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Epidemiology of Candidaemia: A Prospective Comparison between Invasive Candidiasis in Italy and All Over the World

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Introduction

Candida is an important cause of bloodstream infections (BSI), causing significant mortality and morbidity in health care settings [1]. Invasive candidiasis (IC) is a serious disease in hospitalized critically ill and immune-compromised patients [2]. The advances of the supportive therapies, of the complexity of surgical procedures, of the number of elderly people in our society and of the changes in patient demographic characteristics have progressively expanded the population at high risk for fungal diseases. Consequently, the prevalence of *Candida* infection has increased leading to a higher frequency of invasive candidiasis and candidaemia [3,4]. Bloodstream infections sustained by *Candida* species are a major cause of morbidity, hospital length of stay, cost of care and mortality in hospitalized patients, the latter ranking 20-30% of all nosocomial BSIs [5,6] or even more [7].

The epidemiology of candidaemia has been extensively investigated all over the world. The annual incidence of Candida BSI varies greatly by region based on epidemiological studies from Europe and USA (range from 3.0 to 26.2/100,000 inhabitants). Among the North-Europe countries, Norway, Finland and Sweden reported an incidence of 3/100,000 population whereas Denmark reported 8.6/100,000 population in a semi-national survey [8]. In the middle and southern parts of Europe population-based surveys, Switzerland, UK, Scotland, Italy and Spain reported 1.2-8.1/100,000 population [1,9]. Finally, in surveys conducted in Iowa, San Francisco, Atlanta and Connecticut (USA), rates of 6-14/100,000 population have been demonstrated [10] with the exception of the Baltimora area reporting 26.2/100,000 [11]. Then it can be deducted that the incidence of candidaemia varies in different geographical areas so that the study of the local data is crucial for an accurate knowledge of the epidemiological data and consequently for an adequate therapeutic approach [12].

Since early 90s, a trend for a steady enhancement of the incidence of candidaemia has been observed in Europe [13]. Accordingly, in Italy [2], 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. [7], 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, malignancy, total parenteral nutrition, presence of CVC (Central Venous Catheter), previous colonization by *Candida* spp, immunosuppressive treatment, neutropenia etc.

In Policlinico Umberto I°, Sapienza University of Rome, (Mascellino MT et al. 2015, submitted), *Candida albicans* was the most detected species (44%) whereas *non-albicans* strains altogether accounted for 56% being *Candida parapsilosis* the most frequent isolate (32%), followed by *Candida glabrata* (13%), *Candida tropicalis* (7%) and *Candida krusei* with other minor species such as *C. guillermondii*, *C. lusitaniae* and *C. famata* (4%). *C. tropicalis* was significantly higher (p=0.03) in non-Intensive Care Unit patients whereas the opposite was true for *C. parapsilosis*. *C. albicans* showed a greater isolation rate in ICU (58%). In 2015, an isolation peak of *C. parapsilosis* (47%) has been observed overtaking the *C. albicans* detection rate (44%), Probably this is due to the fact that *C. parapsilosis* is reported to be able to attach to polymeric surfaces and generate a biofilm structure, protecting the organisms from the host defences and antifungal drugs, confirming the role of external devices as a leading risk factor for *Candida* infections [14].

All the strains tested were fully susceptible to echinocandins and amphotericin B. Decreased susceptibility to fluconazole was mainly seen with *C. glabrata* and *C. parapsilosis* (MIC 90 respectively 16 and 4 mcg/ml). Caspofungin and voriconazole resulted 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 EUCAST breakpoints 2014 (http://www.eucast.org). Incidence of candidaemia per 10,000 admissions ranged from 6.8 to 12.4 over a 3- year period (2012-2014) (*Mascellino* et al., submitted 2015).

These findings agreed with those reported by other studies performed in Italy that showed similar ranking among the species isolated [1,7,15]. Unlike Italy, *C. glabrata* was the *non-albicans* species detected in USA with a higher frequence in BSI, being *C. parapsilosis* the third species isolated [11]. Therefore it seems as stated before, that the epidemiology of candidaemia varies in the different countries [5,16].

It was estimated that the relative frequency of IC and candidaemia was greater in patients hospitalized in Intensive Care Unit (ICU) considering also that the extensive use of indwelling central venous catheters could contribute to a higher incidence of candidaemia [14,16,17]. However other studies [1,8] have clearly demonstrated that these infections are not just confined to ICU , but rather they are widespread within the hospital with higher rates. The greater incidence of some pathology such as diabetes and other underlying medical conditions may account for a high impact in non-ICU patients. However the distinction between the species distribution and the susceptibility profiles detected in ICU from those in non-ICU environments, has been poorly studied (even among pediatric patients) especially at a local level [18-20], whereas high impact studies have been conducted at a global level [4,10].

In our hospital , a steady rise in the number of yeasts isolated from blood cultures was observed in ICU during 2014 as compared with 2012 (16.7% versus 40.9%, p=0.002) but always lower than the isolation rate in non ICU settings (more than 65%), with values quite similar to those of Bassetti et al. in northern Italy [7]. However, these rates were higher than those reported by Pfaller et al (55.5%), who conducted a worldwide study on the distribution and the resistance to antimycotics of *Candida* species in ICU and non-ICU wards through the Sentry Antimicrobial Surveillance Program [16]. The differences could reflect the local features, such as patient population characteristics, infection control strategies and specific antimicrobial practices [21] as compared with a large study which merged a vast quantity of data.

