

Correlation between genotypes and antifungal susceptibility profiles of *Candida* isolates from pregnant and non-pregnant women in South Africa

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Vulvovaginal candidiasis (VVC) is a common vaginal infection, affecting up to 75% of women of reproductive age at some point in their lives. The leading cause of VVC is *Candida albicans* (*C. albicans*). This study investigates the correlation between genotypes and antifungal susceptibility profiles of *Candida* isolates collected from pregnant and non-pregnant South African women. A total of 72 *Candida* isolates were identified using the Applied Biosystems TaqMan assay and confirmed via germ tube tests and polymerase chain reaction (PCR). All isolates (100%) were identified as *C. albicans*. ABC genotyping revealed that 62.5% of isolates were genotype A, 26.4% were genotype B, and 11.1% were genotype C. Antifungal susceptibility testing using the Sensititre™ YeastOne™ YO10 AST Plate assessed minimum inhibitory concentrations (MIC) for anidulafungin, caspofungin, fluconazole, micafungin, and voriconazole. Fluconazole showed the highest resistance rate at 13.9%, while 86.1% of isolates remained susceptible. Genotype A predominated among isolates resistant to anidulafungin, fluconazole, micafungin, and voriconazole. All caspofungin-resistant isolates were genotype C. Genotype B exhibited no resistance to any antifungals tested, indicating the lowest virulence among the genotypes. These findings suggest that genotypes A and C have higher resistance profiles, emphasising the need for routine VVC screening and resistance surveillance to inform effective *Candida* infection management.

Keywords: vulvovaginal candidiasis, drug resistance, polymerase chain reaction, antifungal agents, pregnancy complications

Introduction

VVC is a prevalent vaginal infection, impacting up to 75% of women of reproductive age at least once during their lifetime.^{1,2} The primary organism behind VVC is *C. albicans*, which is responsible for 70–90% of VVC cases.³ Previous research highlighted a high prevalence of *Candida* infections in Africa and the Middle East, with reported rates of 55.18% and 76.92%, respectively.⁴ In sub-Saharan and central Africa, the infection rate for *C. albicans* was found to be 22.74%, while the South African region had a slightly lower rate of 22.44%. Candidiasis ranks as the fifth most common life-threatening fungal infection, with an estimated mortality rate of 40%.⁵ Symptoms of VVC often include redness around the genital area, inflammation of the genital tract, itching, and a thick, white discharge.⁶

Identifying *Candida* species from culture-positive women is crucial in determining the species responsible for the infection, as well as assessing antimicrobial susceptibility and resistance mechanisms.⁷ Accurate *Candida* species identification is important, as their responses to antifungal drugs can differ, which helps ensure effective therapy and reduces the risk of treatment failure. Various molecular techniques, such as Southern blotting, hybridisation, multilocus sequence typing, and deoxyribonucleic acid (DNA) microsatellite analysis, have been employed for genotyping *Candida* isolates. These genotyping methods classify

strains into clades, which are groups derived from a common ancestor.

Studies have shown that the distribution of these clades is influenced by geographical factors and antifungal resistance patterns, with certain clades linked to specific resistance profiles.⁸ The ABC genotyping method is commonly used for *C. albicans*, where PCR amplification of the 25S ribosomal deoxyribonucleic acid (rDNA) allows classification of the isolates into genotypes A (450 bp [base pair]), B (840 bp), C (450 bp and 840 bp), and D (1 080 bp).⁷ A study by Jafarian et al.⁹ reported genotype A at a prevalence of 57.9%, genotype B at 31.6%, and genotype C at 10.5% among 933 patients, of whom 23 had confirmed *Candida* infections.

Antifungal drug resistance is a significant contributor to the treatment failure of *Candida* infections.¹⁰ Treatment options for candidiasis remain limited, even though various antifungal drugs exist. Based on their mechanisms of action, antifungal drugs used to manage candidiasis are divided into four classes: (1) disruption of cell membrane sterol (polyenes, such as amphotericin B and nystatin), (2) inhibition of the ergosterol biosynthesis pathway (azoles, including fluconazole, voriconazole, posaconazole, and ravuconazole), (3) inhibition of DNA or ribonucleic acid synthesis (flucytosine), and (4) inhibition

of glucan synthesis (echinocandins, such as caspofungin, micafungin, and anidulafungin).¹¹

Fluconazole remains the most frequently used azole for both preventing and treating *Candida* infections. However, prolonged use of this drug can lead to the development of resistance among *Candida* species, reducing its effectiveness. This is supported by previous research, which has shown that resistance to fluconazole among *Candida* species is becoming a growing concern within healthcare systems.¹²

Although global research has advanced in linking *C. albicans* genotypes with antifungal susceptibility profiles, there is a limited amount of international data and a notable lack of data from South Africa. Therefore, addressing this gap is crucial, particularly given the high prevalence of candidiasis in the region and the potential public health implications of increasing treatment resistance. This study aims to explore the correlation between genotypes and the antifungal susceptibility profiles of anidulafungin, caspofungin, fluconazole, micafungin, and voriconazole among *C. albicans* isolates from pregnant and non-pregnant South African women, providing a novel insight into the dynamics of drug resistance. By linking the genotypes to antifungal susceptibility profiles, this research contributes to a better understanding of resistance mechanisms, potentially leading to more effective therapeutic strategies and enhanced regional treatment guidelines.

Methodology

Study setting and population derived from the parent study

This was a sub-study of a broader research project, which focused on diagnosing vaginitis and vaginosis pathogens in women. In the parent study, 150 women were recruited from Victoria Mxenge Hospital in Durban, KwaZulu-Natal, South Africa. Participants in the main study were 18 years or older, provided written informed consent, and agreed to self-collect vaginal swabs, following sample collection instructions from the research team. Data on sexual behaviour, clinical history, and sociodemographic details were gathered from each participant through a structured questionnaire administered by the study team. The recruitment period for the study population spanned from January to August 2022.

Ethical approval for the sub-study

Approval for this sub-study was granted by the Biomedical Research Ethics Committee of the University of KwaZulu-Natal (reference number BREC/00005995/2023).

Laboratory procedures

Sample collection and processing of vaginal swabs from the parent study

Following sample collection, the swabs for *Candida* detection were placed in a 15 ml tube with Cary–Blair transport medium (Neogen, United States) and transported to the laboratory for culture analysis. At the laboratory, the swabs were streaked onto Sabouraud dextrose agar (SDA) plates containing

chloramphenicol (Neogen, United States) and incubated at 35 °C for 48 hours. After incubation, a total of 72 isolates showed positive *Candida* cultures, with 31 isolates derived from pregnant women and 41 from non-pregnant women. These cultures were stored at -80 °C for future use.

Retrieval from storage for the sub-study

The 72 stored *Candida* cultures were retrieved from storage and sub-cultured onto SDA plates containing chloramphenicol and incubated at 35 °C for 48 hours.

