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The Mycology Profile in Immunocompromised Patients of CHU Mohammed VI of Marrakech

Kamissoko Sidiki[1*], Tangara Mariam[1], Belmekia Amine[1], El Hakkouni Awatif[1]

[1]Department of Parasitology-Mycology, Arrazi Hospital, CHU Mohammed VI, Marrakech

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***Corresponding author:** Kamissoko Sidiki
Department of Parasitology-Mycology, Arrazi Hospital, CHU Mohammed VI, Marrakech

Abstract **Original Research Article**

***Introduction*:** This Moroccan study focuses on fungal infections in immunocompromised patients, a particularly vulnerable population. Conducted over two years at CHU Mohamed VI in Marrakech, the research involved 271 patients with various forms of immunosuppression. ***Result*:** The results reveal that Candida spp. led the identified pathogens, accounting for 39.5% of cases, with a predominance of Candida albicans (56%). Dermatophytes occupy the second position (24%), followed by Aspergillus spp. (8.5%). Notably, researchers observed a worrying resistance to fluconazole in 28% of cases, while amphotericin B retains excellent efficacy (98% sensitivity). ***Discussion*:** The detailed analysis shows distinct profiles according to the underlying pathologies : HIV patients mainly present candidiasis, diabetics develop dermatophyte infections, and cases of mucormycosis occur exclusively in the latter population. The most concerned departments are those of infectious diseases, dermatology and hematology. These findings highlight several key issues. On the one hand, early diagnosis requires more sophisticated techniques such as molecular biology. On the other hand, therapeutic management must adapt to the emergence of resistance to common antifungal agents. The authors emphasize the importance of close collaboration between different specialists to optimize the management of these serious infections. ***Conclusion*:** This research provides valuable data for the Moroccan and African context, while confirming some trends observed on a global scale. It also opens up avenues for improving diagnostic and treatment strategies in hospital settings.

Keywords : Mycological Infection, Immunosuppression, Mycological Diagnosis, Morocco.

1. INTRODUCTION

The increasing incidence of infections caused by human fungal pathogens is a major public health problem, particularly in immunocompromised patients [1]. These patients, weakened by diseases such as HIV/AIDS, immunosuppressive treatments (chemotherapy, transplantation) or congenital immune deficits, are particularly vulnerable to invasive mycoses, whose severity and lethal potential are high. Fungi such as *Candida spp., Aspergillus spp.*, and *Cryptococcus neoformans* are frequently involved, with mortality rates reaching 40% for candidemia (Pappas *et al*., 2016) [2], and exceeding 50% for invasive aspergillosis in neutropenic patients [3, 4]. These infections share similarities with some parasitoses, such as Pneumocystis jirovecii *pneumonia*, underlining the complexity of opportunistic infections and the need for an integrated approach. An estimated 6.5 million cases of invasive fungal infections occur worldwide each year, resulting in 3.8 million deaths attributable to the infection [5]. Global Action against Fungal Infections (GAFFI) has recently estimated that 3,300,000 people in Morocco (9% of the population) suffer from a fungal infection each year [6].

Despite diagnostic and therapeutic advances, fungal infections remain under-diagnosed and under-treated due to the difficulty of early diagnosis, increasing resistance to antifungal agents (e.g. *Candida glabrata* resistant to fluconazole, Pfaller and Diekema, 2007) [7], and lack of effective prophylactic strategies.

Faced with these challenges, this study aims to analyze the mycology profile of immunocompromised patients in Morocco, identifying predominant pathogens and assessing associated risk factors.

2. METHODS AND MATERIALS

This is a retrospective descriptive study conducted over 2 years. It took place at the parasitology department of the Mohamed VI hospital in Marrakech.

2.1 Study population

- **Inclusion Criteria**:

To minimize sampling bias, we included all cases of immunocompromised patients (HIV/AIDS, organ transplantation, neutropenia, immunosuppressive therapy, diabetes) in this study showing clinical or biological signs of fungal infection.

