www.journalmsr.com

الجمعية السعودية لجراحة العظام
Saudi Orthopedic Association

Journal of Musculoskeletal Surgery and Research

Article in Press

Original Article

Correlation of native knee joint septic arthritis and bacteremia: A retrospective study

Melissa C. Soderquist, MD[1], Emily Ren, BS[2], Esha R. Kadakia, BS[2], Mark Solarz, MD[1]

[1]Department of Orthopedic Surgery and Sports Medicine, Temple University Hospital, [2]Lewis Katz School of Medicine at Temple University, Philadelphia, Pennsylvania, United States.

***Corresponding author:**
Melissa C. Soderquist, Department of Orthopedic Surgery and Sports Medicine, Temple University Hospital, Philadelphia, Pennsylvania, United States.

mcsoderquist@gmail.com

Received: 01 February 2023
Accepted: 27 February 2023
EPub Ahead of Print: 18 March 2023
Published:

DOI
10.25259/JMSR_28_2023

Quick Response Code:

ABSTRACT

Objectives: Septic arthritis is an orthopedic emergency, delayed treatment results in rapid, and irreversible joint destruction with significant morbidity and mortality. The correlation between the infectious organism(s) isolated from blood and synovial fluid remains unclear. Native joint septic arthritis (NJSA) is often secondary to bacteremia and other contiguous sources of infection. This investigation examined the correlation in infectious organisms between blood and synovial fluid in patients with NJSA and concurrent bacteremia.

Methods: A retrospective chart review was performed on 712 NJSA cases at an urban, level-one trauma center. Patients diagnosed with septic knee arthritis through synovial fluid analysis with white blood cell count >50,000 and/or positive culture from the knee joint on aspiration were included in the study. The organism identified on blood culture in the bacteremic patient was then correlated to the organism found on synovial fluid analysis.

Results: We identified 104 patients at our institution with septic knees; 48 with bacteremia and 56 that did not have bacteremia. Of these patients with bacteremia, 34 patients (70.8%) had the same organism isolated in the knee and the blood. This correlation was statistically significant, with $P = 0.003$. Furthermore, patients with bacteremia underwent a mean of 1.85 ± 0.76 debridement procedures versus 1.21 ± 0.80 procedures in those without ($P = 0.001$).

Conclusion: This study shows a correlation between the organism isolated from the knee and the blood in patients with NJSA in conjunction with bacteremia as well as a correlation between the bacteremic patient and the number of surgical interventions required per patient.

Keywords: Arthrocentesis, Bacteremia, Culture, Knee, Native knee septic arthritis, Septic arthritis

INTRODUCTION

Acute bacterial native joint septic arthritis (NJSA), defined as the pyogenic inoculation of a joint, classically presents as a patient with fever, joint swelling, and joint pain. NJSA is an orthopedic emergency as delayed or inadequate treatment leads to poor health outcomes, including rapid and irreversible destruction of the joint with subsequent disability and significant mortality (case-fatality rate of 11%).[1,2] Common risk factors of NJSA include age >60, pre-existing joint disease, diabetes mellitus (DM), recent trauma, immunosuppression, and substance

How to cite this article: Soderquist MC, Ren E, Kadakia ER, Solarz M. Correlation of native knee joint septic arthritis and bacteremia: A retrospective study. J Musculoskelet Surg Res, doi: 10.25259/JMSR_28_2023

ScientificScholar®
Knowledge is power
Publisher of Scientific Journals

This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 4.0 License, which allows others to remix, transform, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms. ©2023 Published by Scientific Scholar on behalf of Journal of Musculoskeletal Surgery and Research

use. The current incidence of NJSA is approximately two cases/100,000 person-years; however, incidence across all age groups is increasing. It is postulated that this increase can be attributed to an increase in orthopedic-procedure-related infection, the use of immunosuppressant drugs, aging populations, and antibiotic resistance.[2-4]

