REVIEW 10.1111/1469-0691.12539

Global trends in the distribution of *Candida* species causing candidemia

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Abstract

Only five species account for 92% of cases of candidemia (*Candida albicans*, *C. glabrata*, *C. tropicalis*, *C. parapsilosis*, and *C. krusei*); however, their distribution varies in population-based studies conducted in different geographical areas. *C. albicans* is the most frequent species, but considerable differences are found between the number of cases caused by *C. glabrata* and *C. parapsilosis*. Studies from Northern Europe and the USA reported a high number of cases caused by *C. glabrata*, whereas studies from Spain and Brazil demonstrated a lower number of cases caused by *C. glabrata* and a higher number of cases attributed to *C. parapsilosis*. Globally, the frequency of *C. albicans* is decreasing, while that of *C. glabrata* and *C. krusei* is stable, and *C. parapsilosis* and *C. tropicalis* are increasing. Patient characteristics and prior antifungal therapy also have a considerable influence on the distribution and frequency of *Candida* spp., regardless of the geographical area. *C. albicans* is more frequent in patients aged up to 18 years, the frequency of *C. parapsilosis* decreases with age, and *C. glabrata* is more common in the elderly. Finally, the presence of horizontal transmission of *Candida* spp. isolates (reported mainly in patients from the adult medical and post-surgical ICU, patients from oncology–haematology units, and neonates) can affect species distribution.

Keywords: *C. albicans*, *C. glabrata*, *C. parapsilosis*, candidemia, invasive candidiasis, outbreaks, population-based, species distribution
Article published online: 10 February 2014
Clin Microbiol Infect 2014; **20** (Suppl. 6): 5–10

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Background

Fungal infections have become a major problem in hospitals, and the number of episodes of sepsis caused by fungi has been increasing since the early 1990s [1,2]. *Candida* spp. remains the most common cause of invasive fungal infections [3–5], and the incidence of candidemia, which is estimated at 72.8 cases per million inhabitants and year, clearly exceeds that of invasive aspergillosis and mucormycosis [6]. Candidemia is a consequence of advances in health care. During the last 20 years, we have observed an improvement in diagnostic procedures, the development and commercialization of new antifungal agents, and the implementation of strategies to prevent candidemia; nevertheless, the incidence of candidemia has increased [7].

Candidemia is generally diagnosed using blood cultures, although diagnosis remains a challenge for clinicians and microbiologists; in fact, half of all cases of invasive *Candida* infections go undetected in blood cultures [8]. Given these limitations, the true epidemiology and incidence of invasive candidiasis is imprecise. The incidence of candidemia expressed as cases per 100 000 inhabitants has been reported to range from 1 to 8 cases [4]; in a study carried out in Brazil, incidence reported as cases per 100 000 admissions was higher (249 cases per 100 000 admissions) [9]. In a recent 1-year population-based study conducted in Spain (29 hospitals, 773 cases), the incidence of candidemia was 8.1 cases per 100 000 inhabitants, which is similar to that reported in other European studies [10].

Candidemia has an attributable mortality of 15–35% for adults and 10–15% for neonates, and the hospitalization cost for each episode is approximately US$40 000 [11–13]. The rates of

early and late mortality (7 days and 30 days after diagnosis, respectively) are different (13% vs. 30%). Whereas early mortality is associated with factors such as appropriate antifungal therapy and early removal of central venous catheters, late mortality is associated with factors related to the baseline condition of the host [10]. The mortality rate is clearly correlated with a delay in the initiation of appropriate antifungal treatment [14,15]. Incorrect treatment includes absence of antifungal treatment, a delay in initiation, or the use of an inactive agent. Therefore, efforts to minimize these three situations should help to reduce the mortality of candidemia. Knowledge of the frequency of causative species would facilitate appropriate selection of empirical antifungal treatment.

The distribution of *Candida* spp. causing candidemia varies in population-based studies carried out in different geographical areas. Furthermore, notable differences can also be observed between hospital units. However, the frequency of *Candida* species causing candidemia is also dependent on the predisposing conditions of the patients infected, the antifungal agents they receive, and the local hospital-related factors.

This review discusses global trends in the distribution of *Candida* spp. by looking at three main areas: influence of the geographic area, influence of predisposing conditions of the patients, and influence of local hospital epidemiology.

