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# Cutaneous Candidiasis at the Avicenne Military Hospital in Marrakech: A Five-Year Assessment

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**Abstract** **Original Research Article**

***Background***: Candidiasis is a disease caused by yeasts of the genus Candida. They can be mucocutaneous or deep. The objective of this work is to describe the epidemiology of cutaneous candidiasis. ***Patients and Method*:** This retrospective study covers five years (01/2017 to 12/2021). It includes all superficial and deep samples sent to or taken from the mycology-parasitology laboratory of the Avicenne military hospital in Marrakech. ***Results*:** In our series, Candida onychomycosis was most common in women. The age group most affected by *Candida* onychomycosis was between 45 and 60. The majority of patients were outpatients. Onychomycoses were mainly found on the fingers. For epidermomycosis, the sex ratio was 1. No cases were affected by epidermomycosis in the 16 to 30 age group. Most patients with epidermomycosis were outpatients. Involvement of hairless skin accounted for 41.66% of all epidermomycosis diagnosed. For Candida otitis externa, the average age was 44.18 years. The sex ratio M/F was 0.75. Eleven patients were outpatients. The most frequently isolated species was *Candida albicans*. ***Conclusion***: Candidiasis is an opportunistic infection favored by several factors. The *Candida albicans* species remains the most common cause of candidiasis, although *non-albicans* species are increasingly present with the emergence of new strains.

**Keywords***:* Cutaneous candidiasis, *Candida albicans*, onychomycosis, epidermomycosis, candida otitis externa.



## INTRODUCTION

Candidiasis is an opportunistic infection that manifests as superficial or deep-seated damage, often resulting from an imbalance in the microbial flora. The Candida genus comprises over two hundred species, but only ten or so are involved in the disease process, the main one being *Candida albicans*. Many other species are also described, such as *Candida tropicalis*, *Candida parapilosis*, *Candida glabrata* and *Candida krusei*, which are increasingly isolated from biological samples. Cutaneous-mucosal candidiasis includes cutaneous candidiasis (nail candidiasis, epidermomycosis, *Candida* otitis externa, etc.*)* and mucosal candidiasis (genital candidiasis, urinary candidiasis, oral-pharyngeal candidiasis....). They are favored by local factors such as maceration, sweat, humidity and local trauma. Deep-seated or systemic candidiasis involves deep-seated organs (kidneys, lung parenchyma, heart, Etc.). They may be either primary or secondary to candidemia. The incidence of candidiasis is rising remarkably with the emergence of new pathogenic species. Our study aims to investigate the epidemiological profile of cutaneous candidiasis diagnosed at the Avicenne military hospital.

## MATERIAL AND METHODS

We conducted a retrospective study spread over five years from January 1, 2017, to December 31, 2021, involving 2876 mycological samples taken in the parasitology-mycology laboratory at the Avicenne military hospital in Marrakech. Regardless of age, we included patients hospitalized at the hospital or outpatients referred to the parasitology laboratory for mycological sampling in the case of suspected cutaneous candidiasis with a positive culture. We excluded any patient who did not present to the department, any registered patient without any epidemiological information, and any patient with a negative or contaminated culture. From the laboratory mycology registers, we collected age, sex, inpatient or outpatient department, sampling site, direct examination and

culture results. Data were reported and analyzed on a Microsoft Office 2013 Excel file.

Mycological samples are taken by an experienced laboratory technician using sufficient quantities of sterile material at a distance from any local or general antifungal treatment. Because yeasts and bacteria multiply rapidly, the sample is sent immediately to the laboratory or stored at 2-6°C. The sampling method differs according to the site and type of sample. It is a study on a fresh state, either by mounting in an unstained liquid (physiological serum or distilled water) or by using lactophenol blue, which allows better visualization of blastopores or other stains such as May-Grunwald-Giemsa (MGG). In the case of nail scales or fragments, 30% potash is used to lighten the sample before covering it with a clean slide. Two to three drops of sterile physiological water are added to the swab sample. Microscopic observation of the preparation is carried out under a light microscope after 15 minutes of action of the clarifying liquid at low and high magnification (objectives x20, then x40). If positive, fungal elements (mycelial filaments, spores or budding yeasts) can be identified. Cultures are generally performed on Sabouraud's medium supplemented with chloramphenicol (+/-gentamicin) to inhibit associated bacterial growth. Actidione® (cycloheximide) is also frequently added, as it inhibits the growth of most filamentous fungi likely to contaminate cultures. However, it also inhibits the growth of certain pathogenic *Candida* species, such as *Candida glabrata*, *Candida tropicalis* and *Candida parapsilosis.* Yeasts develop after 24 to 48 hours at 27°C to 37°C, with colonies appearing white, creamy and shiny. Yeasts were identified using the blastesis test, the chlamydospore test and API 20 C AUX galleries.

