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Use of the VITEK 2 machine for identification and antifungal sensitivity test of *Candida spp*

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ABSTRACT

In patients with compromised immune systems, infections caused by Candida represent a significant source of illness and death; thus, timely and accurate identification is crucial for effective patient care. A Candida isolate was identified using both conventional techniques and the Vitek-2 system. Antifungal susceptibility testing (AST) was conducted with the Vitek-2 system following the guidelines set forth by the Clinical and Laboratory Standards Institute. The most commonly identified species of Candida was albicans, followed by tropicalis, krusei, parapsilosis, and glabrata. The average agreement rate between the Vitek-2 system and traditional methods exceeded 94%. Most isolates demonstrated sensitivity to amphotericin B (97.67%) and fluconazole (88.95%). The AST agreement rates for fluconazole and amphotericin B were over 94% and more than 99%, respectively, with statistical significance noted ($P < 0.01$).

INTRODUCTION

Antifungal sensitivity test s have increased expanding significance in late decades as etiological specialists of obtrusive contaminations in immune compromised and other basically sick patients (1,3). All the while, the extent of *Candida spp*. including the fluconazole resistant species *C. glabrata* and *C. krusei* (2,4,6). Candida are fungi, unicellular state. eukaryotic growths with completely unexpected properties. For instance, Candida have an impervious to antiinfection agents, sulfamides and other hostile to bacterial operators. Candida cell size (5×10µm), the primary strategy for multiplication is basically by sprouting, and incidentally by budding, and these don't shape spores in or on a fruiting body. Identify of yeantifungal sensitivity test species might be as per a number of properties , for example, cell morphology, physiology, immunology, and molecular (7).

The VITEK2 system is a fully automated instrument for determining the antibiotic susceptibility of bacteria. 51 different taxa, including freshly described species, are included in

the ID-YST database, which takes into consideration subsequent advancements in scientific classification. The new fluorescence-based innovation in the Vitek 2 machinemakes it possible to identify yeantifungal sensitivity test s for up to 15 hours. Clinical isolates or a mix of in-house strains were used in earlier experiments to assess a model of the VITEK 2 that included three physically functional modules (8,9). In recent years, the use of antifungal susceptibility testing (antifungal sensitivity test) in clinical trials has grown. As a result, antifungal drugs with unique modes of action are presented, and antifungal susceptibility testing methods are presented better (10, 11, 12). Invasive fungal infections, particularly candidiasis, are typically believed to respond better to early beginning of proper antifungal treatment (13, 14). The Clinical and Laboratory Standards Institute (CLSI) and, more recently, the antifungal sensitivity test subcommittee of the European Committee for Antimicrobial Susceptibility Testing (eucantifungal sensitivity test) have been providing antifungal sensitivity test reference methodologies for fungi since 1997. At clinical microbiology research facilities, faculty members may be unfamiliar with both of these time-consuming techniques (15, 16, 17, 18, 19, 20). The U.S. Food and Drug Administration has approved two commercial techniques for antifungal sensitivity test of fungus with a few antifungal drugs (FDA): the Etest (biomerieux SA, Marcy Étoile, France) and the Sensititre Yeantifungal sensitivity test One system. However, the performance of these methods is different from the presentation of reference methods. With a yeantifungal sensitivity test sensitivity test that uses the Vitek 2 microbiology system to spectrophotometrically measure Candida growth and analyze susceptibility to flucytosine, amphotericin B, fluconazole, and voriconazole in a fully automated manner, Biomerieux recently expanded its involvement in this field (21, 22, 23). The goal of this study is to assess the Vit. 2 Machine for identifying yeantifungal sensitivity test and performing antimicrobial susceptibility testing (antifungal sensitivity test) in comparison to traditional manual methods.

C. albicans demonstrates a dimorphic growth pattern, primarily existing and multiplying through its phenotype, known as blantifungal sensitivity test ophore or blantifungal sensitivity test oconidia. This organism can transition into various forms, such as yeantifungal sensitivity test and hyphae, in response to environmental signals that are crucial for its virulence. Cells that are elongated and connected to one another are referred to as pseudohyphae, whereas cells identified as true hyphae are characterized by a tubular structure and are separated by transverse septal walls. (26).

Numerous varieties of Candida, with Candida albicans being the most prevalent, can cause the fungal infection known as candidiasis. Clinically, this illness is called candidiasis. These infections come in a wide range of forms, from mild ones like vaginitis and oral thrush to more serious systemic infections like candidemia. These co-infections are especially important in immunocompromised patients, such as those with HIV or cancer, and in patients undergoing non-traumatic emergency surgeries, where strong antibiotics and immunosuppressive medications are frequently used during organ transplants or anti-leukemia treatments (27, 28,29). Below is a quick summary of the signs and symptoms of candidiasis, which vary depending on the location of the infection. A number of antifungal drugs are available and have shown promise in the treatment of candidiasis. The purpose of amphotericin B, fluconazole, and more recent echinocandin class medicines, such as caspofungin, is to combat fungal strains that show resistance to azoles or polyenes (30). The direct inspection is a rapid and efficient way to detect candidiasis. After the afflicted area has been cleaned and prepared, a swab is placed onto a microscope slide. After that, the skin cells are dissolved while the Candida cells are preserved by adding a 10% potassium hydroxide (KOH) solution. This makes it possible to clearly see individual yeantifungal sensitivity test cells and pseudohyphae, which are linked to different species of Candida (31).

SDA media is used to cultivate Candida species because it lowers the pH of the surrounding environment, allowing Candida to flourish while suppressing some bacterial species. This process involves using a sterile swab to swab the diseased location, streaking the swab over SDA media, and then incubating it at 37°C (32, 33). For quick identification of Candida species, chromogenic media (Candida ID CHROM agar) are also suggested (34, 35, 36). These media contain chromogenic compounds that react with enzymes released by candida to produce species-specific colony pigmentations that facilitate simple identification (37).

API Candida was created to help clinical microbiology labs identify the most important medicinal yeantifungal sensitivity test s and organisms that resemble yeantifungal sensitivity test s. B-maltosidase, a-amylase, b-xylosidase, b-glucuronidase, urea hydrolysis, N-acetylb glucosaminidase, and b-galactosidase are among the seven chemical tests that are close to the five sugar tests (glu., galac., sucr., trehal., and raffin.) that are part of the API Candida device. A suspension of candida is introduced into the fluid substrates to immunize the wells. After 24 hours of hatching at 35°C, the outcome shows perusing, and the differentiating pieces of proof are carried out by consulting the list of numerical profiles and a computer application that the producer has provided (38). Simpler, quicker, and more reliable procedures are currently replacing traditional techniques based on the Wickerham osmosis/aging patterns (38). Both automated and manual work identification technologies are employed in clinical microbiology labs; however, the types and quantities of biochemical (starch/enzyme) substrates examined determine how well they identify yeantifungal sensitivity test isolates down to the species level (39). The Auxa Color system employs colorimetric assays to evaluate phenol oxidase production, cycloheximide (actidione) resistance, and digestive substrates, despite having a tiny dataset of only 26 taxa/species. There is another, more intriguing system (38).

The Vitek 2 machinecombines a database of 52 distinct yeantifungal sensitivity test species that has remained consistent since 2000 with the ID-YST (fluorometric) card and the newly developed YST (colorimetric) card. The performance of the system should be continuously assessed to determine whether it can truly keep up with the emergence of rare or novel pathogenic species (40, 41) and potentially with the geographic or source variations of clinical disconnects (42). The system databases should be dynamically updated to include both typical and unusual clinical species. Without a doubt, most of the 60 new clinical yeantifungal sensitivity test s showed resistance to antifungals in vitro (43). could not be gained by phenotypic identifiable evidence, such as testing using the Auxa Color and Programming Interface ID32C system to determine the carbon/nitrogen source osmosis. Furthermore, submolecular identifiable proof based on sequence analysis of the 26S rRNA quality D1/D2 region was required to identify 153 yeantifungal sensitivity test isolates that belonged to both common species with distinctive phenotypic profiles and less common species (44). Compared to traditional phenotypic assays, the depth of species identification/separation would be substantially higher with the recently introduced lattice-assisted laser desorption ionization time of flight (MALDI-TOF) mass spectrometry technique (45). However, the actual use of such a purely biophysical device is still limited to large clinical microbiology research centers in European countries (46, 47).

