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Epidemiological Profile of Candidaemia at Ibn Sina University Hospital, Rabat, Morocco: A Series of 53 Cases

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Abstract

Background: Candidaemia is one of the most frequent invasive fungal infections in hospitals and carries high mortality. Published epidemiological data from Morocco remain fragmentary, which limits the transposition of Western models to our setting. This study aimed to describe the epidemiological and mycological profile of candidaemia diagnosed at Ibn Sina University Hospital, Rabat.

Materials and Methods: A single-centre retrospective descriptive study was conducted in the Central Laboratory of Parasitology-Mycology of Ibn Sina University Hospital, Rabat, over 27 years, from January 1997 to December 2023. All patients, irrespective of age or ward, with at least one blood culture positive for a yeast of the genus *Candida* were included. Identification relied on culture on Sabouraud media and on API *Candida* or API 20C AUX strips (bioMérieux, Marcy-l'Étoile, France). Antifungal susceptibility was assessed with the FUNGITEST method (Bio-Rad, Marnes-la-Coquette, France).

Results: Among 1,724 requests for mycological blood culture, 53 episodes of candidaemia were identified, giving an overall positivity rate of 3.1%. The cohort comprised 28 women and 25 men (male-to-female sex ratio 0.89), with a mean age of 39.5 years, including five neonates (9.4%). Medical intensive care accounted for 54.7% of episodes, ahead of neonatology (9.4%) and cardiovascular surgery (7.5%). Among the 30 isolates identified to species level, *Candida albicans* remained the dominant species (43.3%), but non-albicans species were collectively predominant (56.7%), led by *C. parapsilosis* (23.3%) and *C. tropicalis* (16.7%), while *C. glabrata* remained a minority (10.0%).

Conclusion: The low number of requests and documented cases contrasted with the incidence expected in Morocco and with population-based incidences reported in Europe and the United States, arguing for major under-detection. The rank of *C. parapsilosis* and *C. tropicalis*, ahead of *C. glabrata*, brought our ecology closer to the southern European and Mediterranean pattern than to the North American one. This work documents the ecological shift towards non-albicans species and supports systematic species-level identification, standardised antifungal susceptibility testing according to EUCAST or CLSI, and sentinel surveillance integrated into an antifungal stewardship programme.

Keywords: *Candidaemia; Non-Albicans Candida; Blood Culture; Invasive Fungal Infection; Epidemiology; Candida parapsilosis; Intensive Care; Morocco; Antifungal Resistance; Medical Mycology*

Introduction

Candidaemia is now one of the most frequent invasive fungal infections in hospitals and represents a major public health issue. It ranks among the leading causes of healthcare-associated bloodstream infections, with crude mortality reaching 30% to 60% and a considerable excess hospital cost [1,2]. Worldwide, the annual incidence of candidaemia and invasive candidiasis is estimated at approximately 1,565,000 cases, responsible for nearly 995,000 deaths, corresponding to a case fatality of about 64% [3]. Defined by the isolation of a yeast of the genus *Candida* from at least one blood culture, candidaemia belongs to the broader framework of invasive candidiasis, whose disseminated forms involve deep sites and organs [1,2].

The spectrum of affected patients has widened. Beyond haemato-oncology patients, intensive care, digestive surgery, neonatology, and haemodialysis are now the main reservoirs of cases, owing to the multiplication of invasive devices, exposure to broad-spectrum antibiotics, and parenteral nutrition [1,4]. Diagnosis remains difficult: the sensitivity of blood culture does not exceed 50% in invasive candidiasis, and the time to positivity delays the initiation of treatment [5,6]. These limitations have led to increasing use of empirical treatment, particularly echinocandins, which are now recommended as first-line therapy [2].

In Morocco, despite growing clinician awareness, published epidemiological data remain scarce: the national incidence of candidaemia has only been estimated by modelling, at approximately five cases per 100,000 inhabitants per year [7].

Objective of the Study

The objective of this work was to describe the epidemiological and mycological profile of candidaemia at Ibn Sina University Hospital, Rabat, in order to document local features and guide the diagnostic and therapeutic strategies of our institution.

Materials and Methods

Study design, setting, and period

This was a single-centre retrospective descriptive study conducted in the Central Laboratory of Parasitology-Mycology of Ibn Sina University Hospital, Rabat, over a 27-year period extending from January 1997 to December 2023.