## RESULTS

### 1. Epidemiological data

We included 2876 patients. Females were most affected (67.54%), with an M/F sex ratio of 0.48. The average age was 46, with extremes ranging from 2 months to 81 years. The age group most affected was between 46 and 60. Age was not recorded for 63 patients. 165 patients were outpatients (86.39%), and 26 were inpatients (13.61%).

### 2. Mycological profile:

*Candida albicans* was incriminated in (75.39%) (Figure 1).

### 3. Clinical groups of mucocutaneous candidiasis:

In our series, Candida onychomycosis was most common among women (75.96%), with an M/F sex ratio of 0.31. The age range most affected by Candida onychomycosis was between 45 and 60. Of the 104 patients with Candida onychomycosis, only one was hospitalized, while 103 were outpatients. The location of onychomycoses was observed on the fingers in 67 cases; on the toes in 18 patients, while 6 cases had both locations (Figure 2). The location of 13 onychomycosis samples was not specified. The most common onychomycosis species was *Candida albicans* (84.62% or 88 cases), followed by *Candida glabrata* (5 cases), *Candida tropicalis* (4 cases), *Candida albicans/dubliniensis* complex (4 cases), *Candida famata* (2 cases), *Candida parapsilosis* (2 cases) and a single case of *Candida guilliermondii*.

For epidermomycosis, the sex ratio was 1. No cases were affected by epidermomycosis in the 16 to 30 age group. Age was not recorded for five patients. Most patients with epidermomycosis were outpatients (91.67%). Epidermomycosis were divided into two clinical groups according to the site of involvement: involvement of the folds and involvement of the glabrous skin. Involvement of the glabrous skin represented 41.66% of all epidermomycosis diagnosed (**Table I**). The most frequently isolated species was Candida albicans, with 75% (9 isolates). *Candida parapsilosis* and *Candida famata* were found in just one sample, as was *Candida guillermondii*.

For *Candida* otitis externa, the average age was 44 years, with extremes ranging from 5 to 72 years old. The age group most affected by Candida otomycosis ranged from 46 to 60. The age of patients was not recorded in 3 cases. Eight women (57.14%) were affected by otomycosis, compared with 6 men (42.86%), with an M/F sex ratio of 0.75. Eleven patients were outpatients. The most frequently isolated species was *Candida albicans* in the external auditory canal, with 57.14% (8 cases), followed by *Candida parapsilosis* with 3 cases (21.43%), 2 cases of the *Candida albicans/dubliniensis* complex and a single case of *Candida dubliniensis.*

