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Original article

Surveillance of the epidemiology and antifungal susceptibility of invasive candidiasis: A retrospective study from 2016 to 2020 in a teaching hospital in Sousse, Tunisia

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ABSTRACT

Background: Invasive candidiasis (IC) has emerged worldwide as an important healthcare associated infection caused by *Candida* species. Nowadays, data on the epidemiology of IC and the antifungal susceptibility of *Candida* isolates in Tunisia are still limited. Hence, this study aimed to analyze the incidence, species distribution and antifungal susceptibility of *Candida* strains in the university hospital Sahloul (Sousse, Tunisia). **Methods:** A five-year (2016 to 2020) retrospective study was conducted including all *Candida* isolates recovered from blood, other sterile body fluids and deep-seated samples from hospitalized patients. *Candida* species were identified using the VITEK®2 automated system and the antifungal susceptibilities were determined by the Vitek®2 YST cards and/or the E-test method. **Results:** During the reported period, 138 nonrepetitive *Candida* isolated from separate patients were identified with a mean annual incidence of 1,04 case per 1000 admissions. *Candida albicans (C. albicans)* was the predominant species (42%), followed by *C. parapsilosis* (19,6%), *C. tropicalis* (11,6%) and *C. glabrata* (6,5%). The total resistance rates of fluconazole, voriconazole, amphotericin B and echinocandins were 6,7%, 2,9%, 2,9% and 3,4% respectively. The highest antifungal resistance rates were found with fluconazole (6,7%). This rate significantly increased from 5.3% in 2017 to 10,5% in 2020 (p=0,01). Echinocandins showed excellent in-vitro activities against the majority of *Candida* species. **Conclusion:** The present study provides valuable local surveillance data on the epidemiology and antifungal susceptibilities of invasive *Candida* species which can be useful to guide an appropriate empiric and targeted antifungal therapy.

Introduction

Invasive candidiasis (IC), caused by *Candida* yeasts, is the most common invasive fungal infection among hospitalized patients worldwide. IC has emerged worldwide as an important healthcare associated infection and poses a major public health problem because of its high morbidity and mortality rates, and excess healthcare costs [1].

Historically, *Candida albicans* is the most frequent species causing IC [1,2]. However, the

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increasing of non-albicans *Candida* species has been recognized significantly during the last two decades [3]. Furthermore, non-albicans *Candida* species are often more resistant to antifungal drugs than *C. albicans* which impacts the prognosis of patients with IC [4,5].

Key challenges to the prevention and infection control of IC are based on early diagnosis and rapid initiation of appropriate antifungal therapy [6]. Globally, the distribution of *Candida* species and their antifungal susceptibilities vary considerably with geographical location, institutions and hospital wards [3,7]. Therefore, continued surveillance is needed to draw up adequate preventive and therapeutic strategies.

The aim of this study was to describe species distribution and resistance profiles of *Candida* isolates obtained from IC patients hospitalized in Sahloul University hospital in Sousse region (Tunisia), in order to improve the therapeutic choice in IC cases in the future.

Materials and methods

Patients and data collection

We carried out a retrospective laboratory-based study in 2021. The collected data included all *Candida* strains isolated from 138 IC patients hospitalized in the university hospital Sahloul (Sousse, Tunisia) during five-year period (from 1st January 2016 to 31st December 2020). Fungal specimen data were recovered from normally sterile sites (blood, pleural and peritoneal fluids), biopsy specimens from deep organs (liver, kidney, spleen, pancreas and bones) and central venous catheter (CVC) tips. In case of multiple episodes of IC in the same patient, a subsequent event was considered as independent if developing at least 30 days after the last positive culture related to the previous episode. Patient cultures with two or more fungal species were excluded from the analysis.

The study was approved by the hospital ethics committee to allow the use of laboratory data.

Definitions

The diagnostic criteria of IC were based on the revised definitions of invasive fungal disease (IFD) from the European Organization for the Research and Treatment of Cancer/Mycoses Study Group (EORTC/MSG) consensus [8] and Infectious Diseases Society of America (IDSA) guidelines for the diagnosis and management of intravascular catheter-related bloodstream infection [9]. These criteria include histopathologic, cytopathologic or direct microscopic examination of a specimen obtained by needle aspiration or biopsy from a normally sterile site (other than mucous membranes) showing yeast cell, or the recovery of a yeast by culture of a sample obtained by a sterile procedure from a normally sterile site showing clinical or radiological abnormality consistent with infectious disease process. or isolation of yeasts in blood cultures with signs of infection [10].