Study population: Inclusion and exclusion criteria.

All patients, irrespective of age or hospital ward, with candidaemia defined by the isolation of a yeast of the genus *Candida* from at least one blood culture bottle were included. The date of the first positive sample was taken as the date of the episode, and the initial requesting ward as the reference care unit. Successive positive blood cultures occurring in the same patient within 30 days of the first sample were attributed to a single episode. Yeast isolates not belonging to the genus *Candida*, and strains recovered from sterile sites other than blood such as ascitic or joint fluid, were systematically excluded.

Data collection

Case identification relied on the exhaustive extraction of data from the laboratory bench registers and from the laboratory information system. The variables collected were age, sex, requesting ward, reason for admission, fungal species isolated, associated positive samples from urine, respiratory specimens, and catheter tips, and, when available, the result of antifungal susceptibility testing.

Mycological techniques

Mycological diagnosis relied on direct examination of the blood culture broth followed by systematic subculture on Sabouraud media (plain, with chloramphenicol, and with cycloheximide) incubated at 37°C. Species identification was refined by the analysis of morphological and biochemical characteristics using API *Candida* or API 20C AUX strips (bioMérieux, Marcy-l'Étoile, France), supplemented

where appropriate by latex agglutination tests. Antifungal susceptibility testing was performed with the FUNGITEST method (Bio-Rad, Marnes-la-Coquette, France).

Data analysis and presentation

Data were entered and analysed using SPSS Statistics (IBM Corp., Armonk, NY). The analysis was exclusively descriptive: qualitative variables were expressed as counts and percentages, and quantitative variables as means.

Ethical considerations

The study was based exclusively on anonymised laboratory data generated during routine activity, with no intervention in patient management and no additional sampling.

Results

Over the study period, the Central Laboratory of Parasitology-Mycology received 1,724 requests for mycological blood culture, an average of 64 requests per year, and documented 53 episodes of candidaemia. The overall positivity rate was therefore 3.1%, corresponding to approximately two episodes diagnosed per year across the whole period.

Demographic characteristics

The study population comprised 28 women (52.8%) and 25 men (47.2%), giving a male-to-female sex ratio of 0.89 and indicating a slight female predominance. The cohort was predominantly adult: 48 patients (90.6%) were adults and five patients (9.4%) were neonates hospitalised in neonatology. The mean age of the whole population was 39.5 years. The age distribution thus appeared bimodal, combining a substantial neonatal contingent and a middle-aged adult population, with no notable number of elderly patients.

Distribution by hospital ward

All episodes originated from high-risk hospital sectors. Medical intensive care alone accounted for 29 of the 53 cases, that is 54.7% of the cohort. Next came neonatology, with five cases (9.4%), and cardiovascular surgery A, with four cases (7.5%). Three wards accounted for three cases each (5.7%): surgical intensive care, the emergency department, and the sampling room. The dedicated COVID-19 unit accounted for two cases (3.8%). Finally, four wards were represented by a single episode each (1.9%): endocrinology, the dialysis unit, cardiology B, and visceral surgery A. Grouped by type of activity, critical care sectors comprising medical and surgical intensive care, emergency, neonatology, and the COVID-19 unit accounted for 42 of the 53 episodes, that is 79.2% of the cohort, whereas conventional medical and surgical wards accounted for only 11 cases (20.8%).

Reasons for admission

The reason for admission could be documented in only 16 patients, that is 30.2% of the cohort. Within this subgroup, two causes were equally predominant with three cases each (18.8%): septic shock and major trauma, the latter comprising two cases of polytrauma and one severe craniofacial injury following a road traffic accident. Next, with two cases each (12.5%), came diabetic ketoacidotic coma complicating a urinary tract infection and haematological malignancies, represented by one Burkitt lymphoma and one acute myeloid leukaemia with febrile neutropenia. The remaining six reasons accounted for one case each (6.3%): febrile peritonitis, community-acquired pneumonia, postoperative course, urinary catheter colonisation, myocarditis, and COVID-19.

Overall, severe infectious conditions comprising septic shock, febrile peritonitis, pneumonia, and COVID-19 accounted for six of the 16 documented reasons (37.5%), major trauma for three cases (18.8%), and situations of immunosuppression or metabolic decompensation for four cases (25.0%). Comorbidities, device-related risk factors, and the antifungal treatment received could not be collected in a usable manner.

