



Review article

Clinical outcomes involving patients that develop septic arthritis with methicillin sensitive staphylococcus aureus versus methicillin resistant staphylococcus aureus

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ABSTRACT

Septic Arthritis is an orthopedic emergency that requires prompt diagnosis and treatment. Staphylococcus aureus is the most common pathogen causing septic arthritis. This review seeks to describe clinical characteristics and outcomes associated with patients with methicillin-resistant (MRSA) vs. methicillin-sensitive staphylococcus aureus (MSSA) septic arthritis. The review showed that those infected with MRSA were older, had more chronic medical conditions, and higher values of inflammatory markers. MRSA septic arthritis was also associated with more complications, longer duration of antibiotics, and increased mortality. Thus, health care providers should maintain a high index of suspicion, diagnose, and treat aggressively to prevent adverse outcomes.

1. Introduction and background

Septic arthritis is an infection of a joint cavity, and is an orthopedic emergency that requires prompt diagnosis and treatment. The infection can lead to rapid joint destruction and associated morbidity and mortality. Septic arthritis encompasses infection of the joint caused by bacteria, fungi, mycobacteria, or viruses. Bacterial joint infections are the most common.¹ Septic arthritis usually presents as a mono-microbial infection, but can also present as a poly-microbial infection. Bacterial septic arthritis is estimated to account for 8–27 percent of acutely painful joints in adults.² Risk factors for development of septic arthritis include: age greater than 80, diabetes mellitus, rheumatoid arthritis, presence of a prosthetic joint, recent joint surgery, concurrent skin infection, intravenous drug use, and recent intraarticular corticosteroid injection.³

Overall, Staphylococcus Aureus is the most common pathogen that causes septic arthritis.⁴ Septic arthritis can be caused by both Methicillin Sensitive Staphylococcus Aureus (MSSA) and Methicillin Resistant Staphylococcus Aureus (MRSA). MRSA infection prevalence has increased with the continuously increasing amount of antibiotic resistance.⁵ MRSA infections can present as both hospital acquired and community acquired infections.

Despite the known fact that septic arthritis can be caused by both MSSA and MRSA, there have been a limited number of studies that examine the difference in clinical characteristics and clinical outcomes

of patients that develop septic arthritis caused by these two causative agents. This review aims to stratify the risk of cases of septic arthritis caused by MSSA versus MRSA in order to guide clinicians on management and expected clinical outcomes associated with these microorganisms.

The available literature was searched using the PubMed database with keywords: “septic,” “arthritis,” “MSSA,” “versus,” “and,” “MRSA,” “outcomes.” Articles that compared cases of septic arthritis in individuals of any age caused by MSSA and MRSA were included. Endpoints for this review included clinical outcomes including but not limited to: length of hospital stay; length of antibiotic treatment required; number of operations required; disease recurrence; and sepsis related mortality. 8 papers were identified that fit the aforementioned criteria. A critical appraisal was performed for each article and the methodology and results of the papers are reported in the subsequent review section. Differences in rates of the aforementioned outcomes; relative risk values; odds ratios; confidence intervals; and the corresponding p-values for each article were included in the review of each article.

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2. Review

2.1. Article 1: methicillin resistant staphylococcus aureus versus methicillin sensitive staphylococcus aureus adult haematogenous septic arthritis⁶

A retrospective analysis was performed on all patients presenting to Leeds Teaching Hospital over a five year period with adult haematogenous septic arthritis. The patients included were from primary and tertiary referrals. There was no uniform early time that all patients were enrolled due to the retrospective nature of this prognostic study. All patients that met the inclusion criteria were assessed for clinical outcomes of their septic arthritis for 1 year of follow-up. There is clear definition of the outcomes assessed between MSSA and MRSA groups, but there is no mention of blinding the researchers that evaluated the data and determined the clinical outcomes between the two groups. There were no sub-groups with different prognoses identified therefore there was no adjustment for different prognoses between subgroups.

The results were reported as percentages of the two sub-groups that developed a specific clinical outcome (eg. operative outcome, antimicrobial duration, recurrence, sepsis related mortality). These outcomes were assessed in the one year follow-up for all eligible patients. Continuous variables were analyzed using Student's *t*-test and dichotomous variables were analyzed using Fisher's exact test. There were no reported 95% confidence intervals in this study, but significant results correspond to a *p*-value < 0.05. MRSA patients were significantly older, more likely to have a nosocomial infection, have more chronic medical conditions, and had a stronger association with end-stage renal failure. MSSA patients were significantly more likely to be intravenous drug users. MRSA patients were significantly more likely to be treated with inappropriate empirical antibiotics. MRSA patients did have a strong trend towards a higher all cause 6 month mortality rate than MSSA patients.

