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ORIGINAL ARTICLE

Antifungal susceptibility of non-*albicans Candida* species from blood samples

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Abstract

Introduction: Globally, non-*albicans Candida* (NAC) species have emerged as a notable cause of both healthcare-associated and opportunistic infections. Compared with *Candida albicans*, NAC species are more likely to cause infections fraught with antifungal resistance issues and higher mortality rates. The objectives of this study were to identify the various *Candida* species causing candidaemia in a Malaysian general hospital and to ascertain their antifungal susceptibility profiles. *Materials and Methods:* This 15-month cross-sectional study involved the peripheral blood of patients diagnosed with candidaemia. Conclusive species identification was achieved through matrix-assisted laser desorption ionisation-time-of-flight mass spectrometry (MALDI-TOF MS) while antifungal susceptibility was performed using the colourimetric broth microdilution method. *Results:* A total of 118 non-duplicate *Candida* isolates were analysed during the study period. Out of this total, 47 (39.8%) were *C. albicans*, 25 (21.2%) were *Candida parapsilosis* complex, 24 (20.3%) were *Candida tropicalis*, 19 (16.1%) were *Nakaseomyces glabratus* and three (2.6%) were *Pichia kudriavzevii*. Collectively, the NAC species outnumbered *C. albicans* (60.2% vs. 39.8%). The overall minimal inhibitory concentration at which ≥90% of isolates were inhibited (MIC_{90}) for NAC species was 32 µg/mL for fluconazole, 1 µg/mL for amphotericin B and between 1 to 2 µg/mL for the echinocandins. *Conclusion:* Despite *C. albicans* being the single most frequently isolated species from patients with candidaemia, more than half of candidaemia cases in our centre were caused by NAC species. Generally, although these NAC species were not fluconazole-susceptible, amphotericin B and echinocandins may still be utilised against them.

Keywords: Candida, non-albicans, candidaemia, antifungal, fluconazole, echinocandin

INTRODUCTION

Although more than 200 species of *Candida* have been described so far, 90% of invasive human mycoses are caused by *Candida albicans* and just a handful of non-*albicans Candida* (NAC) species, viz. *Candida tropicalis*, *Candida parapsilosis*, *Nakaseomyces glabratus* (formerly *Candida glabrata*) and *Pichia kudriavzevii* (formerly *Candida krusei*).[1] However, with the dawning of the new millennium, the medical literature has been inundated with reports of NAC species being implicated in a myriad of infections, particularly in critically ill and immunocompromised individuals. Certain NAC species appear to be associated with specific risk factors, such as the overuse of venous catheters (*C. parapsilosis*), the administration of total parenteral nutrition (*C. parapsilosis*) and the presence of an underlying malignancy (*C. tropicalis*).[2] The over-prescription of fluconazole in some centres would also be a selection pressure favouring NAC species that are intrinsically resistant to this antifungal, such as *Pichia kudriavzevii*.[3] Geographical influences on the rising frequency of NAC species have also been reported – for instance, *C. tropicalis* is commonly isolated in Asia and South America,

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while *Nakaseomyces glabratus* is prevalent in Northern and Central Europe, as well as in the USA.[4]

Alarmingly, in many centres, a NAC species has overtaken *C. albicans* as the most frequently isolated yeast from clinical samples. A recent Malaysian study on candidaemia revealed that close to 30% of cases were caused by *C. parapsilosis,* while only 20.1% were attributable to *C. albicans*.[5] Thailand, Malaysia's northern neighbour, is also grappling with a high frequency of NAC infections, with a recent study reporting that almost half of all candidaemia cases were caused by *C. tropicalis*, while only 29% of cases were due to *C. albicans*.[6] The classification of a yeast as a NAC species is not undertaken solely for academic intentions, but rather for practical purposes. Nearly all the commonly isolated NAC species are more likely to be less susceptible to azoles than *C. albicans*, and one of them (i.e. *Candida auris*) even has significant resistance to polyenes.[7] To add fuel to the fire, in some studies, the mortality rate of non-*albicans* candidaemia exceeds that caused by *C. albicans* – it was reported to be 7.7% for *Candida albicans*, 23.7% for *N. glabratus* and as high as 63.6% for *Candida tropicalis*.[8] Therefore, the objectives of this study were to determine the species distribution and antifungal susceptibility profile of the *Candida* isolates that originated from blood specimens in a general hospital in the capital city of the state of Perak, Malaysia.