A standard procedure for conducting an antifungal sensitivity test of Candida by dilution for broth media has been created by the Clinical and Laboratory Standards Institute (CLSI) (48). The results are visually read using this method, which adds subjectivity to the interpretation process. (49, 50, 52, 53) Antifungal sensitivity testing are necessary to track the development of resistance. Conventional identification techniques are time-consuming (51, 54, 55). Furthermore, conventional identification techniques require more time (56,57,58). With a yeantifungal sensitivity test susceptibility test that identifies Candida development, Biomerieux

Vitek 2 has lately increased its presence in this field. The Vitek 2 microbiology systems conduct completely automated testing of susceptibility to flucytosine, amphotericin B, fluconazole, and voriconazole (61, 59, 60). The system makes use of "antifungal sensitivity test cards" that have 64 fluidic wells that automatically fill with samples. A suspension of sterile culture media and various antibiotic concentrations are placed in 64 wells on each card. Additionally, one well serves as a control well and contains only dehydrated culture media free of antibiotics. This fully automated system detects growth or lack thereof by using light attenuation recorded by an optical scanner (62). It is crucial that the samples put into cards are pure microbial isolates because the system uses an optical technique. Colonies on the inoculated agar plates yield a representative isolate, which is subsequently suspended in saline and titrated to 108 CFU/ml. After being linked to an antifungal sensitivity test card, the vial containing the microbial suspension is scanned and put into the Vit. 2 machine . The VITEK cards are filled with the suspension dilution, sealed, and then incubated in the device.

METHODOLOGY

Identification

Eighty-four clinical urine samples and oropharyngeal swabs were randomly selected from a range of healthy and sick people. The isolates were subcultured and purified after all samples were cultivated on Sabouraud agar. By suspending pure subcultures in a 0.45% (wt/vol) NaCl solution until a turbidity equal to the McFarland 2.0 standard was reached, the clinical isolates were identified and speciated using the DensiChek turbidity meter (Biomerieux), a tool for figuring out the optical density of an organism suspension (64)

Antifungal susceptibility testing

According to the manufacturer's guidelines, the turbidity is precisely adjusted to align with the 1.8–2.2 McFarland standard when utilizing inoculum suspensions derived from overnight-cultured specimens in the Vitek 2 antifungal susceptibility testing method (65). Each organism underwent testing using an antifungal susceptibility test card, with a standardized inoculum suspension transferred into a sterile polystyrene test tube known as a Vitek 2 cassette. These prepared cassettes were then placed into the Vitek 2 device for mechanical scanning. The duration of this reading process varied from 9.1 to 27.1 hours, contingent upon the observations made in the drug-free control well (22). The sensitivity of Candida isolates to fluconazole and amphotericin B was assessed through broth microdilution, following the protocols established by the Clinical and Laboratory Standards Institute (CLSI). The minimal inhibitory concentration (MIC) was defined as the lowest drug concentration that produced a discernible decrease in turbidity compared to the control group without medication, adhering to CLSI criteria. The concentrations tested for amphotericin B ranged from 0.016 to 16 mg/ml, while fluconazole concentrations varied from 0.125 to 128 mg/ml. According to CLSI guidelines, MIC breakpoints for fluconazole are categorized as follows: ≤8 mg for susceptible individuals, between 16 and 32 mg for those with intermediate susceptibility, and ≥64 mg for resistant patients.

Statistical analyses

A nonparametric correlation coefficient was used to evaluate the repeatability of antifungal sensitivity test using the Statistical Package for the Social Sciences (version 17.0, SPSS S.L., Madrid, Spain); antifungal sensitivity test was deemed reproducible if the correlation coefficient was $P < 0.05$. Every statistical analysis was carried out. Every test for statistical significance was two-tailed.

RESULTS AND DISCUSSION

Of the 84 isolates of Candida, 75 were correctly recognized by the Vitek 2 ID method. These isolates included Candida albicans (61), Candida tropicalis (6), Candida krusei (5), Candida

glabrata (2), and Candida parapsilosis (1). While Candida tropicalis (1) was identified with poor discrimination, C. albicans (5) were mistakenly identified as C. famata (1), C. parapsilosis (1), and C. albicans (2) (Table 1).

Table 1: Techniques for identifying the Vit. 2 ID system

species	Correctly identified by Vit. 2 system	Misidentified by Vit. 2 system	Low discrimination Correctly by Vit. 2 ID
C. albicans	61	5	2
C. tropicalis	6	0	1
C. krusei	5	0	0
C. parapsilosis	1	1	0
C. glabrata	2	0	0
Total	75	6	3

The Vitek 2 antifungal sensitivity test system showed that 92.4% of isolates of Candida species were sensitive to fluconazole. While 66.6% of non-albicans Candida species (NAC) were sensitive and the remaining 33.4% showed resistance, all Candida albicans isolates were sensitive. Table 2 shows that 90.9% of NAC and all C. albicans isolates (100%) were sensitive. The CLSI broth microdilution method revealed that 97.7% of the isolates of Candida species were amphotericin B sensitive.

Table 2: Candida spp. isolates' profile of antifungal susceptibility testing utilizing the CLSI broth microdilution method and the Vitek 2 system

Species name	Test method	FLU, n (%)		AMB, n (%)	
		Sa (≤8 µg/ml)	Rb (≥ 64 µg/ml)	Sa (≤1 µg/ml))	Rb (≥1 µg/ml)
C. albicans (68)	Vit. 2	68 (100)	0	68 (100)	0
	CLSI	66 (97)	2 (2.9)	68 (100)	0
C. tropicalis (7)	Vit. 2	7 (100)	0	7	7 (100)
	CLSI	5 (71.4)	2 (28.5)	7	7 (100)
C. krusei (5)	Vit. 2	0	5 (100)	3	2 (40)
	CLSI	0	5 (100)	3	2 (40)
C. parapsilosis (**2**)	Vit. 2	2 (100)	0	2 (100)	0
	CLSI	2 (100)	0	2 (100)	0
C. glabrata (**2**)	Vit. 2	1 (50)	1 (50)	2 (100)	0
	CLSI	1 (50)	1 (50)	2 (100)	0

Discussion

The most frequently identified species in standard clinical laboratory assessments include *Candida albicans*, *Candida glabrata*, *Candida tropicalis*, *Candida parapsilosis*, and *Candida krusei* (68). Our analysis indicated that 81% of the identified species were *Candida albicans*. Following this, the next most common species were *Candida tropicalis* at 8.3%, *Candida krusei* at 5.9%, and both *Candida parapsilosis* and *Candida glabrata* at 2.4% each. These findings align with earlier research conducted by Jha et al. (69), which reported that 70% of their total was comprised of *Candida albicans*, followed by *C. tropicalis* (13.33%), *C. krusei* (10%), and both *C. parapsilosis* and *C. stellatoidea* at 3.33%. Additionally, a study by Kumari et al. in 2014 revealed NAC spp. presence in South India (70). In contemporary clinical settings, fluconazole is not advised for treating infections caused by *C. krusei* (76) or for assessing susceptibility to this antifungal agent. The agreement rate for fluconazole between the Vitek 2 antifungal sensitivity testing system and the CLSI broth microdilution method was found to be 97%, closely mirroring the 94.6% agreement noted by Bourgeois et al. (77). Previous research demonstrated that the essential agreement between the Vitek 2 antifungal sensitivity testing system and broth microdilution minimum inhibitory concentrations (MICs) was 93.7% when compared to a reference result from a 48-hour bone mineral density assessment, and reached an agreement of 97.9% with results from a 24-hour broth microdilution test (22). In evaluating drug susceptibility to amphotericin, our findings showed a perfect agreement rate of 100% between the CLSI broth microdilution method and

the Vitek 2 antifungal sensitivity testing system, with correlation coefficient index (CCI) results being statistically significant ($P<0.05$) across all methods employed.

CONCLUSION

A recent study suggests that the Vitek 2 machine improves the identification rate of yeast fungal sensitivity test species isolates while reducing the amount of time required for identification. However, despite their time-consuming nature and sometimes unclear conclusions, traditional identification methods are still regarded as the gold standard and are thus better suited for research uses. As a result, the Vitek 2 machine was developed as a substitute method for yeast fungal sensitivity test species identification and antifungal sensitivity test to guide the selection of appropriate antifungal therapies for better management of opportunistic infections in immunocompromised people.

CONFLICT OF INTEREST:
The authors declare no conflict of interest.

FUNDING:
The study self-funded.

ETHICAL CLEARANCE:

Permission was taken from the concerned authorities. Patients were also informed about the purpose of the study and they all gave their consent to participate in the study.

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