The Epidemiology of Fungaemia at the University Hospital of the West Indies, Kingston, Jamaica

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ABSTRACT

Objectives: *To determine the epidemiology of fungaemia at the University Hospital of the West Indies (UHWI) as well as the incidence of fungaemia at the UHWI over a four-year period.*

Methods*: A cross-sectional survey was conducted over a one-year period (2002). The RapID Yeast Plus Panel Identification kit was used to identify the yeasts found in blood while morphology and dimorphism were used to identify the single mold isolated,* Histoplasma capsulatum. *In addition, a retrospective review of the number of cases of fungaemia at the UHWI over a four-year period from 1998 was done using the laboratory and clinical records in order to determine the incidence over this period.*

Results: *The study showed that Yeast* ***not*** C albicans *(YNCA) accounted for 47% of the isolates while* Candida albicans *accounted for 29%. Of the YNCA species, Candida tropicalis was the most common (75%), followed by* C pseudotropicalis *(12.5%) and C glabrata (12.5%). Cryptococcus sp accounted for 18% of all fungal isolates and there was one isolate (6%) of Histoplasma capsulatum. The medical wards had the most isolates (47%), followed by surgery (29%) and the Intensive Care Unit (ICU) [24%]. While the rate at which fungi were isolated from the blood remained constant over 1998, 1999 and 2001, this doubled in 2002 from 0.26% to 0.5%.*

Conclusion*: Although the incidence of fungaemia at the UHWI has remained relatively low, there was a marked increase in the last year of the study (2002) with a doubling of the number of positive fungal cultures. Candida species account for most cases of fungaemia at the UHWI. However, non-albicans Candida* spp *were more commonly isolated than* C albicans, *a trend that needs to be monitored because of its implications for therapy.*

Epidemiología de la Fungemia en la Hospital Universitario de West Indies, Kingston, Jamaica

A Nicholson, L Rainford

RESUMEN

Objetivos: *Determinar la epidemiología de la fungemia en el Hospital Universitario de West Indies (UHWI) así como la incidencia de la fungemia en UHWI durante un período de cuatro años.*

Métodos: *Se llevó a cabo un estudio transversal por espacio de un año (2002). Se utilizó un kit de paneles para la identificación rápida de levaduras (Rapid Yeast Plus Panel), con el propósito de identificar las levaduras halladas en la sangre, en tanto que la morfología y el dimorfismo fueron usados a fin de identificar los aislados del moho individual,* Histoplasma capsulatum. *Además, se realizó un examen retrospectivo del número de casos de fungemia en el UHWI por espacio de cuatro años desde 1998, usando las historias clínicas e informes de laboratorio, a fin de determinar la incidencia en este período.*

Resultados: *El estudio mostró que las levaduras no C albicans (LNCA) representaban el 47% de los aislados, mientras que la* Candida albicans *representaba el 29%. De las especie LNCA,* Candida tropicalis fue *la más común (75%), seguida de* C pseudotropicalis *(12.5%) y* C glabrata *(12.5%).* Cryptococcus sp *representaba el 18% de todos los aislados fúngicos, y hubo un aislado (6%) de*

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Histoplasma capsulatum. *Las salas de hospitales fueron las que más aislados presentaron (47%), seguidas por las Unidades de cirugía (29%) y las de Cuidados Intensivos (UCI) (24%). Si bien el ritmo al cual los hongos fueron aislados de la sangre permaneció constante durante 1998, 1999, y 2001, el mismo se duplicó en el año 2002 pasando de 0.26% a 0.5%.*

Conclusión: *Aunque la incidencia de la fungemia en el UHWI ha permanecido relativamente baja, se produjo un marcado aumento en el último año de estudio (2002), en el que se duplicó el número de cultivos fúngicos positivos. Las especies de* Candida *son responsables de la mayor parte de los casos de fungemia en el UHWI. Sin embargo, las especies Candida no albicans fueron más comúnmente aisladas que las* C albicans *– una tendencia que necesita ser monitoreada debido a sus implicaciones para la terapia.*

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INTRODUCTION

Fungaemia has been a steadily increasing problem internationally. In the United States of America (USA), *Candida spp* are considered to be the fourth most common hospital associated bloodstream pathogen representing 8–10% of all such infections (1). Bloodstream infections are associated with prolonged hospitalization and increased cost of medical care. In addition, patients with fungaemia are more likely to die during hospitalization than are patients who have bloodstream infections due to other causes (2).

Many factors have been identified as contributing to the increased incidence of fungaemia but most notable are the growing population of immuno-compromised patients with diseases such as AIDS, diabetes mellitus and cancer, premature birth, the common usage of broad-spectrum antibiotics, the emergence of multiple drug-resistant organisms in hospitals, cytotoxic chemotherapy and the use of sophisticated invasive surgical interventions including the use of prostheses and elaborate life-support systems. Newer technologies such as solid organ and bone marrow transplants offered at many hospitals have also been implicated as important risk factors leading to the observed increase (3, 4).