MATERIALS AND METHODS

Study design

This cross-sectional study was conducted over a period of 15 months, from January 2023 until March 2024 in Hospital Raja Permaisuri Bainun (HRPB). HRPB is a 990-bedded hospital situated in Ipoh, the capital city of the Malaysian state of Perak – it is also the third largest Ministry of Health hospital in Malaysia. Non-duplicate *Candida* isolates from the peripheral blood of patients diagnosed with candidaemia requiring antifungal therapy were collected during the study period. This research received ethical approval from Universiti Kebangsaan Malaysia (approval code: UKM PPI/111/8/JEP-2023-502) and from the Ministry of Health of Malaysia's Medical Research and Ethics Committee (research ID: 23-02433-96H). Data were collected from HRPB's laboratory information system and from each patient's file. The data collected encompassed the patient's age, gender, ethnicity, location of stay within the hospital and risk factors for candidaemia (such as the presence of diabetes mellitus, underlying haematological malignancy, ICU admission, prolonged hospitalisation, usage of broad-spectrum antibiotics, usage of antifungal therapy and usage of invasive medical devices).

Isolate identification

During the routine Gram-staining of blood specimens flagged as positive for microbial growth by the BACTEC FX automated blood culture system, any sample that contained gram-positive budding yeast cells was subcultured onto a Sabouraud dextrose agar (SDA) plate and a CHROMagar *Candida* plate for incubation at 30°C for 24-48 hours. Following incubation, each CHROMagar *Candida* plate was examined for the presence of mixed growth (i.e. colonies with more than one distinct colour). Once mixed growth was ruled out, colonies from the SDA plate were subjected to presumptive identification through cornmeal agar culture and definitive identification via matrix-assisted laser desorption ionisation-time-of-flight mass spectrometry (MALDI-TOF MS) (Bruker Daltonics, Germany).

For presumptive identification, a single yeast colony from the SDA plate was picked up using an inoculating loop to cut an "X" on the cornmeal agar. A sterile coverslip was then placed over the "X" using sterile forceps before incubating the plate at 30°C for 24-72 hours. The inoculated cornmeal agar was examined under the light microscope daily and the yeast was speciated by comparing its morphology to that described by Westblade *et al*. (2023).[9]

For definitive identification via MALDI-TOF MS, the extended direct transfer method was used. A single colony from the SDA plate was smeared on a target plate spot. One µL of 70% formic acid was then added onto the smeared plate. Once dry (i.e. within 30 minutes), 1 µL of hydroxycinnamic acid matrix was added. The plate was then analysed by the mass spectrometry machine. The generated results appeared as a list of organisms with corresponding log scores representing the level of accuracy of the identification. A log score of at least 2.0 confirmed the yeast's identity. However if the log score obtained was between 1.7 to 2.0, the identification result was still deemed acceptable provided that the list of species at the top encompass at least three of the same species, there were no other species intermingled in the list of species at the top, the difference in the

log score to the next species was at least 0.2 and the mass spectrometry identification tallied with that of cornmeal agar culture.

Antifungal susceptibility testing

Each *Candida* isolate was tested against nine antifungal drugs (i.e., caspofungin, anidulafungin, micafungin, flucytosine, amphotericin B, fluconazole, itraconazole, voriconazole and posaconazole). Antifungal susceptibility testing was carried out via the colourimetric broth microdilution method using the Sensititre YeastOne YO10 kit (Trek Diagnostic Systems, USA), as per the manufacturer's instructions. Young yeast colonies (approx. 24 hours old) were emulsified in sterile saline and vortexed for 15 seconds to achieve a homogenised suspension. The suspension's turbidity was then adjusted to 0.5 McFarland before transferring 20 µL of it into 11 mL of the YeastOne broth. One hundred µL of the inoculated broth was then pipetted into each well of the Sensititre plate. An adhesive seal was then placed over all the inoculated wells and the inoculated Sensititre plate was incubated at 35°C for 24 hours. If the growth well was red the next day, the minimal inhibitory concentration (MIC) for each antifungal drug was recorded as the lowest drug concentration that inhibited visible fungal growth (i.e. the first blue well). However, if the growth well remained blue or was faintly purple, the plate was re-incubated for another 24 hours before it was re-examined. The relevant Clinical & Laboratory Standards Institute (CLSI) publication was used to interpret the MIC results.[10]

RESULTS

Speciation of yeast isolates

During the study period, the laboratory received blood specimens from 256 individual patients for fungal culture. Out of this total, 118 non-duplicate *Candida* isolates were conclusively identified to the species level. We identified 47 (39.8%) yeast isolates as *C. albicans*, 25 (21.2%) as *C. parapsilosis* complex, 24 (20.3%) as *C. tropicalis*, 19 (16.1%) as *N. glabratus* and three (2.6%) as *P. kudriavzevii*. Collectively, the NAC species outnumbered *C. albicans* (60.2% vs. 39.8%).

Clinicodemographic data of patients

TABLE 1 shows the association between specific variables and the type of candidaemia. Patients with *C. albicans* candidaemia were aged between 32 - 89 years while those with non-*albicans* candidaemia had a wider age distribution of between 2 - 86 years. There was a statistically significant difference between the age medians, with NAC being more likely to cause candidaemia in younger patients. Diabetes mellitus also appeared to be a statistically significant risk factor for NAC, as about two-thirds of all patients with non-*albicans* candidaemia were diabetic.

However, regarding the other risk factors for candidaemia, there was no statistically significant difference between male gender, underlying haematological malignancy, admission to intensive care, prolonged hospitalisation (defined as a hospital stay of at least seven days), broad-

TABLE 1: Association between specific variables or risk factors and the type of candidaemia

Variables or risk factors	*Candida albicans* (n=47)	Non-*albicans* (n=71)	*p*-value
Age in years, median (IQR)	65 (55-75)	59 (44-66)	0.004*
Male gender	28 (59.6)	41 (57.7)	0.844†
Diabetes mellitus	22 (46.8)	48 (67.6)	0.024†
Haematological malignancy	2 (4.3)	5 (7.0)	0.701‡
Admission to intensive care	21 (44.7)	26 (36.6)	0.381†
Prolonged hospitalisation	43 (91.5)	61 (85.9)	0.359†
Broad-spectrum antibiotic usage	40 (85.1)	62 (87.3)	0.731†
Antifungal usage	4 (8.5)	11 (15.5)	0.265†
Invasive medical device insertion	28 (59.6)	51 (71.8)	0.166†

Unless stated otherwise, all data are expressed in n (%); IQR, interquartile range

* derived from Mann-Whitney U test

† derived from Pearson Chi-Square test

‡ derived from Fisher's Exact Test

spectrum antibiotic usage (e.g. a third or fourth generation cephalosporin, a carbapenem, a beta-lactam/beta-lactamase inhibitor combination or a fluoroquinolone), antifungal usage or invasive medical device (i.e. indwelling intravascular catheter) insertion and the type of candidaemia. Prolonged hospitalisation and broad-spectrum antibiotic therapy were the two most notable risk factors for both types of candidaemia, with more than 80% of patients being affected. On the other hand, antifungal usage and underlying haematological malignancy only rarely predisposed patients to either type of candidaemia, as these two risk factors were present in less than 20% of patients.

Antifungal susceptibility testing results

As shown in TABLE 2, among all the species, *C. albicans* had the lowest MIC_{50} and MIC_{90} to fluconazole. Even its MIC_{90} fell within the susceptible range published by the CLSI (i.e. ≤ 2 μg/mL). Although both *C. tropicalis* and *C. parapsilosis* complex had susceptible fluconazole MIC_{50} values (i.e. ≤ 2 μg/mL), the former's MIC_{90} value was SDD (i.e. 4 μg/mL) and the MIC_{90} value of the latter was resistant (⩾ 8 μg/mL). *N. glabratus* had a susceptible-dose-dependent (SDD) MIC_{50} to fluconazole (i.e. ≤ 32 μg/mL) but its corresponding MIC_{90} was resistant (i.e. ⩾ 64 μg/mL). Finally, due to intrinsic resistance, *P. kudriavzeii* is resistant to fluconazole regardless of the MIC reading.

For voriconazole, once again *C. albicans* recorded the lowest MIC_{50} and MIC_{90} values and were within the susceptible range of ≤ 0.12 μg/mL. *C. tropicalis* had voriconazole MIC_{50} and MIC_{90} values that were SDD (i.e. 0.25-0.5 μg/mL). Although both *P. kudriavzeii* and *C. parapsilosis* complex had susceptible voriconazole MIC_{50} values (i.e. ≤ 0.5 μg/mL for the former and ≤ 0.12 μg/mL for the latter), their MIC_{90} readings were SDD (i.e. 1 μg/mL for the former and 0.25-0.5 μg/mL for the latter). The lack of *N. glabratus*-specific voriconazole breakpoints notwithstanding, its MIC_{50} and MIC_{90} values appear to be the highest amongst all the *Candida* species.