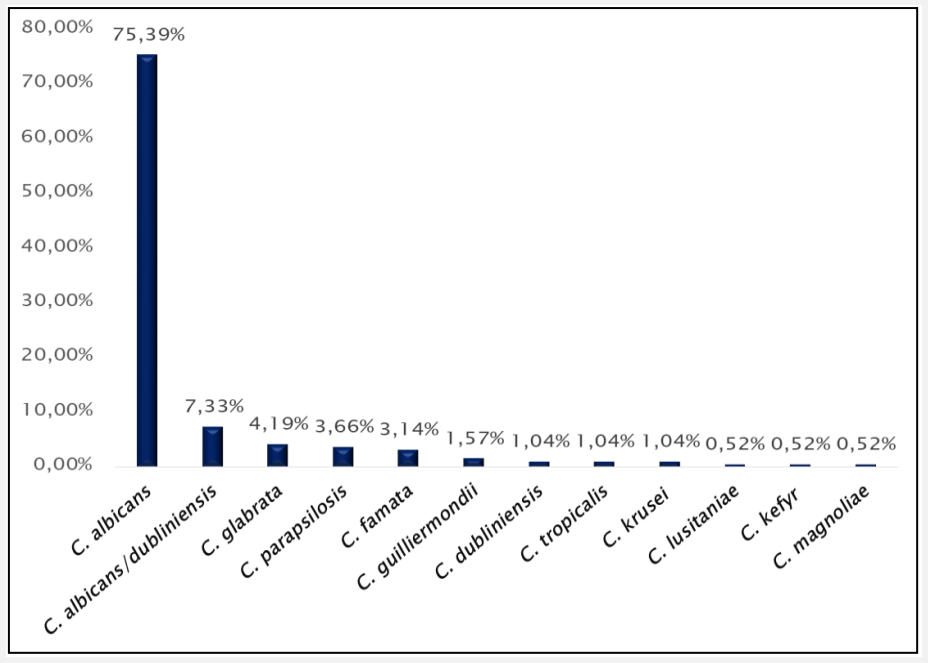


**Figure 1: Distribution of species implicated in cutaneous candidiasis**

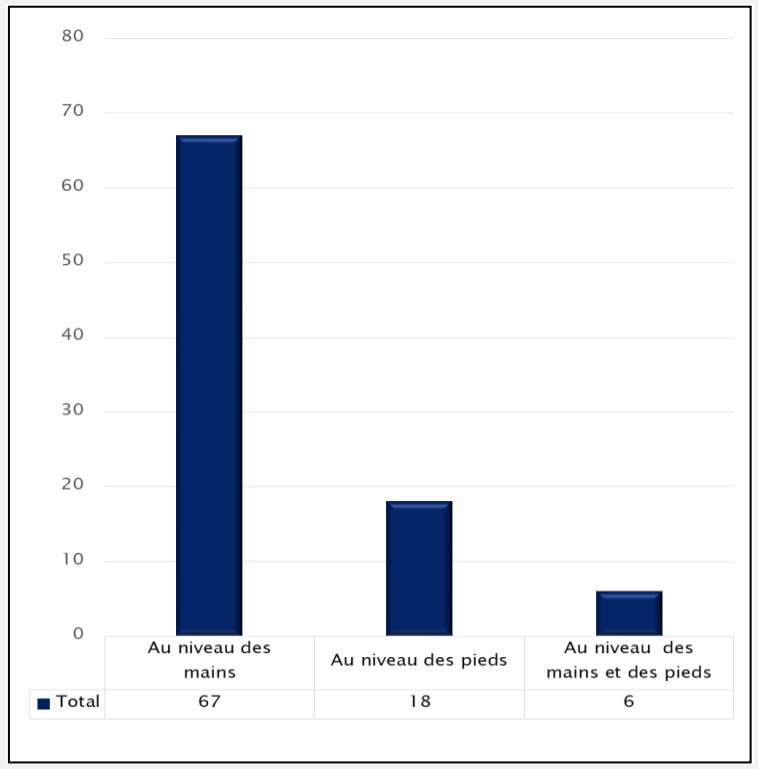


**Figure 2: Distribution of onychomycoses according to location**

**Table I: The distribution of *Candida* epidermomycoses according to location.**

| **Location** | | **Number** | | **Percentage** | |
|---|---|---|---|---|---|
| Folds | Small folds | 6 | | 50,00% | |
| | Large folds | 1 | 7 | 8,33% | 58,33% |
| | Main | 1 | | 8,33% | |
| | Feet | 3 | 5 | 25,00% | 41,66% |
| | Hands and feet | 1 | | 8,33% | |
| Total | | 12 | | 100% | |

## DISCUSSION

Cutaneous mycoses are among the most common dermatological infections worldwide, with a prevalence of 20-25%, depending on the region. They are caused by various pathogens, including dermatophytes, yeasts and molds [1]. The prevalence of fungi varies from region to region and over time due to cultural habits, migratory phenomena, lifestyle changes, population aging, socio-economic conditions, climate change and therapeutic evolution with access to antimicrobial, antifungal and immunosuppressive drugs [2].

Onychomycosis was our series' most frequently reported condition (54%). This aligns with several studies that found nail candidiasis the most frequent clinical group [3-5]. However, in the study carried out in China [3], cutaneous candidiasis dominated the clinical picture, whereas, in the Tunisian study, mucosal candidiasis was the most frequent [4]. In our series, *Candida albicans* remained the most incriminating species, in line with the literature, with a rate of 75% versus only 17% of *non-albicans Candida*. Similar high rates were observed in other studies [4, 5], where *Candida albicans* was the most isolated germ, with proportions of 55% and 67%, respectively, versus 44% and 32% for non-albicans species. In contrast, other studies obtained lower rates, as in India [6], with 36% *Candida albicans.* The high frequency of *Candida albicans* is explained by its ability to survive under challenging conditions and its high pathogenic power [7]:

- Genetic variability is expressed by translating a different genetic code, which prevents using vectors in *Candida albicans.*
- *Candida albicans* exhibit considerable morphological variability. It has several stages: blastospore, pseudomycelium, germ tube, mycelium and chlamydospore, and is capable of spontaneously and reversibly changing from yeast to mycelium. This cellular transition enables it to present two totally different transcriptomes, with differential expression of genes involved in morphology, adhesion, sexual behavior, antigenicity and pathogenicity [8].
- High adhesion capacity on host cells [9].