Species identification

Candida isolates from blood and other sterile body fluid (including pleural and peritoneal fluids), according to the manufacturer's instructions, were collected into both aerobic and anaerobic vials and incubated for at least five days in the BacT/AlerT 3D automated system (bioMérieux, Marcy l'Etoile, France). Biopsy specimens from deep organs (liver, kidney, spleen, pancreas and bones) and central venous catheters tips were inoculated onto blood agar and Sabouraud dextrose agar media. All positive cultures were manually sampled and inoculated onto CAN2® chromogenic agar plates (bioMérieux, France) to ensure the purity and the viability of the cultures. After 48h of incubation at 37°C, isolates were identified by the VITEK®2 automated system (bioMérieux, Marcy-l'Etoile, France).

Antifungal susceptibility

Antifungal susceptibility testing was performed using the VITEK® 2 AST-YSO1 cards (bioMérieux) to determine in-vitro susceptibility to five antifungal drugs (amphotericin b, fluconazole, voriconazole, micafungin and caspofungin). For some resistant fungal strains, an E-test® (Biodisk AB, Solna, Sweden) was also performed to confirm the results, using the RPMI medium. The analysis and interpretation of data were performed according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints.

Statistical analysis

The data were analyzed using IBM SPSS software version 23. The categorical data were compared using Khi2 or Fisher's exact test. A *p* value of 0.05 was significant.

Results

Patient characteristics and specimen distribution

A total of 138 nonrepetitive (i.e. non-duplicated) *Candida* isolates from separate patients were identified over the five-year period. The analysis of

the incidence trend over the study period showed that the mean annual incidence of IC and candidemia were 1,04 per 1000 admissions and 0,45 per 1000 admissions respectively. The incidence of IC increased from 0,86 cases per 1000 admissions in 2016 to 1,79 cases per 1000 admissions in 2020 (p<0,001) **(Figure 1).**

Age range of patients was 1 to 84 years with the median age range of 56 years the male to female sex ratio was 1.3.

Of the *Candida* isolates, 47,8% were from patients hospitalized in the intensive care units (ICUs), followed by surgical wards (29,7%) and medical wards (22,5%). Of the specimen types, 43,5% of *Candida* isolates were recovered from blood, followed by peritoneal fluid (20,3%), CVC tips (18,1%), sterile tissues (15,9%) and pleural fluid (2,2%) **(Table 1).**

Distribution of *Candida* species

Overall, 10 *Candida* species were identified in our study of which the predominant fungal species was *C. albicans* (42%) followed by *C. parapsilosis* (19,6%), *C. tropicalis* (11,6%), *C. glabrata* (6,5%) and *C. famata* (2,9%) **(Table 1).** Over the study period, *C. albicans* was always predominant with a relatively stable frequency (41,7% in 2016 and 41% in 2020). Among non-albicans *Candida* species, the proportion of *C. tropicalis* cases increased from 8,3% to 20,5% (p<0,01) and fluctuations were noticed in the frequency of *C. parapsilosis* cases over the five years. Remarkably, *C. glabrata* strains were mostly isolated from patients aged >65 years (66,7%).

Concerning species distribution by hospital wards, *C. albicans* was always the predominant species followed by *C. parapsilosis* and *C. tropicalis.* In ICUs, *C. albicans* and *C. parapsilosis* were responsible for more than 60% of the cases. In the Surgical department, *C. albicans* was the predominant species (56,1%). In blood cultures, we noticed a high frequency of non-albicans *Candida* species (70%).

In vitro susceptibilities

The results of in vitro antifungal susceptibilities of *Candida* species are summarized in **table (2).**

In our institution, the highest resistance rates were found with fluconazole (6,7% of all isolates). Resistance to fluconazole was mainly seen in *C. glabrata* strains (22,2%) and in uncommon *Candida* species (16%). In fact, fluconazole demonstrated potential in vitro activities against *C. albicans* (98,3% S), *C. parapsilosis* (88,9% S) and *C. tropicalis* (87,5% S).