Confirmatory assays for the isolates

The germ tube test

The germ tube test was conducted to distinguish *C. albicans* from other *Candida* species, such as *C. krusei*, *C. glabrata*, *C. tropicalis*, and *C. parapsilosis*. For this test, 0.5 ml foetal calf serum (Thermo Fisher Scientific, United States) was added to microfuge tubes, and a single colony from the SDA plate culture was mixed into the serum. The tubes were incubated at 37 °C for 2–3 hours. After incubation, wet mount microscopy was used to observe germ tube formation. A positive result for *C. albicans* was indicated by short hyphal (filamentous) extensions emerging laterally from yeast cells without constriction at their origin. Samples without hyphal extensions or with constricted short hyphae at their origin were categorised as negative or as other yeast species.¹³

DNA extraction

DNA extraction from *Candida* cultures was carried out using the PureLink™ Microbiome Kit (Thermo Fisher Scientific, United States) following the manufacturer's protocol. The extracted DNA was stored at -20 °C. A NanoDrop Spectrophotometer (Thermo Fisher Scientific, United States) was used to measure the concentration and purity of the DNA.

Confirmation of *Candida* isolates by real-time PCR

The identity of *Candida* isolates was verified using the Applied Biosystems TaqMan® Assay (Thermo Fisher Scientific, United States), with commercially available primers and probes targeting *C. albicans*, *C. lusitanae*, *C. dubliniensis*, *C. parapsilosis*, *C. glabrata*, *C. tropicalis*, and *C. krusei*. The assays were conducted on the QuantStudio™ 5 Real-Time PCR detection system (Thermo Fisher Scientific, United States). Each PCR reaction had a final volume of 5 µl, consisting of 0.25 µl FAM-labelled probe/primer mix, 1.25 µl FastStart 4X Probe Master Mix (part no. 4444434, Thermo Fisher Scientific, United States), 2 µl template DNA, and 1.5 µl nuclease-free water.

A positive control (TaqMan™ Vaginal Microbiota Extraction Control, cat no. A32039) and a non-template control were included. Amplification involved an initial step at 95 °C for 30 seconds, followed by 45 cycles of denaturation at 95 °C for three seconds, and annealing at 60 °C for 30 seconds. Fluorescent signals from amplified products were detected at the end of the annealing phase, and the QuantStudio™ 5 system software automatically generated raw fluorescent data, including cycle threshold (C_t) mean values.

Genotyping of the *C. albicans* isolates

The isolates were typed using the ABC genotyping method. The 25S *rDNA* gene was amplified from the previously extracted DNA using primers CA-INT-L (5'-ATA AGG GAA GTC GGC AAA ATA GAT CCG TAA-3') and CA-INT-R (5'-CCT TGG CTG TGG TTT CGC TAG ATA GTA GAT-3'). The PCR master mix included 200 nm (nanometres) of each primer, 12.5 µl DreamTaq 2X Master Mix (Thermo Fisher Scientific, United States), 9.5 µl nuclease-free water, and 2 µl template DNA.

The PCR tubes were then placed in a Bio-Rad thermal cycler, and cycling conditions were set to 95 °C for two minutes, followed by 35 cycles of 95 °C for 30 seconds, 60 °C for one minute, and 72 °C for one minute, with a final extension at 72 °C for seven minutes. PCR products were electrophoresed on a 1% agarose gel and visualised using an ultraviolet transilluminator. Based on the yielded band sizes, the *C. albicans* isolates were classified as genotype A (450 bp), genotype B (840 bp), genotype C (450 bp and 840 bp), and genotype D (1 080 bp).¹⁴

Antifungal susceptibility assay for *C. albicans*

Susceptibility testing was conducted using the Sensititre™ YeastOne™ YO10 AST Plate (Thermo Fisher Scientific, United States) to assess the MICs of *C. albicans* isolates against anidulafungin, caspofungin, fluconazole, micafungin, and voriconazole. An inoculum of *C. albicans* for each isolate was prepared to match a 0.5 McFarland standard. From this suspension, 20 µl was added to the Sensititre™ YeastOne™ Broth, followed by adding 100 µl of the inoculum into the microtiter plates. The plates were sealed and incubated at 35 °C for 24–25 hours. The *C. albicans* ATCC 10231 strain served as a control strain, while untreated cultures of each isolate were included as growth controls. All experiments were conducted in triplicate. Table I displays the MIC breakpoints, as per the Clinical and Laboratory Standards Institute guidelines.

Table I: MIC breakpoints per the Clinical and Laboratory Standards Institute guidelines

Antifungal	Susceptible (µg/ml)	SDD (µg/ml)	Resistant (µg/ml)
Anidulafungin	≤ 0.25	0.5	≥ 1
Caspofungin	≤ 0.25	0.5	≥ 1
Fluconazole	≤ 2	4	≥ 8
Micafungin	≤ 0.25	0.5	≥ 1
Voriconazole	≤ 0.12	0.25–0.5	≥ 1

MIC – minimum inhibitory concentration, SDD – susceptible-dose dependent

Results

Confirmatory assays for the obtained isolates

All isolates (72/72, 100%) were confirmed as *C. albicans* based on the germ tube test (Figure 1). Further confirmation was achieved through the quantitative PCR assay using primers and probes specific to *Candida* species. Table II presents the amplification results from the TaqMan assay using these specific probes and primers, indicating that all samples yielded positive amplification. The positive and negative controls also produced the expected results.

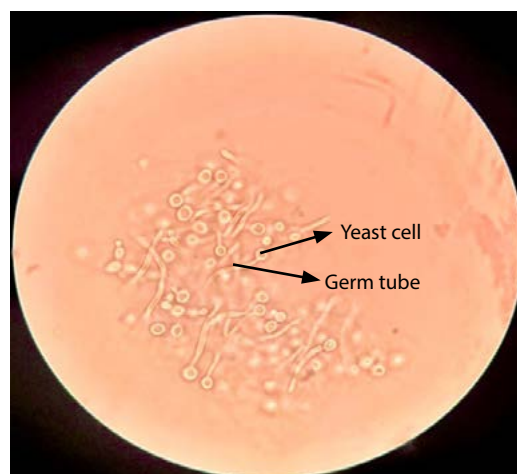


Figure 1: A microscope slide illustrating the results of the germ tube test, which was examined using oil immersion at 100X magnification.

Table II: Results from the TaqMan assay utilising primers and probes specific to *Candida* species, indicating the amplification outcomes for the tested samples

Isolate name	TaqMan assay result (C _t value)
ZMO1	Positive (15.9)
ZMO10	Positive (30.8)
ZMO11	Positive (17.5)
ZMO12	Positive (16.7)
ZMO14	Positive (19.8)
ZMO17	Positive (20.2)
ZMO18	Positive (26.3)
ZMO20	Positive (32.9)
ZMO21	Positive (14.0)
ZMO23	Positive (12.3)
ZMO25	Positive (15.3)
ZMO27	Positive (14.5)
ZMO28	Positive (29.1)
ZMO29	Positive (30.9)
ZMO30	Positive (15.3)
ZMO32	Positive (28.6)
ZMO34	Positive (17.8)
ZMO35	Positive (14.9)
ZMO37	Positive (19.6)
ZMO40	Positive (33.1)
ZMO41	Positive (17)
ZMO42	Positive (31.3)
ZMO43	Positive (17.7)
ZMO44	Positive (24.9)
ZMO47	Positive (16.2)
ZMO53	Positive (28.6)
ZMO54	Positive (17.4)
ZMO56	Positive (17.8)
ZMO58	Positive (17.9)
ZMO59	Positive (18.9)
ZMO60	Positive (15.8)
ZMO62	Positive (24.7)