- **Exclusion Criteria:** Non-Exploitable Records, and Contaminated Samples
- **Sample Size**: 271 patients selected over a period of 2 years in the Mohamed VI university hospital in Marrakech.

2.2 Collection and Mycology Examination

Sampling immunocompromised patients is a delicate procedure for the diagnosis of fungal infections, which can be particularly serious for these individuals due to their weakened immune systems.

Samples received in our department were blood samples from fungal hemoculture vials, tissue samples (biopsies of various tissues), respiratory samples (sputum, broncho-alveolar lavage, bronchial aspiration), Punctures of various liquids (cerebrospinal, joint, pleural, pericardial, ascites...), urinary sampling, skin samples, nails, swabs from various sites, etc. In all cases, sampling was guided by the clinic.

Samples were taken in strict aseptic conditions, collected in sterile vials adapted to the type of sample and sent to the laboratory in accordance with the recommended conditions and deadlines.

Upon receipt of samples, after validation of the pre-analytical stage, a part of each sample was subjected to a systematic direct microscopic examination after treatment according to the nature of the sample: microscopic observation in the fresh state between slide and lamella and after colouring at May Grunwald Giemsa (MGG) of the prepared smears. China ink staining was performed for all CSF received, on centrifugation pellet.

Each sample received was seeded on a Sabouraud dextrose agar (SDA) culture medium with 0.5 g/l chloramphenicol with or without cycloheximide, and incubated at 30-35°C and 25-27°C in an aerobic environment.

The fungal haemocultures were incubated on BD Bactec® system.

Yeast species grown in culture were identified by Vitek ® 2 COMPACT (Biomerieux) and MaldiTof, or Api 20 C AUX biochemical galleries from Biomerieux.

For filamentous fungi (dermatophytes, pseudodermatophytes and molds), the identification was based on the time of growth and the morphological aspects macroscopic and microscopic of the colonies.

Aspergillary serology (ECL.Virclia Lotus Automatic Chemiluminescence Immunoassay (CLIA) produced by Vircell and distributed in Eurobio Scientific) was performed at the clinician's request on (LBA) or serum.

Interpretation of the results considered clinical data, favoring factors, anatomical site of sampling and direct examination and culture results.

2.3 Diagnostic Methods

- **Direct examination and Culture**: Blood samples, sputum, cerebrospinal fluid, and tissue biopsies.
- **Serological tests**: Detection of fungal antigens (galactomannan, β-D-glucan and specific antibodies.
- **Medical imaging**: Computed tomography (CT) and magnetic resonance imaging (MRI) to assess the extent of injury.

2.4 Statistical Analysis

Data was analyzed using SPSS (version 25.0) and collected from the farm forms and imported into an Excel spreadsheet. The statistical study was mainly based on descriptive rather than analytical statistics, without using inferential statistical tests or similar methods.

3. RESULTAT

3.1 Demographic Characteristics of the Population

Parameter	Value	Comments
Average age	46,92±17,52	Extremes (3 – 91) years
Sex ratio (H/F)	1,17/0,86	146 Men (54%) 125 Women (46%)

A wide range (3-91 years) indicates a diversity of the population at risk (child, adult, elderly)

Children (<18 years): (12.3%) mainly in pediatric hematotherapy (84%), with predominance of C. albicans (67%)

Adults (18-65 years): (72.8) peak between 35-50 years (HIV and transplanted)

Elderly (>65 years): (14.9%) 92% with comorbidity

The sex-ratio was in favor of a slight male predominance (54%) but without significant difference in fungal infections

3.2 Distribution of Identified Fungal Pathogens

Pathogenic	Number of cases (%)	Details
Candida spp.	107 (39,5%)	*C. albicans* (56%), *C. glabrata* (3%)
Dermatophytes	65 (24%)	*T. rubrum* (45%), *T. mentagrophytes* (35%)
Aspergillus spp.	23 (8,5%)	*A. fumigatus* (48%), *A. flavus* (43%)
Mucorales	3 (1,1%)	Mucorales spp All in diabetics.

Figure 1 : Distribution of fungal pathogens by type of immunosuppression

The most involved pathogens in this study were yeast of the genus Candida dominated by C. albicans (56%), followed by dermatophytes (T. rubrum 45%) and Aspergillus (A.fumigatus 48%).

3.3 Pathogen Distribution by Hospital Service

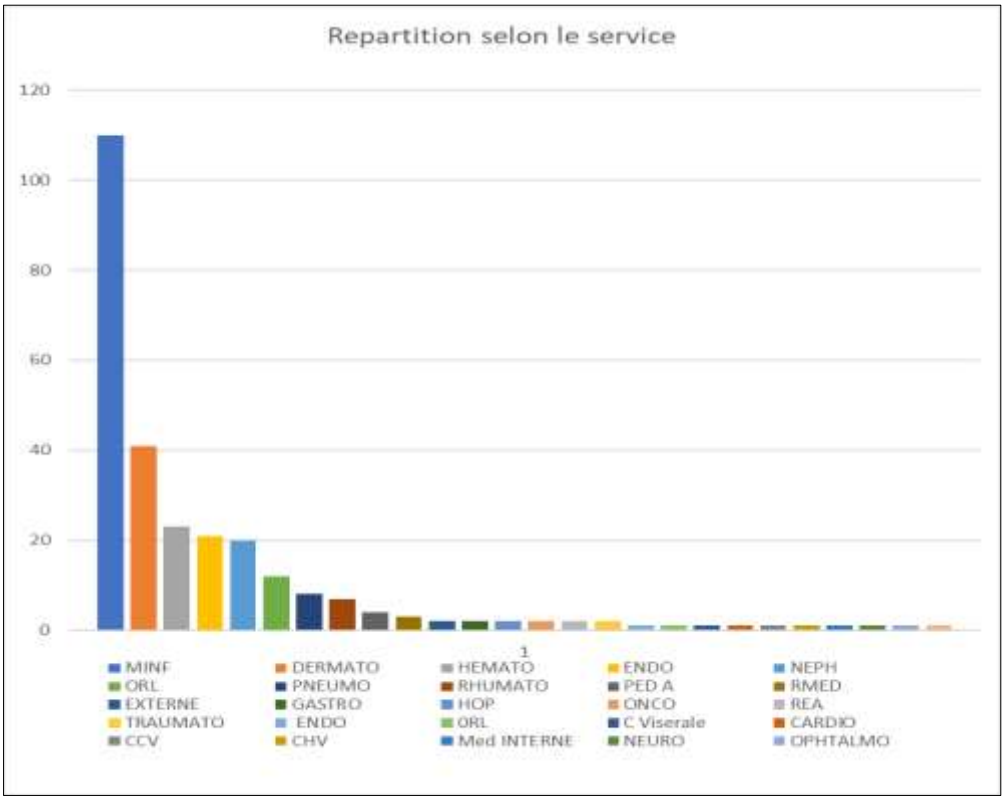

Figure 2 : Fungal pathogen distribution by department

The most affected services were infectious diseases (40.6%), dermatology (15.1%) and clinical hematology (8.5%).

3.4 Distribution According to Immunosuppression

Pathology	NUMBER OF CASES	DOMINANT PATHOGENS	REMARKS
Diabetes	45%	*Candida* spp., dermatophytes (*T. rubrum*), *Aspergillus flavus*	Frequent onychomycosis, associations with *Mucorales* (3 cases).
HIV	30%	*Candida albicans* (70%), *C. dubliniensis* (15%), *Cryptococcus* (1 case)	Predominant oropharyngeal and pulmonary candidiasis.
CHIMIOTHERAPIE	15%	*Candida* spp. (including *resistant C. krusei*), *Aspergillus fumigatus*	High risk of invasive candidiasis.
Transplantation	10%	*Candida* spp., *Aspergillus* spp	Deep infections (storage fluids).

