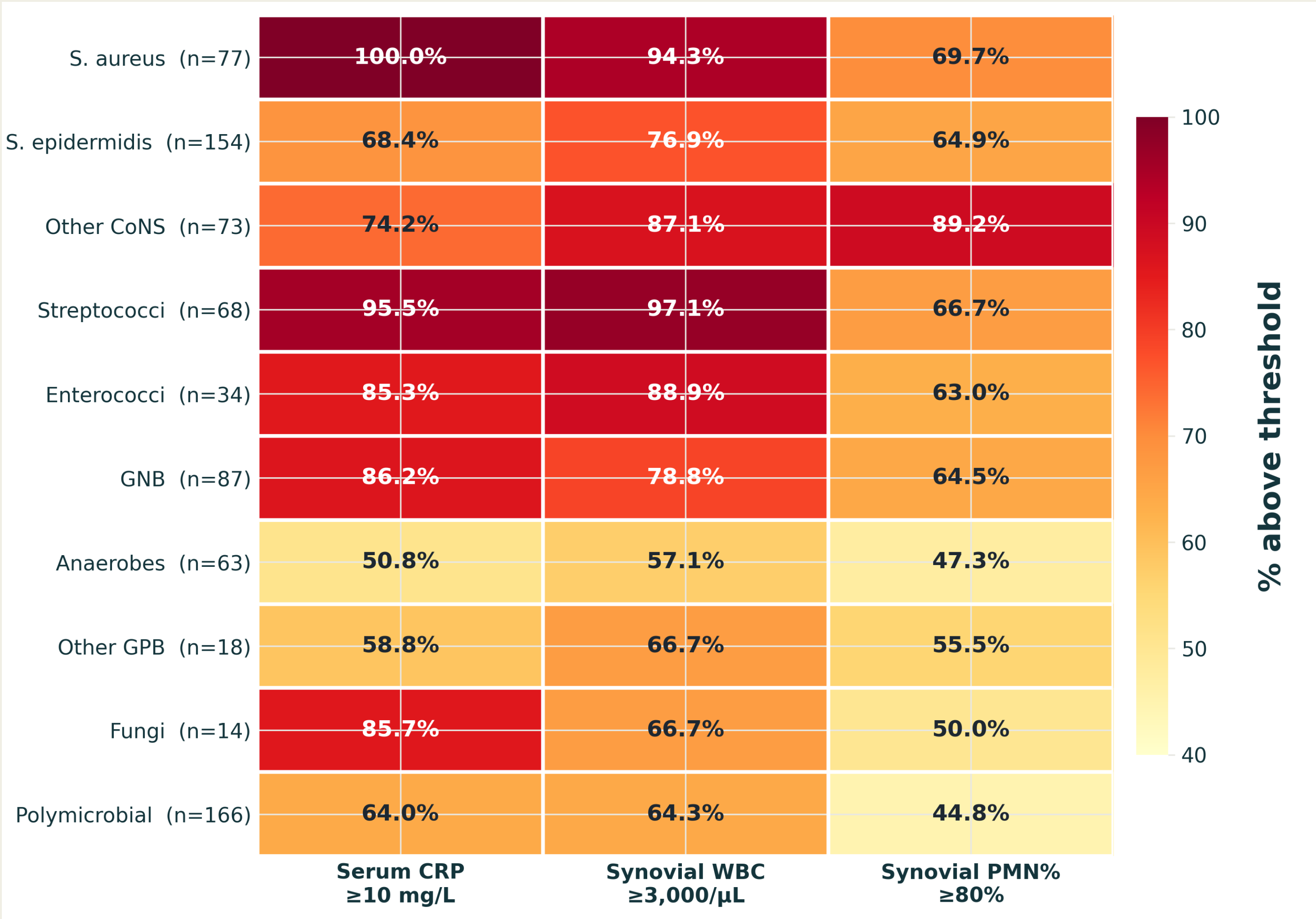


Figure 1: Pathogen-specific probability of exceeding EBJIS biomarker thresholds

Streptococci and *S. aureus* had the highest mean synovial WBC counts (109.5 and 49.0 $\times 10^9/L$, respectively) and the greatest proportion of results above the EBJIS WBC threshold (97.1% and 94.3%). In contrast, only 57.1% of anaerobic and 64.3% of polymicrobial PJIs exceeded the WBC threshold.

At the PMN% $\geq 80\%$ threshold, other CoNS had the highest positivity (89.2%), whereas fewer than half of polymicrobial (44.8%) and anaerobic (47.3%) infections exceeded the threshold despite confirmed PJI.