Candida albicans accounted for 80% of Candidal bloodstream infection at the University of Iowa Hospitals and Clinics in 1984. However, by 1991, it was implicated in less than 50% of these infections with other species such as *C tropicalis* and *C parapsilosis* becoming increasingly more common causes of fungaemia (2). *Candida krusei, C lusitaniae* and *C glabrata* have also been implicated in nosocomial infections. These emerging epidemiological differences have therapeutic and prognostic implications since some *Candida spp* such as *C krusei* and *C glabrata* are resistant to some antifungal agents (5).

At the UHWI, in 1999, *Candida spp* was the seventh most common bloodstream isolate after *Escherichia coli, Klebsiella pneumoniae, Staphylococcus aureus, Streptococcus pneumoniae, Enterobacter spp* and *Enterococcus spp* (unpublished data). The species of *Candida* and the pattern of distribution of the *Candida* isolates were not known.

The aim of this study was to determine the types of fungi implicated in fungaemia at the UHWI and to identify the different species of *Candida* commonly isolated. The incidence of fungaemia over a four-year period was also reviewed to determine whether or not the local data reflected the marked increase in fungal infections reported internationally.

This study provides the only published data on fungal species isolated from blood at the UHWI or in Jamaica. This is important since the overall crude mortality rate associated with fungaemia is high (6). The types of fungi isolated will have implications for empirical therapy because of the variations in susceptibility to commonly used antifungal agents.

MATERIALS AND METHODS

A cross-sectional survey was conducted over a one-year period beginning in January 2002. Fungal isolates found in blood cultures sent to the Department of Microbiology were retrieved and inoculated onto Saboraud Dextrose and Mycobiotic agar. These were incubated at room temperature (25˚C) until growth was detected. Isolates identified as yeast, using Gram stain and biochemical studies, were further identified to the species level using the RapID Yeast Plus Panel Identification kit, (Remel Inc, Norcross, GA). The tests used in this system were based on the microbial degradation of specific substrate detected by various indicator systems.

The single mold isolated was identified by macroscopic examination of the growth, microscopic examination of tease preparation in lactofuchsin stain and appropriate follow-up confirmatory tests.

Duplicates from the same patient were excluded from the study. Laboratory records were reviewed to obtain demographic data for these patients as well as time taken for the culture to become positive. Clinical data on diagnosis, underlying medical conditions, treatment and outcome of the patient were obtained from the medical records. For this study, a case of fungaemia was defined as the isolation of a fungus from a blood culture taken from a patient in hospital (7).

In addition, laboratory records in the Department of Microbiology for a four-year period (1998, 1999, 2001, 2002) were reviewed to determine the incidence of fungaemia over this time. Laboratory data for 2000 were unavailable.

RESULTS

Twenty-nine fungal isolates were identified from blood in the Microbiology Laboratory (UHWI) in 2002. Of these, 20 isolates were retrieved but medical records were available to confirm only 17 of these as cases of fungaemia.

Of the seventeen cases (85%) for which medical records were available, non-albicans species of *Candida* (47%) were most commonly identified followed by *Candida albicans* (29%), *Cryptococcus spp* (18%) and *Histoplasma capsulatum* [6%] (Fig. 1). Of the non-albicans species of

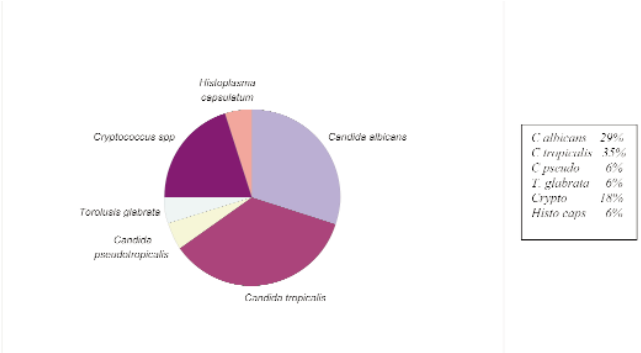

Fig. 1: Distribution of fungal isolates from blood: 2002.

Candida, *Candida tropicalis* was the commonest accounting for 75% of these isolates followed by *Candida pseudotropicalis* and *Candida (Torulopsis) glabrata* accounting for 12.5% each.