NJSA is an uncommon and poorly studied condition despite its significant mortality and adverse health outcomes. This is in part due to the difficulty of rapid and specific diagnosis outside of the careful examination by an experienced physician.[4] When NJSA is present with concomitant bacteremia, the correlation of the infectious organism(s) isolated from blood and synovial fluid remains unclear. NJSA is often secondary to bacteremia and other contiguous sources of infection. These include osteomyelitis or concurrent soft-tissue infection due to the vulnerable vascular synovium allowing bacterial seeding to the joint.[3,5] Patients with polyarticular NJSA are more likely to present with bacteremia compared to monoarticular NJSA.[6] NJSA of unknown etiology is often attributed to transient bacteremia, which potentially complicates accurate diagnosis and treatment plans.[5] The presence of concurrent bacteremia may result in recurrent joint infections, resulting in poor patient outcomes.[7] Polyarticular NJSA, concurrent bacteremia, and recurrent joint infections often necessitate a greater number of surgical procedures and a prolonged course of antibiotics to eradicate the infection.

Staphylococcus aureus is the most common organism isolated from a septic joint. There is also an increasing incidence of Methicillin-resistant *S. aureus* (MRSA) infections and infection with streptococci and Gram-negative rods.[8,9] Specific organisms are correlated with joint distribution, age group, and specific risk factors such as intravenous drug use (IVDU), comorbidities, and geographic location.[2,3,5,9]

Our institution provides comprehensive care to a historically underserved community of lower socioeconomic status. These populations are disproportionately affected by NJSA and may face worse outcomes despite adequate care.[9] This investigation examines the correlation between NJSA and concurrent bacteremia in knee joint infections over time as well as determines any correlation in infectious organisms between blood and synovial fluid in NJSA/bacteremia patients. Reviewing the epidemiology of NJSA and bacteremia specifically within our institution may contribute to more tailored clinical decision-making, management, and further insight into the clinical characteristics of this condition.

MATERIALS AND METHODS

After obtaining approval from our university's Institutional Review Board, a retrospective chart review was performed on 712 NJSA cases presented to an urban, level-one trauma center between January 1, 2011, and March 31, 2021. The chart review was conducted using our electronic medical record, International Classification of Diseases – Ninth Revision (ICD-9) codes 711.06, as well as Tenth Revision (ICD-10), codes M00.869. Native knee septic joint arthritis was specified using these codes.

In this study, NJSA was defined as a pathogenic infection of the native joint, diagnosed through synovial fluid analysis with a white blood cell (WBC) count >50,000, and/or positive culture from the knee joint on aspiration.[10] Patients were included if they were diagnosed with NJSA of the knee from age 18 years to 89 years. After clinical chart review, patients who did not have NJSA based on synovial WBC count >50,000 or positive culture from the knee joint on aspiration or surgical intervention were excluded from the study.

The medical record was reviewed for the following information: Age, gender, race, ethnicity, zip code, insurance status, body-mass index (BMI), comorbidities, Charlson comorbidity index, location, infectious organism isolated, IVDU status, mono versus polyarticular infection, presence and mechanism of bacteremia, recurrent or first infection, immunosuppressant medication, smoking status, surgical history, HIV status, hepatitis C status, DM status, history of rheumatologic disorders, history of steroid injections, date of initial infection, serum C-reactive protein (CRP), serum WBC count, synovial WBC count, neutrophil percent, serum procalcitonin, and treatment outcome. If available, the Kocher criteria (non-weight-bearing, temperature >38.5°C/101.3°F, erythrocyte sedimentation rate (ESR) >40 m/h, and WBC >12,000 cells/mm^3) were noted.

Data analysis

Statistical analysis was performed using only de-identified data. Baseline and demographic characteristics were summarized using descriptive statistics. We examined the association of bacteremia, comorbidities, BMI, demographic information, WBC count, percent polymorphonuclear leukocytes, and the number of surgical procedures with the presence of NJSA. We conducted Chi-squared tests for categorical variables and *t*-tests for continuous variables, comparing the groups of patients with and without bacteremia. We used $P < 0.05$ denoting statistical significance and no adjustment for the multiple comparisons.

RESULTS

From ICD-9 and ICD-10 codes, 200 patients were identified with septic arthritis in the selected period. After manual chart review, 104 of these patients were identified as having NJSA of the knee based on a WBC count >50,000 cells/mm^3 or by organism growth on culture from aspiration or operative intervention. Of these patients, 48 (46.1%) were found to be bacteremic. Demographic information is shown in [Table 1].