2.2. Article 2: changing patterns of acute hematogenous osteomyelitis and septic arthritis: emergence of community-associated methicillin-resistant staphylococcus aureus⁷

This retrospective chart review conducted at Le Bonheur Children's Medical Center at the University of Tennessee Health Science Center in Memphis, Tennessee between 2000 and 2004 included children diagnosed with acute hematogenous osteoarticular infections. All patients enrolled in the study must have had no more than 14 days of symptoms prior to presentation at the hospital. Patient records were obtained throughout the duration of their hospitalization until discharge. The goal of this study was to determine total and pathogen-specific incidence rates of acute hematogenous osteoarticular infections and to compare clinical and demographic features of children with MRSA infections with those with MSSA infections. Outcomes were clearly defined as duration of symptoms before clinical presentation, laboratory parameters upon admission and follow-up, number of calendar days in the hospital, number of calendar days with fever and positive blood cultures, culture results, radiographic assessments, surgical and non-surgical procedures, antimicrobial therapy, complications, duration of therapy and short-term outcomes. There were no prognostic factors that were adjusted for in this study.

Data was analyzed using Kruskal-Wallis tests, χ^2 analysis, or Fisher exact test where appropriate. Results showed increasing incidence of total infections but the rate of MSSA infections remained constant throughout the course of the study while the rate of MRSA infections increased from 4%-40%. There were no differences in the duration of fever or pain before the diagnosis. There was significantly increased risk for subperiosteal abscess formation, requirement of surgical procedures, and mean length of hospital stay in patients with MRSA infections as compared to those with MSSA infections. However, there was no increase in the rate of developing chronic osteomyelitis despite the increase in the severity of community acquired MRSA infections. This

study reported that 46 of 47 MRSA infections in the community of focus were susceptible to clindamycin. Ultimately, this study recommended that careful evaluation for subperiosteal and muscle or soft-tissue abscess as well as other complications must be conducted to ensure prompt resolution of MRSA infections, which are potentially life-threatening. This study recommends antibiotic coverage of MRSA in empiric management of osteoarticular infections, though antibiotic susceptibility in your respective communities should drive the choice in antibiotic.

2.3. Article 3: community-acquired methicillin-resistant staphylococcus aureus musculoskeletal infections: emerging trends over the past decade⁸

This is a retrospective chart review conducted at Children's Hospital of Philadelphia, a tertiary-care children's hospital, between 2001 and 2010 that included previously healthy children and adolescents below the age of 19 years of age with acute musculoskeletal *S. aureus* infections. The goal of the study was to identify epidemiological trends of MRSA and MSSA infections in the Philadelphia community over a decade by comparing patient age, gender, infection type, dates of admission and discharge, MRI studies, CRP levels at presentation, number of surgical procedures performed, antibiotic treatment regimens, length of inpatient treatment, and complications during hospitalization between the two groups. There is no uniform early time that all patients were enrolled in this study due to the retrospective nature of the study. Patient records were obtained and the follow-up period was the length of the patient's hospital stay. The outcomes in this study were clearly defined, however there was no mention of blinding the researchers to the clinical outcomes described in this study. There was no adjustment for different prognostic factors between the two groups.

Patients were divided into two cohorts for data analysis: culture positive MRSA and culture positive MSSA. The data were analyzed by using a 2-sample Student's *t*-test and Mann-Whitney *U* test for continuous variables and Pearson χ^2 test was used to compare categorical data. A *p*-value < 0.05 was considered statistically significant. The prevalence of patients with culture positive MRSA infections in the community of focus increased threefold over the studied 10 year period. MRSA infections were also associated with a significant increase in CRP levels at admission, length of hospital stay, and number of surgical interventions. These results increase awareness of these rising trends and provide a scaffold to counsel patients and family members on the increased risk for complications and other sequelae posed by MRSA infections.

2.4. Article 4: adult native septic arthritis in an inner city hospital: effects on length of stay⁹

A retrospective analysis of all patients presenting with native joint infections between 1999 and 2008 were identified. It is unclear whether the patients included were from a primary or tertiary center. There is no uniform early time that all patients were enrolled due to the retrospective nature of this prognostic study. There is no mention of the length of follow-up. The study primarily examined the length of hospital stay between the different infectious organisms and did not examine any other clinical outcomes, so it seems as though length of follow-up is not applicable in this study. There is clear definition of the outcome assessed (length of stay) between MSSA and MRSA groups, but there is no mention of blinding the researchers. The study did adjust for prognostic factors including past medical comorbidities.

The results were reported as length of stay between the different groups of patients including those with MSSA and MRSA infections. Spearman's correlation and Mann Whitney U-Tests were performed to assess for statistically significant difference between the two groups in regards to length of stay after developing the infection. Confidence intervals for the length of stay between groups with MSSA and MRSA were not reported. There was no statistically significant difference in

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