Echinocandins (EC), represented by caspofungin and micafungin, exhibited potent in vitro activities against the majority of *Candida* strains: all *C. albicans*, *C. tropicalis* and *C. glabrata* tested strains were susceptible to EC. Decreased susceptibility to EC was especially observed among *C. parapsilosis* isolates (88,9% S) with also high MIC90 (1 µg/mL). Remarkably, two *Candida* strains (one *C. guilliermondii* and one *Candida* species) were multidrug-resistant and exhibited resistance to all amphotericin B, fluconazole, caspofungin and micafungin.

Trends of antifungal resistance over the 5-year study period

The evolution of resistance rates of five antifungal agents against *Candida* species over the five-year study period are represented in **figure (2).**

The resistance rates of fluconazole decreased from 8,3% to 5,3% between 2016 and 2017, and then significantly increased from 5,3% in 2017 to 10,5% in 2020 (p=0,01), without significant increase in any particular species. Resistance to amphotericin B was rare over the study period with resistance rates ranging from 4,1% to 5,1%. Concerning Echinocandin (caspofungin and micafungin) resistance emerged only in 2020 (8,1%).

Table 1. Clinical characteristics of patients and species distribution of the *Candida* isolates.

Patients Characteristic	Number (%) of isolates						
	Total	***C. albicans***	***C. parapsilosis***	***C. tropicalis***	***C. glabrata***	***C. famata***	**Others[a]**
Number of patients (%)	**138 (100)**	**58 (42)**	**27 (19,6)**	**16 (11,6)**	**9 (6,5)**	**4 (2,9)**	**24 (17,4)**
Gender							
Female	60 (43,5)	27 (45)	14 (23,3)	8 (13,3)	3 (5)	2 (3,3)	6 (10)
Male	78 (56,5)	31 (39,7)	13 (16,7)	8 (10,3)	6 (7,7)	2 (2,6)	18 (23)
<18	18 (13)	7 (38,9)	4 (22,2)	2 (11,1)	---	1 (5,6)	4 (22,2)
18-49	27 (19,6)	11 (40,7)	4 (14,8)	3 (11,1)	1 (3,7)	---	8 (29,6)
50-65	41 (29,7)	18 (43,9)	8 (19,5)	6 (14,6)	2 (4,9)	1 (2,4)	6 (14,6)
>65	52 (37,7)	22 (42,3)	11 (21,2)	5 (9,6)	6 (11,5)	2 (3,8)	6 (11,5)
Ward Type							
ICU	66 (47,8)	24 (36,4)	16 (24,2)	7 (10,6)	5 (7,6)	1 (1,5)	13 (19,7)
Surgical department	41 (29,7)	23 (56,1)	4 (9,8)	3 (7,3)	3 (7,3)	2 (4,9)	6 (14,6)
Medical department	31 (22,5)	11 (35,5)	7 (22,6)	6 (19,4)	1 (3,2)	1 (3,2)	5 (16,1)
Separated year							
2016	24 (17,4)	10 (41,7)	7 (29,2)	2 (8,3)	1 (4,2)	---	4 (16,6)
2017	20 (14,5)	7 (35)	2 (10)	2 (10)	2 (10)	2 (10)	5 (25)
2018	31 (22,5)	13 (41,9)	8 (25,8)	2 (6,5)	1 (3,2)	---	7 (22,6)
2019	24 (17,4)	12 (50)	3 (12,5)	2 (8,3)	2 (8,3)	2 (8,3)	3 (12,5)
2020	39 (29,3)	16 (41)	7 (17,9)	8 (20,5)	3 (7,7)	---	5 (12,8)
Separated sites							
Blood	60 (43,5)	18 (30)	17 (28,3)	9 (15)	4 (6,7)	3 (5)	9 (15)
CVC[b]	25 (18,1)	10 (40)	7 (28)	4 (16)	---	1 (4)	3 (12)
Peritoneal fluid	28 (20,3)	22 (78,6)	---	---	3 (10,7)	---	3 (10,7)
Sterile tissues[c]	22 (15,9)	5 (22,7)	3 (13,6)	3 (13,6)	2 (9,1)	---	9 (40,9)
Pleural fluid	3 (2,2)	3 (100)	---	---	---	---	---

Notes: a This included C. krusei (3), C. dubliniensis (3), C. guilliermondii (2), C. ciferrii (2), C. lusitaniae (1) and *Candida* spp. (15) (unidentifiable species). b central venous catheter. c This included kidney (13), pancreas (3), liver (3), spleen (1), bile (1) and bone (1).