Table II: Continued

Isolate name	TaqMan assay result (C _t value)
ZMO63	Positive (16.8)
ZMO65	Positive (26.6)
ZMO67	Positive (19.3)
ZMO68	Positive (29.6)
ZMO69	Positive (25.1)
ZMO71	Positive (12.4)
ZMO72	Positive (21.5)
ZMO75	Positive (18.5)
ZMO77	Positive (17)
ZMO79	Positive (27.9)
ZMO80	Positive (19.2)
ZMO81	Positive (22)
ZMO82	Positive (29.0)
ZMO83	Positive (16.5)
ZMO84	Positive (20.2)
ZMO85	Positive (19.1)
ZMO86	Positive (15.4)
ZMO87	Positive (18.8)
ZMO88	Positive (16.9)
ZMO89	Positive (16.4)
ZMO91	Positive (14.6)
ZMO94	Positive (14.9)
ZMO95	Positive (18.8)
ZMO96	Positive (15.1)
ZMO97	Positive (16.3)
ZMO98	Positive (17.9)
ZMO99	Positive (28.3)
ZMO102	Positive (16.0)
ZMO103	Positive (15.2)
ZMO107	Positive (27.2)
ZMO110	Positive (31.1)
ZMO119	Positive (18.8)
ZMO128	Positive (15.9)
ZMO132	Positive (15.5)
ZMO135	Positive (32.2)
ZMO141	Positive (14.9)
ZMO142	Positive (31.1)
ZMO145	Positive (31.7)
ZMO146	Positive (13.6)
ZMO147	Positive (13.7)

C_t – cycle threshold

Genotyping analysis

All 72 isolates (100%) produced positive PCR results (Figures 3, 4, 5, 6, 7, and 8). Figure 2 shows that most of the isolates (45/72, 62.5%) exhibited a 450 bp band, classified as genotype A. Nineteen isolates (19/72, 26.4%) displayed a 840 bp band size, assigned to genotype B. Additionally, eight isolates (8/72, 11.1%) yielded two band sizes of 450 bp and 840 bp, corresponding

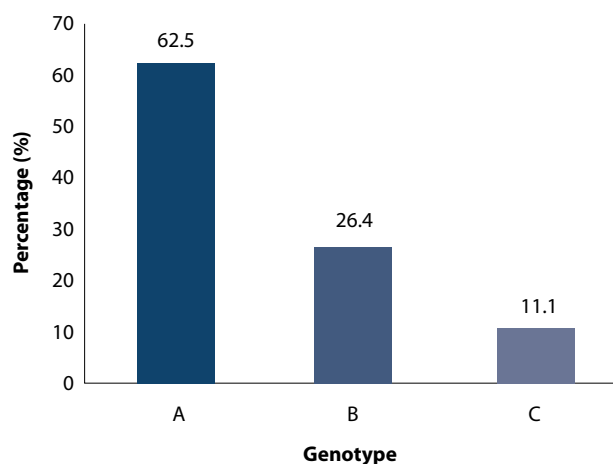
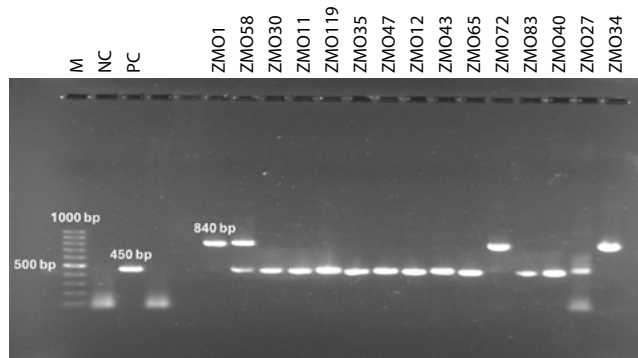
Figure 2: The percentages of *C. albicans* genotypes.

Figure 3: An agarose gel displaying positive amplicons generated for *C. albicans* isolates is shown, with observed band sizes of 450 bp, 840 bp, and a combination of both 450 bp and 840 bp. M represents the 100 bp DNA molecular ladder (ThermoFisher Scientific), NC indicates the negative control (no template DNA added), PC denotes the positive control (*C. albicans* ATCC 10231 strain), along with 15 clinical isolates of *C. albicans*.

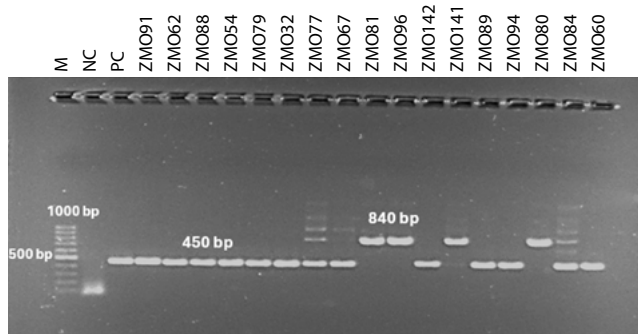


Figure 4: An agarose gel illustrating positive amplicons generated for *C. albicans* isolates is presented, with observed band sizes of 450 bp and 840 bp. M indicates the 100 bp DNA molecular ladder (ThermoFisher Scientific), NC represents the negative control (no template DNA added), PC denotes the positive control (*C. albicans* ATCC 10231 strain), and the gel includes 17 clinical isolates of *C. albicans*.

to genotype C. No isolates were classified as genotype D, since the 1 080 bp band was not detected. A detailed summary of the assigned genotypes is shown in Table III.

Antifungal susceptibility assays

For anidulafungin, 91.7% of the 72 isolates tested (66/72) were susceptible, exhibiting MICs ≤ 0.25 $\mu\text{g/ml}$. Additionally, 1.4% of

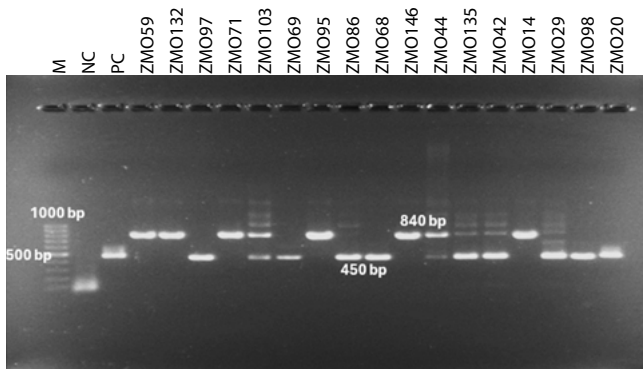


Figure 5: An agarose gel is presented, displaying positive amplicons generated for *C. albicans* isolates. The observed band sizes include 450 bp, 840 bp, and a combination of both 450 bp and 840 bp bands. M indicates the 100 bp DNA molecular ladder (ThermoFisher Scientific), NC represents the negative control (no template DNA added), PC denotes the positive control (*C. albicans* ATCC 10231 strain), along with 17 clinical isolates of *C. albicans*.