Although MIC data for itraconazole, posaconazole and amphotericin B were also determined, there were no current CLSI breakpoints at the time of writing to facilitate interpretation – the last CLSI document that actually published breakpoints for these specific agents was released in 2008 (i.e. 14 years before the release of document M27M44S). Document M27M44S also advised against using some of these previous breakpoints because they were published with minimal clinical data and could be incorrect. However, it can be seen that each NAC had MIC_{50} and MIC_{90} values that were either equal or higher than that of *C. albicans*, indicating that the possibility of resistance to these agents is also more likely with NAC.

Interestingly, for 5-flucytosine, both *N. glabratus* and *C. tropicalis* had lower MIC_{50} values compared with *C. albicans*. However, *N. glabratus* and *C. tropicalis* had a corresponding 5-flucytosine MIC_{90} values that either equaled or exceeded that of *C. albicans*, respectively. Both *P. kudriavzevii* and *C. parapsilosis* complex had MIC_{50} and MIC_{90} values that were either equal to or higher than that of *C. albicans.* We are however unable to interpret these MIC values because document M27M44S did not publish any 5-flucytosine breakpoints.

Where the echinocandin antifungals are concerned, *C. albicans* had the lowest MIC_{50} and MIC_{90} values and were deemed susceptible to each of all three agents (i.e. MIC ≤ 0.25 μg/mL). Although the NAC species had echinocandin MIC_{50} and MIC_{90} values that either equaled or exceeded that of *C. albicans*, their MICs were still considered susceptible (i.e. ≤ 0.25 μg/mL for *C. tropicalis* and *P. kudriavzevii*, ≤ 0.12 μg/mL for *N. glabratus*, and ≤ 2 μg/mL for *C. parapsilosis* complex). Due to *in vitro* methodological issues, the CLSI specified a separate set of breakpoints for *N. glabratus* against micafungin (i.e. ≤ 0.06 μg/mL to denote susceptibility, instead of ≤ 0.12 μg/mL as specified for the other echinocandins). However, despite these stricter breakpoints, our *N. glabratus* isolates still had susceptible micafungin MIC_{50} and MIC_{90} values.

DISCUSSION

Close to 1.6 million people have invasive candidiasis every year, with nearly a million of these patients succumbing to the infection, resulting in a mortality rate in excess of 60%.[11] Candidaemia is regarded as the most common form of invasive candidiasis and is unequivocally defined as the isolation of *Candida* sp. from at least one blood culture.[12] Thus, enrolling subjects for the study was straightforward, as each subject needed just one blood culture which yielded *Candida* sp. Out of 256 patients with blood fungal culture requests, 118 had *Candida* spp. in their blood, resulting in a candidaemia rate of approximately 46% among patients being

TABLE 2: Antifungal susceptibility testing results for the various *Candida* spp. isolated.

Antifungal agent	*Candida albicans* (n=47)	*Candida tropicalis* (n= 24)	*Pichia kudriavzevii* (n= 3)	*Candida parapsilosis* complex (n= 25)	*Nakaseomyces glabratus* (n=19)	All NAC (n=71)
FZ						
MIC_{50}	0.5	2	64	1	16	2
MIC_{90}	1.0	4	64	8	128	32
VZ						
MIC_{50}	0.015	0.25	0.5	0.015	0.5	0.25
MIC_{90}	0.060	0.25	1.0	0.250	2.0	1.00
IZ						
MIC_{50}	0.12	0.25	0.5	0.12	0.5	0.25
MIC_{90}	0.25	0.50	0.5	0.25	2.0	1.00
PZ						
MIC_{50}	0.03	0.25	0.5	0.06	1	0.25
MIC_{90}	0.12	1.00	0.5	0.12	8	1.00
AB						
MIC_{50}	0.5	1	1	0.5	1	1
MIC_{90}	0.5	1	2	1.0	2	1
5F						
MIC_{50}	0.12	0.06	16	0.12	0.06	0.06
MIC_{90}	0.12	0.25	16	0.50	0.12	1.00
MF						
MIC_{50}	0.015	0.03	0.25	1	0.015	0.06
MIC_{90}	0.015	0.06	0.25	2	0.030	2.00
AF						
MIC_{50}	0.06	0.12	0.12	1	0.06	0.12
MIC_{90}	0.12	0.12	0.12	2	0.12	2.00
CF						
MIC_{50}	0.06	0.25	0.25	0.5	0.06	0.25
MIC_{90}	0.12	0.25	0.25	1.0	0.12	1.00