Species distribution

Species-level identification was obtained for 30 of the 53 episodes (56.6%); for the remaining 23 episodes (43.4%), identification was not documented in the registers. Mycological analysis of the 30 identified isolates showed a predominance of *Candida albicans*, found in 13 cases (43.3%). Non-albicans species nevertheless collectively represented the majority of isolates, with 17 strains (56.7%). They were led by *C. parapsilosis*, isolated seven times (23.3%), and *C. tropicalis*, isolated five times (16.7%). *C. glabrata* accounted for only three isolates (10.0%) and *C. krusei* for a single one (3.3%); a final isolate was identified to genus level only (*Candida* sp., 3.3%). The albicans to non-albicans ratio was therefore 43.3% versus 56.7%, and the two leading non-albicans species, *C. parapsilosis* and *C. tropicalis*, together accounted for 40.0% of the identified isolates (Figure 1).

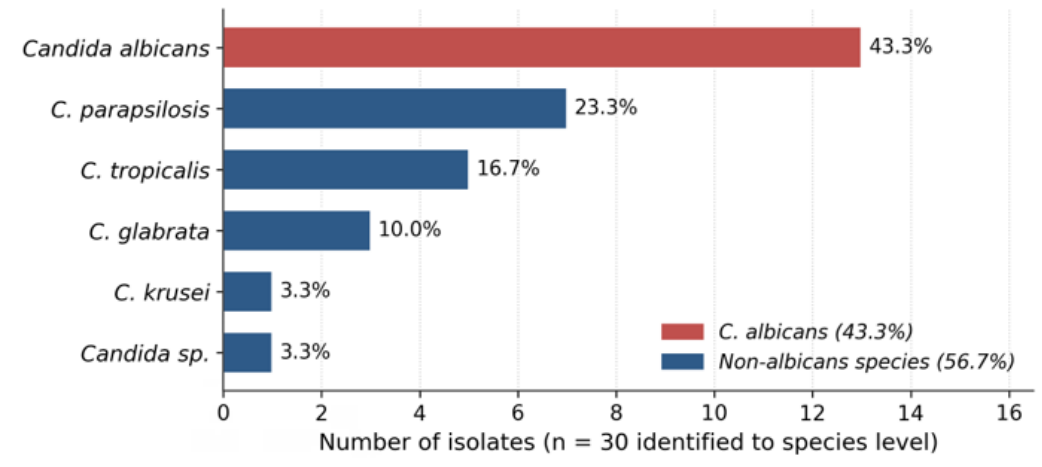

Figure 1: *Distribution of the Candida species isolated from the 30 episodes identified to species level. Candida albicans remained the leading species (43.3%), while non-albicans species were collectively predominant (56.7%), led by C. parapsilosis (23.3%) and C. tropicalis (16.7%).*

Co-isolation of *Candida* from other sites, namely urine, respiratory specimens, and catheter tips, was frequently found in intensive care patients, reflecting the systemic nature of the infection and prior multisite colonisation. The results of antifungal susceptibility testing performed with the FUNGITEST method could not be exploited in a homogeneous manner across the whole period and are therefore not reported.

Discussion

This series of 53 episodes of candidaemia constitutes the longest retrospective observation available at Ibn Sina University Hospital, Rabat. It provides useful elements of comparison with recent international data while highlighting the structural limitations of mycological diagnosis in our setting.

The positivity rate of 3.1% observed in our series lies in the lower range of published data. For comparison, the European meta-analysis by Koehler., *et al*. found a pooled population incidence of 3.88 episodes of candidaemia per 100,000 person-years, reaching 5.5 episodes per 1,000 intensive care admissions, with 30-day mortality of 37% [8]. Active population-based surveillance by the Centers for Disease Control and Prevention Emerging Infections Program across four sites between 2012 and 2016 reported a mean crude incidence

of 8.7 cases per 100,000 inhabitants, with in-hospital case fatality of 25% [9]. In Morocco, the only available national estimate, obtained by deterministic modelling, evaluated the incidence of candidaemia at approximately five cases per 100,000 inhabitants per year, that is nearly 1,800 episodes expected annually nationwide [7].