In conclusion, invasive fungal infections represent an increasing challenge both in ICU and in non-ICU clinical settings. The knowledge of the local epidemiology and of the susceptibility profiles are factors of paramount importance for the clinical management of these potentially lethal infectious diseases. The shift from *C. albicans* towards other species of *Candida* has been noticed all over the world in the last decades [22].

References

1. Bassetti M, Merelli M, Righi E, Diaz-Martin A, Rosello EM, Luzzati R,et al.(2013) Epidemiology, species distribution, antifungal susceptibility, and outcome of candidaemia across five sites in Italy and Spain. J Clin Microbiol 51: 4167-4172.
2. Mascellino MT, Raponi G, Oliva A, Mastroianni CM, Vullo V (2012) Candidaemia in immune-compromised hosts: incidence and drugs sensibility. J Clin Exp Pathol 2: 1-5.
3. Concia E, Azzini AM, Conti M (2009) Epidemiology, incidence and risk factors for invasive candidiasis in high-risk patients. Drugs 1: 5-14.
4. Pfaller MA, Diekema DJ (2007) Epidemiology of invasive candidiasis: a persistent public health problem. Clin Microbiol Rev 20: 133-163.
5. Tortorano AM, Prigitano A, Lazzarini C, Passera M, Deiana ML, et al. (2013) A 1-year prospective survey of candidaemia in Italy and changing epidemiology over one decade. Infection 41: 655-662.
6. Matsumoto E, Boyken L, Tendokar S, Mc Danel J, Castanheira M, et al. (2014) Candidaemia sueveillance in Iowa: emergence of echinocandin resistance. Diagn Microb Infect Dis 79: 205-208.
7. Bassetti M, Taramasso L, Nicco E, Molinari MP, Mussap M, et al. (2011) Epidemiology, species distribution, antifungal susceptibility and outcome of nosocomial candidaemiain a tertiary care hospital in Italy. PLoS One 6: e24198.
8. Tortorano AM, Kibbler C, Peman J, Bernhardt H, Klingspor L, et al. (2006) Candidaemia in Europe: epidemiology and resistance. Int J Antimicrob Agents 27: 359-366.
9. Marchetti O, Bille J, Fluckiger U, Eggimann P, Ruef C, et al. (2004) Fungal Infection Network of Switzerland. Epidemiology of candidaemia in Swiss tertiary care hospitals: secular trends, 1991-2000. Clin Infect Dis 38: 311-320.
10. Diekema D, Arbefeville S, Boyken L, Kroeger J, Pfaller M (2012) The changing epidemiology of healthcare-associated candidaemia over three decades. Diagn Microbiol Infect Dis 73: 45-48.
11. Lockhart SR, Iqbal N, Cleveland AA, Farley MM, Harrison LH, et al. (2012) Species identification and antifungal susceptibility testing of Candida bloodstream isolates from population-based surveillance studies in two U.S. cities from 2008 to 2011. J Clin Microbiol 50: 3435-3442.
12. Tortorano AM, Dho G, Prigitano A, Breda G, Grancini A, et al. (2012) Invasive fungal infections in the intensive care unit: a multicentre, prospective, observational study in Italy (2006-2008). Mycoses 55: 73-79.
13. Lass-Florl C (2009) The changing face of epidemiology of invasive fungal disease in Europe. Mycoses 52: 197-205.
14. Ferreira JAG, Carr JH, Starling CEF, de Resende MA, Donlan RM (2009) Biofilm formation and effect of caspofungin on biofilm structure of Candida species bloodstream isolates. Antimicrob Agents Chemother 53: 4377-4384.
15. De Rosa FG, Trecarichi EM, Montrucchio C, Losito AR, Raviolo S, et al. (2013) Mortality in patients with early- or late-onset candidaemia. J Antimicrob Chemother. 68: 927-935.
16. Pfaller MA, Messer SA, Moet GJ, Jones RN, Castanheira M (2011) Candida bloodstream infections: comparison of species distribution and resistance to echinocandin and azole antifungal agents in Intensive Care Unit (ICU) and non-ICU settings in the SENTRY Antimicrobial Surveillance Program (2008-2009). Int J Antimicrob Agents 38: 65-69.
17. Zilberberg MD, Shorr AF. (2009) Fungal infections in the ICU. Infect Dis Clin North Am. 23: 625-642.
18. Leroy O, Gangneux JP, Montravers P, Mira JP, Gouin F, et al. (2009) Epidemiology, management, and risk factors for death of invasive Candida infections in critical care: a multicenter, prospective, observational study in France (2005-2006). Crit Care Med 37: 1612-1618.
19. Puig-Asensio M, Padilla B, Garnacho-Montero J, Zaragoza O, Aguado JM, et al. (2014) Epidemiology and predictive factor for early and late mortality in Candida bloodstream infections: a population-based surveillance in Spain. Clin Microbiol Infect 20: 245-254.
20. Fridkin SK, Kaufman D, Edwards JR, Shetty S, Horan T (2006) Changing incidence of Candida bloodstream infections among NICU patients in the United States: 1995-2004. Pediatrics 117: 1680-1687.
21. Tumbarello M, Posteraro B, Trecarichi EM, Fiori B, Rossi M, et al. (2007) Biofilm production by Candida species and inadequate antifungal therapy as predictors of mortality for patients with candidaemia. J Clin Microbiol 45: 1843-1850.
22. Cleveland AA, Harrison LH, Farley MM, Hollick R, Stein B, et al. (2015) Declining incidence of candidaemia and the shifting epidemiology of Candida resistance in two US metropolitan areas, 2008-2013: results from population–based surveillance. PLoS One 10: e0120452.