All data are expressed in µg/mL; MIC_{50}, minimal inhibitory concentration at which ≥50% of isolates are inhibited; MIC_{90}, minimal inhibitory concentration at which ≥90% of isolates are inhibited; FZ, fluconazole; VZ, voriconazole; IZ, itraconazole; PZ, posaconazole; AB, amphotericin B; 5F, 5-flucytosine; MF, micafungin; AF, anidulafungin; CF, caspofungin; NAC, non-*albicans Candida*.

investigated for invasive fungal infections. However, the true candidaemia rate among such patients in HRPB may even be higher, because while blood cultures are specific, they are known to lack sensitivity. This is the basis for some authors recommending up to four blood culture sets within 24 hours to achieve a yield exceeding 90%, which is often impractical in resource-limited settings.[12] When only positive cultures were considered, *Candida* spp. were isolated from 118 of 151 blood cultures which yielded fungal pathogens, leading to an isolation rate of 78%. This essentially means that *Candida* was by far the most prevalent fungal pathogen causing invasive fungal infections in HRPB during the study period.

As emphasised earlier, merely stating that "*Candida* species" was isolated when releasing a culture report is no longer sufficient due to the different mortality rates and antifungal resistance

profiles associated with the various *Candida* spp. Although ribosomal large subunit DNA (LSU rDNA) sequencing is regarded as the reference standard for yeast identification, it is not widely available in most diagnostic laboratories in Malaysia. Fortunately, when compared with LSU rDNA sequencing, MALDI TOF-MS has been reported to be able to correctly identify more than 98% of yeast isolates and 100% of the top five *Candida* species.[13] The performance of MALDI-TOF MS even surpassed that of multiplex PCR, which only managed to identify 87% of yeast isolates correctly.[13] Thus, we resorted to using MALDI TOF-MS for conclusive identification of our yeast isolates. Apart from the top five *Candida* species mentioned earlier, we did not encounter any other species in our cohort, further strengthening the accuracy of our species identification using mass spectrometry.

In the 1990s, *C. albicans* was still the foremost species causing candidaemia episodes, with some regions reporting a lion's share of up to 70%.[14] Roughly three decades later, our study revealed that *C. albicans* was still the predominant singular *Candida* species causing candidaemia in HRPB. While this is a relief to some extent, it is unfortunately not the species that caused the greatest number of candidaemia episodes because it accounted for slightly less than even 40% of cases. The prevailing NAC species causing candidaemia in our cohort was *C. parapsilosis* (accounting for 21%), followed very closely by *C. tropicalis* (20%) – candidaemia episodes caused by just these two NAC species already outnumbered those caused by *C. albicans*. The situation is even bleaker in countries neighbouring Malaysia. A recent study conducted in a hospital in Java, Indonesia revealed that *C. albicans* was found in even less than a quarter of candidaemia cases.[15] Like us, *C. parapsilosis* was also the most dominant NAC causing candidaemia in this Indonesian study, albeit with a much higher percentage of 37%.[15] In Thailand, which also neighbours Malaysia, researchers in a Bangkok hospital found that only 29% of candidaemia was attributable to *C. albicans*.[6] However, unlike our study, the principal NAC species causing candidaemia in this Thai study was *C. tropicalis* (49%), while *C. parapsilosis* only accounted for 5% of cases.[6]

We found that a younger age was significantly associated with non-*albicans* candidaemia – this observation echoes that of a Chinese study, in which age above 60 years was found to be a statistically significant demographic variable favouring *albicans* candidaemia.[16] We postulate that this observation is related to the age-dependent differences in the composition of the human normal flora, particularly in the gut. This is because from the gut, *Candida* spp. can translocate and disseminate to the bloodstream.[17] Investigators studying the gut colonisation of *C. albicans* found that subjects aged between 50 - 59 years were less colonised than other age groups, although the investigators believe this might be associated with this specific generation of study subjects rather than the specific age of the subjects.[18] Coincidentally, this age range of 50 – 59 years lies well within the age IQR of our cohort of non-*albicans* candidaemia patients – whether the patients in this age range are more likely to have NAC in their guts is uncertain and warrants further study.