Table 2. In vitro antifungal susceptibility results of 138 isolates to five antifungal agents.

Species and Antifungal Agents	MIC (µg/mL)			Number (%) of isolates in each category			
	Range	50%	90%	S	I	R	NT
Candida albicans (n=58)							
Amphotericin B	≤0,25-2	≤0,25	0,5	57 (100)	1 (1,7)		
Fluconazole	≤0,5-32	≤0,5	1	57 (98,3)		1 (1,7)	
Voriconazole	≤0,12-0,25	≤0,12	≤0,12	57 (98,3)		1 (1,7)	
Caspofungin	≤0,12-025	≤0,12	≤0,12	30 (100)			28
Micafungin	≤0,016	≤0,016	≤0,016	30 (100)			28
Candida parapsilosis (n=27)							
Amphotericin B	≤0,25-16	≤0,25	1	25 (92,6)		2 (7,4)	
Fluconazole	≤0,5-32	≤0,5	4	24 (88,9)	1 (3,7)	2 (7,4)	
Voriconazole	≤0,12-4	≤0,12	≤0,12	26 (96,3)		1 (3,7)	
Caspofungin	≤0,12-8	0,25	1	15 (88,9)	2 (11,1)	1 (5,6)	9
Micafungin	≤0,016-4	≤0,016	1	15 (88,9)	2 (11,1)	1 (5,6)	9
Candida tropicalis (n=16)							
Amphotericin B	≤0,25-1	≤0,25	1	16 (100)			
Fluconazole	≤0,5-8	1	8	14 (87,5)	2 (12,5)		
Voriconazole	≤0,12-1	≤0,12	≤0,12	16 (100)			
Caspofungin	≤0,12-0,25	≤0,12	≤0,12	11 (100)			5
Micafungin	≤0,016	≤0,016	≤0,016	11 (100)			5
Candida glabrata (n=9)							
Amphotericin B	≤0,25-0,5	≤0,25	0,5	9 (100)			
Fluconazole	≤0,5-32	16	32	1 (11,1)	6 (66,7)	2 (22,2)	
Voriconazole	≤0,12-0,25	≤0,12	0,25	8 (88,9)	1 (11,1)		
Caspofungin	≤0,12-0,25	≤0,12	0,25	9 (100)			
Micafungin	≤0,016	≤0,016	≤0,016	9 (100)			
Others[a] *(n= 28)*							
Amphotericin B	≤0,25-16	≤0,25	1	26 (92,9)		2 (7,1)	
Fluconazole	≤0,5-32	≤0,5	8	19 (76)	2 (8)	4 (16)	3[b]
Voriconazole	≤0,12-4	≤0,12	0,5	26 (100)		2 (7,1)	
Caspofungin	≤0,12-8	≤0,12	0,25	18 (90)		2 (10)	8
Micafungin	≤0,016-4	≤0,016	≤0,016	18 (90)		2 (10)	8

Notes. a: Others includes: *C. famata* (4), *C. krusei* (3), *C. dubliniensis* (3) *C. guilliermondii* (2), *C. ciferrii* (2), *C. lusitaniae* (1), and *Candida* spp. (13).b: *C. krusei* (intrinsic resistance to Fluconazole). Abbreviations: S: susceptible; I: intermediate; NT: not tested

Figure1. Incidence of invasive candidiasis and candidemia (2016-2020)

