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Ernest Mario School of Pharmacy

Risk Factors and Clinical Outcomes of Candidemia Associated with Severe COVID-19

Deepali Dixit, PharmD, BCPS, BCCCP, FCCM¹; Polly Jen, PharmD, BCPS, BCIDP, AAHIVP²; Tyler D. Maxwell, BS, PharmD³; Steven Smoke, PharmD, BCPS, BCIDP⁴; James Andrew McCracken, PharmD¹; Maria Cardinale-King, PharmD, BCCCP¹; Aditi Haribhakti, PharmDc¹; Purvi Patel, MD⁵; Eris Cani, BS, PharmD, BCIDP, BCPS³; Seohyun (Claudia) Choi, PharmD, BCCCP⁶; Sugeet Jagpal, MD⁵; Tilly Varughese, MD⁵; Luis L. Tatem, MD⁷; Tanya Bhowmick, MD⁵

¹Ernest Mario School of Pharmacy – Rutgers, The State University of New Jersey; ²Newark Beth Israel Medical Center; ³Touro College of Pharmacy; ⁴Cooperman Barnabas Medical Center; ⁵Robert Wood Johnson Medical School; ⁶University of Washington, School of Pharmacy; ⁷SUNY Downstate Medical Center

Background

- Research regarding secondary infections in COVID-19 initially focused on bacterial infections, but attention on the relevance of secondary fungal infection in COVID-19 management is growing¹⁻⁴
- Emerging reports have observed that patients infected with SARS-CoV-2 have an increased risk of candidemia
- Limited literature exist addressing risk factors and clinical outcomes of candidemia in patients infected by SARS-CoV-2
- Candidemia in patients with COVID-19 has been reported in variable rates, ranging from 0.8% to 14%⁵
- Furthermore, in COVID-19 patients with secondary candidemia, the mortality rates range from 40% to 70%, underlining the urgency for a better understanding of the relationship between these infections
- The objective of our study is to identify the clinical characteristic, outcomes and risk factors outcomes of patients with severe COVID-19 and candidemia

Methods

- This multicenter, retrospective, case-control study included patients with severe COVID-19 who were diagnosed with secondary candidemia from eight academic medical centers between August 2020 and August 2021
- Cases: ≥ 18 years old with a confirmed diagnosis of severe COVID-19 and candidemia
- Control: ≥ 18 years of age with a confirmed diagnosis of severe COVID-19 were randomly selected from the same day admission as cases in a 2:1 ratio
- Primary outcome was to evaluate risk factors and clinical outcomes of patients with COVID-19 and fungal co-infection
- All study measures and outcomes were first summarized overall and by case-control groups using range, median with interquartile for continuous measures, or frequency with percentage for categorical measures
- Ordinal measures were summarized using median with IQR or frequency with percentages

Patient Characteristics

	COVID-19 Only n= 184	COVID-19 + Candidemia n = 91	p-value
Age (yr), median (IQR)	67 (59-76)	62 (54.5-72)	0.01
Charlson Comorbidity Index at Admission, median (IQR)	4 (2-7)	3 (2-5)	0.02
Respiratory Rate Oxygenation Index at Admission, median (IQR)	10.3 (5.4-17.8)	6.2 (3.9-15)	0.01
ICU Admission, n (%)	107 (58.2)	80 (87.9)	<0.01
SOFA Score at ICU Admission, median (IQR)	8 (4-10)	7.5 (4-10)	0.79
In-hospital Mortality, n (%)	74 (40.2)	62 (68.1)	<0.01

