

Title: Antimicrobial stewardship during COVID-19 : An analysis of culture negative patients receiving extended antimicrobials

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Background: Covid is associated with symptoms, clinical findings and lab abnormalities that raise concern for secondary infections. Excess antimicrobial use despite low rates of secondary infections has been reported and presents a continuing challenge for antimicrobial stewardship programs (ASPs), particularly during Covid-19 surges. The objective of this study was to analyze the appropriateness of antimicrobial use in patients with extended antimicrobial therapy during two distinct Covid-19 hospital surges.

Methods: An observational, retrospective, cohort study was conducted for COVID-19 patients who were admitted to our 548-bed community teaching hospital between November-December 2021 (Delta-predominant phase) and January-February 2022 (Omicron-predominant phase) and received antibiotics for more than 4 days without positive cultures. Demographic and clinical data was obtained from the institutional data warehouse. Infectious diseases-trained researchers evaluated the appropriateness of antimicrobials based on diagnostic and clinical reporting, and institutional antimicrobial stewardship guidelines. Patients were considered to have probable secondary bacterial infection if they had 2 of the following: fever, unexplained leukocytosis, worsening secretions, hypoxia and/or imaging. Outcomes of interest included confirmed infections and excess antimicrobial days. Categorical and continuous variables were analyzed by Chi-square tests, Fischer's Exact test, and Mann-Whitney U tests, respectively. Statistical significance was defined as $P \leq 0.05$.

Results: A total of 87 patients were included in the study. Fifty-six patients and 31 patients were identified in the Delta-predominant and Omicron-predominant groups, respectively. The groups were similar with higher vaccination rates in the Omicron-predominant group (37.5% vs. 64.5%; $p=0.016$). Patients in the Omicron-predominant group required less ventilation (39.3% vs. 16.1%; $p=0.025$). There were no differences in infectious diseases consultation, immunomodulator or remdesivir use, antimicrobials classes prescribed, and antimicrobial days of therapy or duration between cohorts. There was also no difference in length of stay, 30-day mortality, or 30-day readmissions. Infections were confirmed in 78.6% and 83.9% ($p=0.55$) of groups with pneumonias accounting for 60.7% and 40.9%, respectively. Excess antibiotic use occurred in 14.3% of patients during the Delta-predominant group and 3.1% in the Omicron-predominant group ($p=0.149$). There was no difference in the duration of inappropriate antimicrobial use between groups in patients without infections (5 days vs. 5 days; $p=0.24$).

Conclusion: Results demonstrated that most antimicrobial use was appropriate in a challenging patient population lacking positive cultures to guide therapy. Inappropriate antimicrobial utilization occurred demonstrating continued opportunities for our institutional ASP.