Figure 3 : Distribution of pathologies

- **HIV**: Dominance of *Candida albicans* (mucous membranes) and rarity of aspergilloses (except in case of associated neutropenia).
- **Diabetes**: Preponderance of dermatophytes (nails) and risk of angio-invasive mycoses (*Mucorales*, *Aspergillus*).

3.5 DISTRIBUTION ACCORDING TO THE NATURE OF THE WITHDRAWAL

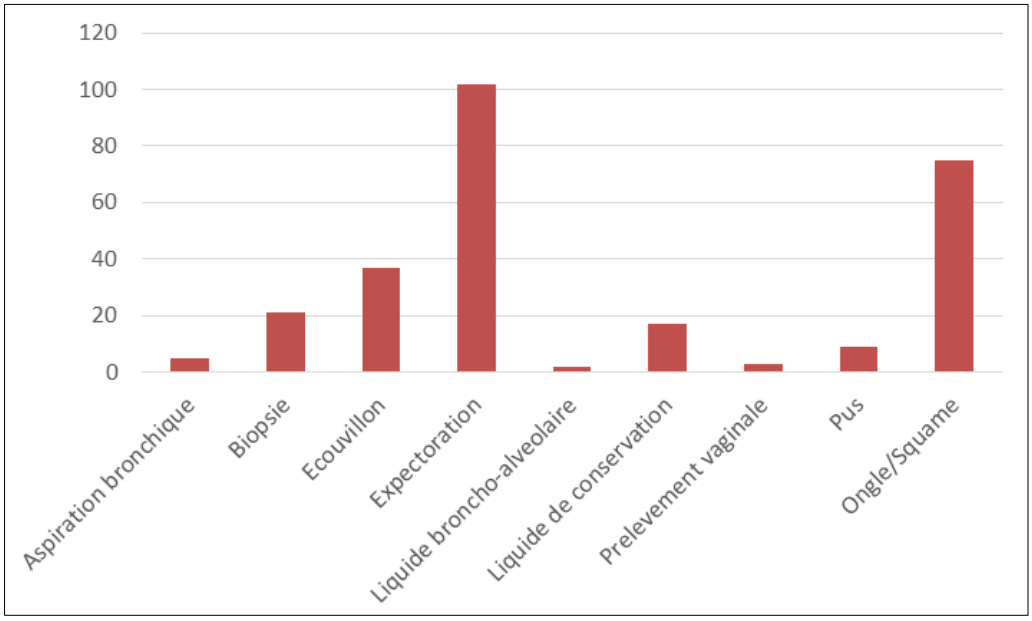

Figure 4 : Breakdown of the nature of the levy

Sputum was the most common type of sampling (38%), followed by nail/scaly samples (28%).

3.6 MAPPING OF RESISTANCES

Antifungal *Candida albicans*	Global Sensitivity	Resistance
Fluconazole	89%	11%
Voriconazole	93%	7%
Caspofungine	94%	6%
Amphotericin B	98%	2%

The table shows that amphotericin B was sensitive (98%) followed by caspofungine (94%), which is an excellent alternative with rare resistance. Voriconazole (93%) remains effective despite moderate resistance, and fluconazole (89%).

4. DISCUSSION

Fungal infections in immunocompromised patients are a major public health problem, associated with high morbidity and mortality. Our study, conducted on 271 patients of the CHU Mohamed VI of Marrakech, aimed to describe important epidemiological, diagnostic and therapeutic data on the mycological profile of this vulnerable population. The results confirm global trends while highlighting local particularities that merit further analysis.