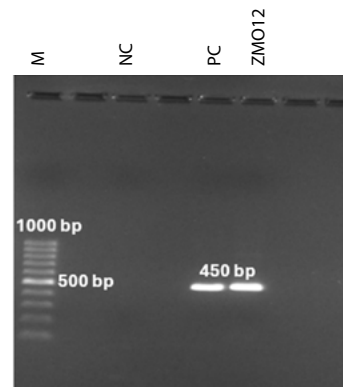


Figure 8: One clinical isolate of *C. albicans* in an agarose gel showing the positive amplicons generated, with observed band sizes at 450 bp. M – 100 bp DNA molecular ladder (Thermo Fisher Scientific), NC – negative control (no template DNA added), PC – positive control (*C. albicans* ATCC 10231 strain)

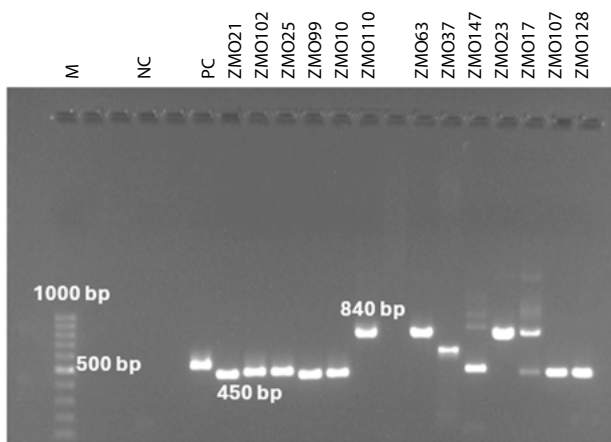


Figure 6: An agarose gel is shown, displaying positive amplicons generated for *C. albicans* isolates. The observed band sizes include 450 bp, 840 bp, and a combination of both 450 bp and 840 bp bands. M denotes the 100 bp DNA molecular ladder (ThermoFisher Scientific), NC indicates the negative control (no template DNA added), PC represents the positive control (*C. albicans* ATCC 10231 strain), and the gel includes 13 clinical isolates of *C. albicans*.

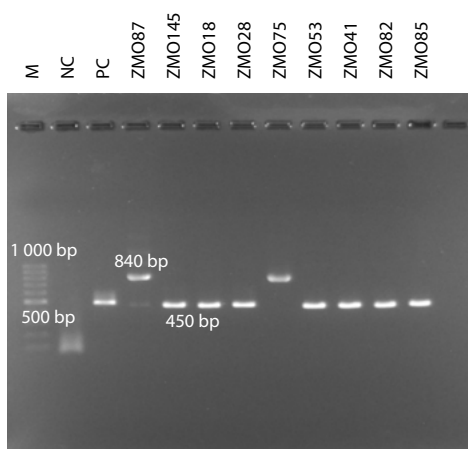


Figure 7: An agarose gel is presented, showing positive amplicons generated for *C. albicans* isolates. The observed band sizes include 450 bp, 840 bp, and a combination of both 450 bp and 840 bp bands. M indicates the 100 bp DNA molecular ladder (ThermoFisher Scientific), NC represents the negative control (no template DNA added), PC denotes the positive control (*C. albicans* ATCC 10231 strain), and the gel contains nine clinical isolates of *C. albicans*.

Table III: Assignment of genotypes for individual isolates based on the banding patterns obtained

Isolate name	PCR product size (bp)	Genotype
ZMO1	840	B
ZMO10	450	A
ZMO11	450	A
ZMO12	450	A
ZMO14	840	B
ZMO17	450 & 840	C
ZMO18	450	A
ZMO20	450	A
ZMO21	450	A
ZMO23	840	B
ZMO25	450	A
ZMO27	450	A
ZMO28	450	A
ZMO29	450	A
ZMO30	450	A
ZMO32	450	A
ZMO34	840	B
ZMO35	450	A
ZMO37	840	B
ZMO40	450	A
ZMO41	450	A
ZMO42	450 & 840	C
ZMO43	450	A
ZMO44	450 & 840	C
ZMO47	450	A
ZMO53	450	A
ZMO54	450	A
ZMO56	450	A
ZMO58	450 & 840	C
ZMO59	840	B
ZMO60	450	A
ZMO62	450	A
ZMO63	840	B

Table III: Continued

Isolate name	PCR product size (bp)	Genotype
ZMO65	450	A
ZMO67	450	A
ZMO68	450	A
ZMO69	450	A
ZMO71	840	B
ZMO72	840	B
ZMO75	840	B
ZMO77	450 & 840	C
ZMO79	450	A
ZMO80	840	B
ZMO81	840	B
ZMO82	450	A
ZMO83	450	A
ZMO84	450 & 840	C
ZMO85	450	A
ZMO86	450	A
ZMO87	840	B
ZMO88	450	A
ZMO89	450	A
ZMO91	450	A
ZMO94	450	A
ZMO95	840	B
ZMO96	840	B
ZMO97	450	A
ZMO98	450	A
ZMO99	450	A
ZMO102	450	A
ZMO103	450 & 840	C
ZMO107	450	A
ZMO110	840	B
ZMO119	450	A
ZMO128	450	A
ZMO132	840	B
ZMO135	450 & 840	C
ZMO141	840	B
ZMO142	450	A
ZMO145	450	A
ZMO146	840	B
ZMO147	450	A

PCR – polymerase chain reaction, bp – base pair

the isolates (1/72) were classified as susceptible-dose dependent (SDD) to anidulafungin, with a 0.5 µg/ml MIC. Meanwhile, 6.9% of the isolates (5/72) showed resistance to anidulafungin, displaying MICs \geq 1 µg/ml (Supplementary Table I).

For caspofungin, 94.4% of the 72 isolates tested (68/72) were susceptible, exhibiting MICs \leq 0.25 µg/ml. Additionally, 2.8% of the isolates (2/72) were classified as SDD to caspofungin, with a 0.5 µg/ml MIC. Similarly, 2.8% of the isolates (2/72) were resistant

to caspofungin, displaying MICs \geq 1 µg/ml (Supplementary Table II).

For fluconazole, 86.1% of the 72 isolates tested (62/72) were susceptible, exhibiting MICs \leq 2 µg/ml. Conversely, 13.9% of the isolates (10/72) were found to be resistant to fluconazole, with MICs \geq 8 µg/ml (Supplementary Table III).

For micafungin, 90.3% of the 72 isolates tested (65/72) were susceptible, exhibiting MICs \leq 0.25 µg/ml. Additionally, 5.5% of the isolates (4/72) were classified as SDD to micafungin, with a 0.5 µg/ml MIC. Furthermore, 4.2% of the isolates (3/72) were resistant to micafungin, displaying MICs \geq 1 µg/ml (Supplementary Table IV).

For voriconazole, 86% of the 72 isolates tested (62/72) were susceptible, exhibiting MICs \leq 0.12 µg/ml. Additionally, 7% of the isolates (5/72) were classified as SDD to voriconazole, with MICs ranging from 0.25 µg/ml to 0.5 µg/ml. Furthermore, another 7% of the isolates (5/72) were resistant to voriconazole, displaying MICs \geq 1 µg/ml (Supplementary Table V).

Table IV presents the susceptibility profiles of *C. albicans* isolates against anidulafungin, caspofungin, fluconazole, micafungin, and voriconazole.

Table IV: Susceptibility profiles of *C. albicans* isolates to anidulafungin, caspofungin, fluconazole, micafungin, and voriconazole ($n = 72$)

Antifungal	Susceptibility profile		
	Susceptible	SDD	Resistant
Anidulafungin	66 (91.7%)	1 (1.4%)	5 (6.9%)
Caspofungin	68 (94.4%)	2 (2.8%)	2 (2.8%)
Fluconazole	62 (86.1%)	0 (0%)	10 (13.9%)
Micafungin	65 (90.3%)	4 (5.5%)	3 (4.2%)
Voriconazole	62 (86%)	5 (7%)	5 (7%)

SDD – susceptible-dose dependent

Correlation between susceptibility profiles and genotypes

Table V presents the correlation between anidulafungin susceptibility patterns and *C. albicans* genotypes. Among the 66 isolates that were susceptible to anidulafungin, 41/66 (62.1%) were classified as genotype A, 18/66 (27.3%) as genotype B, and 7/66 (10.6%) as genotype C. The single isolate (1/1, 100%) that was SDD to anidulafungin was assigned to genotype B. Among the five isolates resistant to anidulafungin, 4/5 (80%) were classified as genotype A and 1/5 (20%) as genotype C.

Table VI illustrates the correlation between caspofungin susceptibility patterns and *C. albicans* genotypes. Among the 68 isolates that were susceptible to caspofungin, 43/68 (63.2%) were classified as genotype A, 19/68 (28%) as genotype B, and 6/68 (8.8%) as genotype C. The isolates that were SDD to caspofungin (2/2, 100%) were both assigned to genotype A. Additionally, the isolates resistant to caspofungin (2/2, 100%) were both classified as genotype C.

Table V: Correlation between the susceptibility profile of anidulafungin and *C. albicans* genotypes

Genotype	Susceptibility pattern		
	Susceptible (n = 66)	SDD (n = 1)	Resistant (n = 5)
A	41 (62.1%)	0 (0%)	4 (80%)
B	18 (27.3%)	1 (100%)	0 (0%)
C	7 (10.6%)	0 (0%)	1 (20%)

SDD – susceptible-dose dependent

Table VI: Correlation between the susceptibility profile of caspofungin and *C. albicans* genotypes

Genotype	Susceptibility pattern		
	Susceptible (n = 68)	SDD (n = 2)	Resistant (n = 2)
A	43 (63.2%)	2 (100%)	0 (0%)
B	19 (28%)	0 (0%)	0 (0%)
C	6 (8.8%)	0 (0%)	2 (100%)

SDD – susceptible-dose dependent

Table VII: Correlation between the susceptibility profile of fluconazole and *C. albicans* genotypes

Genotype	Susceptibility pattern	
	Susceptible (n = 62)	Resistant (n = 10)
A	37 (59.7%)	8 (80%)
B	19 (30.6%)	0 (0%)
C	6 (9.7%)	2 (20%)

SDD – susceptible-dose dependent

Table VIII: Correlation between the susceptibility profile of micafungin and *C. albicans* genotypes

Genotype	Susceptibility pattern		
	Susceptible (n = 65)	SDD (n = 4)	Resistant (n = 3)
A	40 (61.5%)	3 (75%)	2 (66.7%)
B	18 (27.7%)	1 (25%)	0 (0%)
C	7 (10.8%)	0 (0%)	1 (33.3%)

SDD – susceptible-dose dependent

Table IX: Correlation between the susceptibility profile of voriconazole and *C. albicans* genotypes

Genotype	Susceptibility pattern		
	Susceptible (n = 62)	SDD (n = 5)	Resistant (n = 5)
A	37 (59.7%)	5 (100%)	3 (60%)
B	19 (30.6%)	0 (0%)	0 (0%)
C	6 (9.7%)	0 (0%)	2 (40%)

SDD – susceptible-dose dependent

Table VII presents the correlation between fluconazole susceptibility patterns and *C. albicans* genotypes. Among the 62 isolates that were susceptible to fluconazole, 37/62 (59.7%) were classified as genotype A, 19/62 (30.6%) as genotype B, and 6/62 (9.7%) as genotype C. Of the 10 isolates that were resistant to

fluconazole, 8/10 (80%) were assigned to genotype A, while 2/10 (20%) were assigned to genotype C.

Table VIII illustrates the correlation between micafungin susceptibility patterns and *C. albicans* genotypes. Among the 65 isolates that were susceptible to micafungin, 40/65 (61.5%) were classified as genotype A, 18/65 (27.7%) as genotype B, and 7/65 (10.8%) as genotype C. Of the four isolates that were SDD to micafungin, 3/4 (75%) were assigned to genotype A, while 1/4 (25%) was assigned to genotype B. Among the three isolates that were resistant to micafungin, 2/3 (66.7%) were classified as genotype A, and 1/3 (33.3%) as genotype C.

Table IX presents the correlation between voriconazole susceptibility patterns and *C. albicans* genotypes. Among the 62 isolates that were susceptible to voriconazole, 37/62 (59.7%) were classified as genotype A, 19/62 (30.6%) as genotype B, and 6/62 (9.7%) as genotype C. All isolates (5/5, 100%) that were SDD to voriconazole were assigned to genotype A. Among the five isolates that were resistant to voriconazole, 3/5 (60%) were classified as genotype A, while 2/5 (40%) were classified as genotype C.

Discussion

Globally, *Candida* species account for a substantial proportion of fungal infections related to women's healthcare.² *C. albicans* is responsible for over 80% of yeast infections.¹⁵ This study aimed to link the distribution of *C. albicans* genotypes with the antifungal susceptibility profiles of anidulafungin, caspofungin, fluconazole, micafungin, and voriconazole in 72 *C. albicans* isolates obtained from the vaginal swabs of pregnant and non-pregnant patients at the Victoria Mxenge Hospital in Durban, South Africa.

ABC genotyping analysis of 25S *rDNA* is a molecular typing technique widely used to detect variations among *Candida* species, playing an important role in linking specific genotypes to antifungal resistance and serving as a valuable tool for epidemiological research.^{7,16} In the current study, most of the 72 isolates were identified as genotype A (62.5%), followed by genotype B (26.4%) and genotype C (11.1%). These findings align with those of another study, which reported genotype A as the most prevalent among all *C. albicans* isolates (54.69%), followed by genotype B (34.38%) and genotype C (10.94%).¹⁷

This study is consistent with findings from research conducted in Iraq on patients with VVC. Among the 54 *C. albicans* isolates examined in that study, genotype A was the most prevalent, accounting for 50%, followed by genotype B at 29.62%, and genotype C at 20.37%.¹⁸ A study conducted in northeast Brazil on women with vaginal *Candida* infections also identified genotype A as the most prevalent (93.6%), followed by genotype C (6.4%). Notably, genotypes B and D were not detected in that study.¹⁹ However, in a study from Palestine, 55% of the vaginal *Candida* isolates had genotype C, followed by genotypes A (32.4%) and B (12.6%).²⁰ An Iranian study also found genotype C as the most common (83.5%), followed by genotype B (12.6%) and genotype A (3.9%).²¹ These observed genotype variations may be attributed to differences in geographical regions.

The resistance of *Candida* species to antifungal treatments remains a major challenge in managing fungal infections.²² In this study, we assessed the in vitro susceptibility of 72 *C. albicans* isolates to five antifungal agents: anidulafungin, caspofungin, fluconazole, micafungin, and voriconazole. Anidulafungin, caspofungin, and micafungin are part of the echinocandin class of antifungals, while fluconazole and voriconazole are classified as azole antifungals. Resistance to these drugs can lead to treatment failure. *Candida* species show the highest prevalence of resistance to azole antifungals.

Vaginal *C. albicans* isolates are known to exhibit high resistance rates to fluconazole.²³ Among these isolates, 91.7% demonstrated susceptibility to anidulafungin, while 6.9% exhibited resistance. For caspofungin, 94.4% were susceptible, with 2.8% showing resistance. Regarding fluconazole, 86.1% of isolates were susceptible, and 13.9% were resistant. Micafungin showed a susceptibility rate of 90.3%, with 4.2% resistance. Lastly, voriconazole had a susceptibility rate of 86%, and 7% of isolates were resistant. Caspofungin and micafungin demonstrated lower resistance rates than anidulafungin, fluconazole, and voriconazole. Among the antifungal agents tested, fluconazole exhibited the highest resistance rates.

These results align with findings from another study, which reported resistance rates for caspofungin (1%), fluconazole (9%), and voriconazole (6%).²⁴ Similarly, a study conducted in China demonstrated low resistance rates against anidulafungin, caspofungin, and micafungin, while higher resistance rates were noted for fluconazole and voriconazole.²⁵ High resistance rates to fluconazole and voriconazole have also been observed in additional studies from China and Bulgaria.^{26,27} In contrast, research conducted in Tanzania revealed lower resistance rates, with 3.1% for fluconazole and 3.6% for voriconazole.²⁸ Research on antifungal resistance among *Candida* species is valuable as it offers up-to-date data on resistance patterns, aiding in evaluating empirical treatment guidelines. Variations in antifungal susceptibility profiles among *C. albicans* can be attributed to geographic differences and variations in the populations studied.

The current study also described the correlation between the detected *C. albicans* genotypes in relation to the susceptibility profiles of anidulafungin, caspofungin, fluconazole, micafungin, and voriconazole. Of the 66 isolates susceptible to anidulafungin, 62.1% belonged to genotype A, 27.3% were genotype B, and 10.6% were genotype C. Among the five isolates resistant to anidulafungin, 80% were categorised as genotype A, with the remaining 20% classified as genotype C. For caspofungin susceptibility, 63.2% of the 68 isolates were identified as genotype A, 28% as genotype B, and 8.8% as genotype C, while both caspofungin-resistant isolates were genotype C. Of the 62 fluconazole-susceptible isolates, 59.7% were genotype A, 30.6% were genotype B, and 9.7% were genotype C. For the 10 fluconazole-resistant isolates, 80% were identified as genotype A, and 20% as genotype C. Regarding micafungin, 61.5% of the 65 susceptible isolates were genotype A, 27.7% were genotype B, and 10.8% were genotype C. Among the three micafungin-

resistant isolates, 66.7% were genotype A, and 33.3% were genotype C. Finally, of the 62 isolates susceptible to voriconazole, 59.7% were genotype A, 30.6% were genotype B, and 9.7% were genotype C. Among the five voriconazole-resistant isolates, 60% were genotype A, and 40% were genotype C.

The study demonstrated that most isolates susceptible to the five antifungal agents were predominantly of genotype A, followed by genotype B, and then genotype C. Among the isolates resistant to anidulafungin, fluconazole, micafungin, and voriconazole, most were identified as genotype A, with the remainder being genotype C. Notably, all isolates resistant to caspofungin were of genotype C. No resistant isolates were classified as genotype B, demonstrating that this genotype had a 0% resistance rate, the lowest among the genotypes studied.

However, other studies conducted in China assessing *C. albicans* genotypes against azole antifungals revealed that genotype A isolates showed lower resistance rates than those of genotype B.^{23,29} Another study conducted in Jordan found that all *Candida* isolates collected from women with vaginal candidiasis were susceptible to fluconazole, resulting in a 0% resistance rate among genotypes A, B, and C.³⁰ Lastly, a study conducted in China revealed that *C. albicans* 25S rDNA genotypes belonging to group A exhibited significantly lower susceptibility rates to fluconazole than genotypes B and C.³¹

To our knowledge, no South African studies have linked the genotypes of *C. albicans* isolates from pregnant and non-pregnant women to the antifungal susceptibility profiles of anidulafungin, caspofungin, fluconazole, micafungin, and voriconazole. In this study, most *C. albicans* isolates were identified as genotype A and exhibited resistance to anidulafungin, fluconazole, micafungin, and voriconazole, while caspofungin-resistant isolates were all classified as genotype C. This indicates that genotypes A and C are more virulent than genotype B. Currently, there is limited research on the correlation between *Candida* genotypes and antifungal susceptibility patterns; a gap in the literature that this study addresses.

Study limitations

The study faced a few limitations. The small sample size may have been a reason for the study's inability to detect non-*albicans* *Candida* species. Additionally, since the research was conducted in a single geographical area and the participants were all recruited from a single clinic, it may not fully represent the broader population. However, given that Victoria Mxenge Hospital serves as a central tertiary hospital, it does reflect a wider portion of Durban's population.

Conclusion

Most *C. albicans* isolates collected from both pregnant and non-pregnant South African women demonstrated susceptibility to anidulafungin, caspofungin, fluconazole, micafungin, and voriconazole. Genotype A was the most prevalent *C. albicans* genotype among women in Durban, South Africa. The isolates susceptible to the five antifungal agents were mainly genotype A, followed by genotype B, and then genotype C. Among isolates

showing resistance to anidulafungin, fluconazole, micafungin, and voriconazole, the majority were classified as genotype A, with the remaining resistant isolates identified as genotype C. All isolates resistant to caspofungin belonged to genotype C. No resistance to any tested antifungal drugs was found among isolates of genotype B, suggesting it is the least virulent strain of *C. albicans*. Additional research is necessary to investigate the occurrence of other genotypes, such as genotype D, and to establish their correlation with antifungal resistance patterns. Future studies can now focus on the mechanisms behind resistance in local isolates. Currently, antifungal resistance patterns for commonly used treatments of *Candida* infections are not being monitored in our local setting, highlighting a need for resistance surveillance to mitigate the risk of future untreatable infections.

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Conflict of interest

The authors declare no conflict of interest.

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Ethical approval

This study was approved by the Biomedical Research Ethics Committee of the University of KwaZulu-Natal (reference number BREC/00005995/2023).

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Correlation between genotypes and antifungal susceptibility profiles of *Candida* isolates from pregnant and non-pregnant women in South Africa

Supplementary Material

Supplementary Table I: *C. albicans* isolates: MICs and susceptibility profiles to anidulafungin

Isolate name	MIC (µg/ml)	Susceptibility profile
ATCC	0.12	Susceptible
ZMO1	0.06	Susceptible
ZMO10	0.12	Susceptible
ZMO11	0.12	Susceptible
ZMO12	< 0.015	Susceptible
ZMO14	0.12	Susceptible
ZMO17	0.12	Susceptible
ZMO18	0.06	Susceptible
ZMO20	0.12	Susceptible
ZMO21	0.03	Susceptible
ZMO23	0.03	Susceptible
ZMO25	0.12	Susceptible
ZMO27	0.25	Susceptible
ZMO28	0.12	Susceptible
ZMO29	0.12	Susceptible
ZMO30	0.12	Susceptible
ZMO32	< 0.015	Susceptible
ZMO34	< 0.015	Susceptible
ZMO35	0.12	Susceptible
ZMO37	0.06	Susceptible
ZMO40	0.06	Susceptible
ZMO41	0.03	Susceptible
ZMO42	< 0.015	Susceptible
ZMO43	0.12	Susceptible
ZMO44	0.12	Susceptible
ZMO47	0.12	Susceptible
ZMO53	< 0.015	Susceptible
ZMO54	0.12	Susceptible
ZMO56	0.12	Susceptible
ZMO58	0.12	Susceptible
ZMO59	0.03	Susceptible
ZMO60	0.03	Susceptible
ZMO62	0.12	Susceptible
ZMO63	0.03	Susceptible
ZMO65	0.12	Susceptible
ZMO67	0.06	Susceptible
ZMO68	1	Resistant
ZMO69	< 0.015	Susceptible
ZMO71	< 0.015	Susceptible
ZMO72	0.12	Susceptible
ZMO75	0.06	Susceptible
ZMO77	0.03	Susceptible
ZMO79	0.12	Susceptible
ZMO80	0.12	Susceptible
ZMO81	< 0.015	Susceptible
ZMO82	< 0.015	Susceptible
ZMO83	0.12	Susceptible
ZMO84	0.12	Susceptible
ZMO85	2	Resistant
ZMO86	< 0.015	Susceptible
ZMO87	0.5	Susceptible-dose-dependent
ZMO88	0.12	Susceptible
ZMO89	0.12	Susceptible
ZMO91	0.06	Susceptible
ZMO94	0.06	Susceptible
ZMO95	0.12	Susceptible
ZMO96	0.12	Susceptible
ZMO97	0.06	Susceptible
ZMO98	0.06	Susceptible
ZMO99	< 0.015	Susceptible
ZMO102	< 0.015	Susceptible
ZMO103	0.12	Susceptible
ZMO107	< 0.015	Susceptible
ZMO110	< 0.015	Susceptible
ZMO119	< 0.015	Susceptible
ZMO128	0.12	Susceptible
ZMO132	< 0.015	Susceptible
ZMO135	4	Resistant
ZMO141	< 0.015	Susceptible
ZMO142	1	Resistant
ZMO145	1	Resistant
ZMO146	0.06	Susceptible
ZMO147	0.06	Susceptible

MICs - minimum inhibitory concentrations

Supplementary Table II: *C. albicans* isolates: MICs and susceptibility profiles to caspofungin

Isolate name	MIC ($\mu\text{g/ml}$)	Susceptibility profile
ATCC	0.12	Susceptible
ZMO1	0.06	Susceptible
ZMO10	0.5	Susceptible-dose-dependent
ZMO11	0.25	Susceptible
ZMO12	0.06	Susceptible
ZMO14	0.06	Susceptible
ZMO17	0.06	Susceptible
ZMO18	0.03	Susceptible
ZMO20	0.12	Susceptible
ZMO21	0.12	Susceptible
ZMO23	0.06	Susceptible
ZMO25	0.06	Susceptible
ZMO27	0.12	Susceptible
ZMO28	0.06	Susceptible
ZMO29	0.12	Susceptible
ZMO30	0.12	Susceptible
ZMO32	< 0.008	Susceptible
ZMO34	0.12	Susceptible
ZMO35	0.12	Susceptible
ZMO37	0.03	Susceptible
ZMO40	0.06	Susceptible
ZMO41	0.06	Susceptible
ZMO42	1	Resistant
ZMO43	0.12	Susceptible
ZMO44	0.12	Susceptible
ZMO47	0.12	Susceptible
ZMO53	0.03	Susceptible
ZMO54	0.12	Susceptible
ZMO56	0.06	Susceptible
ZMO58	0.12	Susceptible
ZMO59	0.06	Susceptible
ZMO60	0.06	Susceptible
ZMO62	0.06	Susceptible
ZMO63	0.03	Susceptible
ZMO65	0.06	Susceptible
ZMO67	0.06	Susceptible
ZMO68	0.5	Susceptible-dose-dependent
ZMO69	< 0.008	Susceptible
ZMO71	< 0.008	Susceptible
ZMO72	0.06	Susceptible
ZMO75	0.03	Susceptible
ZMO77	0.12	Susceptible
ZMO79	0.12	Susceptible
ZMO80	0.12	Susceptible
ZMO81	0.06	Susceptible
ZMO82	0.06	Susceptible
ZMO83	0.12	Susceptible
ZMO84	0.06	Susceptible

ZMO85	< 0.008	Susceptible
ZMO86	< 0.008	Susceptible
ZMO87	0.25	Susceptible
ZMO88	0.06	Susceptible
ZMO89	0.12	Susceptible
ZMO91	0.06	Susceptible
ZMO94	0.06	Susceptible
ZMO95	0.12	Susceptible
ZMO96	0.03	Susceptible
ZMO97	0.03	Susceptible
ZMO98	0.06	Susceptible
ZMO99	0.06	Susceptible
ZMO102	0.03	Susceptible
ZMO103	0.06	Susceptible
ZMO107	< 0.008	Susceptible
ZMO110	0.03	Susceptible
ZMO119	< 0.008	Susceptible
ZMO128	0.12	Susceptible
ZMO132	< 0.008	Susceptible
ZMO135	8	Resistant
ZMO141	< 0.008	Susceptible
ZMO142	0.25	Susceptible
ZMO145	0.25	Susceptible
ZMO146	0.12	Susceptible
ZMO147	0.06	Susceptible

MICs - minimum inhibitory concentrations

Supplementary Table III: *C. albicans* isolates: MICs and susceptibility profiles to fluconazole

Isolate name	MIC ($\mu\text{g/ml}$)	Susceptibility profile
ATCC	2	Susceptible
ZMO1	0.25	Susceptible
ZMO10	64	Resistant
ZMO11	32	Resistant
ZMO12	0.25	Susceptible
ZMO14	0.5	Susceptible
ZMO17	0.5	Susceptible
ZMO18	0.25	Susceptible
ZMO20	0.5	Susceptible
ZMO21	< 0.12	Susceptible
ZMO23	0.25	Susceptible
ZMO25	0.5	Susceptible
ZMO27	0.25	Susceptible
ZMO28	0.25	Susceptible
ZMO29	0.5	Susceptible
ZMO30	0.12	Susceptible
ZMO32	< 0.12	Susceptible
ZMO34	0.12	Susceptible
ZMO35	64	Resistant
ZMO37	0.5	Susceptible

ZMO40	0.25	Susceptible
ZMO41	0.5	Susceptible
ZMO42	< 0.12	Susceptible
ZMO43	0.5	Susceptible
ZMO44	32	Resistant
ZMO47	4	Susceptible
ZMO53	< 0.12	Susceptible
ZMO54	0.5	Susceptible
ZMO56	0.25	Susceptible
ZMO58	0.25	Susceptible
ZMO59	0.5	Susceptible
ZMO60	< 0.12	Susceptible
ZMO62	2	Susceptible
ZMO63	0.25	Susceptible
ZMO65	8	Resistant
ZMO67	0.5	Susceptible
ZMO68	0.5	Susceptible
ZMO69	< 0.12	Susceptible
ZMO71	< 0.12	Susceptible
ZMO72	0.25	Susceptible
ZMO75	0.5	Susceptible
ZMO77	< 0.12	Susceptible
ZMO79	2	Susceptible
ZMO80	0.5	Susceptible
ZMO81	0.5	Susceptible
ZMO82	< 0.12	Susceptible
ZMO83	0.25	Susceptible
ZMO84	0.5	Susceptible
ZMO85	8	Resistant
ZMO86	< 0.12	Susceptible
ZMO87	2	Susceptible
ZMO88	1	Susceptible
ZMO89	0.5	Susceptible
ZMO91	0.25	Susceptible
ZMO94	0.25	Susceptible
ZMO95	0.5	Susceptible
ZMO96	< 0.12	Susceptible
ZMO97	0.5	Susceptible
ZMO98	0.5	Susceptible
ZMO99	< 0.12	Susceptible
ZMO102	< 0.12	Susceptible
ZMO103	2	Susceptible
ZMO107	< 0.12	Susceptible
ZMO110	< 0.12	Susceptible
ZMO119	< 0.12	Susceptible
ZMO128	32	Resistant
ZMO132	< 0.12	Susceptible
ZMO135	> 256	Resistant
ZMO141	< 0.12	Susceptible
ZMO142	8	Resistant

