ABSTRACT

There is an increase in non-albicans Candida (NAC) vulvovaginal candidiasis which is attributed to overuse of antifungal therapy and this has led to antifungal resistance. This study was aimed at determining the antifungal resistance pattern of some clinical isolates of Candida species. Eighty-eight (88) isolates were used which included Candida tropicalis (34), Candida Parapsilosis (21), Candida albicans (20), Candida krusei (7) and Candida glabrata (6). The drugs used were Fluconazole (25µg), Ketoconazole (10µg), Voriconazole (1µg), Nystatin (100Units), Amphotericin B (20µg), Flucytosine (1µg), Clotrimazole (10µg) and Itraconazole (50µg). The susceptibility testing was carried out using the M44-A standard method for yeast disk diffusion testing. Results showed that the percentages of Candida species resistant to Fluconazole, Ketoconazole, Voriconazole, Amphotericin B, Flucytosine, Clotrimazole and Itraconazole and Nystatin were 52.3%, 61.9%, 35.2%, 19.3%, 86.4%, 34.1%, 45.5% and 44.3%, with inhibition zone diameters ≤14mm, ≤20mm, ≤13mm, <10mm, ≤11mm, ≤11mm, ≤13mm and no inhibition zone diameter respectively. Candida krusei was the most resistant species with 100% resistance to each of Fluconazole, Ketoconazole, Voriconazole, Amphotericin B, Flucytosine, Clotrimazole and Itraconazole.
1. INTRODUCTION

Serious fungal infections afflict millions of patients annually resulting in more than 1,350,000 deaths. The most serious fungal infections occur as a consequence of other serious health problems such as asthma, AIDS, cancer, and organ transplantation, and they all require antifungal therapy for a successful outcome. Failure to treat effectively either because of diagnostic delays or missed diagnosis often leads to death or serious illness. This recognition has resulted in a significant increase in antifungal agents use for the treatment and prevention of fungal infections. Yet, therapeutic options are limited; as the most widely used antifungal drugs comprise only a few chemical classes including azoles, polyenes, and echinocandins [1,2].

Candida species are well known for causing infections in mouth, skin, and vagina in humans [3]. The second most common cause of abnormal discharge after bacterial vaginosis in healthy women of reproductive age is vulvovaginal candidiasis [4]. Some studies have reported that three fourth (75%) of women will experience an episode of vulvovaginal candidiasis in their lifetimes, 50% of these will experience at least a second episode, and 5–10% of all women experience recurrent vulvovaginal candidiasis [5,6,7]. Candida albicans is the most common cause of vulvovaginal candidiasis, although the frequency of vulvovaginal candidiasis caused by other Candida species, such as C. tropicalis, C. glabrata, and C. krusei is increasing [8].

Candidiasis is a fungal infection caused by the yeast Candida. Candida can cause infections if it grows out of control or if it enters deep into the body (for example, the bloodstream or internal organs like the kidney, heart, or brain). Some types of Candida are resistant to the antifungals used to treat them [2,9]. Antimicrobial resistance occurs naturally over time, usually through genetic changes. New resistance mechanisms are emerging and spreading globally, threatening our ability to treat common infectious diseases, resulting in prolonged illness, disability, and death. However, the misuse and overuse of antimicrobials is accelerating this process [10,11].

Although Candida albicans, which causes most Candida infections in people has very low levels of drug resistance, other types of Candida are frequently resistant and more deadly [3]. Yeast infections resistant to antifungal agents have been increasing and their frequency will likely continue to increase [8].

In South Eastern Nigeria, little is known about the distribution and antifungal resistance pattern of Candida species isolated from clinical samples, high vaginal swabs inclusive. Most often, in vitro susceptibility testing is used most importantly to detect resistance as well as to select agents with likely activity for a given infection. Many clinical laboratories do not have the capacity to test Candida for drug resistance, limiting the ability to guide treatment and track resistance [3]. [8] Also noted that lack of expertise in the field can also be incriminated as a factor. This study was, therefore aimed at determining the antifungal resistance pattern of Candida species isolated from high vaginal swabs of women attending a hospital in Enugu State, South East Nigeria to a host of antifungal drugs.
2. MATERIALS AND METHODS

2.1 Source of Test Microorganisms

The test microorganisms were isolated from high vaginal swab (HVS) specimens of women attending the Obstetrics and Gynecology Unit of the University of Nigeria Teaching Hospital (UNTH) Ituku/Ozalla, Enugu State, Nigeria as described [12]. These organisms included Candida tropicalis (34), Candida Parapsilosis (21), Candida albicans (20), Candida krusei (7) and Candida glabrata (6). In all, there were eighty-eight (88) yeast microorganisms.

2.2 Standardization of Inoculum and in vitro Antifungal Susceptibility Testing Using Commercial Antifungal Discs

Using a sterile wire loop, discrete colonies each of 24 hours pure culture of the Candida isolates was picked and inoculated into 5ml of sterile 0.85% saline. The turbidity of the suspension was adjusted and then matched visually with 0.5 McFarland standards which is equivalent to 1 x 10^6 colony forming units per ml (CFU/ml). The antifungal susceptibility testing was carried out using one of four standard methods for antifungal susceptibility testing, that is M44-A for yeast disk diffusion testing [13] released by the Clinical and Laboratory Standards Institute (CLSI), formerly the NCCLS (National Committee on Clinical Laboratory Standards). Eight antifungal drugs were used: Fluconazole (25µg), Ketoconazole (10µg), Voriconazole (1µg), Nystatin (100Units), Amphotericin B (20µg), Fluycytosine (1µg), Clotrimazole (10µg) and Itraconazole (50µg) (Oxoid, UK and Abtek, Liverpool). Mueller Hinton Agar (TM MEDIA, TITAN BIOTECH LTD, Rajasthan, India) was prepared according to the manufacturer’s instructions and poured into Petri dishes (plates). Each plate was seeded with 0.2ml of the standardized inoculum and spread plated evenly on the surface of the agar. The above antifungal discs were then aseptically placed (using sterile forceps) on the surface of the agar plates by pressing each disc down firmly to ensure complete, level contact with the agar. The plates were left for 30 minutes at room temperature on the laboratory bench for pre-diffusion and then incubated in an inverted position at 30°C for 24 hours. After the incubation period, the inhibition zone diameter was measured and recorded in millimeter (mm) using a transparent ruler [14]. The antifungal susceptibility of the isolates was interpreted as susceptible (S), Susceptible Dose-Dependent (SDD) or Intermediate (I) and Resistant (R). The results were interpreted in line with the Clinical and Laboratory Standards Institute guidelines [14] and [15].

3. RESULTS AND DISCUSSION

3.1 In vitro Susceptibility Profile of the Candida Species to Fluconazole

It was observed in this study that 27 (30.7%) of the Candida isolates were susceptible to Fluconazole, 15 (17%) were susceptible dose-dependent and 46 (52.3%) were resistant. Candida glabrata was the most susceptible (50%) followed by Candida parapsilosis (42.9%). Meanwhile, the highest resistance (85.7%) was shown by Candida krusei. In fact, none of the Candida krusei isolate was susceptible to Fluconazole (Table 1). This resistance (52.3%) is very much higher than the 2.6% reported by [16] in Korea. Also, the 25%, 29.4%, 42.9% and 50% susceptibilities respectively observed for Candida albicans, Candida tropicalis, Candida parapsilosis and Candida glabrata does not agree with the > 90% respectively observed for Candida albicans, Candida tropicalis, Candida parapsilosis and 84.3% for Candida glabrata by [17] in Kuala Lumpur, Malaysia. The result of 17% susceptible dose-dependent isolates recorded in this study is similar to 13.8% susceptible dose-dependent isolates previously recorded [16]. Also, the 0% susceptibility of Candida krusei to Fluconazole observed in the present study agrees with the 0% susceptibility previously reported [16]. Similarly, [18] reported 100% resistance of Candida krusei to Fluconazole. Isolates of Candida krusei are considered resistant to Fluconazole irrespective of the MIC [16]. This calls for identification of the particular etiologic agent (Candida species) and sensitivity testing to avoid ineffective and inappropriate therapy.

3.2 In vitro Susceptibility Profile of the Candida Species to Ketoconazole

Twelve (13.6%) out of the 88 Candida isolates were susceptible, 22 (25%) were susceptible dose-dependent and 54 (61.4%) were resistant. Candida krusei was the most resistant (71.4%) followed by Candida albicans (70%) while Candida parapsilosis was the most susceptible dose-dependent species (Table 2). Candida albicans had a 15% susceptibility to
ketoconazole which is very much lower than the 73% susceptibility reported by [19]. [19] also reported a 33.55% resistance of Candida krusei against ketoconazole which is lower than the 71.4% resistance observed in the present study. However, [20] reported a high resistance (83.3%) for Candida krusei against ketoconazole which is similar to the high resistance (71.4%) observed in the present study.

3.3 In vitro Susceptibility Profile of the Candida Species to Clotrimazole

From the in vitro susceptibility profile of the Candida species to Clotrimazole (Table 3), it was observed that 37(42.0%) of the Candida isolates were susceptible, 21 (23.9%) were susceptible dose-dependent while 30 (34.1%) were resistant. The highest resistance (71.4%) was observed with Candida krusei while Candida parapsilosis was the most susceptible (57.1%). Candida tropicalis was the most susceptible dose-dependent species (32.4%) and also the least resistant species (26.5%). Candida albicans had 30% susceptibility and 40% resistance to Clotrimazole (Table 3). [21] Reported 36.2% sensitivity and 63.8% resistance of Candida albicans against Clotrimazole. In a similar study carried out in Northwest Ethiopia, [22] reported that of the 96 Candida isolates tested against Clotrimazole, only 7 (7.3%) were resistant. This is very much lower than the 34.1% resistance recorded in the present study. [22] Reported a much higher susceptibility (77.2%) of Candida albicans in their study. The 66.7% resistance of Candida tropicalis against Clotrimazole reported by [21] in Jos, North Central Nigeria is much higher than the 26.5% resistance recorded in the present study. However, [21] reported 75.4% resistance against Clotrimazole by Candida krusei which is similar to the 71.4% observed in the present study.

Table 1. In vitro susceptibility profile of the Candida Species to Fluconazole (25µg)

| Species          | Total number | S (%) | SDD (%) | R (%) |
|------------------|--------------|-------|---------|-------|
| Candida albicans | 20           | 5(25) | 3(15)   | 12(60)|
| Candida tropicalis | 34         | 10(29.4) | 8(23.5) | 16(47.1) |
| Candida parapsilosis | 21    | 9(42.9) | 2(9.5) | 10(47.6) |
| Candida krusei   | 7            | 0(0)  | 1(14.3) | 6(85.7) |
| Candida glabrata | 6            | 3(50) | 1(16.7) | 2(33.3) |
| **Total**        | **88**       | **27(30.7)** | **15(17.0)** | **46(52.3)** |

Key: S = Susceptible; SDD = Susceptible Dose Dependent; R = Resistant

Table 2. In vitro susceptibility profile of the Candida Species to Ketoconazole (10µg)

| Species          | Total number | S (%) | SDD (%) | R (%) |
|------------------|--------------|-------|---------|-------|
| Candida albicans | 20           | 3(15) | 3(15)   | 14(70) |
| Candida tropicalis | 34         | 5(14.7) | 8(23.5) | 21(61.8) |
| Candida parapsilosis | 21    | 3(14.3) | 8(38.1) | 10(47.6) |
| Candida krusei   | 7            | 0(0)  | 2(28.6) | 5(71.4) |
| Candida glabrata | 6            | 1(16.7) | 1(16.7) | 4(66.7) |
| **Total**        | **88**       | **12(13.6)** | **22(25.0)** | **54(61.9)** |

Key: S = Susceptible; SDD = Susceptible Dose Dependent; R = Resistant

Table 3. In vitro Susceptibility Profile of the Candida Species to Clotrimazole (10µg)

| Species          | Total number | S (%) | SDD (%) | R (%) |
|------------------|--------------|-------|---------|-------|
| Candida albicans | 20           | 6(30.0) | 6(30.0) | 8(40.0) |
| Candida tropicalis | 34         | 14(41.2) | 11(32.4) | 9(26.5) |
| Candida parapsilosis | 21    | 12(57.1) | 3(14.3) | 6(28.6) |
| Candida krusei   | 7            | 2(28.6) | 0(0.0)  | 5(71.4) |
| Candida glabrata | 6            | 3(50.0) | 1(16.7) | 2(33.3) |
| **Total**        | **88**       | **37(42.0)** | **21(23.9)** | **30(34.1)** |

Key: S = Susceptible; SDD = Susceptible Dose Dependent; R = Resistant
3.4 In vitro Susceptibility Profile of the Candida Species to Amphotericin B

Susceptible isolates were 61(69.3%) while 10 (11.4%) and 17 (19.3%) were susceptible dose-dependent and resistant respectively. The species that was most resistant to Amphotericin B was Candida krusei (42.9%) followed by Candida albicans (25.0%). Candida tropicalis was the most susceptible (79.4%) followed by Candida parapsilosis (76.2%). There were no susceptible dose-dependent and resistant isolates of Candida parapsilosis and Candida glabrata respectively (Table 4). [23] reported a much lower resistance (15.75%) of Candida krusei against Amphotericin B. Candida tropicalis was the most susceptible (79.4%) followed by Candida parapsilosis (76.2%). [24] Reported 100% susceptibility of Candida albicans, Candida tropicalis, Candida parapsilosis and Candida glabrata to Amphotericin B. There were no susceptible dose-dependent isolates of Candida parapsilosis while Candida glabrata showed no resistance to Amphotericin B (Table 4). This agrees with the findings of [17] who reported there were no susceptible dose-dependent isolates of Candida parapsilosis and also 0% resistance of Candida glabrata against Amphotericin B. Other researchers have also documented 0% resistance of Candida glabrata against Amphotericin B [20,19].

3.5 In vitro Susceptibility Profile of the Candida Species to Flucytosine

The in vitro susceptibility profile of the Candida isolates to Flucytosine is shown in Table 5. Seventy-six (86.4%) of all the isolates were resistant, 6 (6.8%) were intermediate and also 6 (6.8%) were susceptible. The interpretive categories for Flucytosine are the same categories used to interpret bacterial testing. These categories include susceptible (S), intermediate (I), and resistant (R), with Intermediate (I) being substituted for the susceptible dose-dependent category. All the isolates (100%) of Candida albicans, Candida krusei and Candida glabrata were resistant to Flucytosine. [25] reported 80% resistance of Candida albicans in the United Kingdom. The method used to determine the susceptibility of the isolates can influence the results. It has been suggested that the disk method is a sensitive but not necessarily specific method to determine Flucytosine susceptibility of Candida albicans [25]. A very low susceptibility of 4% and 2% was observed with Candida tropicalis and Candida parapsilosis respectively. Only 6 isolates of Candida tropicalis (17.6%) were susceptible dose-dependent.

3.6 In vitro Susceptibility Profile of the Candida Species to Voriconazole

For Voriconazole, 46 (52.3%) of the Candida isolates were susceptible, 11 (12.5%) were susceptible dose-dependent and 31 (35.2%) were resistant. Candida parapsilosis isolates were the most susceptible (66.7%) followed by Candida krusei (57.1%) and Candida tropicalis (52.9%). There were no susceptible dose-dependent isolates of Candida krusei (Table 6). A 100% susceptibility of Candida tropicalis and Candida parapsilosis to Voriconazole has been observed by some other researchers [17,16] which conflicts with the present study. Also, in a similar research carried out by [26] in Venezuela, none of the Candida species was found to be resistant to Voriconazole. In another study by [24] in Turkey, all 200 (100%) isolates of Candida species were susceptible to Voriconazole. [27] recorded 89.9% susceptibility of all the Candida species isolated from samples from oral candidiasis and diaper dermatitis lesions collected from children referring to private and public clinics in Ilam, Iran. This 89.9% susceptibility is much higher than the 52.3% observed in the present study. These variations in susceptibility profile may be explained by the differences in the hospital, the underlying disease of the patient, clinical specimen analyzed as well as the geographical location where the studies were carried out [26].

| Table 4. In vitro Susceptibility Profile of the Candida Species to Amphotericin B (20µg) |
|---------------------------------|---------------|---------------|---------------|
| Species                        | Total number | S (%)         | SDD (%)       | R (%)         |
|--------------------------------|---------------|---------------|---------------|
| Candida albicans               | 20            | 12(60.0)      | 3(15.0)       | 5(25.0)       |
| Candida tropicalis             | 34            | 27(79.4)      | 3(8.8)        | 4(11.8)       |
| Candida parapsilosis           | 21            | 16(76.2)      | 0(0.0)        | 5(23.8)       |
| Candida krusei                 | 7             | 3(42.9)       | 1(14.3)       | 3(42.9)       |
| Candida glabrata               | 6             | 3(50.0)       | 3(50.0)       | 0(0.0)        |
| Total                          | 88            | 61(69.3)      | 10(11.4)      | 17(19.3)      |

Key: S = Susceptible; SDD = Susceptible Dose Dependent; R = Resistant
Table 5. *In vitro* Susceptibility Profile of the *Candida* Species to Flucytosine (1µg)

| Species          | Total number | S (%) | I (%) | R (%) |
|------------------|--------------|-------|-------|-------|
| Candida albicans | 20           | 0(0.0)| 0(0.0)| 20(100.0) |
| Candida tropicalis | 34          | 4(11.8)| 6(17.6)| 24(70.6) |
| Candida parapsilosis | 21       | 2(9.5)| 0(0.0)| 19(90.5) |
| Candida krusei   | 7            | 0(0.0)| 0(0.0)| 7(100.0) |
| Candida glabrata | 6            | 0(0.0)| 0(0.0)| 6(100.0) |
| **Total**        | **88**       | **6(6.8)**| **6(6.8)**| **76(86.4)** |

Key: S = Susceptible; I = Intermediate; R = Resistant

Table 6. *In Vitro* Susceptibility Profile of the *Candida* Species to Voriconazole (1µg)

| Species          | Total number | S (%) | SDD (%) | R (%) |
|------------------|--------------|-------|---------|-------|
| Candida albicans | 20           | 7(35.0)| 5(25.0)| 8(40.0) |
| Candida tropicalis | 34         | 18(52.9)| 2(5.9)| 14(41.2) |
| Candida parapsilosis | 21      | 14(66.7)| 3(14.3)| 4(19.0) |
| Candida krusei   | 7            | 4(57.1)| 0(0.0)| 3(42.9) |
| Candida glabrata | 6            | 3(50.0)| 1(16.7)| 2(33.3) |
| **Total**        | **88**       | **46(52.3)**| **11(12.5)**| **31(35.2)** |

Key: S = Susceptible; SDD = Susceptible Dose Dependent; R = Resistant

3.7 *In vitro* Susceptibility Profile of the *Candida* Species to Itraconazole

Twenty-seven (30.7%) of the *Candida* isolates were susceptible while 21 (23.9%) and 40 (45.5%) were susceptible dose-dependent and resistant respectively. *Candida parapsilosis* was the most susceptible (42.9%) followed by *Candida tropicalis* (35.3%) while *Candida glabrata* was the most resistant (83.3%) followed by *Candida albicans* (65.0%). There were no susceptible isolates of *Candida glabrata* (Table 7). [26] reported 27.6% resistance of *Candida* isolates in Venezuela while [27] recorded 38.3% susceptibility in Iran. In one study, 85.7% of *Candida parapsilosis* and more than 90% of *Candida tropicalis* isolates were susceptible to Itraconazole [16]. In their research, [27] found out that the resistance of *Candida albicans* to Itraconazole was 43.8% which is lower than that (65.0%) observed in the present study. There were no susceptible isolates of *Candida glabrata* which does not agree with the 83.4% susceptibility reported by [16].

3.8 *In vitro* Susceptibility Profile of the *Candida* Species to Nystatin

Table 8 shows the *in vitro* susceptibility profile of the *Candida* isolates to Nystatin. It can be seen from the table that 33 (37.5%), 16 (18.2%) and 39 (44.4%) of the isolates were susceptible, susceptible dose-dependent and resistant respectively. *Candida glabrata* was the most susceptible (66.4%) followed by *Candida parapsilosis* (52.4%) while *Candida albicans* was the most resistant (55.0%) followed by *Candida tropicalis* (50.0%) and *Candida krusei* (42.9%). This disagrees with the findings of [28] and [19] that showed a 100% susceptibility of all *Candida* isolates to Nystatin. [21] reported that out of 139 *Candida* isolates, 26 (18.7%) and 113 (81.3%) were sensitive and resistant to Nystatin respectively which does not agree with the results of the present study. [27] observed 95.3% susceptibility of all different *Candida* species in Ilam, Iran. *Candida glabrata* was the most susceptible (66.4%) followed by *Candida parapsilosis* (52.4%) while The resistance by *Candida albicans*, *Candida tropicalis* and *Candida krusei* against Nystatin in this study is much lower than the 70.7%, 100% and 82.0% respectively reported by [21].

In the overall, the highest susceptibility was recorded for Amphotericin B to which 61 (69.3%) of the 88 *Candida* isolates were susceptible followed by Voriconazole (52.3%) and Clotrimazole (43.0%). [27] also recorded the highest susceptibility (99.3%) by all different *Candida* isolates to Amphotericin B. [29] detected 100% susceptibility to Amphotericin B by all strains of *Candida* isolated in Turkey. [30] reported that all of 50 *Candida* species (except 1 strain of *Candida tropicalis*) isolated in Central-Western Brazil were susceptible to Amphotericin B. The present study also agrees with that of [22] who reported that Amphotericin B was the most effective drug to which all isolates of *Candida* species except *C. krusei* were 100% sensitive. Other reports of very high susceptibility of *Candida* species to Amphotericin B have been
Table 7. In vitro susceptibility profile of the Candida species to itraconazole (50µg)

| Species             | Total number | S (%) | SDD (%) | R (%) |
|---------------------|--------------|-------|---------|-------|
| Candida albicans    | 20           | 4(20.0) | 3(15.0) | 13(65.0) |
| Candida tropicalis  | 34           | 12(35.3) | 11(32.4) | 11(32.4) |
| Candida parapsilosis| 21           | 9(42.9) | 4(19.0) | 8(38.1) |
| Candida krusei      | 7            | 2(28.6) | 2(28.6) | 3(42.9) |
| Candida glabrata    | 6            | 0(0.0) | 1(16.7) | 5(83.3) |
| **Total**           | **88**       | **27(30.7)** | **21(23.9)** | **40(45.5)** |

Key: S = Susceptible; SDD = Susceptible Dose Dependent; R = Resistant

Table 8. In vitro susceptibility profile of the Candida species to nystatin (100units)

| Species             | Total number | S (%) | SDD (%) | R (%) |
|---------------------|--------------|-------|---------|-------|
| Candida albicans    | 20           | 6(30.0) | 3(15.0) | 11(55.0) |
| Candida tropicalis  | 34           | 9(26.5) | 8(23.5) | 17(50.0) |
| Candida parapsilosis| 21           | 11(52.4) | 3(14.3) | 7(33.3) |
| Candida krusei      | 7            | 3(42.9) | 1(14.3) | 3(42.9) |
| Candida glabrata    | 6            | 4(66.4) | 1(16.7) | 1(16.7) |
| **Total**           | **88**       | **33(37.5)** | **16(18.2)** | **39(44.4)** |

Key: S = Susceptible; SDD = Susceptible Dose Dependent; R = Resistant

documented [17,31,24]. Owing to its high toxicity (especially nephrotoxicity) and low bioavailability (when administered orally), Amphotericin B is not regularly prescribed or used extensively. This may account for the high sensitivity when compared with other antifungal drugs [22]. Amphotericin has a broad spectrum of action and presents a low incidence of fungal resistance even after a half century of clinical use. One major disadvantage of Amphotericin B is its nephrotoxicity [32,33].

