

# Invasive Candidiasis



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## KEYWORDS

- *Candida* • Invasive candidiasis • Antifungals • Bloodstream infection
- Fungal infection

## KEY POINTS

- *Candida* is a leading cause of hospital-acquired bloodstream infections, in particular in patients admitted to intensive care units.
- Non-culture-based molecular diagnostic assays have the potential to improve time to treatment, thereby improving morbidity and mortality.
- Echinocandins are the treatment of choice for most cases of invasive candidiasis.
- Targeted antifungal prophylaxis decreases rates of invasive candidiasis and may influence mortality.

## INTRODUCTION

Invasive infection due to *Candida* species is a condition associated with medical progress. It is a common health care-associated infection and is widely recognized as a major cause of infection-related morbidity and mortality. There are at least 15 distinct *Candida* species that cause human disease, but more than 95% of invasive disease is caused by the 5 most common pathogens: *C albicans*, *C glabrata*, *C tropicalis*, *C parapsilosis*, and *C krusei*. Serious infections due to these organisms are generally referred to as invasive candidiasis (IC). Mucosal *Candida* infections, including those involving the oropharynx, esophagus, and vagina, are not part of this review. Rather, the focus of this review is on the epidemiology, pathogenesis, diagnosis, clinical manifestations, and management of IC.

## EPIDEMIOLOGY

Candidemia ranks as the third or fourth most common cause of health care-associated bloodstream infection (BSI) and is a leading cause of BSIs in the intensive care unit (ICU). A recent multicenter point-prevalence survey identified *Candida* spp as the most common health care-associated bloodstream pathogen.<sup>1</sup> At least 50% of episodes of candidemia occur in an ICU setting, reflecting the complexity of illness usually associated with

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this infection. There are well-recognized risk factors associated with IC that apply to all hospitalized persons but especially to those in an ICU. Premature low-birth-weight neonates are at extraordinary high risk of candidemia, and the highest incidence of candidemia occurs in the neonatal ICU. The most common risk factors include the presence of an indwelling central venous catheter (CVC), exposure to broad-spectrum antibacterial agents, prolonged ICU stay with or without assisted ventilation (greater than 3 days), recent major surgery, necrotizing pancreatitis, any type of hemodialysis, and immunosuppression.<sup>2,3</sup> A more complete list of risk factors for IC is depicted in **Table 1**.

Community-acquired candidemia is a relatively new observation in the United States and other developed countries, reflecting the increasing utilization of parenteral outpatient antimicrobial therapy through a permanent or semipermanent venous access device (eg, Hickman catheter, peripherally inserted cannulated catheter).<sup>4</sup> This phenomenon has led to the observation that as many as 20% to 30% of patients with candidemia are categorized as health care associated and community acquired.

Species distribution is important in all forms of candidiasis; there is considerable geographic, center-to-center, and unit-to-unit variability in the prevalence of pathogenic *Candida* species.<sup>5-9</sup> Indeed, candidiasis is not one but rather several diseases, with each *Candida* species presenting its own unique characteristics with respect to tissue tropism, propensity to cause invasive disease, virulence, and antifungal susceptibility. A working knowledge of the local epidemiology and rates of antifungal resistance is critical in making informed clinical and therapeutic decisions while awaiting culture and susceptibility data.

In the United States, *C albicans* accounts for approximately 50% of bloodstream *Candida* isolates. *C glabrata* is the second most common bloodstream pathogen, representing up to 25% to 30% in some series.<sup>10</sup> *C glabrata* is more common among patients aged greater than 60 years and in solid organ transplants. This pathogen is uncommon in the neonatal ICU (NICU).<sup>5</sup> *C tropicalis* and *C parapsilosis* generally represent 10% to 15% of isolates, depending on the region and the study population. For example, in Latin America, *C parapsilosis* and *C tropicalis* are both more common in adults than *C glabrata*.<sup>9</sup> *C tropicalis* is recognized commonly in India, Latin America, and other tropical and subtropical regions. *C krusei* is the least common of the 5 major species and is a prominent pathogen among patients with hematologic malignancies and others who have received prolonged azole prophylaxis.

<b>Immunocompromised</b>	<b>Nonimmunocompromised</b>	<b>Neonates</b>
In addition to →	Broad-spectrum antibiotics	← In addition to
Granulocytopenia	Any type of renal dialysis	Gestational age
Stem cell transplant	Central venous catheter	Low APGAR
Mucositis	IV drug use	Length of NICU stay
Graft vs host disease	Severity of illness	H <sub>2</sub> blockers
Type of chemotherapy	Total parenteral nutrition	Shock
Organ transplants	GI perforation or surgery	Intubation
	<i>Candida</i> colonization	GI disease
	Diabetes	Congenital malformations
	Length of stay in ICU	
	Pancreatitis	
	Sepsis	

**Abbreviations:** GI, gastrointestinal; GVHD, graft-versus-host disease; IV, intravenous; NICU, neonatal ICU.

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