Table 1: The demographic information of patients with and without bacteremia.

	No bacteremia *n*=56		Bacteremia *n*=48		*P*-value
	Mean	S.D.	Mean	S.D.	
Age (years)	49.13	13.78	48.42	16.76	0.813
BMI	29.94	11.10	27.39	7.48	0.183
Sex					
Male	46		32		0.07
Female	10		16		
Race					
Black	21		18		0.83
Hispanic/ Latino	13		9		
White	17		18		
Other	5		3		
Ethnicity					
Hispanic	15		9		0.33
Non-Hispanic	41		39		
Insurance					
Private	24		16		0.53
Medicaid	20		20		
Medicare	9		11		
Uninsured/ Other	3		1		

S.D.: Standard deviation

[Table 2] demonstrates the organism isolated in the synovial fluid in patients without bacteremia. We found that of these 48 patients with bacteremia, 16 (33.3%) of these patients' blood cultures isolated MRSA, 12 (25%) isolated methicillin-susceptible *S. aureus* (MSSA), and 20 (41.7%) isolated other organisms. These organisms included *Streptococcus agalactiae*, *Pseudomonas aeruginosa*, *Streptococcus dysgalactiae*, *Bacillus cereus*, and *Klebsiella pneumoniae*. Of these patients with bacteremia, 34 (70.8%) patients had the same organism isolated in the knee and the blood. Ten (20.8%) patients had a growth on blood cultures, but no organism was isolated on cultures from the knee. Four (8.3%) patients had different organisms isolated in the blood and the knee. This was statistically significant, with $P = 0.003$ [Table 3].

[Table 4] shows the mean values and standard deviations of the serum and synovial fluid analysis in both groups. There was no significant difference between CRP, WBC count in the blood, neutrophil count in the blood, WBC count of the knee synovial fluid, and neutrophil count from the knee synovial fluid. The mean CRP of the patients without bacteremia was 75.95 mg/L, whereas the mean CRP of the bacteremic patients was 58.5 mg/L. The mean WBC count in the serum of the patients without bacteremia was 12.32 cells/mm^3, whereas in the patients with bacteremia was 14.63 cells/mm^3. The WBC count of the synovial fluid of the patients without bacteremia was 83.37k cells/mm^3, whereas the mean WBC count of the synovial fluid in the patients with bacteremia was 65.91k cells/mm^3. This was not statistically significant.

Table 2: The organism isolated in the knee synovial fluid in patients without bacteremia.

No bacteremia (*n*=56)		
Knee synovial fluid organism	MSSA	16
	MRSA	11
	Other	12
	No Growth	17

MSSA: Methicillin-susceptible *Staphylococcus aureus*, MRSA: Methicillin-resistant *Staphylococcus aureus*

Table 3: The correlation of organisms identified in the blood and the knee.

Correlation of blood and knee organism		
Organism	**Number of patients**	***P*-value**
MSSA/MSSA	9	0.003
MRSA/MRSA	12	
Other/Other	13	
No growth in knee	10	
Different organism in blood versus knee	4	

MSSA: Methicillin-susceptible *Staphylococcus aureus*, MRSA: Methicillin-resistant *Staphylococcus aureus*

Table 4: The CRP, serum WBC analysis, and knee joint synovial fluid analysis for all patients included in this study.

	No bacteremia (*n*=56)		Bacteremia (*n*=48)		*P*-value
	Average	S.D.	Average	S.D.	
CRP	75.95	111.45	58.50	101.74	0.421
WBC serum (K/microL)	12.32	5.11	14.63	7.72	0.073
PMNs serum (%)	74.23	12.32	77.24	12.28	0.639
WBC synovial fluid (K/ microL)	83.37	105.39	65.91	64.61	0.380
PMNs synovial fluid (%)	89.21	11.17	86.18	15.62	0.297

WBC: White blood cell, PMNs: Polymorphonuclear leukocytes, CRP: C-reactive protein, S.D.: Standard deviation

[Table 5] shows the number of patients with selected medical comorbidities with or without bacteremia that were found to have a septic knee. The only comorbidity in this case that was statistically significant was recent bacteremia.