ZMO145	16	Resistant
ZMO146	< 0.12	Susceptible
ZMO147	0.25	Susceptible

MICs - minimum inhibitory concentrations

Supplementary Table IV: *C. albicans* isolates: MICs and susceptibility profiles to micafungin

Isolate name	MIC (µg/ml)	Susceptibility profile
ATCC	0.015	Susceptible
ZMO1	< 0.008	Susceptible
ZMO10	0.25	Susceptible
ZMO11	0.015	Susceptible
ZMO12	0.015	Susceptible
ZMO14	0.015	Susceptible
ZMO17	0.015	Susceptible
ZMO18	0.015	Susceptible
ZMO20	0.015	Susceptible
ZMO21	0.015	Susceptible
ZMO23	0.015	Susceptible
ZMO25	0.015	Susceptible
ZMO27	0.015	Susceptible
ZMO28	< 0.008	Susceptible
ZMO29	0.5	Susceptible-dose-dependent
ZMO30	0.015	Susceptible
ZMO32	< 0.008	Susceptible
ZMO34	0.015	Susceptible
ZMO35	0.015	Susceptible
ZMO37	< 0.008	Susceptible
ZMO40	< 0.008	Susceptible
ZMO41	< 0.008	Susceptible
ZMO42	< 0.008	Susceptible
ZMO43	0.015	Susceptible
ZMO44	0.015	Susceptible
ZMO47	0.015	Susceptible
ZMO53	< 0.008	Susceptible
ZMO54	0.015	Susceptible
ZMO56	0.015	Susceptible
ZMO58	< 0.008	Susceptible
ZMO59	0.015	Susceptible
ZMO60	< 0.008	Susceptible
ZMO62	0.015	Susceptible
ZMO63	< 0.008	Susceptible
ZMO65	0.06	Susceptible
ZMO67	< 0.008	Susceptible
ZMO68	1	Resistant
ZMO69	< 0.008	Susceptible
ZMO71	< 0.008	Susceptible
ZMO72	0.015	Susceptible
ZMO75	< 0.008	Susceptible
ZMO77	0.03	Susceptible

ZMO79	0.06	Susceptible	ZMO29	< 0.008	Susceptible
ZMO80	0.03	Susceptible	ZMO30	< 0.008	Susceptible
ZMO81	< 0.008	Susceptible	ZMO32	< 0.008	Susceptible
ZMO82	< 0.008	Susceptible	ZMO34	< 0.008	Susceptible
ZMO83	0.015	Susceptible	ZMO35	2	Resistant
ZMO84	0.03	Susceptible	ZMO37	0.015	Susceptible
ZMO85	2	Resistant	ZMO40	< 0.008	Susceptible
ZMO86	< 0.008	Susceptible	ZMO41	< 0.008	Susceptible
ZMO87	0.5	Susceptible-dose-dependent	ZMO42	< 0.008	Susceptible
ZMO88	0.015	Susceptible	ZMO43	< 0.008	Susceptible
ZMO89	0.015	Susceptible	ZMO44	1	Resistant
ZMO91	< 0.008	Susceptible	ZMO47	0.25	Susceptible-dose-dependent
ZMO94	< 0.008	Susceptible	ZMO53	< 0.008	Susceptible
ZMO95	0.03	Susceptible	ZMO54	< 0.008	Susceptible
ZMO96	0.015	Susceptible	ZMO56	< 0.008	Susceptible
ZMO97	0.015	Susceptible	ZMO58	< 0.008	Susceptible
ZMO98	0.015	Susceptible	ZMO59	< 0.008	Susceptible
ZMO99	< 0.008	Susceptible	ZMO60	< 0.008	Susceptible
ZMO102	< 0.008	Susceptible	ZMO62	0.12	Susceptible
ZMO103	0.03	Susceptible	ZMO63	< 0.008	Susceptible
ZMO107	< 0.008	Susceptible	ZMO65	0.12	Susceptible
ZMO110	< 0.008	Susceptible	ZMO67	< 0.008	Susceptible
ZMO119	< 0.008	Susceptible	ZMO68	< 0.008	Susceptible
ZMO128	0.015	Susceptible	ZMO69	< 0.008	Susceptible
ZMO132	< 0.008	Susceptible	ZMO71	< 0.008	Susceptible
ZMO135	> 8	Resistant	ZMO72	< 0.008	Susceptible
ZMO141	< 0.008	Susceptible	ZMO75	< 0.008	Susceptible
ZMO142	0.5	Susceptible-dose-dependent	ZMO77	< 0.008	Susceptible
ZMO145	0.5	Susceptible-dose-dependent	ZMO79	0.25	Susceptible-dose-dependent
ZMO146	0.015	Susceptible	ZMO80	< 0.008	Susceptible
ZMO147	< 0.008	Susceptible	ZMO81	< 0.008	Susceptible

MICs - minimum inhibitory concentrations

Supplementary Table V: *C. albicans* isolates: MICs and susceptibility profiles to voriconazole

Isolate name	MIC (µg/ml)	Susceptibility profile
ATCC	0.06	Susceptible
ZMO1	< 0.008	Susceptible
ZMO10	1	Resistant
ZMO11	0.5	Susceptible-dose-dependent
ZMO12	< 0.008	Susceptible
ZMO14	0.015	Susceptible
ZMO17	< 0.008	Susceptible
ZMO18	< 0.008	Susceptible
ZMO20	0.015	Susceptible
ZMO21	< 0.008	Susceptible
ZMO23	< 0.008	Susceptible
ZMO25	< 0.008	Susceptible
ZMO27	< 0.008	Susceptible
ZMO28	< 0.008	Susceptible

ZMO82	< 0.008	Susceptible
ZMO83	< 0.008	Susceptible
ZMO84	0.015	Susceptible
ZMO85	0.12	Susceptible
ZMO86	< 0.008	Susceptible
ZMO87	0.03	Susceptible
ZMO88	0.06	Susceptible
ZMO89	< 0.008	Susceptible
ZMO91	< 0.008	Susceptible
ZMO94	< 0.008	Susceptible
ZMO95	< 0.008	Susceptible
ZMO96	< 0.008	Susceptible
ZMO97	< 0.008	Susceptible
ZMO98	< 0.008	Susceptible
ZMO99	< 0.008	Susceptible
ZMO102	< 0.008	Susceptible
ZMO103	0.12	Susceptible
ZMO107	< 0.008	Susceptible
ZMO110	< 0.008	Susceptible

ZMO119	< 0.008	Susceptible
ZMO128	1	Resistant
ZMO132	< 0.008	Susceptible
ZMO135	> 8	Resistant
ZMO141	< 0.008	Susceptible
ZMO142	0.5	Susceptible-dose-dependent
ZMO145	0.5	Susceptible-dose-dependent
ZMO146	< 0.008	Susceptible
ZMO147	< 0.008	Susceptible

MICs - minimum inhibitory concentrations