Our study has also shown that among the known risk factors for candidaemia, only underlying diabetes mellitus was significantly associated with non-*albicans* candidaemia. It has already been well-known for decades that hyperglycaemia increases the risk of candidiasis. Hyperglycaemia can impair humoral host defence mechanisms, particularly those related to neutrophil functions (e.g. chemotaxis and phagocytosis).[19] Moreover, the binding of glucose to complement C3 hinders the attachment of this protein to the surface of the microbe, resulting in impairment of opsonisation.[19] Although researchers in Bangkok, Thailand also found that a higher proportion of patients with non-*albicans* candidaemia had diabetes mellitus (i.e. 33.3% vs. 28.9%), their data did not reach statistical significance.[6] Likewise, a Chinese study conducted in Beijing also found that a higher percentage of candidaemia patients with diabetes mellitus had non-*albicans* candidaemia (i.e. 45.6% vs. 36.7%), although this was also not statistically significant.[20] On the contrary, another Chinese study conducted in Hangzhou found it was *C. albicans* that was significantly associated with candidaemia in diabetic patients.[16] Thus, it is likely that the association between diabetes mellitus and non-*albicans* candidaemia is geographically dependent.

Our study has shown that NAC species have higher fluconazole MIC values than *C. albicans*, echoing the findings of numerous other researchers from around the globe over the past decade.[16,21-22] The fluconazole MIC_{90} results for all our NAC species (with the exception of *C. tropicalis*) were outright resistant. Although our *C. tropicalis* isolates had a fluconazole MIC_{90}

which was SDD (instead of resistant), cross-resistance to other azole drugs is a noteworthy concern with this species, with a jaw-dropping azole cross-resistance rate of 90% being reported in certain patient groups.[16] Not surprisingly, our *C. tropicalis* isolates also had a voriconazole MIC_{90} reading that was SDD. Although the corresponding itraconazole and posaconazole MIC_{90} readings for *C. tropicalis* were also higher, it is unclear at the time of writing if the azole cross-resistance extends to these agents as well because specific susceptibility testing breakpoints have yet to be published.[10] In any case, itraconazole is primarily used to treat mucosal (but not invasive) candidiasis, while posaconazole is a mould-active agent which is not indicated for primary candidiasis therapy.[23] Thus, for NAC species with high fluconazole MICs, antifungal agents from other classes (e.g. polyenes and echinocandins) need to be contemplated for candidaemia therapy.

A guideline on candidiasis by the Infectious Diseases Society of America (IDSA) "strongly recommends" an echinocandin as the first-line antifungal agent and lipid formulation amphotericin B as an alternative therapy for treating candidaemia in both neutropenic and non-neutropenic patients.[23] The availability of CLSI breakpoints for echinocandins allowed us to ascertain that all our *Candida* isolates were susceptible to all three agents tested (i.e. micafungin, anidulafungin and caspofungin). With regard to amphotericin B (the sole polyene tested), the absence of CLSI breakpoints prompted us to refer to epidemiological cut-off values (ECVs) instead to predict drug susceptibility. Essentially, any *Candida* sp. with an amphotericin B MIC exceeding 2.0 μg/mL is considered "non-wild type" and likely to have a mutational or acquired resistance mechanism to the drug.[24] Thus, by relying on ECVs, all our isolates (including the NAC species) were predictably amphotericin B-susceptible. Lamentably, due to the lack of generic echinocandin brands in the HRPB formulary at the time of writing, a single vial of an echinocandin can cost, depending on the specific agent, between 30 to over a hundred-fold that of a vial of fluconazole. Likewise, a vial of lipid formulation amphotericin B is more than 90 times more expensive than a vial of fluconazole. Therefore, it is improbable that the IDSA's recommendation on echinocandins and lipid formulation amphotericin B can be fully adopted by hospitals with limited resources. More likely, fluconazole will continue to be widely prescribed in hospitals with a low NAC prevalence and the conventional form of amphotericin B (which is more nephrotoxic but substantially cheaper than its lipid formulation) will continue to be favoured if a non-azole drug is necessitated.

CONCLUSION

In keeping with global trends, more than half of candidaemia cases in HRPB during the study period were caused by NAC species. As a silver lining to this bleak situation, *C. albicans* was still the single most frequently isolated species from patients with candidaemia. However, a NAC species should be considered when yeasts are first detected in blood cultures of patients who are younger than 60 years or if diabetes mellitus is also a co-morbidity. While our *C. albicans* isolates were undoubtedly susceptible to fluconazole, the same cannot be said of our NAC isolates – the overall MIC_{90} of these NAC species was 30 times higher than that of *C. albicans*. Although amphotericin B and echinocandins can still be utilised against NAC species, these non-azole antifungal agents do come with a markedly heftier price tag. Similar prevalence studies need to be conducted from time to time to detect evolving trends in antifungal susceptibility patterns.

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