Our study reveals that Candida spp. (39.5%) and dermatophytes (24%) are the fungal pathogens most frequently isolated in immunocompromised individuals, followed by Aspergillus spp. (8.5%). These results are consistent with literature data, where *Candida albicans* remains the main agent of invasive mycoses, especially in HIV and transplanted patients (Pappas *et al*., 2018) [8], but also increasing rates of non-albicans species have been noted worldwide, most likely linked to an increase in the misuse of antifungal drugs [9]. The prevalence of dermatophytes in diabetics (45%) is explained by their tropism for keratinized tissues (nails, skin) and the impact of hyperglycemia on immune function (Rodriguez *et al*., 2020), and a similar study was conducted at the AVICENNE military hospital in Marrakech, which was 41% consistent with our study [10]. Male predominance (54%) could be explained by greater exposure to risk factors (agricultural work, poorly controlled diabetes).

The high prevalence of *Candida albicans* (70%) among HIV patients in this population reflects its role as a marker for advanced immunosuppression (CD4 < 200/mm 3). On the other hand, the rarity of aspergilloses

(except in cases of associated neutropenia) highlights the importance of lymphocytes in the defense against *Aspergillus* (Bongomin *et al*., 2017) [11], and a study conducted at the University Hospital of Fez, shows us the rarity of often underdiagnosed aspergillary infection and highlights the frequency of aspergillary grafting in tuberculosis patients [12].

The frequent association between diabetes and infections caused by dermatophytes (*T. rubrum*) or Mucorales (1.1%) confirms the increased risk of angioinvasive mycoses in this population (Cornely *et al*., 2019) [13].

The presence of *Candida non-albicans* (including *resistant C. krusei*) and Aspergillus fumigatus *in patients undergoing chemotherapy or transplant reflects their prolonged exposure to antifungal drugs and hospital environments (Pfaller et al., 2019)* [14]. These species are susceptible to outbreaks and have reduced sensitivity to fluconazole [15].

Direct examination and culture, although standard, have limited sensitivity, especially for *Aspergillus* and Mucorales (Donnelly *et al*., 2020) [16]. In our study, sputum (main sample analyzed) identified Aspergillus in *only 8.5% of cases, highlighting the need for additional methods.*

Galactomannan and β-D-glucan antigen are tests that have improved early diagnosis of invasive aspergillosis, but their interpretation must take into account false positives (β-lactam antibiotics, dialysis) (Taccone *et al*., 2021) [17].

Fungal PCR, although not systematized in our study, represents a major advance for the rapid detection of fungal DNA in sterile samples (Clancy and Nguyen, 2018) [18].

Our study confirms a resistance to fluconazole in 11% of isolates, this to be explained by long-term treatments or therapeutic interactions. Fluconazole remains sensitive in the majority of cases a candida albicans but mainly presents resistance to *C. glabrata* and *C. krusei*, CDC (2020). Our result is a little lower than [19], which had found 96%. In contrast, amphotericin B (98% sensitivity) and echinocandins (94%) remain effective, but their use is limited by toxicity and cost. New-generation antifungal drugs such as isavuconazole and posaconazole provide an alternative to voriconazole with a better tolerance profile (Maertens *et al*., 2016) [20].

Surveillance of *Candida auriset from azolé*-resistant Aspergillus *is crucial, recently the WHO published a list of* priority fungal pathogens in which two species of candida (Candida albicans, candida auris*) are considered critical priority groups (WHO, 2021)* [21].

This study presents limitations such as the standardization of fungal PCR and integration of genomic sequencing (NGS) for accurate identification, and the combined use of biomarkers (galactomannan + β-D-glucan + PCR) to reduce false negatives.

5. RECOMMENDATIONS

- Propose a diagnostic/therapeutic protocol adapted to local resources.
- Raise awareness of the rational use of antifungal drugs to reduce resistance.
- Strengthening mycology laboratories in regional hospitals.

6. CONCLUSION

Our study confirms the prevalence of candidiasis and aspergillosis in immunocompromised Moroccan, with particularities related to diabetes and HIV. The main challenges remain early diagnosis, control of resistance and access to innovative antifungal drugs. A multidisciplinary approach involving microbiologists, infectiologists and pharmacists is essential to improve the management of these life-threatening infections.

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