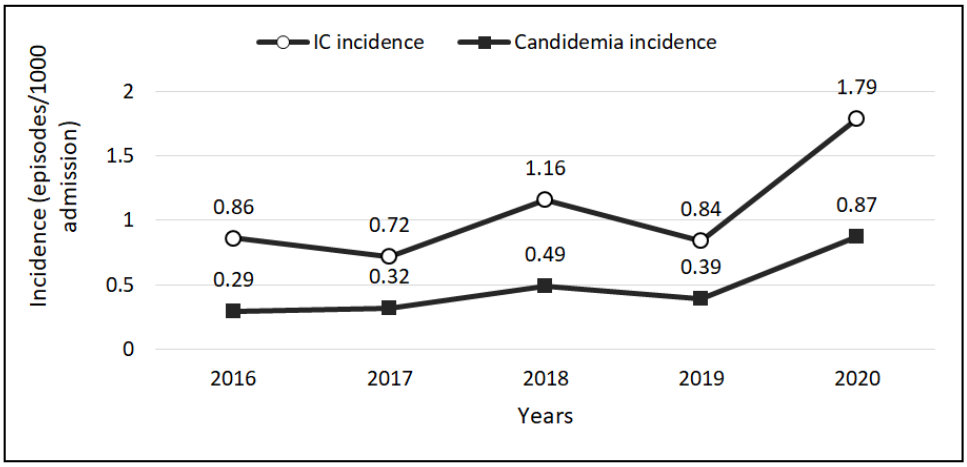
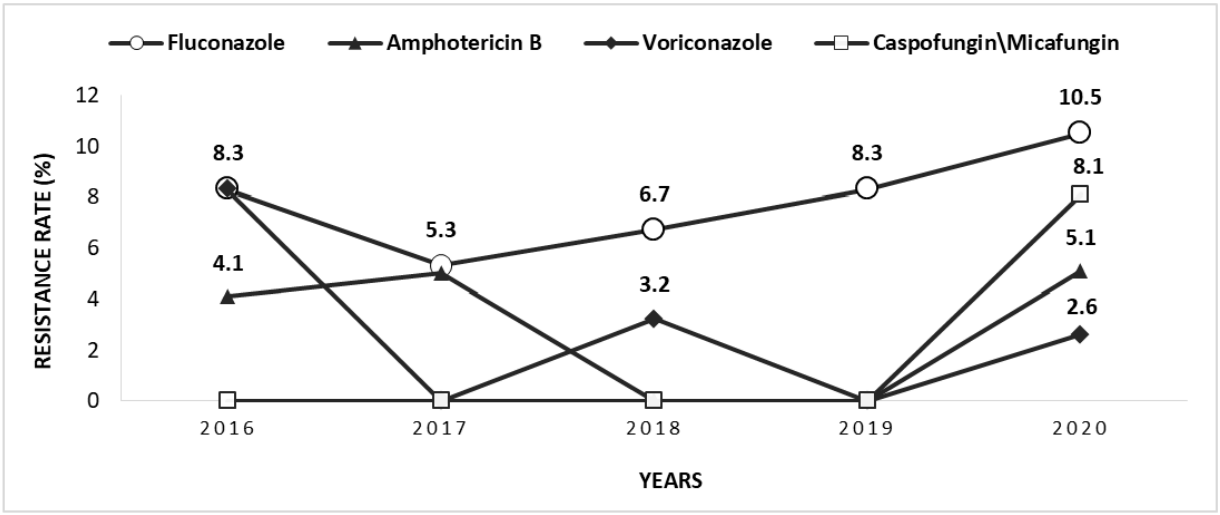


Figure2. Resistance trend of five antifungal agents in *Candida* isolates from 2016 to 2020.



Discussion

This retrospective study describes a laboratory-based, 5-year surveillance of invasive candidiasis (IC) infections in Sahloul University hospital in Sousse (Tunisia). During the study period, the incidence of IC has doubled from 0,86 to 1,79 cases per 1000 admissions (p<0,01), and the incidence of candidemia increased 3-fold from 0,29 to 0,87 cases per 1000 admissions (p<0,001). Our results, as many studies worldwide, present a significant increase in the incidence of IC in the last decade emphasizing the huge impact of these infections [11,12]. The mean annual incidence of IC (1,04 cases per 1000 admissions) is on accordance with the global incidence of IC which varies from 0,3 to 5 per 1000 admissions according to hospital-based studies [13,14]. Unfortunately, in Tunisia similar local studies focused only on candidemia or specific populations, like neonates [15-17].