Patients with bacteremia underwent a mean of 1.85 ± 0.76 debridement procedures versus 1.21 ± 0.80 procedures in

those without (P = 0.001). Eleven patients with bacteremia underwent three or more irrigation and debridement procedures, whereas seven patients without bacteremia underwent three or more procedures [Table 6].

DISCUSSION

We identified 104 patients at our institution with septic knees; 48 (46.1%) with bacteremia and 56 (53.8%) that did not have bacteremia. There were no significant differences in the patient demographic information between these two groups, including age, BMI, gender, race, ethnicity, and insurance provider [Table 1]. The etiology of septic arthritis can be difficult to identify. However, several known risk factors have been detailed in previously published literature, including age >60 years, recent bacteremia, DM, cancer, cirrhosis, renal disease, drug or alcohol abuse, recent surgery, history of steroid use, and rheumatoid arthritis.[11] We found that of these 48 patients with bacteremia, 16 of these patients' blood cultures isolated MRSA, 12 isolated MSSA, and 20 isolated other organisms. These other organisms included *S. agalactiae*, *P. aeruginosa*, *S. dysgalactiaee*, *B. cereus*, and *K. pneumoniae*. Of these patients with bacteremia, 34 patients had the same organism isolated in the knee and the blood. Mechanistically, this is easy to understand as NJSA is introduced into a joint either as a result of hematogenous spread or by direct inoculation.[2] This correlation was statistically significant with P = 0.003.

Table 5: The correlation between medical comorbidities in patients with or without bacteremia that were found to have a septic knee.

	Number of patients		*P*-value
	No Bacteremia (*n*=56)	Bacteremia (*n*=48)	
Reinfection	15	11	0.65
Age > 60	10	13	0.26
Recent bacteremia	3	30	<0.01
DM	17	17	0.58
Cancer	6	4	0.68
Liver disease	4	3	0.86
Renal disease	10	10	0.70
CVD	13	16	0.25
HTN	30	25	0.88
Dementia	1	2	0.47
COPD	4	5	0.55
Connective tissue disease	0	3	0.06
Peptic ulcer	0	2	0.12
Hemiplegia	1	1	0.91
AIDS	2	1	0.65
Substance use disorder	38	30	0.57
History of steroid use	10	8	0.87
Recent surgery	20	20	0.53
Rheumatoid	0	3	0.06
Smoking	22	24	0.27
HIV	7	4	0.49
Hepatitis C	23	24	0.36

DM: Diabetes mellitus, CVD: Cardiovascular disease, HTN: Hypertension, COPD: Chronic obstructive pulmonary disease, AIDS: Acquired immunodeficiency syndrome

Table 6: The number of surgical interventions required in patients with NJSA with and without bacteremia.

Number of surgical interventions			
	Bacteremia (*n*=48)	No bacteremia (*n*=56)	P-value
0	4	6	<0.001
1	26	23	
2	15	12	
3+	11	7	

Furthermore, in our study, ten patients had a growth on blood cultures, but no organism was isolated on cultures from the knee. This is possibly due to early antibiotic administration, a bacterial inhibitor such as complement, or an organism that is difficult to grow on synovial culture media, such as *Kingella*.[12-14] Four patients had different organisms isolated in the blood and the knee. Mathews *et al.* found that in patients where bacteria were not isolated from the joint, microorganisms were detected in blood culture in 11% and from other sources in 7%, reinforcing the importance of appropriate cultures.[15] Due to the concern for the development of rapid joint destruction, empiric broad-spectrum antibiotics are typically initiated directly following joint aspiration.[8] The results of our study would support early empiric antibiotic selection based on the organism isolated from blood culture results when available in those patients with bacteremia and concurrent NJSA. This would allow for earlier tailored antibiotic administration in patients with no growth on knee aspiration culture, as blood cultures are often drawn at the time of presentation to the hospital.