Onychomycoses are caused by fungi, which can be dermatophytes, non-dermatophyte molds or yeasts. They are not only contagious and unsightly but often recurrent [10, 11]. On the other hand, Candidiasis onychomycosis is uncommon, accounting for only 10% to 20% of cases [12]. They are mainly observed in patients exposed to favorable factors such as microtrauma, certain professions with prolonged exposure to water and sugar (catering and food professions), diseases such as psoriasis, trophic disorders of the lower limbs in elderly subjects, hyperhidrosis of the hands, peripheral vascular diseases, diabetes and HIV infection. Other factors include ageing, corticosteroids, immunosuppressants and broad-spectrum antibiotics [13].

Nail involvement was the main site of cutaneous candidiasis in our study, with a prevalence of 54.45%. Similar rates were reported in other national and international studies [3, 5, 14, 15]. In our survey, onychomycosis was more frequent in women, with a prevalence of 75.96% versus 24.04% in men, with an M/F sex ratio of 0.3. This same trend was observed in several similar studies carried out in Indonesia (116), Brazil [17], Serbia (118) and Japan [19], with 75%, 75%, 84.7% and 72.46% of cases, respectively. This clear predominance of women may be due to cultural and behavioral factors, such as household chores with prolonged, repeated contact with water and cleaning products, wearing protective gloves, excessive manicure care, microtrauma, and aesthetic concern expressed mainly by women. Physiological differences, such as the slower rate of nail growth and the finer structure of the nail plate in women (0.5 mm vs. 0.6 mm in men), may also be involved.

Regarding age, the preponderance of onychomycoses was observed in adults over 46. The 0 to 15 and 16 to 30 age groups were the least affected. These results concur with those reported in Serbia [18] and Brazil [17], with an average age of 50 and 65, respectively. A study carried out in Indonesia [16] and Senegal [20] confirmed this predominance in adults over 46, with a prevalence of 53.7% and 50.1%, respectively. These results can be explained by reduced nail growth, poor blood circulation, repeated microtrauma and the inability to ensure adequate nail care, general factors such as diabetes and immune response deficiency usually present in older people, and venous insufficiency more accentuated with age [21]. Onychomycosis, on the other hand, is rarely seen in children due to the rapidity of nail regrowth, the different structure of the nail bed, the small nail surface and the rarity of trauma in young children [22]. Advanced age can be deemed as a risk factor for onychomycosis.

Concerning lesion location, the results of our series confirm the literature's findings that candida onychomycosis is more common in the fingernails. Indeed, our study found that 73.62% of cases were localized to the fingernails, compared with 19.78% to the toes and 6.59% to both. This clinical distribution aligns with national and international studies [23, 5, 24, 25, 26, 27, 28, 18, 29, 30]. In contrast, lower prevalences of hand localizations were reported in Saudi Arabia [31] at 53.3% and in Indonesia [16], where hand involvement was present in 22.62% of all patients and associated finger and toenail involvement in 42.59%. These results may be explained by patient neglect of this type of localized foot disease [28], contact with detergents and citrus fruits, and prolonged hand contact with water. Nail involvement of the toes is rare and often indicates

superinfection of onycholysis of another origin (haematoma, psoriasis) [32]. In Indonesia, farmers and fishermen tend to work barefoot. They are, therefore, more exposed to nail trauma and prolonged foot contact with water or damp environments, which may explain the more frequent cases of candida onychomycosis of the toes. *Candida albicans* was the species most implicated in candida onychomycosis. Indeed, our study reported a rate of 84.62% or 88 cases. At the same time, NCAC species were less isolated and represented by *Candida glabrata* with 5 cases, *Candida tropicalis* with 4 cases, *Candida famata* (2 cases), *Candida parapsilosis* (2 cases) and a single case of *Candida guilliermondii*. Several studies reported similar mycological profiles [23, 5, 24, 25, 26, 27, 28, 18, 29, 30]. In contrast, other authors have reported that NCAC species are the most frequent etiology in Colombia [33], Iran [30], Taiwan [34], France (Lyon region) [35], Serbia [18] and Brazil [17]. A comparison of the results reveals a change over time in the *Candida* species isolated. In fact, the relative frequency of the albicans species has decreased while that of the other species has increased. Furthermore, in the literature, the NCAC species most frequently isolated in candida onychomycosis is *Candida parapsilosis*, whereas, in our series, it was present in only 2 cases.