Several factors converge to explain this gap. First, the intrinsic sensitivity of blood culture does not exceed 50% in invasive candidiasis, a well-documented limitation that justified the concept of the missing 50% described by Clancy and Nguyen and the development of non-culture tests including mannan antigen and anti-mannan antibody, beta-D-glucan, polymerase chain reaction, and T2*Candida* [5]. Second, the absence of systematic use of yeast-dedicated blood culture bottles and of a continuously monitored automated blood culture system reduced diagnostic yield; the study conducted at Ibn Rochd University Hospital in Casablanca, which used Mycosis IC/F bottles on a BACTEC instrument (Becton Dickinson, Franklin Lakes, NJ), illustrated the contribution of this approach in the Moroccan context [10]. Third, frequent exposure to empirical or prophylactic antifungal therapy before sampling decapitated a proportion of episodes [1,2]. Finally, the small number of requests suggests a lack of clinical suspicion and insufficient clinico-biological communication rather than a lack of analytical resources.

This under-documentation is not specific to our centre. The systematic review by Okoye., *et al*. devoted to invasive candidiasis in Africa identified only 18,293 cases over nearly 45 years (1976-2021), of which 82% were reported by South Africa alone, highlighting a major data deficit for the whole continent, including North Africa [11].

Our series was distinguished by a slight female predominance (male-to-female sex ratio 0.89), in contrast with the majority of international cohorts. United States population surveillance found a higher incidence in men (9.4 versus 8.0 per 100,000) [9]; paediatric and adult series from Asia and South Asia similarly reported a male predominance of about 60% [12,13]. Given the limited size of our series, this inversion of the sex ratio must be interpreted with caution: it very probably reflects the case mix of the wards concerned rather than a sex-related risk factor.

The most striking difference concerned age: the mean age of 39.5 years in our cohort was much lower than in series from high-income countries. In the United States, the incidence of candidaemia was highest after 65 years (25.5 per 100,000) [9]; in Bahrain, the mean age of a recent series of 430 episodes reached 65.7 years, with mortality of 85.5% [14]. Three elements may explain this gap: the younger national demographic structure; the case mix of Moroccan medical intensive care, marked by a high proportion of major trauma and sepsis in young adults; and the relative weight of the neonatal contingent [9].

The five neonatal cases (9.4%) constituted an important epidemiological signal. Neonatal candidaemia falls within a well-identified risk profile comprising prematurity, very low birth weight, central venous catheter, parenteral nutrition, and prolonged antibiotic therapy, and is characterised in most series by a predominance of *C. parapsilosis*: 56.3% of paediatric episodes in a seven-year Turkish series [12] and 28.2% in a Chinese paediatric cohort in which neonates represented 40.5% of cases [13]. The coexistence in our series of a neonatal contingent and a high proportion of *C. parapsilosis* was therefore entirely consistent and points towards horizontal, hand-borne transmission linked to intravascular devices.

Our mycological profile confirmed the ecological transition described worldwide: *C. albicans* remained the leading species isolated (43.3%), but non-albicans species became collectively predominant (56.7%). This evolution is now well established: the systematic review conducted for the World Health Organization Fungal Priority Pathogens List documented a decrease in the relative proportion of infections due to *C. albicans* compared with other *Candida* species, while confirming its place as the leading species responsible for invasive candidiasis worldwide [15,16].

The originality of our series lay in the rank of the non-albicans species. The second species was *C. parapsilosis* (23.3%), followed by *C. tropicalis* (16.7%), with *C. glabrata* (now *Nakaseomyces glabratus*) remaining a minority (10.0%). This profile differed clearly from the

North American and northern European pattern, in which *C. glabrata* occupies second place: 39% *C. albicans*, 28% *C. glabrata*, and 15% *C. parapsilosis* in the CDC surveillance [9]; 45% *C. albicans* and 35% *C. glabrata* in a recent series from Minnesota [17]. It was, however, very close to the southern European and Mediterranean pattern: the Greek national survey placed the *C. parapsilosis* complex first (41%) ahead of *C. albicans* (37%), with a doubling of the proportion of *C. parapsilosis* between 2009 and 2018 [18]. It also matched data from the Arabian Peninsula, where *C. albicans* remained the most frequent species but the second species varied between countries with a general rise in non-albicans species [19], data from East Asia where *C. parapsilosis* (31.9%) and *C. tropicalis* (21.5%) rivalled *C. albicans* (32.2%) [20], and data from Latin America and the Caribbean, where *C. albicans* and *C. tropicalis* predominated [21]. Across the African continent, the systematic review by Okoye., *et al*. found a distribution very close to ours, with 32.6% *C. albicans* and 30.4% *C. parapsilosis* [11].

