

Yeast Infections: Epidemiological and Mycological Profile of Different Yeasts Isolated at the Hassan II University Hospital of Fez

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Background and study aim: The current study aims to identify the epidemiological and etiological profile of all the yeast infections diagnosed in the laboratory of Parasitology-Medical Mycology of the CHU HASSAN II of Fez.

Patients and Methods: This is a retrospective study spread over 5 years, from November 2015 to November 2020, concerning 3672 mycological samples, and including superficial samples taken in the Parasitology-Medical Mycology laboratory (nail scales, skin, scalp, various swabs ...) as well as deep samples (CSF, BAL, blood culture ...), received from different hospital services of the Hassan II University Hospital of Fez. Among these samples, 472 patients were confirmed as carriers of superficial or deep yeast infection after a mycological study (direct examination + culture) of each sample.

Results: Of these 3672 patients, 472 were confirmed as carriers of yeast infections, that is a prevalence of 12.8 %. The average age of our patients is 37.61 years.

Yeast mycotic disease was more common in women than in men, with a sex ratio M/F=0.76. *Candida sp* was the prevalent genus (92.37%), followed by *Cryptococcus sp* (3.38%), *Geotrichum sp* (2.33%), *Trichosporon sp* (1.48%), and *Malassezia sp* (0.42%). These different fungi were responsible for different clinical conditions, some isolated from superficial samples dominated by onychomycosis (38.34%), and others from deep samples dominated by fungemia (31, 19%).

Conclusion: Yeast diseases are becoming more and more known, ranging from simple superficial damage to systemic infection. *Candida albicans* is the most commonly identified species, but with the emergence of new species, the incidence of non *albicans Candida* and other yeasts is continuously increasing. Therefore, given their different susceptibility to antifungal agents, their identification remains necessary.

INTRODUCTION

The yeast infections are the infections caused by yeast fungi, which have a very broad clinical spectrum.

Compared to the whole fungal world, the number of yeasts encountered in human pathology is very low. They have different biological characteristics, but they are essentially opportunistic, they express their pathogenicity only when there are risk factors. *Candida albicans* represents the most commonly implicated species, however, other non *albicans* species such as *Candida tropicalis*, *Candida parapsilosis*, *Candida glabrata*, and *Candida krusei*, are increasingly being reported as agents

of mycoses. Other yeasts of the genus: *Trichosporon*, *Malassezia*, *Geotrichum* and *Cryptococcus* may exceptionally be the cause of superficial mycosis, as they can be responsible for deep systemic infections in immunocompromised patients. The current study aims to determine the epidemiological profile of yeast mycosis at the Hassan II University Hospital in Fez, and to show that the clinical spectrum of yeast fungal infections is very broad, ranging from skin and nail superinfection to systemic dissemination.

MATERIALS AND METHODS

Study design: It is a retrospective study

Study settings: This is a monocenter study concerned all mycological samples from patients hospitalized in the different departments of the Hassan II University Hospital of Fez, HASSAN II University Hospital is a tertiary referral center in the North of Morocco , and also from other patients coming from other clinical center for a mycological sample, during the period from November 2015 to November 2020 . This work exploited the data reported on the registers kept at the laboratory of Parasitology-Mycology of the CHU HASSAN II of Fez.

Inclusion criteria:

- Patients with a yeast infection.
- Any age
- Both gender
- whatever their immune status

Exclusion criteria:

- All species of fungi that are not part of the yeast fungi were not included in the study.

The samples were processed in two steps: direct examination, the objective of which was the analysis of the product with direct observation in the fresh state, after clarification, or after staining (MGG) and the systematic culture of the sample in three media (Sabouraud , Sabouraud added with chloramphenicol and Sabouraud added with cycloheximide).

A sample is considered positive when a fungus is detected on direct examination and on culture when it is a superficial sample. Deep samples are considered positive when direct examination and/or culture are positive.

The isolation and identification of fungal elements were based on morphological (macroscopic and microscopic examination), phenotypic (filamentation test), biochemical (use of sugar assimilation tests (galleries)), and immunological (agglutination tests of latex particles sensitized by monoclonal antibodies) , as well as the use of indirect diagnostic methods (Research of circulating antigens) necessary to diagnose invasive mycoses often fatal in immunocompromised patients.