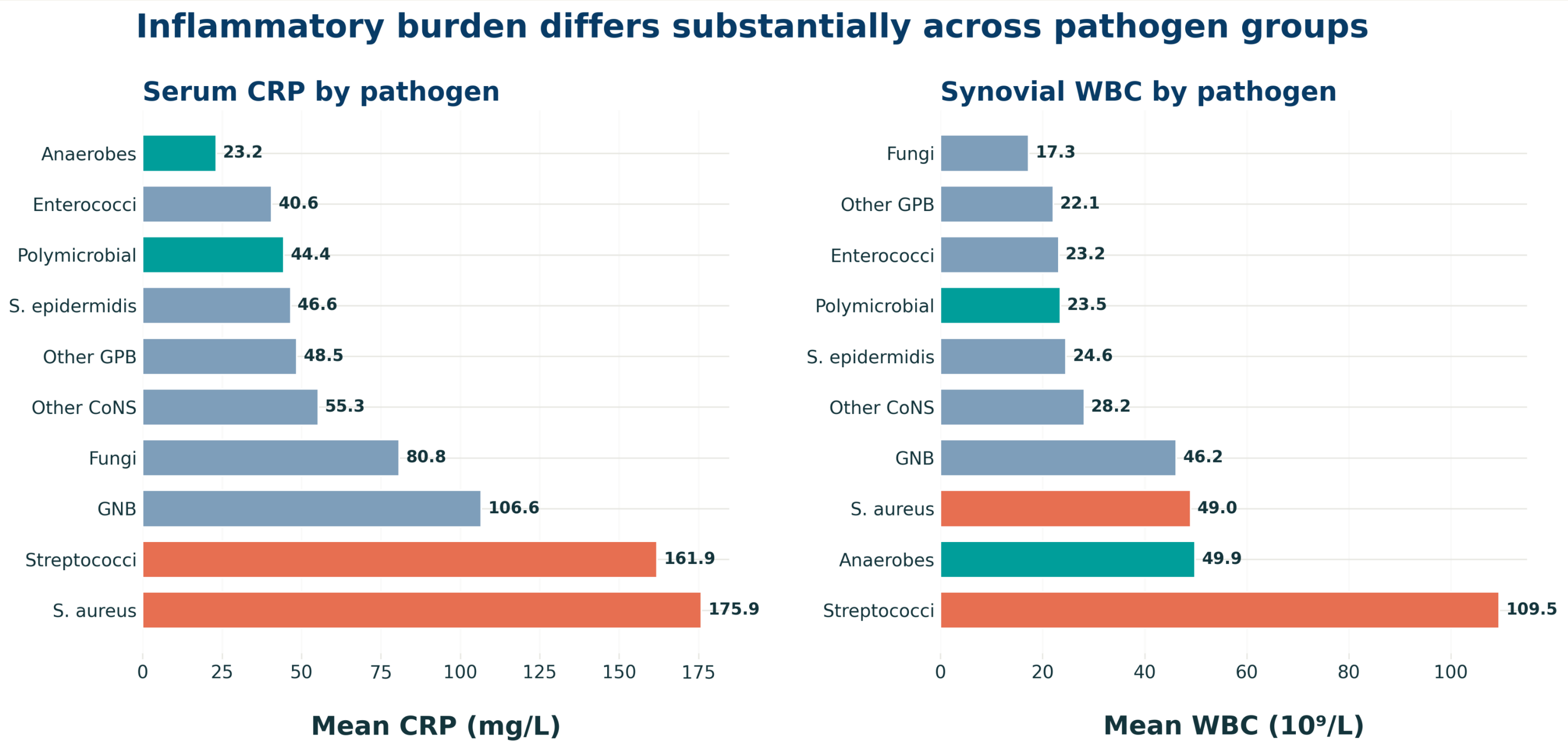


Figure 2: Mean levels of serum CRP and synovial WBC

S. aureus and streptococci had the highest mean serum CRP levels (175.9 and 161.9 mg/L, respectively). All *S. aureus* PJIs exceeded the CRP ≥ 10 mg/L threshold, compared with only 50.8% of anaerobic PJIs.

Pathogen-specific inflammatory marker profile in chronic hip and knee PJI				
Pathogen group	n	Mean serum CRP (mg/L)	Mean synovial WBC ($10^9/L$)	Mean PMN (%)
S. aureus	77	175.9	49.0	80.5
S. epidermidis	154	46.6	24.6	75.2
Other CoNS	73	55.3	28.2	85.9
Streptococci	68	161.9	109.5	80.8
Enterococci	34	40.6	23.2	79.1
GNB	87	106.6	46.2	73.1
Anaerobes	63	23.2	49.9	67.2
Other GPB	18	48.5	22.1	81.3
Fungi	14	80.8	17.3	68.2
Polymicrobial	166	44.4	23.5	64.3

Overall comparison across 10 pathogen groups: serum CRP and synovial WBC, $p < 0.001$; PMN%, $p = 0.006$.

Figure 3: Pathogen-specific mean inflammatory marker profile in chronic hip and knee PJI

Monomicrobial PJI showed higher serum CRP, synovial WBC, and PMN% than polymicrobial PJI (all $p \leq 0.004$). Within polymicrobial PJI, the number of co-infecting pathogens was not associated with biomarker levels (all $p > 0.16$); however, high-virulence combinations had higher synovial WBC ($p < 0.001$) and serum CRP ($p = 0.001$) than low-virulence combinations.

Conclusion

- ✓ Routine PJI biomarkers are pathogen dependent.
- ✓ Low-virulence bacteria, anaerobes, and polymicrobial infections often fall below established EBJIS thresholds, posing a clinically significant risk of false-negative results.
- ✓ In polymicrobial PJI, attenuated biomarker levels are related to virulence composition rather than the number of detected pathogens.
- ✓ Do not exclude PJI solely on normal routine markers when anaerobic or polymicrobial infection is clinically plausible.