Influence of the Geographical Area

The list of *Candida* species causing candidemia is long and continues to expand as a consequence of more precise identification. The ARTEMIS DISK Global Antifungal Surveillance Study includes a large registry of invasive *Candida* isolates collected from 127 medical centers worldwide (39 countries). Data from this registry showed that only five species (*C. albicans*, *C. glabrata*, *C. tropicalis*, *C. parapsilosis*, and *C. krusei*) accounted for 92% of cases of candidemia [16]. *C. albicans* was the most common cause of candidemia worldwide, accounting for 62% of cases [7,16].

However, the ranking of the abovementioned 'top 5' species is variable. Fig. 1 summarizes the proportion of cases

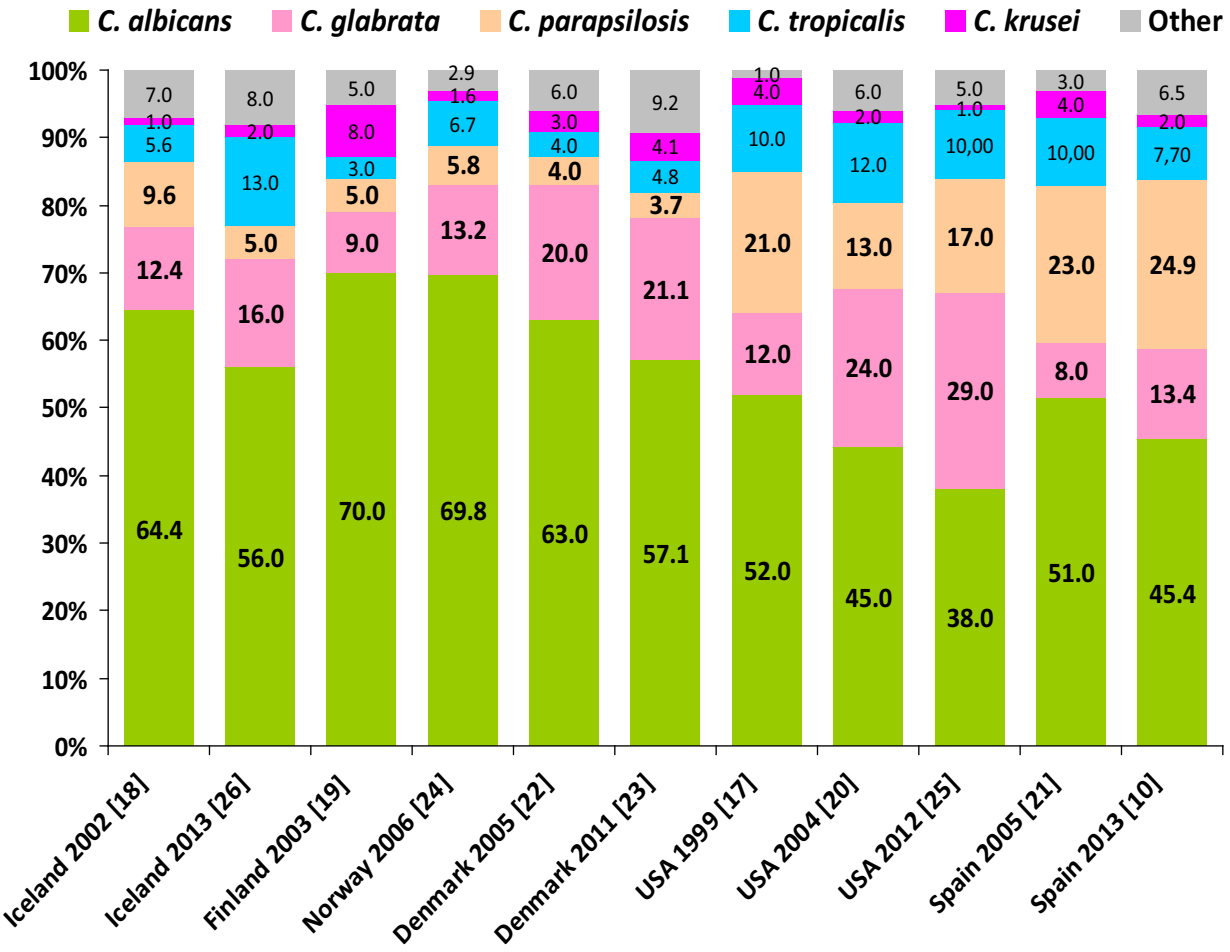

FIG. 1. Proportion of the most relevant Candida species from population-based studies reporting on candidemia in different countries.