The highest resistance was observed with Fluconazole to which 76 (86.4%) out of the 88 Candida isolates were resistant followed by Ketoconazole (61.4%) and Fluconazole (52.3%). Fluconazole has been one of the most widely used drugs for treating candidiasis [34]. In fact, Fluconazole is the most widely used drug for treating candidiasis [35] generally, and is the most commonly prescribed antifungal used for most Candida albicans infections [36]. Thus, wide spread and prolonged use of azoles promote rapid development of the phenomenon of multidrug resistance, which poses a major problem in antifungal therapy [34]. In the present study, Voriconazole was the second antifungal drug to which most (52.3%) of the Candida species were susceptible. Being a second-generation, synthetic triazole derivative of Fluconazole, it can be used to treat infections caused by Fluconazole-resistant Candida species [37]. Meanwhile, the highest number of susceptible-dose dependent Candida isolates was observed with Ketoconazole (25%), followed by Clotrimazole and Itraconazole, each recording 23.9% and then, Nystatin (18.2%). The Candida isolates categorized as being susceptible-dose dependent (SDD) is in recognition that yeast susceptibility is dependent on achieving maximum blood levels. Thus, an isolate with an SDD category implies clinical efficacy when higher than normal dosage of a drug can be used and maximal possible blood levels achieved [38].

Candida tropicalis was the species with the highest susceptibility (79.4%) to Amphotericin B followed by Candida parapsilosis (76.2%) and 66.7% respectively to Amphotericin B and Voriconazole. Fig. 1 shows the activity of some of the antifungal drugs against Candida tropicalis. Candida krusei was the species with the least susceptibility showing 0% susceptibility to each of Fluconazole, Ketoconazole and Fluocytosine (Fig. 2). It is critically noted that Fluconazole is not recommended for Candida krusei and it has also been stated that Candida krusei should not be tested against Fluconazole to which it is intrinsically resistant [39]. In a review by [40], it was documented that out of 1, 075 Candida krusei isolates tested against Fluconazole, 96.6% was resistant to the drug. Also, Candida glabrata showed 0% susceptibility to each of Fluocytosine and Itraconazole while Candida albicans showed 0% susceptibility to Fluocytosine only. Candida glabrata has been documented of being able to develop high-level resistance after exposure to azole antifungals [41]. Also Candida glabrata was the only Candida species with 0% resistance to Amphotericin B.
4. CONCLUSION

In the present study, the percentages of Candida species resistant to Fluconazole, Ketoconazole, Voriconazole, Nystatin, Amphotericin B, Flucytosine, Clotrimazole and Itraconazole were respectively 52.3, 61.9, 35.2, 44.3, 19.3, 86.4, 34.1 and 45.5%. Candida krusei was the most resistant species with 100% resistance to each of Fluconazole, Ketoconazole and Flucytosine. Candida tropicalis was the species with the highest susceptibility (79.4%) to Amphotericin B followed by Candida parapsilosis. The drug to which most of the Candida species were susceptible was Amphotericin B followed by Voriconazole while Flucytosine was the drug with the highest resistance followed by Ketoconazole and Fluconazole.

Based on the findings of the present study, Voriconazole is recommended for vaginal candidiasis especially in the study area and also especially for infections caused by Fluconazole-resistant Candida species. This study also recommends that sensitivity testing be carried out before antifungal therapy. Due to the fact that indiscriminate use of drugs (including antifungal drugs) is generally common in this part of the world, it should be avoided to reduce the development and spread of resistance.

DISCLAIMER

The products used for this research are commonly and predominantly used products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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