The medical wards had the highest number of isolates (47%) followed by 29% from the surgical wards and the ICU with 24% of the isolates (Fig. 2). *Cryptococcus spp* ac-

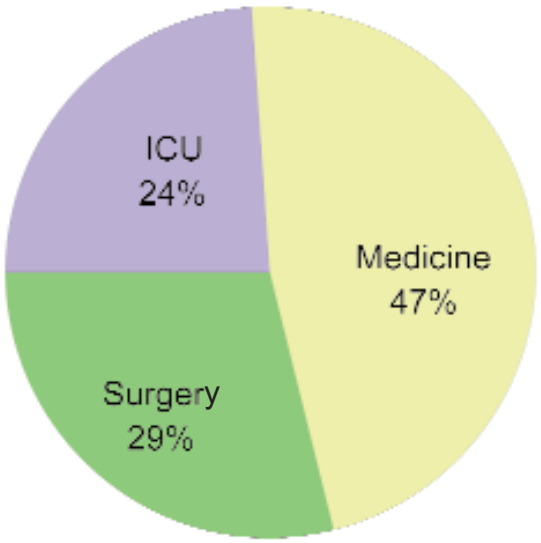

Fig. 2: Distribution by Wards/Service.

counted for 18% of the bloodstream fungal isolates and there was only one case (6%) of *Histoplasma capsulatum* which was found in the blood of a 16-year old HIV-positive female patient.

These isolates were recovered from the blood of patients ranging in age from 4–82 years, with most of the patients falling within the > 60-year old age group. The number of cases was lowest in the 0–20-year old age group (Fig. 3).

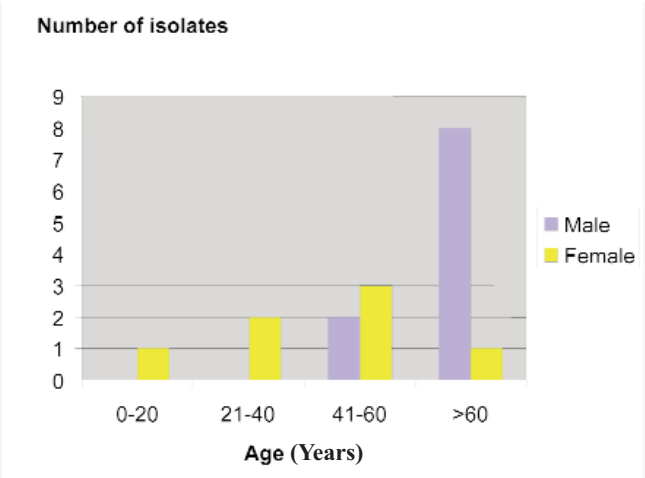

Fig. 3: Distribution of isolates by age and sex.

Some of the factors found to be associated with fungaemia in this study included previous antibiotic use (13 cases), diabetes mellitus (5 cases), hypertension (5 cases), malignancy (3 cases), surgery (6 cases) and a positive HIV status (4 cases).

The rate at which fungi were isolated remained fairly constant over 1998, 1999 and 2001. In 1998, 0.27% (13/4, 774) of all blood samples submitted to the laboratory for culture yielded a positive fungal culture (95% CI 0.12, 0.42). In 1999, 0.23% (10/4, 437) of all blood cultures yielded a positive fungal culture (95% CI 0.09, 0.37). In 2001, 0.27% (15/5,592) of all blood cultures yielded a positive fungal culture (95% CI 0.13, 0.41). In 2002 however, this rate doubled to 0.5% (29/5,893) of all blood cultures (95% CI 0.31, 0.67).

DISCUSSION

This study showed that non-albicans Candida species were actually more commonly isolated than *Candida albicans* at the UHWI with *C tropicalis* being the most common of these. This is an important finding since *C albicans,* which has been traditionally regarded as the more common and significant pathogen, is the only species routinely identified at the UHWI, while all other *Candida* species are reported as 'Yeast not *Candida albicans* (YNCA)'. However, while *C albicans* remains the most commonly isolated fungus from bloodstream infections in some countries, there appears to be a

trend emerging where the non-*albicans* species are increasing in incidence.

In Canada from 1992–1994, *Candida albicans* was the commonest cause of candidaemia followed by *Candida parapsilosis* and *Candida tropicalis*. It was also found that the mortality rate associated with Candidaemia was high but varied among the species implicated, with only *C parapsilosis* being associated with a lower mortality rate than infection with *C albicans* (8). In some studies, *C parapsilosis* was recorded as one of the more commonly isolated non-albicans Candida species (9) but this species was not isolated in this study. In Finland, although *C albicans* was found to be the commonest cause of fungal bloodstream infection over a five-year period from 1995, non-albicans Candida species such as *C glabrata, C parapsilos, C krusei* and *C tropicalis* were found to have become more common (7).

