

## Candidemia and Severe COVID-19 – Which Risk Factors are Modifiable?

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Since the beginning of the SARS-CoV-2 pandemic, a hallmark of the disease has been slow recovery. In the United States, nearly 30% of patients with COVID-19 require admission to the intensive care unit with a median hospital length of stay of 15 days [1]. Add in the first line treatment of steroids combined with excessive antibiotic use and you have a recipe for candidemia [2].

Prevalence and mortality of candidemia remain unchanged for the past decade in spite of improvements in many other areas of hospital-acquired infections [3]. Risk factors for candidemia come in two groups: the medical diagnoses of the patient and the actions we take to care for them. The bulk of candidemia occurs in hospitalized patients with a large proportion of patients having central venous access [4, 5]. In many respects, it falls into the realm of infection prevention and antimicrobial stewardship. Two memorable images come to mind: rows of IV pumps and dialysis machines strung up outside of ICU rooms and patients in the prone position, the former to protect healthcare workers from excessive entries and preservation of personal protective equipment in short supply and the latter to maximize oxygenation [6-8].

In this issue of *Clinical Infectious Diseases*, Seagle et al report the epidemiology of candidemia during the early months of the pandemic, crucially comparing to two different non-COVID cohorts, preceding and concurrent. While there are limitations and missing data, there are important differences to highlight and learn from as candidemia in the setting of COVID-19 represents a truly unique patient population. Patients with COVID-19 had less liver disease but more diabetes and obesity, fewer prior hospitalizations and surgery but more ICU time, mechanical ventilation, and acute dialysis. Figure 1 tells the story. Rather than a peak with long tail, the landscape has shifted: the prolonged ICU stays of COVID-19 patients gives way to a wide plateau of candidemia cases.

While the epidemiology of candidemia has shifted slightly over time to include more community acquired infections, it remains an illness of the healthcare environment as seen here with >80% falling into the healthcare-associated and healthcare onset categories. COVID-19 cases pushed this further to ~95% healthcare related and nearly twice as many diagnosed in the ICU. With so many differences between patients, it is difficult to make comparison regarding their outcomes. They are just too different. Instead, we should focus on how we got here, and what can be done differently now and next time around. How many features are modifiable vs. inevitable? I keep coming back to those two evolving extensions of clinical infectious diseases – infection prevention and antimicrobial stewardship. As the old saying goes, an ounce of prevention is worth a pound of cure.

This brings us back to our images of devices outside rooms, long extension tubing sometimes draping along the floor on the way back to the proned patient. Shah et al provide an excellent breakdown of the risks and benefits of devices moved outside the room, and, fortunately, they continued to track this data and report it in comparison to a baseline cohort prior to moving devices outside the room [7, 9]. The authors did not find an increase central line associated bloodstream infections (CLABSIs) or other complication rates in spite of this arrangement of devices while successfully reducing the number of times nurses entered the room. Meanwhile other centers have reported a noted increase in CLABSIs on their COVID units compared to non-COVID units [10]. It is important to understand this dynamic more broadly and over a longer duration given ~80% of patients in the current study had a central venous catheter in place.

Similarly, nearly all patients received antibiotics during the two weeks preceding their candidemia diagnosis. Yet bacterial co-infections with COVID at the time of admission are rare [11, 12]. How

many patients received antibiotics, “just in case?” There is still so much work to do. In spite of a pandemic unfolding in front of our eyes showing the devastation that a virus can cause without any help from other pathogens, our addiction to antibiotics could not be broken. How will this change? ID physicians, at least in our current iteration, are not the answer. We are too scarce of a resource, highly regionalized. Year after year, numerous ID fellowship training slots go unfilled. Will the pandemic change that?

In the end, this is a starting point. What is the true reality experienced nationwide? As this new illness diverges from our baseline understanding of candidemia, further investigation must follow. What were source control rates? What are the new risk factors? Which are modifiable, which are unavoidable? Is candidemia in this setting a pre-morbid diagnosis? More patients in the combined pandemic cohort died in 48 hours, and approximately 1/3 of all deaths in the COVID-19 cohort occurred in this initial 48-hour period. Was this a function of the early days of the pandemic or candidemia in a unique patient population?

When considering fungal infections as neglected diseases, candidemia is generally not included [13]. We cannot neglect the data learned here; we must build upon it. Investment must follow. We need to identify the modifiable risk factors and learn how to mitigate with infection prevention controlled trials. We need to expand the reach of antimicrobial stewardship with accountable antibiotic prescribing for all – viral sepsis is a proven entity. Our patients deserve a better tomorrow.

**Notes:**

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