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Research Brief

Risk factors for healthcare-associated infection among patients hospitalized with COVID-19 infection

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Introduction

The occurrence of healthcare-associated infections (HAIs) increased during the coronavirus disease 2019 (COVID-19) pandemic,[1–3] with the most substantial increase for central line-associated bloodstream infection (CLABSI), and methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremia,[4,5] reversing a multi-decade national trend of decreasing occurrence of these infections and leading to speculation that infection prevention practices had degraded as a result of the pandemic.

The observed increase in HAIs during the COVID-19 pandemic has been linked to increased susceptibility specifically in patients with COVID-19.[6] However, the contributing modifiable and unmodifiable factors have not been described.

Methods

This cross-sectional retrospective analysis was conducted using data collected in the course of clinical care of patients hospitalized with COVID-19 between March 2020 and December 2022 at 182 inpatient facilities affiliated with a system of community hospitals. The diagnosis of COVID-19 was based on lab-confirmed COVID-19, via either molecular or antigen testing, during the encounter or within 30 days of admission without lab-confirmed negative tests prior to admission. CLABSI and MRSA HAIs were measured using National Healthcare Safety Network case definitions and standard HAI surveillance by trained infection preventionists.

Potential risk factors for CLABSI or MRSA were collected from the electronic inpatient record. Logistic regression was used to determine risk factors associated with either HAI. Statistical analysis was completed in R (version 4.1.2).

Results

Among the 321,721 patients hospitalized with COVID-19, we observed 326 MRSA infections (0.1% of all patients) and 628 CLABSIs (0.9% of patients with a central line). MRSA and CLABSI HAIs are more common among patients with higher morbidity as measured by Elixhauser comorbidity scores (mean+/–SD; MRSA vs no MRSA: 15.09+/–10.22 vs 8.07+/–9.08; CLABSI vs no CLABSI: 15.6+/–11.0 vs 12.8+/–10.2). Patients with MRSA versus those without also had higher acuity, as measured by increased ICU utilization (46.3% (151) versus 23.0% (73,627)) and mechanical ventilation (22.4% (73) versus 5.8% (18,694)) within 3 days of admission. A similar higher acuity was seen in patients with CLABSI versus those without (ICU utilization: 62.9% (395) vs 48.7% (35080); mechanical ventilation: 37.9% (238) versus 20.9% (15070)). A longer length of stay (LOS) was also observed in patients with MRSA or CLABSI versus the unaffected counterparts (mean+/–SD days before HAI, MRSA: 18.32+/–20.24 vs 7.91+/–10.61; CLABSI: 20.2+/–15.3 vs 15.1+/–15.6). See the supplemental table for additional demographics of the analysis population.

Identified risk factors (Table 1) included higher comorbidity score on admission, longer LOS, admission to ICU, ventilator support, use of steroids, use of other immunosuppressive agents, and race/ethnicity. Of patients who received steroids, 51% (110,480) received the daily dose equivalent of ≤6 mg of dexamethasone, and 36% (76,773) received the equivalent of >6 mg of dexamethasone. The highest odds ratios relate to the use of strongly immunosuppressive therapies. Because of the correlation between high-dose steroid use and lower age, an interaction term was included. Notably, age does not show a significant association with HAI, independent of the likelihood of receiving high-dose steroids. High-dose steroids correlate with 2–4 times higher odds of infection in those <65 years of age and >65 years of age for either HAI. Tocilizumab and/or baricitinib were associated with nearly twice the odds of HAI. The association for race reached significance with CLABSI only and demonstrated a higher risk among those identifying as Hispanic/Latino or other nonwhite, non-black category.

Discussion

In our analysis of a large multistate population of inpatients with COVID-19, we found that the odds of developing MRSA or CLABSI HAIs were associated with strong immunosuppressive therapies, patient comorbidities, and higher acuity at admission. The odds of infection are most significantly elevated by treatment with immunosuppressive agents such as tocilizimab, baricitinib, and most especially higher-dose steroids. This suggests a potentially modifiable factor that could help address the previously

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Table 1. Logistic regression for odds of HAI in patients with COVID-19

	MRSA		CLABSI	
	Adjusted OR	95% CI	Adjusted OR	95% CI
ICU within 3 days of admission	1.41	(1.08, 1.84)	1.12	(0.92, 1.36)
Mechanical ventilation within 3 days of admission	1.78	(1.30, 2.45)	1.75	(1.44, 2.13)
Length of stay (days, before HAI)	1.01	(1.01, 1.01)	1.00	(1.00, 1.01)
Tocilizumab or baricitinib (before HAI)	1.92	(1.43, 2.58)	1.76	(1.45, 2.13)
Dexamethasone <= 6 mg (before HAI)	1.61	(1.27, 2.05)	1.19	(1.00, 1.43)
Elixhauser comorbidity score	1.06	(1.05, 1.07)	1.03	(1.02, 1.04)
Race/ethnicity Reference: White				
Black/African American	0.77	(0.55, 1.09)	1.11	(0.87, 1.42)
Hispanic/Latino	1.09	(0.83, 1.43)	1.90	(1.58, 2.29)
Other/unknown	1.11	(0.74, 1.65)	1.59	(1.21, 2.08)
Age/high-dose steroid interaction Reference: <=65, no high-dose steroids				
<=65, high-dose steroids	4.40	(3.03, 6.39)	2.57	(1.96, 3.36)
>65, no high-dose steroids	0.84	(0.54, 1.30)	0.72	(0.51, 1.00)
>65, high-dose steroids	2.46	(1.66, 3.66)	1.77	(1.34, 2.35)

Note. HAI, healthcare-associated infection; COVID-19, coronavirus disease 2019; MRSA, methicillin-resistant *Staphylococcus aureus*; CLABSI, central line-associated bloodstream infection; CI, confidence interval.

identified increased occurrence of HAIs in patients hospitalized with COVID-19.[6] This finding is particularly notable given that dexamethasone at high doses has been found to also be associated with poorer outcomes in COVID-19 patients, and formal guidance now advises against its use.[7,8] The correlation between HAI risk and race/ethnicity has been observed in other studies and is deserving of further investigation.[9,10] Limitations of this study include that this is a retrospective analysis, and there may be factors with a true association with HAI that were not identified or introduce bias.

This study demonstrates the potential to decrease the occurrence of HAI among inpatients with COVID-19 through judicious use of immunosuppressive therapies, and awareness of the increased risk when such therapies are used appropriately. These findings allow clinicians to be alert to those patients with COVID-19 at the highest risk for HAI and potentially reduce those risks.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/ice.2024.142.

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Competing interests. None.

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