Epidemiology of Fungal Infections at an Infectious Disease Reference Centre in Malaysia

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ABSTRACT

Introduction: Epidemiology of fungal infections in an infectious disease reference centre is different from other institutions. This study aimed to look at the scenario of fungal infections at an infectious disease reference centre in Malaysia. **Methods:** All positive fungal cultures from an infectious disease reference centre were identified by routine mycology laboratory methods. Patient demographic, laboratory and clinical data were collected and analyzed. Duplicate data were excluded. **Results:** Middle-aged Malay males were the most common group. However, increased proportions of Chinese, Myanmar and Indonesians reduced the Malay predominance in HIV-positive group. In all patients, *Candida* species represented 64.1% isolates, followed by *Cryptococcus neoformans* (14.7%) and *Penicillium marneffei* (14.7%). Among HIV-positive individuals, *C. neoformans* (37.9%) was the most common species, followed by *P. marneffei* (35.6%) and all *Candida* species (17.2%). In contrast to other non-infectious disease reference centres, common causes of fungaemia included *P. marneffei* (43.5%), *Candida* species (25.8%), *C. neoformans* (24.2%) and *H. capsulatum* (6.5%). **Conclusion:** The prevalence of fungal infection at an infectious disease reference centre is different from other non-infectious disease reference centres. This may have an impact on current antifungal practice especially empiric antifungal therapy, patient morbidity and mortality.

KEYWORDS: Infectious disease, fungal infection, HIV, fungaemia, Malaysia

INTRODUCTION

Fungal infections are becoming more common to cause morbidity and mortality among hospitalized patients. The increasing population of immunocompromised individuals is a major factor in the emergence of opportunistic fungal infections. The human immunodeficiency virus (HIV) disease epidemic has been shown to be responsible for dramatic increases in cryptococcosis, penicilliosis and histoplasmosis.[1] In Malaysia, most HIV patients are referred to a centralized infectious disease reference centre in Sungai Buloh Hospital, located in the suburbs of Kuala Lumpur. As HIV patients are at increased risks for fungal infections, the concentration of this group of patients in a single centre may result in a different fungal epidemiological profile as compared with a general hospital, non-infectious disease reference centre. Since its inauguration in September 2006, there has been no study to look at the types of fungi isolated from patients in Hospital Sungai Buloh. Therefore, this study aimed to determine the fungal epidemiological profile of an infectious disease reference centre in Malaysia.

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MATERIALS AND METHODS

This was a cross-sectional study conducted at Hospital Sungai Buloh, Malaysia; a 620-bedded infectious disease reference centre in the country. It acts as a tertiary referral centre for various cases of infectious diseases in Malaysia, especially HIV/AIDS. However, it also caters for other specialties, including general medicine, surgery, orthopaedics, obstetrics and gynaecology and paediatrics.

Culture results from all specimens were included in the study. Specimens were inoculated onto Sabouraud Dextrose Agar (SDA - Difco Laboratories, UK) media. Yeastlike organisms from normally sterile sites were inoculated onto a chromogenic agar (BBL™CHROMagar™, UK) to rule out mixed fungal infections. Yeasts were identified by using commercially-prepared carbohydrate assimilation tests, ID 32C (bioMérieux, France). Moulds were identified by macroscopic and microscopic examinations. A mature growth on SDA was examined macroscopically for its surface colour, texture and reverse-side colour; and microscopically by tease mount / scotch tape preparation with

lactophenol cotton blue dye for pigmentation, hyphae, macroconidia, microconidia and fruiting structures. Repeated positive isolates from the same specimen, from the same patient that yielded the same fungal species within three months were regarded as recurrent infection and were excluded from the study. Patient demographic, clinical and laboratory data were obtained from the computer Total Hospital Information System. The data included age, gender, ward, laboratory request number, date of specimen taken, organism isolated and patients' HIV status. The data were anonymized by removing the names and medical record numbers. Statistical analysis was performed using IBM SPSS Statistics version 18.0 (IBM Corporation, New York, USA). The study was approved by the Medical Research and Ethics Committee, Universiti Kebangsaan Malaysia Medical Centre (UKMMC).

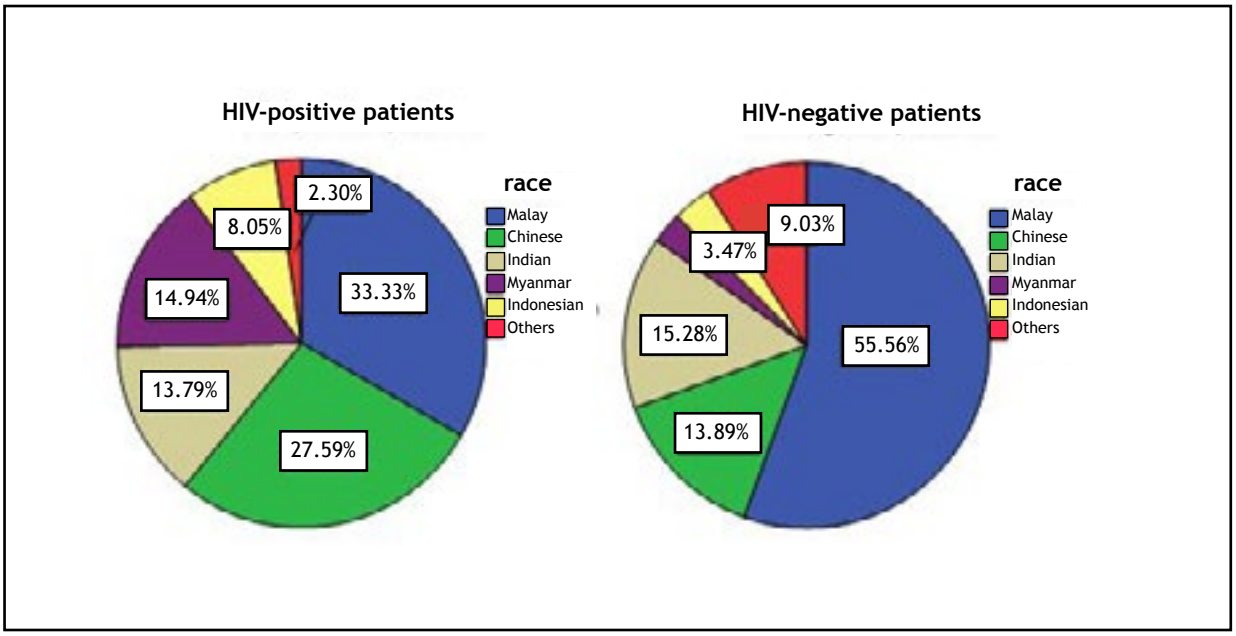
Table I. Demographics of patients with positive fungal cultures

	HIV-positive patients n = 87 (%)		HIV-negative patients n = 144 (%)		All patients n = 231 (%)		p-value by Pearson's Chi-square
Gender							
Male	75	(86.2)	96	(66.7)	171	(74.0)	<0.001
Female	12	(13.8)	48	(33.3)	60	(26.0)	
Age group							
<18 y	0	(0)	20	(13.9)	20	(8.7)	<0.001
≥18 y	87	(100)	124	(86.1)	182	(91.3)	
Mean age ± SD	39.1 ± 9.8		43.7 ± 22.7		41.9 ± 19.0		<0.001

RESULTS

Two-hundred-thirty-one clinical samples were included in the study such as urine (42.9%), blood (32.0%), cerebrospinal fluid (8.7%), respiratory specimens (6.1%), tissue (3.9%), dermatological specimens (3.1%), body fluids (2.2%), bone marrow aspirate (0.9%) and pus (0.4%). Two-hundred-thirty-one patients were included, where 87 (37.7%) were HIV-positive individuals. Adult male patients aged 18 years and above were the most common group (Table I). Gender, age group and mean ages were significantly different between the HIV-positive and HIV-negative groups (p-values of <0.001).

Figure 1: Difference in race distributions among HIV-positive and HIV-negative populations (p-value<0.001)



The distribution of races was significantly associated with HIV status. Among the HIV-negative individuals, the Malays comprised more than half (55.6%) of patients, followed by Chinese and Indians. However, among HIV-positive individuals, only one-third were Malays. Chinese, Myanmar, Indonesian and other races formed the other two-thirds of patients (Figure 1). Other races included Vietnamese, Bangladeshi, Pakistani, Caucasians and other East Asians. The most common groups of fungi isolated were yeasts (80.5%), followed by thermally dimorphic fungi (16.9%) and moulds (2.6%). Among isolates, *Candida albicans* was the most commonly isolated. The distribution of isolates among HIV-positive and HIV-negative individuals differed significantly (p-value <0.001). Among HIV-positive individuals, *Cryptococcus neoformans* (37.9%) was the most common species, followed by *Penicillium marneffei* (35.6%) and all *Candida* species (17.2%). Among HIV-negative individuals, thermally dimorphic fungi and *Cryptococcus neoformans* no longer were the most common isolates (Table II). There were 62 adult cases of fungaemia, of which *P. marneffei* was the most common fungus isolated (43.5%); followed by *Candida* species (25.8%), *C. neoformans* (24.2%) and *H.capsulatum* (6.5%).

Table II. Prevalence of fungal isolates among all, HIV-positive and HIV-negative patients (p-value by Pearson's chi-square test <0.001)

		All patients		HIV-positive		HIV-negative	
		n = 231 (%)		n = 87 (%)		n = 144 (%)	
Yeasts		**186**	**(80.5)**	**50**	**(57.5)**	**136**	**(94.4)**
	Candida albicans	69	(29.9)	8	(9.2)	61	(42.4)
	Candida glabrata	9	(3.9)	1	(1.1)	8	(5.6)
	Candida tropicalis	6	(2.6)	0	(0)	6	(4.2)
	Candida parapsilosis	3	(1.3)	0	(0)	3	(2.1)
	Candida lusitaniae	1	(0.4)	0	(0)	1	(0.7)
	Candida spp.	60	(26.0)	6	(6.9)	54	(37.5)
	Cryptococcus neoformans	34	(14.7)	33	(37.9)	1	(0.7)
	Trichosporon spp.	4	(1.7)	2	(2.3)	2	(1.4)
Dimorphic fungi		**39**	**(16.9)**	**36**	**(41.4)**	**3**	**(1.7)**
	Penicillium marneffei	34	(14.7)	31	(35.6)	3	(2.1)
	Histoplasma capsulatum	5	(2.2)	5	(5.7)	0	(0)
Moulds		**6**	**(2.6)**	**1**	**(1.1)**	**5**	**(3.5)**
	Fusarium spp.	3	(1.3)	1	(1.1)	2	(1.4)
	Curvularia spp.	1	(0.4)	0	(0)	1	(0.7)
	Aspergillus niger	1	(0.4)	0	(0)	1	(0.7)
	Paecilomyces lilacinus	1	(0.4)	0	(0)	1	(0.7)
	Total	**231**	**(100)**	**87**	**(100)**	**144**	**(100)**

DISCUSSION

All age groups were affected. The most commonly affected age groups in this study were adults aged 18 years and above. A high male-to-female ratio (2.9:1) was noted in our patient population. Almost half of male patients were infected with HIV (43.9%) compared to (20.0%) in female patients. The distributions of mycoses among all patients were highest in Malays, followed by Chinese and Indians; however, this may reflect normal ethnic distribution in Malaysia. The distribution of race between HIV-positive group and HIV-negative group differed significantly (p<0.001). Malay predominance in HIV-negative group was significantly diminished by increases in Chinese, Myanmar and Indonesian proportions. This data reflects a negative impact of immigrants to the overall population health status in Malaysia. A strict policy must be enforced by the government to prevent spread of HIV among the immigrants and local population.

Almost two-thirds (62.6%) of positive fungal cultures came from the infectious disease (ID) and general medical wards. This finding may be attributed to the patient population in those wards with serious underlying medical conditions, including HIV as compared with other wards. *Penicillium marneffe*i and *C. neoformans* were the most common species isolated (38% each), followed by *C. albicans* (8%) and *H. capsulatum* (5%). Cryptococcosis and penicillosis were reported in about 20% and 7% of patients with AIDS in northern Thailand, respectively.[2]

The distribution of fungal isolates is not uniform throughout the world. In our study, the most common fungal species isolated from all cases was *Candida albicans* (29.9%); followed by *Candida spp.* (26.0%), *Penicillium marneffei* (14.7%) and *Cryptococcus neoformans* (14.7%). However, among 62 adult cases of fungaemia, *P. marneffei* was the most common fungus isolated (43.5%); followed by

Candida species (25.8%), *C. neoformans* (24.2%) and *H. capsulatum* (6.5%). This is in contrast to other studies involving two university hospitals in Malaysia, where *Candida* species were the most common isolates in fungaemia.[3,4] These two centres are tertiary level referral centres but are not designated as infectious disease centres. *Penicillium marneffei* infection is an important disease among HIV-infected persons in Southeast Asia. The disease has now been reported among HIV-infected persons in Thailand, Myanmar, Vietnam, Cambodia, Malaysia, north-eastern India, Hong Kong, Taiwan, and southern China.[5] A similar study in San Francisco Bay Area hospitals involving similar high-HIV population as in our study, showed a different pattern of fungal distributions. In that study, *Candida* species accounted for most of the infections, followed by *Cryptococcus, Coccidioides, Aspergillus* and *Histoplasma*.[6] Among candidaemia cases in our study, *C. albicans* were still the most common *Candida* species isolated (55%); followed by *C. glabrata* (20%), *C. parapsilosis* (15%) and *C. tropicalis* (10%). In some hospitals, the proportion of cases of candidaemia due to *C. glabrata* is strikingly higher among patients who are >60 years of age.[7] Other studies in Malaysia gave varying reports of the most common *Candida* species isolated from blood. Universiti Kebangsaan Malaysia Medical Centre reported *C. albicans* as the most common species isolated (40%) followed by *C. tropicalis* (32%) and *C. parapsilosis* (10%)[4] whereas Universiti Malaya Medical Centre reported *C. parapsilosis* as the most common species isolated (51.0%) followed by *C. tropicalis* (25.5%) and *C. albicans* (11.8%).[3]

In conclusion, the prevalence of fungal infection at an infectious disease reference centre is different from other non-infectious disease reference centres. This may have an impact on current antifungal practice, particularly for empiric antifungal therapy, which in turn may affect patient morbidity and mortality.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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