The distribution of IC cases showed that IC cases are mainly found among patients hospitalized in ICUs (47,8%), followed by surgical wards (29,7%). In fact, patients admitted to ICU are at high risk of IC and *Candida* species has become the third most common cause of infection in the ICUs worldwide [18,19]. In addition, patients underwent a recent surgery, especially digestive, are at risk of developing IC [14,20,21]. However, the high proportion of IC in ICUs in our study (47,8%), is due to the absence of oncology, hematology-oncology and neonate units in our hospital which usually have a large proportion of IC cases [22].

Among *Candida* species, *C. albicans* was the most frequent etiologic agent of IC in our study

(42% of the isolates). In recent years, we are witnessing a change in the ecology of *Candida* species with a trend towards non-albicans *Candida* species [4,7]. This fact seems to apply to Tunisia because the proportion of IC cases caused by *C. albicans* found in our study (42%) is lower than that overall in a study conducted in the region of Sousse (64%) 10 years earlier [16]. This change seems to be linked to the selective pressure associated with the excessive use of antifungal drugs, to individual patient risk factors and clonal outbreaks [2,3].

In this study, *C. parapsilosis* was the most common non-albicans *Candida* species (19,6%), in accordance with some studies which reported an increase in the frequency of IC due to *C. parapsilosis* in Tunisia [15,23]. In Algeria, *C. parapsilosis* was even ranked first with 36,6% of all IC isolates [24]. Fluctuations in the proportion of IC cases caused by *C. parapsilosis* over the five years is probably linked to his ability to cause nosocomial outbreaks [25]. Indeed, *C. parapsilosis* adheres to catheters, colonize intravascular devices and prosthetic materials and has also been frequently isolated from human hands suggesting that colonization on healthcare worker's hands may lead to infection [25].

During the five-year study period, the proportion of *C. tropicalis* isolates increased significantly from 8,3% to 20,5% (p<0,01). In a previous study conducted in Sfax region (Tunisia) in 2011, *C. tropicalis* was the most common species (37,7%) responsible for candidemia [15]. Recently, this species was also reported as the most prevalent yeast species causing candidemia in Algeria [26]. Indeed, *C. tropicalis* is considered by many as the second most virulent *Candida* species, behind *C. albicans* [27].

Species distribution by specimens showed that non-albicans *Candida* species was especially seen in blood cultures (70%) and CVC (60%) with high frequencies of *C. parapsilosis* which was the most isolated species, right after *C. albicans*. This is probably linked to its particularity as a typically commensal of human skin and its ability to colonize medical devices as explained earlier [25].

The distribution of *Candida* species according to different wards of Sahloul Hospital showed that *C. albicans* was mostly isolated in surgical wards (56,1%). The preponderant involvement of C. albicans in peritonitis (78,6%), which occurs mostly in surgical environment, explains its high frequency in Surgical department. Our results are consistent with other studies which reported that C. albicans is responsible of 58% to 73% of *Candida* peritonitis [28,29]. In the other hand, non-albicans *Candida* species were more frequently isolated in ICUs (63,6%) which is consistent with literature [13,30].

The emergence of drug-resistant *Candida* strains has become a serious threat to patients with IC worldwide [25]. In our study, the fluconazole (FCZ) resistance rate was the highest (6,7%) in all *Candida* strains followed by echinocandins (EC) (3,4%), amphotericin B (AmB) (2,9%), and voriconazole (VCZ) (2,9%). Overall, resistance to antifungal agents varies among *Candida* species.

For AmB, we noticed high MIC ranges (≤0,25-16 µg/ml) and two resistant strains to AmB among the less-common/unidentified *Candida* species. Globally, despite 50 years of polyenes use, resistance to AmB remains exceptional but higher MIC values and some resistances have been demonstrated with the less-common *Candida* species samely to our results [31].

Regarding to azoles, we found high-level FCZ resistance with *C. glabrata* (22,2%) strains, similar to the resistance rate reported by **Sellami et al.** (Tunisia) in 2011 (23,5%) [15]. Indeed, this specie is well-known for its high rates of azoles resistance and possesses the capacity to develop resistance after the first contact with this drug [32]. However, the resistance rate of *C. glabrata* strains found in our study is higher than the global average (8 to 16%) [7,33,34]. This is probably due to the massive use of FCZ in Tunisia, particularly in our institution, due to its availability and low cost compared to other drugs [35]. In the same way, *C. parapsilosis* FCZ resistance rate (7,4%) was higher than global surveillance data (0 to 5,4%) [2,33,34]. In the last years, *C. parapsilosis* strains have been found to be increasingly resistant to azoles worldwide [36]. For *C. tropicalis*, we did not find any resistance strain to FCZ. This is reassuring compared to the 3% FCZ resistance rate reported by **Sellami et al.** and the 31,5% recently reported in Algeria [15,26]. The less-common *Candida* species, also exhibited high FCZ resistance rate (16%) and a high MIC90 (8 µg/ml). All *C. krusei* isolates were resistant to FCZ (100%). This was expected because *C. krusei* has an intrinsic resistance to FCZ [36]. In addition, one *C. guilliermondii* and three unidentified isolates (*Candida* species) were resistant to FCZ. According

to **Colombo et al.** in 2017, *C. guilliermondii* has an intrinsic decreased susceptibility to azoles [31].

As *Candida* species have become more resistant to azoles, the use of EC to treat IC has increased worldwide [25]. In our study, overall resistance to EC was 3,4%. Among *Candida* species, *C. parapsilosis* had a resistance rate of 5,6% and a high MIC90 (1 µg/ml) with caspofungin. These results are not so worrying since *C. parapsilosis* has an intrinsic low susceptibility to EC, with MIC values for EC being naturally higher than other *Candida* species [25]. Despite that, infected patients respond well to EC treatments even with high MIC values, but a higher dose of caspofungin (100 mg/24h) with

Candida parapsilosis systemic infections is recommended [38]. In our study the fact that all *C. glabrata* strains were susceptible to EC is reassuring because a rising EC resistance of C. glabrata in the USA was reported and poses a serious challenge for clinical therapy [39].

In recent years, multidrug-resistant (MDR) *Candida* species are starting to emerge due to the widespread (and misuse) of antifungal drugs [31]. Globally, *C. glabrata* and *C. auris* are the main *Candida* species associated with multidrug-resistance [31]. Fortunately, until today, there was no evident proof of the presence of *C. auris* in Tunisia. Nevertheless, we must remain vigilant especially when it comes to unidentified/less-common *Candida* species. In our study, two strains (one unidentified strain, *Candida* species and one *C. guilliermondii*) were simultaneously resistant to three antifungal agents, AmB, FCZ and EC. The VITEK®2 system used in our study was reported to misidentify *C. auris* as *C. haemulonii, C. famata* or *C. lusitaniae* [40-42]. Indeed, further investigations are planned for these two MDR strains in order to identify these strains by molecular sequencing or by using matrix-assisted laser desorption ionization time of flight mass spectrometry (MALDI-TOF MS) [40-42].

Conclusion

The present study provides valuable local surveillance data on the epidemiology and antifungal susceptibilities of invasive *Candida* species in Sahloul University hospital (Sousse, Tunisia), which can be useful to guide an appropriate empiric and targeted antifungal therapy. We noted that in ICUs, IC were mainly caused by non-albicans *Candida* species. These species exhibited high FCZ resistance and represented a large proportion of candidemia and catheter-related candidemia cases. Therefore, knowing the lack of financial means, the early use of echinocandins as first-line treatment, as recommended worldwide [38], should be prioritized with ICU patients. In surgical department, C. albicans was the most involved species, especially in *Candida* peritonitis. This species exhibited low antifungal resistance rates. Therefore, the use of FCZ for these patients is still approved as recommended by the European Society of Intensive Care Medicine and the European Society of Clinical Microbiology and Infectious Diseases which stipulate that FCZ can be used in less severe patients and in setting with low rate of FCZ resistance [38]. We recommend a continuous surveillance of the local epidemiology in order to detect any potential changes in *Candida* species distribution and antifungal susceptibilities.

Study limitations

Our study had some limitations. First, this was a retrospective conducted at a single hospital. However, to the best knowledge, it is the first report about invasive candidiasis in Tunisia. Other reports focused only on candidemia or some specific populations. Second, the absence of oncology, hematology-oncology and neonate units in our hospital, may underestimate the impact of these infections, but at the same time, shows their high incidence in ICU and surgical wards. To remedy these limitations, a parallel prospective study was carried out in ICUs in order to better understand the impact of IC.

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