Results

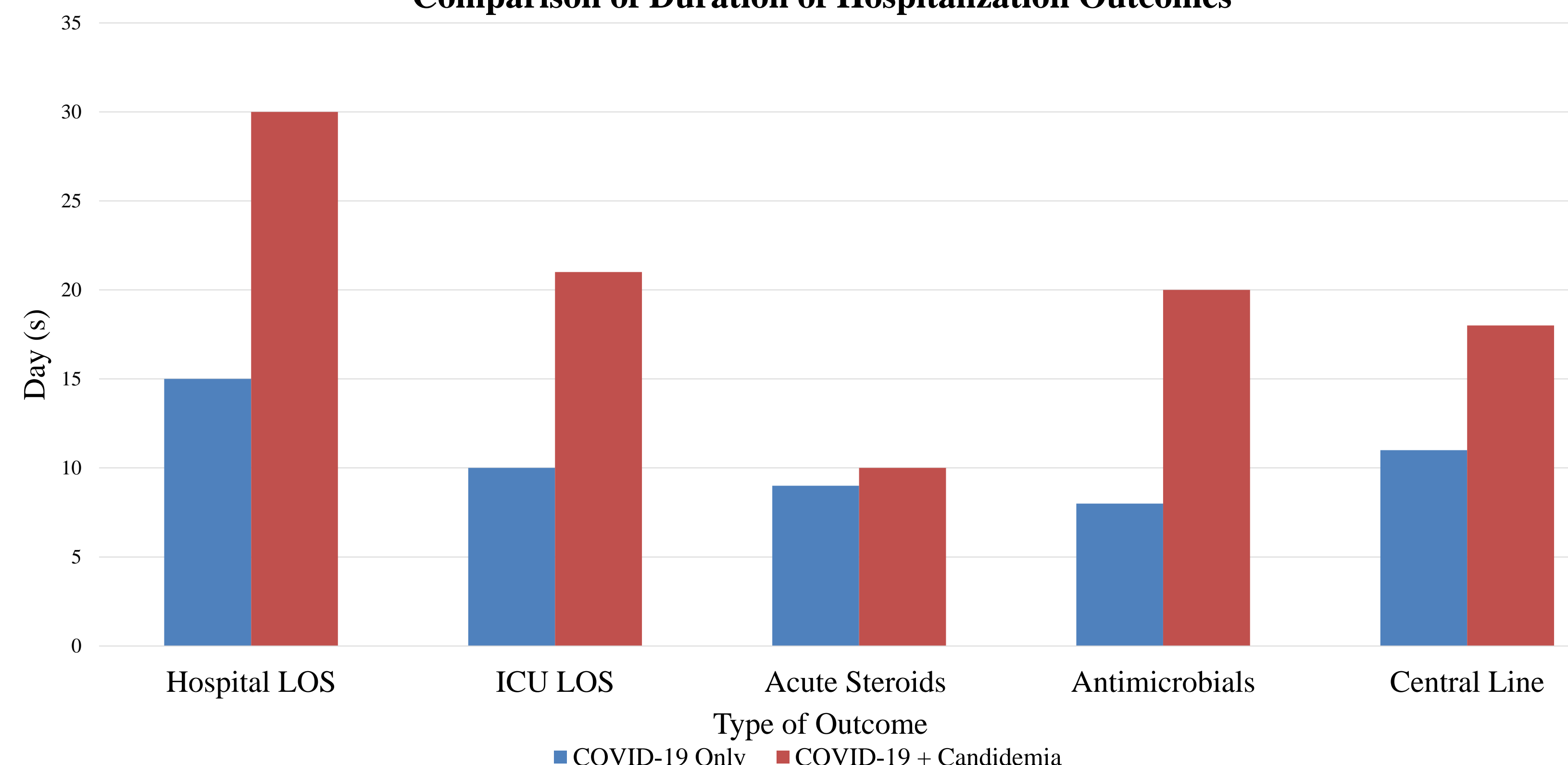
Candidemia Characteristics

	COVID-19 + Candidemia n = 91
Time from COVID-19 dx to Candidemia dx (d), median (IQR)	18 (11-26)
Time from Candidemia dx to Antifungal tx Initiation (hr), median (IQR)	3 (0.8-13.5)
Time from Candidemia dx to Microbiological Clearance (d), median (IQR)	2 (0-4)
Total Duration of Antifungal tx (d), median (IQR)	11 (3-15)

Hospitalization Details and Outcomes

	COVID-19 Only n = 184	COVID-19 + Candidemia n = 91	p-value
Acute Steroid Use, n (%)	128 (69.6)	68 (74.7)	NA
Biologics Use, n (%)	74 (26.9)	40 (44.0)	<0.01
Antimicrobial Use, n (%)	165 (89.7)	91 (100)	<0.01
Central Line Placed, n (%)	88 (47.8)	86 (94.5)	< 0.01
Mechanical Ventilation at Admission, n (%)	71 (38.6)	63 (69.2)	<0.01
Continuous Infusion of Paralytics, n (%)	25 (13.6)	40 (44.0)	NA

Comparison of Duration of Hospitalization Outcomes



Discussion

- This is the largest multicenter, case-control study to date that identifies risk factors for the development of candidemia and demonstrates substantially higher in-hospital mortality among those with COVID-19 and secondary candidemia compared with those without candidemia
- It is reported that candidemia is seen earlier (within 2 weeks) during hospital stay among COVID-19 patients compared to patients without COVID-19^{6,7}
- We observed a median of 18 days for the development of candidemia in COVID-19 patients in our study
- However, the reasons for these findings are uncertain other than additive impact of risk factors, such as higher and earlier use of steroids (as stated in other reports) and disease severity^{6,7}
- In previous research, in-hospital mortality in patients with candidemia ranged from 25% to 40%^{7,8}
- Whereas our study found a higher mortality rate of 68% in patients with candidemia and COVID-19, which is significantly higher than mortality rate of COVID-19 patients without candidemia
- Additionally, COVID-19 may cause acute respiratory distress syndrome, which may require mechanical ventilation and high dose steroid therapy, and potentially increase the risk of candidemia^{7,9,10}
- However, our study did not demonstrate mechanical ventilation or corticosteroids as risk factors for candidemia among COVID-19 patients
- Independent risk factors for candidemia identified in our study were the use of central lines, biologics, and paralytic therapy
- Interestingly, our study demonstrated that the use of paralytic therapy was associated with candidemia, which was not previously described
- Similar to previous studies, our study also observed an increased use and longer duration of broad-spectrum antibiotics in COVID-19 patients that developed candidemia
- The median duration of antibiotics was 8 days for COVID-19 patients and 20 days for patients with COVID-19 and candidemia
- *C. albicans* was the most frequently isolated pathogen as observed in our study
- Timely diagnosis of candidemia remains a challenge with current standard microbiology techniques
- In addition to others, our study reports a trend for certain risk factors for candidemia that are more prevalent in critically ill patients

Conclusions

- Our study demonstrated COVID-19 patients with candidemia required ICU admission and received biologics, antibiotics, paralytic infusions, and central lines more frequently prior to developing candidemia than patients without candidemia
- Clinicians should consider implementing protocols for surveillance and prevention of complications associated with infection

Author Contact Information

Email: ddixit@pharmacy.rutgers.edu



References: