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RESEARCH ARTICLE

CANDIDEMIAS IN HOSPITALIZED PATIENTS OF THE BAIXADA FLUMINENSE REGION, PROVINCE OF RIO DE JANEIRO, BRAZIL

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ABSTRACT

Sepsis by *Candida* species are nowadays one of the leading causes of morbidity and mortality, especially in hospitalized, immunocompromised patients and newborn with high health risk levels. The objective of this research is to investigate the incidence of candidemias in patients hospitalized at the Baixada Fluminense region, Province of Rio de Janeiro, Brazil, and identify species of the genus *Candida* which causes sepsis on these patients. Blood samples from 1213 patients with clinical suspects of sepsis were collected between January 2010 and December 2014 and seeded on the nutrient broth Brain Heart Infusion. Positive cultures for yeast cells were transplanted into Sabouraud dextrose agar medium and the fungal growth obtained was identified by biochemical tests of BioMerieux–Vitek system. 31 cases of candidemia were diagnosticated, which corresponded to a prevalence rate of PC =2,56. The isolated species of the genus *Candida* were: 14 cases of *Candida albicans* (Dominance Coefficient , DC=45,16%), two cases *of C. krusei* (DC=6,45%), four cases of *C. stellatoidea* (DC=12,90%), one case *of C. glabrata* (DC=3,23%), two cases of *C. parapsilosis* (DC=6,45%) and eight cases of *C. tropicalis* (DC=25,81%). The results highlighted the need for continued attention to patients hospitalized to possible infections by *Candida* species which causes candidemias.

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INTRODUCTION

Attempting to an increasing number of cases of sepsis and the hypothesis that species of the *Candida* genus could be inducing this manifestation in patients of hospitals of the Baixada Fluminense region, Province of Rio de Janeiro, Brazil, this research was carried out considering the fact that microbial infections produced by bacteria and fungi are among the most frequent causes of death in hospital environment. Such infections are usually acquired during the hospitalization of patients (Veronesi and Focaccia, 2013; Tirabochi *et al.*, 2007). Systemic fungemias are important causes of mortality and morbidity, mainly due to frequent invasive procedures. The administration of broad spectrum antifungal agents may also change the biological characteristics of the microorganisms (Veronesi and Focaccia, 2013). Due to this approach, some researchers focused on the study of sepsis, specially by species of the genus *Candida*, such as Ruiz *et al*. (2013) and Cuetera *et al*. (2006) who commented about the high importance of fungal infections and demonstrated that systemic candidiasis is described in approximately 30% of patients with malignant tumors and 25% of patients who received bone marrow transplants. *Candida* yeasts have a wide distribution in the environment and pollution occurs through human and animal feces; these agents are also constituents of the normal microbiota and participate in some pathogenesis. Candidosis of the oral mucosa, commonly called creamy stomatitis or "thrush", is characterized by the presence of white, mucosa-adherent plaques with a membranous appearance. This clinical

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form is the most frequent in critically ill people or newborns of mothers with vaginal candidiasis; can reach the pharynx, larynx, esophagus, or even disseminate hematogenously (Coura, 2013; Galvan and Mariscal, 2006). *Candida* species spread under amphibious conditions, considered to be a dynamic and intermediate situation between symbiosis and antibiosis, which requires a balance between the host and the microflora of the organism. Modifications that change the parasite-host interrelationship cause the microorganism to begin a parasitic action (Soares *et al.*, 2013). Almost always the infection by species of the genus *Candida* have an endogenous origin, caused by yeasts which constituted previously the normal microbiota of the patient. In these circumstances, the digestive tract would constitute the main gateway of the microorganism to the circulatory system. In neutropenic patients there would be lesions in the digestive mucosa, which can favour the passage of the fungus from the intestinal lumen to the bloodstream. In neutropenic patients, blood invasion would be preceded by colonization of the digestive tract and subsequent translocation of the fungus through the intestinal wall. Other factors responsible for the cited changes, considered as natural body defence, may originate from the patient's own health situation: diseases that induce severe immunological changes (diabetes, neoplasia, acquired immunodeficiency, major burns) or as a result of the use of antibiotics that destroy normal flora and, in this case, predispose the proliferation of *Candida* species. Presence of intravenous catheters, parenteral nutrition, monitoring systems, intravascular prosthesis, multiple abdominal surgery, organ transplantation and treatment with corticoids may also trigger candidemia on weakened patients (Galvan and Mariscal, 2006; Carmeño and Cuesta, 2012). This research of *Candida* species as pathogens in hospitalized was developed with the objective of investigating the incidence of candidemia in hospitalized patients in the Baixada Fluminense region, province of Rio de Janeiro, Brazil, identifying the *Candida* species that cause candidemia in these patients.

MATERIALS AND METHODS

The research has observational, individualized and transversal design, with convenience sampling of 1.213 hospitalized patients with clinical suspect of sepsis. From each patient three venous blood samples were collected, with an interval of one hour and preferably during febrile access. The samples were seeded in test tubes containing 50 ml of Brain Heart Infusion broth and incubated at 37°C. Samples were withdrawn from the tubes every 24 hours and stained by Gram method. Yeast positive cultures were transported to Petri dishes containing the Sabouraud-dextrose agar medium, sealed with adhesive tape and incubated at 37°C. Cultures were considered negative when there was no fungal growth after 12 days of incubation. The growth obtained from the culture was identified by the morphotinctorial characteristics of Gram staining and microscopic observation of Gram positive yeast cells. The final identification of the yeast colonies was performed by biochemical test kits of BioMerieux-Vitek system. The identity of *Candida albicans* was confirmed by the observation of germ tube formation in yeast when exposed to blood serum and also by serological agglutination reaction for yeast exposure to anti-*C. albicans* serum. For statistic purposes, patients were stratified by age group, with arbitration of six classes based on the amplitude of the age distribution, calculating the class interval in 14 years. Established the age classes, health indicators were calculated as the prevalence coefficient (PC), and the dominance coefficient (CD), the trend of the phenomenon, and tested for differences between coefficients by chi-square test with significance level of 5% for the Type I9 error (Serra-Freire, 2002). All procedures of the survey are in accordance with the Declaration of Helsinki. The research project was approved by the Commission of Ethics in Research of the Iguaçu University – UNIG.

RESULTS

A conclusive diagnosis was made in 31 cases of sepsis by species of the genus *Candida* from a total of 1213 patients, corresponding to a prevalence coefficient PC=2.56%. The following species were isolated: *Candida albicans* 14 cases (PC=1.15%), *C. krusei* two cases (PC=0.16%), *C. stellatoidea* four cases (PC=0.33%), *C. glabrata* one case (PC=0.08%), *C. parapsilosis* two cases (PC=0.16%), and *C. tropicalis* eight cases (PC=0.66%). Among the isolated species, *C. albicans* was dominant with DC=45.16%, followed by *C. tropicalis*

Table 1. Dominance coefficient (DC) and prevalence coefficient (PC) of Candida species isolated from the blood of patients of hospital network of cities of Baixada Fluminense region, Province of Rio de Janeiro, Brazil, from January 2010 to December 2014, considering the age class of the patients

Age class (years) of the examined patients (Nº)		Class 6 H 20	Class 21 H 35	Class 36 H 50	Class 51 H 65	Class 66 H 80	Class > 80	Sum 6 H >80
		36	88	169	339	491	90	1.213
Species	Indicator	Candidemia cases by species of the agente by sample						
Candida albicans	Nº	0	0	1	5	7	1	14
	DC (%)	0	0	3,23	16,13	22,58	3,23	45,16
	PC (%)	0	0	0,08	0,42	0,58	0,08	1,16
Candida krusei	Nº	1	1	0	0	0	0	2
	DC (%)	3,23	3,23	0	0	0	0	6,45
	PC (%)	0,08	0,08	0	0	0	0	0,17
Candida stellatoidea	Nº	0	2	1	0	1	0	4
	DC (%)	0	2,45	3,23	0	3,23	0	12,90
	PC (%)	0	0,17	0,08	0	0,08	0	0,33
Candida glabrata	Nº	0	0	0	1	0	0	1
	DC (%)	0	0	0	3,23	0	0	3,23
	PC (%)	0	0	0	0,08	0	0	0,08
Candida parapsilosis	Nº	0	0	0	1	1	0	2
	DC (%)	0	0	0	3,23	3,23	0	6,45
	PC (%)	0	0	0	0,08	0,08	0	0,17
Candida tropicalis	Nº	0	2	0	2	4	0	8
	DC (%)	0	6,45	0	6,45	12,90	0	25,81
	PC (%)	0	0,17	0	0,17	0,33	0	0,66
S u m	Nº	1	5	2	9	13	1	31
	DC (%)	3,23	16,13	6,45	29,03	41,93	3,23	100,00
	PC (%)	0,08	0,41	0,16	0,74	1,09	0,08	2,56

Table 2. Frequency of species of the genus *Candida* isolated from hospitalized patient's blood of the hospital network of cities of the Baixada Fluminense region, Province of Rio de Janeiro, Brazil, from January 2010 to December 2014, considering the age class of the patients

Age class (years) of the examined patients (Nº)		Class 6 H 20	Class 21 H 35	Class 36 H 50	Class 51 H 65	Class 66 H 80	Class > 80	Sum 6 H >80
		36	88	169	339	491	90	1.213
Species	Frequency	Frequency of candidemia/species of the agente by age class						
Candida albicans	Nº	0	0	1	5	7	1	14
	(%)	0	0	7,14	35,72	50,00	7,14	100,00
Candida krusei	Nº	1	1	0	0	0	0	2
	(%)	50,00	50,00	0	0	0	0	100,00
Candida stellatoidea	Nº	0	2	1	0	1	0	4
	(%)	0	50,00	25,00	0	25,00	0	100,00
Candida glabrata	Nº	0	0	0	1	0	0	1
	(%)	0	0	0	100,00	0	0	100,00
Candida parapsilosis	Nº	0	0	0	1	1	0	2
	(%)	0	0	0	50,00	50,00	0	100,00
Candida tropicalis	Nº	0	2	0	2	4	0	8
	(%)	0	25,00	0	25,00	50,00	0	100,00
S u m*	Nº	1	5	2	9	13	1	31
	(%)	2,78[b]	5,68[a]	1,18[b]	2,65[b]	2,65[b]	1,11[b]	2,56[a]

Obs.: Exponents with equal letters on the same line indicate non-significant difference (p> 0.05), when the letters are different the difference is significant.

(DC=25.81%). The small number of positive cases in each class, with a nominal variable, does not allow a more elaborated statistical analysis, however the health indicators reveals important situations for the health of the hospitalized patients (Table 1). In all age groups candidemia cases were registered (Table 1), but the infection was significantly more expressive (p<0,05) at the age class between 21 and 35 years, considering the number of samples and positive cases on each age class (Table 2). The relationship between the number of candidemia cases and the age of the patient occurred with increasing tendency (y=1.57 + 1.027x), but the calculated correlation coefficient (r=-0.31) is acceptable and true, and indicates that in the sample the relative frequency of cases is greater in adults and old, with regressing trend among the older patients.

DISCUSSION

The results obtained of the blood cultures of patients hospitalized in the hospital network of Baixada Fluminense allow us to consider nosocomial fungal infections as relevant causes of morbidity and perhaps mortality. These results are consistent with those of Jarvis (1995) when he demonstrated between 1980 and 1990 that more than 70% of fungal infections in 180 hospitals evaluated were caused by species of the genus *Candida*. Tortorano *et al*. (2004) reported the occurrence of *C. albicans* infection (DC=96%) and *C. krusei* (DC=4%) in 56.8% of carcinomatous patients, and associated the cases with the patients' physical conditions and the treatment they were submitted. As found in the Baixada Fluminense region, there is dominance of *C. albicans*, but there are also infections by other species of the genus *Candida*. Gurgel (1998) studied patients from intensive care units who registered a high incidence of candidemia and pointed out the existence of several intrinsic factors that favoured the infection. This author accords with the inferences of Karlowicz *et al*. (2000) who demonstrated that infections by *Candida* species are a very serious epidemiological problem with several risk factors, such as candidemia in neonates or patients hospitalized in intensive care units. Moreira (2005) and Sanchez and Aguirre (2007) agreed with Karlowicz *et al*. (2000) affirming that candidemia is indeed a frequent disease in sick and neonates born with low weight. According to these authors, the frequency of candidemia increased in recent years due to better survival levels of high-risk newborns and correlated with prolonged antibiotic therapy, invasive procedures, parenteral nutrition and immature immune system face to the risk of infection. During the research, Karlowicz *et al*. (2000) found 17 cases of *C. albicans* candidemia, 7 cases of *C. parapsilosis* and 7 cases of *C. tropicalis*, with a mortality rate of 33.3%. Daad and Tahawi (2001) researched the influence of several clinical variables on the development and outcome of candidemia, based on 655 positive blood cultures, finding 31 cases (4.7%) of fungemia by species of the genus *Candida*. They commented that all cases of candidemia were "in hospital" infection and occurred after 48 hours of hospitalization, corroborating the results of Thuler *et al*. (1991). These authors isolated *C. albicans*, *C. tropicalis* and *C. parapsilosis*, correlating the use of venous catheters, stay period in intensive care units and antibiotic therapy with broad bacterial spectrum to the increased cases frequency. Débora *et al*. (1999) identified 11.6% of children and 88.4% of adults with candidemia in 415 cases evaluated from 14 hospitals in various regions of Canada. The most frequent species were *C. albicans* with 286 cases (68.2%), *C. parapsilosis* with 43 cases (10.4%), *C. glabrata* with 34 cases (8.2%), *C. tropicalis* with 27 cases 6.5%) and other *Candida* species with 18 (4.3%). The authors mention that the coefficient of lethality was about 46%. In these patients, the risk factors related to infection and death were to be aged over 60 years, antibacterial therapy, permanency time in intensive care units, malignant diseases, cytotoxic chemotherapy and neutropenia. The research revealed that the highest correlation index was found between hospitalization and age, still poorly demonstrated, considering the trend of the phenomenon and the calculated correlation coefficient.

França *et al*. (2008) mentioned that the endogenous origin of candidemia due to translocation phenomenon is the main source of the disease, but some species such as *C. parapsilosis* may originate exogenously, mainly by the use of venous catheters and the colonized hands of healthcare professionals who attend the patient. Our experience with patients hospitalized in hospitals of the cities of Baixada Fluminense corroborates these statements, since the venous catheters when removed are sent to culture, and the presence of species of the genus *Candida* is often revealed, showing that in these cases there is a possibility of fungal invasion to the organism and may cause candidemia. In Soweto, South Africa, Kreusch and Karstaedt (2013) reported the isolation of *Candida albicans*

from blood cultures of 22 HIV-infected patients who had a CD4 cell count below 70/µl, with a mortality rate of 73%. Our studies on candidemia in patients from the cities of Baixada Fluminense, province of Rio de Janeiro, showed a percentage of 2.56% for sepsis by species of the genus *Candida*; lower than those found in Soweto. Such differences may be related to the living conditions of the studied populations and peculiarities about the implantation of microorganisms, nutritional factors, immunodepression among other factors. Some relevant aspects to be considered are the citations of Veronesi & Focaccia (2013) on the treatment of hospital infections caused by species of the genus *Candida*. They cited that inadequate treatment induces the emergence of mutant strains which are resistant to systemic antimycotics and, in these cases, the high rates of recurrence may contribute to their spread. This information shows the need for epidemiological markers to discover the origin of these infections in hospitals.

Motoa *et al*. (2016) studied the infections caused by species of *Candida* genus in patients hospitalized in Intensive Care Units in Colombia between 2010 and 2013. Among the 2.680 isolated fungi, *Candida* species represented 94.5% of the total, with similar proportions between *C. albicans* and other species of the genus (48.3% and 52.7%, respectively). They commented that in blood samples, *C. albicans* was the most frequent, a result that resembles the results of our research in the Baixada Fluminense region (45.16% prevalence for *C. albicans* and 54.84% for other *Candida* species).

Conclusion

From the analysis of the results of the research, the conclusions are: candidemia was diagnosed in hospitalized patients in the Baixada Fluminense region, province of Rio de Janeiro. Among the 1.213 patients evaluated, 31 cases were diagnosed, corresponding to 2.56% of the studied patients. The identified species were: *Candida albicans* 14 (45.0%), *C. krusei* 2 (6.5%), *C. stellatoidea* 4 (13.0%), *C. glabrata* 1 (3.0%), *C. parapsilosis* 2 (6.5%), and *C. tropicalis* 8 (26.0%). Generalized infections by species of the genus *Candida* constitute a serious threat to the health of the affected ones, mainly when is diagnosed later, and can lead to death over 50% of infected patients. Therefore, blood cultures should be performed early as a routine exam in all patients with suspect of sepsis. There are no ideal measures for prophylaxis, considering that these fungal agents constitute the normal biota of the organism and attack when they find favourable conditions for its implantation. These results on candidemias in the region of Baixada Fluminense shall stimulate health professionals to continue the investigation of sepsis by fungal elements and alert to the risk of these condition to hospitalized patients.

