

Euro Pathology 2018: Epidemiology of Candidaemia: A Prospective Comparison between Invasive Candidiasis in Italy and All Over the World - Maria Teresa Mascellino - Department of Public Health and Infectious Diseases, Sapienza University of Rome, Italy.

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Abstract

Candida is a major cause of blood circulation infections (BSI), causing significant mortality and morbidity in healthcare settings. Invasive candidiasis (IC) is a serious disease in critically ill and immunocompromised hospital patients. Advances in supportive therapies, the complexity of surgical procedures, the number of elderly people in our society and changes in the demographics of patients have gradually increased the population at high risk for fungal diseases. As a result, the prevalence of Candida infection has increased, resulting in a higher frequency of invasive candidiasis and candidaemia. Infections in the blood circulation suffered by Candida species are a major cause of morbidity, length of stay in hospital, cost of care and mortality in hospitalized patients, the latter ranking 20-30% of all BSI nosocomials or more.

Introduction

Candida is a major cause of blood circulation infections (BSI), causing significant mortality and morbidity in healthcare settings. Invasive candidiasis (IC) is a serious disease in critically ill and immunocompromised hospital patients. Advances in supportive therapies, the complexity of surgical procedures, the number of elderly people in our society and changes in the demographics of patients have gradually increased the population at high risk for fungal diseases. As a result, the prevalence of Candida infection has increased, resulting in a higher frequency of invasive candidiasis and candidaemia. Infections in the blood circulation suffered by Candida species are a major cause of morbidity, length of stay in hospital, cost of care and mortality in hospitalized patients, the latter ranking 20-30% of all BSI nosocomials or more.

The epidemiology of candidaemia has been widely studied worldwide. The annual incidence of Candida BSI varies considerably by region, based on

epidemiological studies conducted in Europe and the United States (from 3.0 to 26.2 / 100,000 inhabitants). Among the northern European countries, Norway, Finland and Sweden reported an incidence of 3/100 000 inhabitants, while Denmark declared 8.6 / 100,000 inhabitants in a semi-national survey. In central and southern Europe, population-based surveys, Switzerland, the United Kingdom, Scotland, Italy and Spain reported 1.2 to 8.1 / 100 000 inhabitants. Finally, in surveys carried out in Iowa, San Francisco, Atlanta and Connecticut (USA), rates of 6-14 / 100,000 inhabitants have been demonstrated with the exception of the Baltimore area with 26.2 / 100,000 [11]. We can then deduce that the incidence of candidaemia varies by geographic area, so that the study of local data is crucial for a precise knowledge of epidemiological data and therefore for an adequate therapeutic approach. Since early 90s, a trend for a steady enhancement of the incidence of candidaemia has been observed in Europe. Accordingly, in Italy, it has been observed that the frequency with which Candida was cultured from BSI, increased over the time with a significant enhancement in the number of isolates from 2010 to 2012. This observation parallels to that of Bassetti et al, who showed increased incidence of candidaemia from 2008 until 2010 in a study performed in a tertiary care hospital in northern Italy.

Risk factors for Candida BSI are well known and mainly include broad spectrum antibiotic therapy, malignant neoplasm, total parenteral nutrition, presence of CVC (central venous catheter), previous colonization by Candida spp, immunosuppressive therapy, neutropenia, etc.

In Policlinico Umberto I °, Sapienza University of Rome (Mascellino MT et al. 2015, submitted), Candida albicans was the greatest detected species (44%), while non-albicans strains represented 56% in total, Candida

parapsilosis being the most common isolate. (32%), followed by *Candida glabrata* (13%), *Candida tropicalis* (7%) and *Candida krusei* with other minor species such as *C. guilliermondii*, *C. lusitanae* and *C. famata* (4%). *C. tropicalis* was significantly higher ($p = 0.03$) in non-resuscitated patients while the reverse was true for *C. parapsilosis*. *C. albicans* showed a higher isolation rate in ICU (58%). In 2015, an isolation peak of *C. parapsilosis* (47%) was observed, exceeding the detection rate of *C. albicans* (44%). and generate a biofilm structure, protecting organisms from host defenses and antifungal drugs, confirming the role of external devices as the main risk factor for *Candida* infections.

All the strains tested were fully sensitive to echinocandins and amphotericin B. A decrease in sensitivity to fluconazole was mainly observed with *C. glabrata* and *C. parapsilosis* (MIC 90 respectively 16 and 4 $\mu\text{g/ml}$). Caspofungin and voriconazole have been shown to be the most potent antimycotics with higher MICs of caspofungin for *C. parapsilosis*. All isolates were wild-type organisms and no acquired resistance was detected based on the EUCAST 2014 breakpoints (<http://www.eucast.org>). The incidence of candidaemia per 10,000 admissions varied from 6.8 to 12.4 over a 3-year period (2012-2014) (Mascellino et al., Submitted in 2015).

These results are in agreement with those reported by other studies carried out in Italy which showed a similar classification among the isolated species. Unlike Italy, *C. glabrata* was the non-*albicans* species detected in the United States with a higher frequency of BSI, *C. parapsilosis* being the third isolated species. It therefore seems, as indicated above, that the epidemiology of candidaemia varies from country to country.

It has been estimated that the relative frequency of ICD and candidaemia is higher in patients hospitalized in the intensive care unit (ICU), also considering that extensive use of indwelling central venous catheters may contribute to higher incidence. High candidaemia. However, other studies have clearly shown that these infections are not limited to intensive care, but are more common in hospitals with higher rates. The higher incidence of certain pathologies such as diabetes and

other underlying medical conditions may explain a high impact in non-resuscitated patients. However, the distinction between the distribution of species and the sensitivity profiles detected in the intensive care unit compared to those in a non-resuscitated environment has been poorly studied (even in pediatric patients), in particular at the local level, while studies high impact have been carried out around the world.

Conclusion:

In conclusion, invasive fungal infections represent a growing challenge both in ICU and in non-ICU clinical settings. Knowledge of local epidemiology and sensitivity profiles are factors of paramount importance for the clinical management of these potentially fatal infectious diseases. The passage of *C. albicans* to other *Candida* species has been observed worldwide in recent decades

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