RESULTS

The study population consisted of patients who came from different health facilities for a mycological examination at the laboratory of parasitology and medical mycology of the HASSAN II University Hospital of Fez .During the study period, we collected a total of 3672 mycological samples, of which 472 were confirmed positive for yeast infection, with a sex ratio M/F equal to 0.76 in favor of women. The age of the patients varied from 0 months to 88 years with an average of 37.61 years.

During the study period, the number of specimens varied from year to year with an average of 612 specimens per year. The annual incidence of cases is shown in **table and figure 1**.

We note that the lowest prevalence of positive samples for yeast infections predominate in 2019 and 2020. This decrease can only be explained by the containment that was imposed following the covid 19 pandemic.

The different samples were either superficial samples collected in the Parasitology-Mycology Department (n=237 or 50,21 %) or deep samples from different departments of the Hassan II University Hospital of Fez (n=235 or 49,78 %), these services were grouped into 4 main categories: Intensive Care, Surgery, Hematology and Oncology (adults and children), and Medicine. (**Table 2**)

We note that the most exposed services are intensive care (41.27%) and onco-hematology (24.68%).

Onychomycosis are the most common superficial infections in our series with 181 cases or 76.05%, followed by mycosis of the ENT sphere with 19 cases (7.98%), mycosis of the scalp with 16 cases (6.72%), and finally epidermomycosis (13 cases) and genital mycosis (9 cases).

As for deep samples, they are dominated by fungemia with 73 cases or 31.19% and broncho-pulmonary samples with 70 cases or 29.91%.

The yeast infections observed in our study were due to 5 genera of yeast. The genus *Candida* remains the most frequently implicated yeast in both superficial mycosis (93.27%) and deep mycosis (91.45%).

The *albicans* species represents 50% of superficial yeast infections and 42.73% of deep

yeast infections. It is implicated in 48.06% of nail mycosis and 64.2% of lung mycosis.

The non *albicans* species were predominant in deep samples, mainly in blood cultures, of which *Candida tropicalis* was in first place, followed by *Candida parapsilosis*, *Candida glabrata* and *Candida krusei* (Table 3).

The *Cryptococcus* genus is mainly represented by *Cryptococcus neoformans* affecting 6.83% of deep mycosis, it was isolated in 16 cases, mainly from serum and cerebrospinal fluid, with only one case of cutaneous cryptococcosis.

Geotrichum sp was identified in 11 specimens (2.33% of cases), of which 08 cases were onychomycosis.

Other yeasts such as *Malassezia sp* and *Trichosporon sp* were mainly involved in superficial skin mycosis, representing 0.4% of cases.

Regarding the immune status of the patients, we find that 56.77% (n=268) are immunocompetent, while 43.22% (n=204) have different types of immunosuppression. The distribution of the different yeasts isolated according to the immune status of the patients is shown in Table 4. There is a predominance of *Cryptococcus sp* (n=12) in immunocompromised patients, and other species in immunocompetent ones.

Table1: Annual prevalence of yeast cases

Years	Total number of samples taken	The cases of yeast infections listed					A.I (%)	
		<i>Candida sp</i>	<i>Cryptococcoccus sp</i>	<i>Geotrichum sp</i>	<i>Trichosporon sp</i>	<i>Malassezia sp</i>		
2015	52	20	0	3	0	0	23	44,2%
2016	731	162	2	7	2	1	174	23,8%
2017	801	80	1	0	3	1	85	10,61%
2018	832	77	4	1	1	0	83	9,9%
2019	760	60	2	0	0	0	62	8,1%
2020	496	37	7	0	1	0	45	9,07%
total	3672	436	16	11	7	2	472	

(A.I : annual incidence)