Patients with MRSA infections warrant special consideration, given the increasing resistance to vancomycin.[16] In particular, some strains of MRSA are positive for the virulence factor panton-valentine leucocidin cytotoxin, which enables them to survive in neutrophils. These strains are associated with fulminant infections and have accounted for the increased frequency of joint infections in the USA.[2] In addition, antibiotic duration in uncomplicated septic arthritis is recommended for 3–4 weeks. However, in the bacteremic patient, this may not be sufficient.[17] McBride *et al.* found an average antibiotic duration of 40 days in 302 patients with large joint septic arthritis.[9] It was not specified if these patients had concurrent bacteremia. Ascione *et al.* utilized arthroscopic debridement techniques and noted CRP normalization in <4 weeks in patients on IV antibiotics.[18] Shukla *et al.* treated patients with native hip septic arthritis with arthroscopic

lavage. Then, they kept patients on IV antibiotics until their CRP was in a normal range and then placed them on oral antibiotics for 2 weeks.[19] There is currently a paucity of data regarding the duration of antibiotic therapy recommended for patients with concurrent bacteremia at the time of infection.[16]

Furthermore, [Table 5] outlines the association between medical comorbidities in patients with septic knees with and without bacteremia. These results found that recent bacteremia was related to an increased likelihood of NJSA. Medical comorbidities remain an important risk factor for knee septic arthritis, particularly in immunocompromised patients, but do not confer increased risk when associated with bacteremia.[15] Rheumatoid arthritis and other connective tissue diseases requiring treatment with disease modifying anti-rheumatic drugs have been found to confer an increased risk of septic arthritis irrespective of adequate therapy.[16] McBride *et al.* found a correlation between septic arthritis and those patients who had a surgical procedure within the past 3 months or a skin or soft-tissue infection, rheumatoid arthritis, gout, or end-stage renal disease on dialysis.[9]

In addition, [Table 6] shows the number of surgical interventions in patients with a septic knee with and without bacteremia. Patients with bacteremia underwent a mean of 1.85 ± 0.76 debridement procedures versus 1.21 ± 0.80 procedures in those without (P = 0.001). Jung *et al*. found that patients with systemic sepsis had a higher incidence of recurrent infection and, therefore, required a greater number of surgical interventions.[7] Early diagnosis and treatment are instrumental in limiting patients' morbidity and mortality.[20,21] This has important implications for patients as well as the health-care system. A greater number of surgical interventions is indicative of more difficulty treating the septic joint, possibly due to increased hematogenous seeding of the joint, making the infection more difficult to eradicate. Patients with septic arthritis of the knee have decreased function compared to the contralateral knee, with bacteremia possibly increasing patient mortality and difficulty with joint salvage.[22] Furthermore, increased surgical interventions result in a longer length of stay in the hospital, resulting in greater health-care costs.

The limitations of this study include patients from a single institution, which can limit the scope of practice. In addition, with this being a retrospective chart review, there are inherent limitations, including missing charts and limited data availability.

CONCLUSION

This study shows a correlation between the organism isolated from the knee and the blood in patients with NJSA in conjunction with bacteremia. It also demonstrates a correlation between the bacteremic patient and the number of surgical interventions required per patient. This has significant health-care implications regarding antibiotic therapy in the patient with bacteremia and concurrent NJSA of the knee. More investigation could be performed, looking at the outcomes and function in patients with NJSA with bacteremia compared to those without bacteremia in the future.

AUTHORS' CONTRIBUTIONS

Author/s testifies that all persons designated as authors qualify for authorship and have checked the article for plagiarism. If plagiarism is detected, all authors will be held equally responsible and will bear the resulting sanctions imposed by the journal thereafter. ER and ERK collected and organized data. MCS organized data, performed statistical analysis, and wrote the initial and final drafts. MS designed the study and critically reviewed and approved the final draft. All authors have critically reviewed and approved the final draft and are responsible for the manuscript's content and similarity index.

ETHICAL APPROVAL

This study was approved by the Temple University Hospital Institutional Review Board, IRB #28389, on May 1, 2021.

DECLARATION OF PATIENT CONSENT

The authors certify that In this retrospective chart review they have obtained all appropriate patients consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

FINANCIAL SUPPORT AND SPONSORSHIP

This study did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CONFLICTS OF INTEREST

There are no conflicting relationships or activities.