This distribution was not neutral in terms of prevention. The predominance of *C. parapsilosis* is classically associated with skin and hand carriage, biofilm formation on intravascular devices, and parenteral nutrition [2]. Its epidemic potential is further supported by the description of fluconazole-resistant clonal genotypes carrying the ERG11 Y132F substitution, disseminated across several hospitals in Spain and Italy [22,23]. Its high frequency in our series therefore constituted a signal in favour of reinforcing hand hygiene and catheter management, as much as an epidemiological marker.

The concentration of more than half of the episodes in medical intensive care (54.7%) was in full agreement with international data: the incidence of candidaemia is highest in intensive care, reaching 5.5 episodes per 1,000 admissions according to the European meta-analysis [8], and invasive candidiasis is the leading invasive fungal infection in this setting [4,24], even though the precise estimation of its incidence in intensive care remains methodologically difficult [25]. The risk factors identified in the CDC surveillance, namely a central venous catheter in 73% of patients, systemic antibiotic therapy in the preceding 14 days in 77%, and recent surgery in 33%, closely matched the reasons for admission found in our documented subgroup: septic shock, polytrauma, peritonitis, cardiovascular surgery, haemodialysis, diabetic decompensation, and haematological malignancies [9].

The frequency of urinary, respiratory, and catheter co-isolation observed in our series underlined the systemic nature of the infection and the importance of prior multisite colonisation as a pathophysiological step. It requires a rigorous search for secondary foci including endocarditis, endophthalmitis, osteoarticular involvement, and deep abscesses, in line with global management recommendations, which advise ophthalmological examination and echocardiography in at-risk patients as well as source control, in particular early removal of central venous catheters [2].

The issue of resistance surveillance extends beyond our series. The proportion of *C. parapsilosis* isolates not susceptible to fluconazole has increased markedly in global surveillance programmes, in connection with the expansion of the ERG11 Y132F genotype [26]. In *C. glabrata*, azole resistance mainly involves overexpression of efflux pumps [27]. Finally, the emergence of *Candida auris*, whose frequency is increasing in international surveillance programmes [28] and whose management remains difficult [29], calls for particular vigilance: no isolate of this species was identified in our series, but this absence could also reflect the limitations of the phenotypic identification techniques used over the period.

Our study did not allow homogeneous exploitation of antifungal susceptibility data, since the FUNGITEST method used over the period is a semi-quantitative technique that is now obsolete and does not allow determination of minimum inhibitory concentrations or classification of isolates according to current clinical breakpoints. Current recommendations require species-level identification and determination of minimum inhibitory concentrations according to EUCAST or CLSI reference methods, or by a validated commercial system [2].

From a therapeutic standpoint, global ECMM, ISHAM, and ASM recommendations favour an echinocandin as first-line treatment of candidaemia, with oral step-down to fluconazole after documentation of susceptibility and clinical improvement, catheter removal, and reassessment at 48 to 72 hours [2].

Limitations of the Study

This study has several limitations. Its retrospective and single-centre design restricts the generalisability of the findings. Mortality data, comorbidities, device-related risk factors, and antifungal treatment received could not be collected in a usable manner. Species-level identification was obtained for only 56.6% of episodes, which may have introduced a selection bias in the distribution reported. Finally, antifungal susceptibility results were not exploitable.

Conclusion

This retrospective study contributes to filling the deficit of Moroccan epidemiological data on candidaemia and clarifies the fungal ecology specific to Ibn Sina University Hospital, Rabat. It highlights three main messages: a very probable under-detection of candidaemia, attested by numbers of mycological blood culture requests and of documented cases well below expected incidences; a confirmed ecological transition towards non-albicans species, with a Mediterranean-type profile dominated by *C. parapsilosis* and *C. tropicalis*; and a concentration of cases in medical intensive care and neonatology, two sectors in which device-related prevention is decisive. Strengthening clinico-biological synergy, modernising the diagnostic chain, and implementing standardised surveillance of antifungal resistance are the priority levers for improving early diagnosis and the prognosis of these infections.

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