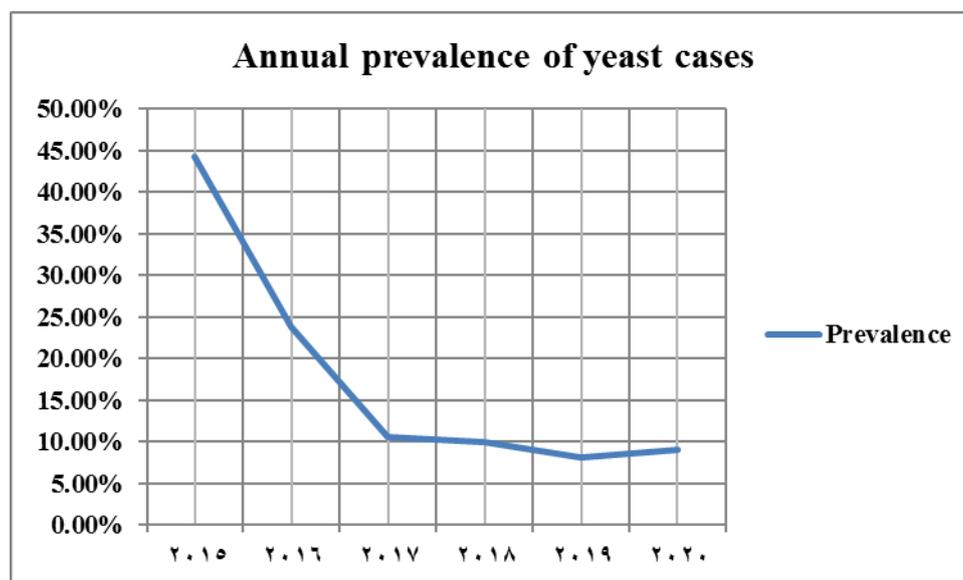


Figure 1: Annual prevalence of yeast cases

Table 2: Distribution of deep samples received (n = 235) in the parasitology-mycology department according to the service of hospitalization.

Service	%(n=235)
Surgery	12,76% (n=30)
Medicine	21,27% (n=50)
Intensive Care	41,27% (n=97)
Hematology and Oncology	24,68% (n=58)

Table 3: Distribution of the main yeast species according to samples.

			<i>Candida sp</i>						<i>Cryptococcus sp</i>	<i>Geotricum sp</i>	<i>Trichosporon sp</i>	<i>Malassezia sp</i>	
			<i>C.A</i>	<i>C.T</i>	<i>C.P</i>	<i>C.G</i>	<i>C.K</i>	others NAC					
SM	Nail	181	87	12	14	0	0	54	0	8	6	0	
	Skin	12	5	3	0	1	0	1	0	1	0	1	
	Scalp	16	8	0	0	0	3	5	0	0	0	0	
	ENT	19	13	0	0	1	3	2	0	0	0	0	
	Sphere												
	Genital Sphere	9	6	0	0	3	0	0	0	0	0	0	
DM	Serum	81	21	13	12	12	6	8	9	0	0	0	
	CSF	8	1	0	0	0	0	1	6	0	0	0	
	Cornea	14	3	3	2	1	2	3	0	0	0	0	
	Urine	13	6	2	0	2	1	2	0	0	0	0	
	Respiratory tract	70	45	5	0	4	2	11	0	2	0	1	
	Pus	20	12	1	1	0	2	4	0	0	0	0	
	Biopsy	7	3	0	0	0	0	2	1	0	1	0	
	KT	10	5	1	2	2	0	0	0	0	0	0	
	other liquids	12	4	2	0	3	2	1	0	0	0	0	
	Total	472	219	42	31	29	21	94	16	11	7	2	

C.A : *Candida albicans* *C.T* : *Candida tropicalis* *C.P* : *Candida parapsilosis*
C.G : *Candida glabrata* *C.K* : *Candida krusei* CNA : non albicans *Candida*
SM : superficial mycosis DP : deep mycosis

Table 4: Distribution of the different yeasts identified according to the immune status of the patients.

yeasts	immune status		Total
	immunocompetent	immunocompromised	
<i>Candida</i>	113	106	219
<i>Candida non albicans</i>	137	80	217
<i>Cryptococcus sp</i>	4	12	16
<i>Geotricum sp</i>	7	4	11
<i>Malassezia sp</i>	1	1	2
<i>Trichosporon sp</i>	5	2	7
	268	204	472

DISCUSSION

In recent years, fungal infections involving yeast fungi have gained considerable importance, not only because of their superficial localizations, but especially because of their deep invasions

due to increasingly aggressive treatments, transplants and immunosuppression [1].

The spectrum of yeast fungal flora in our study is rich and varied. We have noticed that superficial yeast infections, dominated by onychomycosis,

are more frequent than deep yeast infections. This increase may be related to the increased need of patients to be treated for these affections, and to the systematic realization of mycological samples in front of the least suspicion of a superficial mycosis. Invasive yeast infections affecting very vulnerable patients, either because of an underlying pathology or because of immunosuppressive therapy, are continuously increasing [1].

Superficial mycosis, whether cutaneous or phanerial, are a common reason for dermatological consultation. As for our study, onychomycosis dominated the superficial mycosis encountered, whose isolated fungal spectrum was reserved by *Candida albicans*. [2,3].

Invasive candidiasis accounts for approximately 80% of all systemic fungal infections. *Candida sp* is currently the fourth most common microorganism in the world causing nosocomial sepsis (8 to 10%) [4]. In our study and most studies, *Candida albicans* remains the leading species (40-73%) [5,6].

Candida albicans is the most prevalent species both in our series and in other studies [2, 3,4]. However, in recent decades, we have observed an increase in the prevalence of non *albicans Candida* species in both deep and superficial areas, particularly *Candida parapsilosis* and *Candida glabrata* [1]. This may be due not only to changes in the fungal spectrum, but also to improved identification techniques, particularly chromogenic medium, which allows better identification of the association between non *albicans Candida* and *albicans Candida* [1].

Candida tropicalis ranks second in our series, which is consistent with other studies [7,8], while it was ranked the third species in other series [9,10]. It was mainly identified in nails and blood cultures. However, *Candida parapsilosis* comes in third position, its frequency has increased significantly, and this has also been noticed in Latin America, and Spain where it occupied the second and first place respectively (25%) [11,12]. Exogenous acquisition of this species is usually associated with intravascular access and parenteral nutrition [5].

Candida glabrata and *Candida krusei* occupy fourth and fifth place, respectively, in the present study, whose emergence is attributed primarily to their natural resistance to fluconazole. In

contrast, *Candida glabrata* is the only species that has been steadily increasing over the past decade in the United States, accounting for 20-24% of candidemias [5]. But, it is less common in most other countries, studies from Europe [13], Taiwan [14], and Canada [15,16] indicate that *Candida glabrata* has not increased despite excessive use of fluconazole in these countries.

Emerging strains of non *albicans Candida* have been isolated such as *Candida kefyr* and *Candida famata*, but they remain in the minority although their isolation rate has increased in recent years [5].

Cryptococcosis is an opportunistic mycosis, frequently observed in HIV infected subjects, its neuromeningeal form is constantly increasing in Morocco [17]. It occurs occasionally in immunocompetent subjects, and in the present study, we have collected two cases of cryptococcosis in immunocompetent patients.

Geotrichosis and trichosporonosis are diseases caused by yeasts usually isolated from the skin and nails [18]. The pathogenic role of these yeasts in superficial involvement is still poorly defined because it is difficult to determine simple colonization from real infection [19,20].

For *Geotrichum*, we isolated in our series 8 cases of onychomycosis, 2 cases in a sputum sample, and one case of intertrigo. For each of these cases, the mycological examination showed the presence of yeasts on direct examination and the culture was pure and abundant without isolation of another etiological agent as recommended for the involvement of a mold [21]. Under these same conditions, we identified *Trichosporon sp* in 6 cases of onychomycosis and in one skin biopsy. Furthermore, *Trichosporon sp* onychomycosis is not uncommon, as a Korean study found *Trichosporon sp* to be the second most common cause of onychomycosis [22]. These cases should prompt reconsideration of the pathogenicity of these emerging fungi, especially since these superficial infections could be invasive infection [19]

Malassezia sp has been implicated in this series in 2 cases, The yeasts of the genus *Malassezia* are yeasts that have undergone a crucial taxonomic evolution and a great interest in human and animal pathology. These microorganisms, colonizing the superficial layer of the skin, can pass from the commensal state to the parasitic due to several exogenous and

endogenous factors causing various skin diseases such as: pityriasis versicolor which is the clinical form most described in the literature [23].

CONCLUSION

Isolation of a yeast does not always indicate its pathogenicity. The results obtained must be taken into consideration according to the clinical data and the presence of possible risk factors. The therapeutic protocol for mycoses is based on local antifungal topicals for localized forms and systemic treatment for disseminated forms.

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Ethical approval: Approved.

HIGHLIGHTS

- The incidence of fungal infections involving yeast fungi has increased considerably in recent years
- Clinical spectrum of yeast infections is very broad, ranging from simple superficial damage to systemic infection.
- *Candida albicans* is the most commonly identified species
- With the emergence of new species, the incidence of non-*albicans Candida* and other yeasts is constantly increasing.

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