Results similar to those of this study were obtained in North India where a five-year study showed that most episodes of candidaemia were caused by species other than *C albicans* with *C tropicalis* being the most common followed by *C albicans*. Other *candida* species implicated there included *C parapsilos* and *C glabrata*. This was also found in other parts of India (10).

A study done in Italy, showed a shift in the species of *Candida* causing fungaemia with the proportion due to *C albicans* decreasing while that due to other species such as *C parapsilos* and *C tropicalis* and *C glabrata* increased (11). *C tropicalis* is an important pathogen and has been reported to be a common cause of fungaemia in both oncology and non-oncology patients. It is thought to be acquired in ways similar to *C albicans* with similar risk factors such as prior treatment with multiple antibiotics and prior haemodialysis (2).

The increased use of fluconazole in some countries has lowered the incidence of fungaemia (12). However, the use of fluconazole as antifungal prophylaxis may result in a shift towards non-*albicans sp* of *Candida* since some species such as *C krusei*, may be innately resistant to this drug (13, 3). At the UHWI, fluconazole is not used prophylactically but is used empirically to treat nosocomial fungaemia. At Anderson Cancer Centre in Houston, there was a relative decrease in *C albicans* and *C tropicalis* infections and an increase in *C krusei* and *C glabrata* infections. This was thought to be due to the use of fluconazole prophylaxis which provides strong protection against the development of *C tropicalis* and *C albicans* infection in comparison with other species (14).

The fact that one of the YNCA isolates was *Candida (Torulopsis) glabrata* is important to note because there have been reports of resistance in this species to one of the more commonly used antifungal agents, Amphotericin B (2). In addition, it has been observed that *C albicans* and *C glabrata*, which were initially susceptible to fluconazole, may develop resistance during treatment and some species of *Candida* such as *Candida krusei* are intrinsically resistant to fluconazole (5). This further reinforces the value of identifying the species involved in infections so that treatment may be monitored closely.

The practice in the laboratory at the UHWI of identifying only *C albicans* species to the species level should be re-examined. The emergence of changing trends reported by other studies and the results of this study, suggest the need to also monitor the emergence of non-*albicans* species since such emergence has significant implications for prognosis and therapy.

Of significance also is the fact that *Cryptococcus sp* accounted for 20% of the fungal bloodstream isolates and all were from HIV-positive patients. This underscores the impact of the increasing HIV-positive population in Jamaica on the incidence of fungaemia and may explain why the highest incidence of fungaemia was found on the medical wards (35%). In 1995, it was reported that since 1987, the annual AIDS case rate in Jamaica doubled every two years with 69% of individuals dying with AIDS (15). A study in Finland showed no patient with fungaemia and a positive HIV status reflecting the low prevalence of HIV infection in that country (7).

It is important to note that blood cultures are taken from all patients with a clinical diagnosis of sepsis and are routinely cultured for bacteria and yeast. Although the actual numbers of positive fungal blood cultures remain relatively low, there was a doubling of the number in the last year of the study. This trend should be monitored very closely since the incidence of fungaemia is expected to increase with the continued increase in the HIV-positive population and as there is an increased use of prostheses in surgical procedures. In addition, the flora may become even more diverse with the occurrence of other types of fungi such as *Aspergillus, Fusarium, Acremonium* and *Paecilomyces* species (16).

The relatively low numbers of positive fungal blood cultures may be explained by the fact that while many of the factors associated with fungaemia, such as heavy usage of broad spectrum antibiotics especially in the ICU (17) and a growing immunocompromised population are a problem in Jamaica, other factors such as bone marrow transplant are noticeably absent from this setting and organ transplants are not commonly done here.

It is important, however, to monitor fungal isolates at the UHWI so that emerging trends can be detected early.

The limitations of study include the relatively small sample size and the fact that risk factors were not assessed. However some associations that were observed between fungaemia and underlying clinical conditions included previous antibiotic use, a positive HIV status, surgery, malignancy and diabetes mellitus. Factors associated with fungaemia were common among hospitalized patients therefore it was often not clear what the predisposing factors for the development of these infections were. Some factors such as indwelling catheters provide a route of entry for the organism while others such as malignancy and chemotherapy act by inducing immunosuppression (3).

The dynamic nature of the factors involved in the cause and incidence of fungaemia makes the monitoring of fungaemia an important tool to detect emerging trends.

This study showed that *Candida* species were the most important cause of fungaemia at the UHWI. However, similar to some other countries, non-albicans Candida species were more common than *C albicans.* In addition, *Cryptococcus sp* was found to be the most significant isolate in the HIV-positive population.

The doubling of the positive fungal blood cultures seen in the final year of the study provides cause for concern. There should be continued surveillance to monitor the incidence of fungaemia and the species involved so that emerging trends can be detected and empirical antifungal therapy monitored accordingly.

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