REFERENCES

Cermeño, J.R., Cuesta, Y.H. 2012. Seroprevalencia de citomegalovírus (CMV) en patients infectados con el vírus de inmunodeficiencia humana (HIV) en el estado Bolivar, Venezuela. *Rev Soc Venezuela Microbiol*., 232: 70-74.

Coura, R. 2013. Dinâmica das Doenças Infecciosas e Parasitárias. Ed Guanabara Koogan, Rio de Janeiro.

Cuetera, M.S., Alambra, A., Del Palacio, A. 2006. Diagnóstico microbiológico tradicional de la candidiasis invasora en el paciente crítico no neutropénico. *Rev Iberoam Micol*., 23: 4-7.

Daad, A.H., Tahawi, A.T. 2001. Candidemia at a University Hospital: epidemiology, risk factors and predictors of natality. *Ann Saudi Med*., 21(3-4): 178-182.

Debora, L.R., Rotstein, C., Nicolle, L.E., Iannou, S. 1999. Candidemia at selected Canadian sites: Results from the fungal disease registry, 1992-1994. *Can Med Asoc J*., 160 (4): 493-499.

França, J.C.B., Ribeiro, C.E.L., Queiroz-Telles, F. 2008 Candidemia em um hospital terciário Brasileiro: incidência, frequência das diferentes espécies, fatores de risco e susceptibilidade aos antifúngicos. *Rev Soc Bras Med Trop*., 4(1): 23-28.

Galvan, B., Mariscal, F. 2006. Epidemiología de la candidemia in ICI. *Rev Iberoam Micol*., 23: 12-15.

Gurgel, J.A.H. 1998. Epidemiology and risk factors in nosocomial candidemia. *UNIMAR Ciencias*, 7(1): 19-21.

Jarvis, W.R. 1995. Epidemiology of Nosocomial Fungal Infections with Emphasis on *Candida* species. *J Clin Infect Dis*., 20: 1526-1530.

Karlovicz, M.G., Hashimoto, L.N., Kelly-Jr, R.E. 2000. Should control venous catheters be removed as soon as candidemia in delected in neonats? *Pediatric*, 106: 63.

Kreusch, A., Karstaedt, A.S. 2013. Candidemia among adults in Soweto, South Africa. *Intern J Infect Dis*., 7(8): 621-623.

Moreira, M.E.L. 2005. Controvérsias a respeito da sepse fúngica no pré-termo extremo. Profilaxia e esquema terapêuticos. *J Ped*., 81(1): 53-58.

Motoa, G., Muñoz, J.S., Oñate, J., Pallares, C.J., Hernández, C., Villegas, M.V. 2016. Epidemiology of *Candida* isolates from Intensive Care Units in Colombia from 2010 to 2013. *Rev Iberoam Micol*., 34(1): 17-22.

Ruiz, L.S., Khouri, S., Hahn, R.C., Silva, E.G., Oliveira, V.K.P., Gandra, R.F., Paula, C.R. 2013. Candidemia by Species of *Candida parapsilosis* complex in childres's hospital: prevalence, biofilm production and antifungal susceptibility. *Mycopathol J*., 175(3-4):231-239.

Sanchez, J.R., Aguirre, J.J.M. 2007. Factores asociados a mortalidad por fungemias causadas por *Candida* sp. en niños. *Bol Med Hosp Infant Mexico*, 54: 91-98.

Serra-Freire, N.M. 2002. Planejamento e Análise de Pesquisas Parasitológicas. EdUFF, Niteroi.

Suarez, B.L., Alvarez, M.I., Bernal, M., Callazos, A. *Candida* species and other yeasts in the oral cavities of type 2 diabetic patients in Cali, Colombia. *Colomb Med*., 44 (1): 26-30.

Thuler, L.C.S., Macambira, R.P., Jóia, P.F.F. 1991. Alterações da microbiota em pacientes hospitalizados. *J Bras Med*., 60: 14-22.

Tiraboschi, I.N., Carnevale, S., Benetucci, A., Fernandez, N., Kurlat, I., Foccoli, M. *et al.* 2007. Brote de candidemia por *Candida albicans* en neonatología. *Rev Iberoam Micol.*, 24:263-267.

Tortorano, A.M., Peman, .J, Bemhardt, H., Kibblei, C.C., Kingspor, H. 2004. Epidemiology candidemia in Europe. *Europ J Clin Microbiol Infect Dis*., 23: 317-322.

Veronesi R., Focaccia R. 2013. Tratado de Infectologia, Ed Atheneu, Rio de Janeiro.

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