Epidermomycosis candidiasis is a skin infection most often caused by *Candida albicans.* In our study, epidermomycosis accounted for 6.28% of all diagnosed cutaneous candidiasis. This result is in agreement with that obtained in the same laboratory [23] in 2015, with a prevalence of 6.16%, while higher rates were reported in Rabat [5] with a majority of 28.35%, in Dakar [2] and China [3] with 14.43% and 52.36% respectively. In our series, there was an equal distribution of the two sexes with six male and six female cases, whereas, in 2015, we found a male predominance in the same laboratory [23] with a rate of 58.82%. Moreover, most authors have affirmed this male predominance [37, 38, 25, 36]. This may be explained by men's greater physical activity, which exposes them to perspiration and maceration. Of all the epidermomycosis diagnosed in our series, most patients were adults over 60. This may be explained by factors favoring intertrigo's appearance, such as rubbing and maceration, primarily found in elderly unattended patients and those who sweat profusely. This finding is in line with those described in similar Moroccan studies [5, 25, 23, 24], in China [3], Japan (119), France [39] and Algeria [40], where adults aged over 60 were most affected. Our results show that the preferred location for candidiasis is intertrigo, with 5 cases of inter-digito-plantar intertrigo and one case of inter-digito-palmar intertrigo, and the ample folds, followed by hairless skin, especially on the feet. These results align with other studies reported in Algeria [40] and Tunisia [41]. In our series, there was a higher prevalence of localization in the feet, in contrast to the literature [42-44]; this may be linked to the high level of physical activity and the use of occlusive footwear in military patients, causing moisture and maceration of the inter-toe spaces [43].

Candida otomycoses are fungal ear infections caused by the *Candida* genus. They account for 5 to 30% of all otitis externa, most often chronic or subacute. However, they can also affect the middle ear and, in severe cases, even the inner ear [45]. The diagnosis of fungal otitis is based on clinical data. When in doubt, a mycological examination is of great value [46]. Fungal otitis is frequently encountered in tropical and subtropical zones due to environmental conditions (scorching and humid climate). It is favored by manipulating the external auditory canal (EAC) and its cleaning, either with cotton swabs or administering ear drops and wearing hearing aids [47] and the presence of dermatosis in the EAC, particularly eczema [45]. The prevalence of *Candida* otomycosis varies from country to country. In Tunisia [48], *Candida* is the most prevalent species of fungal infection of the EAC, accounting for 62.7%, while in Serbia [49], the prevalence of candida otomycosis is almost similar to that of mold (45.6%/48.9%). These rates of otomycosis highlight the progressive importance of fungi in the development of ear infections. The variation in the prevalence of candida otomycosis may be due to inclusion criteria, the geographical location studied, climatic conditions, and the value of mycological examination in diagnosing fungal otomycosis. Concerning gender, a slight female predominance was observed, with an M/F sex ratio of 0.75. This has been observed in other studies, notably those carried out in Iran [50] and Serbia [49], while other studies carried out in India [51], Nigeria [52] and Spain [53] noted a predominance of males. This variation in results shows that gender is not a factor in otomycosis. In our work, the strains incriminated in otomycoses are dominated by *C. albicans*, which does not exist in a saprophytic state on skin and dander. Therefore, any isolation of *C. albicans* from an ear swab must be considered pathogenic. This predominance is also observed in Serbia [49] and China [54]. However, *Candida parapsilosis* was the most implicated in several studies [49, 50, 54], whereas it was isolated in only 21.43% of cases in our series. In the literature, *Candida parapsilosis* is most often implicated in chronic, non-acute otitis externa [55]. This difference in results can be explained by the method on which the study is based (morphological or molecular), hence the need for molecular studies to provide precise data concerning the microbial epidemiology of otomycosis.

## CONCLUSION

Candidiasis is a public health problem, and its incidence rises steadily as the population at risk increases. Diagnosis is generally tricky and requires a combination of anamnestic, clinical and mycological data. The ideal management approach is to prevent local and general risk factors parallel with antifungal treatment. The results of our study confirm the continuing change in the mycological profile of candidiasis due to the emergence of several new species and the trend towards non-albicans species, which are becoming more and more frequent. However, *Candida*

*albicans* is still the species most frequently incriminated in cutaneous-mucosal and deep-seated infections.

**Conflict of Interest:** No

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