REFERENCES

1. Mathews CJ, Kingsley G, Field M, Jones A, Weston V, Phillips M, *et al*. Management of septic arthritis: A systematic review. Postgrad Med J 2008;84:265-70.
2. Mathews CJ, Weston VC, Jones A, Field M, Coakley G. Bacterial septic arthritis in adults. Lancet 2010;375:846-55.
3. Goldenberg DL. Septic arthritis. Lancet 1998;351:197-202.
4. García-Arias M, Balsa A, Mola EM. Septic arthritis. Best Pract

Res Clin Rheumatol 2011;25:407-21.
5. Clerc O, Prod'hom G, Greub G, Zanetti G, Senn L. Adult native septic arthritis: A review of 10 years of experience and lessons for empirical antibiotic therapy. J Antimicrob Chemother 2011;66:1168-73.
6. Lieber SB, Fowler ML, Zhu C, Moore A, Shmerling R, Paz Z. Clinical characteristics and outcomes in polyarticular septic arthritis. Joint Bone Spine 2018;85:469-73.
7. Jung SW, Kim DH, Shin SJ, Kang B, Who Y, Yang S. Septic arthritis associated with systemic sepsis. Int Orthop 2018;42:1-7.
8. Ross JJ. Septic arthritis. Infect Dis Clin North Am 2005;19:799-817.
9. McBride S, Mowbray J, Caughey W, Wong E, Luey C, Siddiqui A, *et al*. Epidemiology, management, and outcomes of large and small native joint septic arthritis in adults. Clin Infect Dis 2020;70:271-9.
10. Kocher MS, Mandiga R, Zurakowski D, Barnewolt C, Kasser J. Validation of a clinical prediction rule for the differentiation between septic arthritis and transient synovitis of the hip in children. J Bone Joint Surg Am 2004;86:1629-35.
11. Elsissy JG, Liu JN, Wilton PJ, Nwachuku I, Gowd AK, Amin NH. Bacterial septic arthritis of the adult native knee joint: A review. JBJS Rev 2020;8:e0059.
12. Yagupsky P, Peled N, Katz O. Epidemiological features of invasive *Kingella kingae* infections and respiratory carriage of the organism. J Clin Microbiol 2002;40:4180-4.
13. Hughes JG, Vetter EA, Patel R, Schleck C, Harnsen S, Turgeant L, *et al*. Culture with BACTEC Peds Plus/F bottle compared with conventional methods for detection of bacteria in synovial fluid. J Clin Microbiol 2001;39:4468-71.
14. Hepburn MJ, Fraser SL, Rennie TA, Singleton C, Delgado B. Septic arthritis caused by *Granulicatella adiacens*: Diagnosis by inoculation of synovial fluid into blood culture bottles. Rheumatol Int 2003;23:255-7.
15. Mathews CJ, Coakley G. Septic arthritis: Current diagnostic and therapeutic algorithm. Curr Opin Rheumatol 2008;20:457-62.
16. Sharff KA, Richards EP, Townes JM. Clinical management of septic arthritis. Curr Rheumatol Rep 2013;15:332.
17. Ross JJ. Septic arthritis of native joints. Infect Dis Clin North Am 2017;31:203-18.
18. Ascione T, Balato G, Mariconda M, Rosa D, Rizzo M, Pagliano P. Post-arthroscopic septic arthritis of the knee: Analysis of the outcome after treatment in a case series and systematic literature review. Eur Rev Med Pharmacol Sci 2019;23:76-85.
19. Shukla A, Beniwal SK, Sinha S. Outcome of arthroscopic drainage and debridement with continuous suction irrigation technique in acute septic arthritis. J Clin Orthop Trauma 2014;5:1-5.
20. Ballard A, Burkhalter WE, Mayfield GW, Dehne E, Brown P. The functional treatment of pyogenic arthritis of the adult knee. J Bone Joint Surg Am 1975;57:1119-23.
21. Samilson RL, Watkins MB, Winters DM. Acute suppurative arthritis. J Bone Joint Surg Am 1956;38:1313-20.
22. Sreenivas T, Nataraj AR, Menon J. Acute hematogenous septic arthritis of the knee in adults. Eur J Orthop Surg Traumatol 2013;23:803-7.