



Increased COVID-19 Mortality Risk: A Systematic Review of Clinical Outcomes in Patients Co-infected with COVID-19 and Staphylococcus Aureus

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Objective: Endemic to the hospital environment, *Staphylococcus aureus* is a leading bacterial pathogen causing deadly infections such as bacteremia and endocarditis. In past viral pandemics, it has been the principal cause of secondary bacterial infections, significantly increasing patient mortality rates. Our world now combats the rapid spread of COVID-19, leading to a pandemic with a death toll greatly surpassing those of many past pandemics. However, the impact of co-infection with *Staphylococcus aureus* remains unclear. Therefore, we aimed to systematically review the literature in order to describe the clinical outcomes of COVID-19 and *Staphylococcus aureus* co-infection.

Methods: Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, searches were conducted in PubMed, Scopus, Ovid MEDLINE, CINAHL, ScienceDirect, medRxiv, and the WHO COVID-19 database. Original research articles that were in English, included patients infected with both COVID-19 and *Staphylococcus aureus*, and provided a description of clinical outcomes for patients were eligible. For the final articles that were selected, the following data was extracted: type of staphylococcal species, onset of co-infection, patient sex, age, symptoms, hospital interventions, and clinical outcomes.

Results: Searches generated a total of 779 articles, and of those, a total of 26 studies were eligible for this review. In total, there were 68 co-infected patients. In addition to COVID-19 infection, 63.8% of patients were infected with methicillin-sensitive *Staphylococcus aureus* (MSSA), and 36.2% were infected with methicillin-resistant *Staphylococcus aureus* (MRSA); a single patient was infected with both strains of *Staphylococcus aureus*. 60.3% were diagnosed with hospital-acquired MSSA or MRSA (HA-MSSA or HA-MRSA) infection. 57.4% of patients were male, and mean patient age was 60.4 years (SD = 15.7). Fever, cough, and shortness of breath were the most frequently reported symptoms. Aside from antibiotics, the most common hospital interventions were corticosteroids (25.7%) and intubation with mechanical ventilation (61.8%). There was a total of 43 deaths (63.2%) reported.

Conclusions: Co-infection with COVID-19 and *Staphylococcus aureus* has been shown to considerably increase the risk of patient mortality during hospital admission. Unfortunately, the most common treatments for COVID-19 in our study, corticosteroids and intubation with mechanical ventilation, are significant risk factors for bacterial infection. Our findings emphasize the imperative of COVID-19 vaccination to prevent hospitalization for COVID-19 treatment and the subsequent susceptibility to hospital-acquired *Staphylococcus aureus* co-infection.