

Mortality rate from Candida infections remains high in Brazil, despite therapeutic advances

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Candida albicans. Credit: Wikipedia.

An article published in the *Journal of Fungi* analyzing bloodstream infection by fungi of the genus Candida, and comparing data for the periods 2010–11 and 2017–18 in Brazil, shows the persistence of extremely high mortality rates despite advances in therapeutic practices. Candidemia is the world's most prevalent nosocomial (hospital-acquired) invasive fungal infection. Its incidence varies globally from 0.33 to 6.51



episodes per 1,000 admissions.

The <u>comparative analysis</u> used data from 616 cases treated in 11 public and <u>private hospitals</u> (369 in the first period and 247 in the more recent period).

Treatment with echinocandins, the current initial antifungals of choice, intensified from 13% to 41%, but without affecting mortality rates, showing that other factors should be investigated.

"We have a late diagnosis problem. Diagnosis still depends exclusively on blood culture. Fungal culture and identification in the laboratory take time and the sensitivity of this method is low, with as many as 50% false negatives. Time is crucial to <u>patient survival</u>. We need to save time by investing in better techniques that don't depend on culture, including molecular diagnosis and use of biomarkers," said Caroline Agnelli, first author of the article. She is a Ph.D. candidate specializing in research on infectious and parasitic diseases at the Federal University of São Paulo (UNIFESP).

Another shocking revelation in the article is the number of people who receive no treatment at all. "Two out of every ten aren't treated for lack of diagnostic resources. At least half of those who do receive treatment die. Data collected by colleagues in Porto Alegre [state capital of Rio Grande do Sul] from more than 120 Latin American medical centers shows that only one in ten hospitals have the resources for an effective diagnostic approach in medical mycology—and this applies to several fungal infections," said Arnaldo Colombo, last author of the article and a professor at UNIFESP.

For the researchers, the study shows that mortality rates have not fallen despite the knowledge accumulated on the natural history of invasive infections by Candida, in contrast with other neglected fungal diseases.



"Patient prognosis is multifactorial, but we know what can make all the difference: early administration of antifungal medication combined with timely and effective control of the source of the infection, including central line removal," Agnelli said.

Candidemia is a complication that usually appears in critical patients hospitalized for long periods, particularly in intensive care units (ICUs), taking <u>broad-spectrum antibiotics</u> and corticosteroids, or requiring an invasive procedure such as dialysis or surgery, especially abdominal. Use of central venous catheters is a risk factor, but the proportion of early removal in candidemia cases remained below 50% throughout the study period.

"The decision to remove a central line should be individualized for reasons of safety, disease severity and clinical conditions, of course. However, it should be prioritized whenever possible in order to improve the patient's prognosis," Agnelli said.

The fungus that causes hospital-acquired candidemia is the same one that naturally colonizes the gastrointestinal tract and is familiar to women as the cause of vaginal candidiasis (yeast infection). "It's inoffensive if your immune system is in order and you're not in hospital, where it can move from colonization to invasive disease, especially owing to the use of antibiotics, which favors dysbiosis—an imbalance in the gut, with an increase in the Candida population—and the use of invasive medical procedures to treat the patient. Under conditions associated with low immunity and a hospital environment, 'living with the enemy' in good health becomes living with the enemy dangerously," Colombo said.

Change of profile and other studies

Mortality rates were unacceptably high and remained unchanged



throughout the study period despite wider use of echinocandins. For the researchers, this was probably associated with changes in the population at risk and improvable treatment strategies. "There was a change of profile. We found that age didn't increase, but the quality of aging was different. There have been more comorbidities recently. Patients admitted to hospital have been hospitalized before, sometimes on several occasions," Agnelli said.

The median age of the patients was similar in both periods (62 and 65), and there were no significant differences in initial clinical severity. In the more recent period, however, the number with more than three comorbidities doubled (to 29%, up from 16% in 2010), as did the proportion undergoing dialysis (15%, up from 8% in 2010). Patients in the more recent period presented with candidemia sooner, and 40% had been hospitalized previously (compared with 21% in 2010).

"We found a 14-day mortality rate of about 35% and a 30-day mortality rate of about 50%. These are very high rates. Some years ago, we asked why and compared them with the rates in other countries," Colombo said, citing a <u>study</u> conducted in partnership with researchers in Spain. Mortality was significantly lower among the Spanish patients even though they were older than the Brazilians.

"Diagnosis was a factor here, too, but it was clear that they removed central lines sooner, controlled infective focus effectively, and began administering the right antifungal earlier. In Brazil, the bacterial sepsis protocol recommended for patients in intensive care is often ignored in cases of fungal infection. The timing of the start of therapeutic management is crucial as far as prognosis is concerned. The study showed this very clearly," Agnelli said.

Methodology and challenges



Collection of medical history and laboratory data up to 30 days from confirmation of candidemia was based on a routine laboratory-based surveillance protocol, including demographics, underlying medical conditions, <u>risk factors</u> and conditions associated with candidemia, such as use of broad-spectrum antibiotics, chemotherapy, steroids, prior abdominal surgery, central venous catheter at the time of diagnosis, parenteral nutrition, identification of Candida species, clinical severity, antifungals prescribed, time to start of treatment, time to catheter removal, and all-cause mortality at 14 and 30 days from diagnosis of candidemia. The species was identified by a local laboratory, and the material was sent to UNIFESP's Special Mycology Laboratory for confirmation.

The group has been conducting epidemiological surveillance research for a long time, with the collaboration of hospitals, facilitating similarity among clinical records. "However, it's no simple task to collect this data accurately. Oversight and auditing are needed, as well as painstaking analysis to merge databases and make correct comparisons," Colombo said.

"The technology hasn't advanced enough to help with database merging. It's necessary to review criteria constantly in order to align all the variables so that the populations and samples are comparable," Agnelli said.

More information: Caroline Agnelli et al, Prognostic Trends and Current Challenges in Candidemia: A Comparative Analysis of Two Multicenter Cohorts within the Past Decade, *Journal of Fungi* (2023). DOI: 10.3390/jof9040468

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