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► To cite this version:

J. Guitard, A.P. Bellanger, J. Dorin, S. Cassaing, A. Capitaine, et al.. Current knowledge and practice of *Candida auris* screening in France: A nationwide survey from the French Society of Medical Mycology (SFMM). *Journal of Medical Mycology = Journal de Mycologie Médicale*, 2024, 34 (3), pp.101490. 10.1016/j.mycmed.2024.101490 . hal-04675511

HAL Id: hal-04675511

<https://amu.hal.science/hal-04675511v1>

Submitted on 22 Aug 2024

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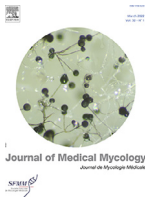
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ELSEVIER

Contents lists available at ScienceDirect

Journal of Medical Mycology

journal homepage: www.elsevier.comJournal of Medical Mycology
Journal of Mycology

Research Paper

Current knowledge and practice of *Candida auris* screening in France: A nationwide survey from the French Society of Medical Mycology (SFMM)

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ARTICLE INFO

Article History:

Received 13 November 2023

Revised 27 May 2024

Accepted 3 June 2024

Available online 4 June 2024

Keywords:

Candida auris

Screening

Diagnosis

National survey

France

ABSTRACT

Due to large outbreaks observed worldwide, *Candida auris* has emerged as a major threat to healthcare facilities. To prevent these phenomena, a systematic screening should be performed in patients transferred from regions where the pathogen is highly endemic. In this study, we recorded and analyzed French mycologists' current knowledge and practice regarding *C. auris* screening and diagnosis. Thirty-six centers answered an online questionnaire. Only 11 (30.6 %) participants were aware of any systematic screening for *C. auris* for patients admitted to their hospital. In the case of post-admission screening, axillae/groins ($n = 21$), nares ($n = 7$), rectum ($n = 9$), and mouth ($n = 6$) alone or various combinations were the body sites the most frequently sampled. Only six centers (8.3 %) reported using a commercially available plate allowing the differentiation of *C. auris* colonies from that of other *Candida* species, while five laboratories (13.8 %) had implemented a *C. auris*-specific qPCR. Considering the potential impact on infected patients and the risk of disorganization in the care of patients, it is crucial to remember to biologists and clinicians the utmost importance of systematic screening on admission.

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Introduction

Candida auris has emerged as a significant fungal pathogen over the last decade that now poses a serious threat due to its potential to trigger extensive hospital outbreaks and its common resistance to available antifungal drugs [1–4]. Moreover, *C. auris* is responsible for severe infections such as candidemia or bone infections, with a fatality rate estimated at 40 % [5–7]. This, among other factors, led the World Health Organization to classify *C. auris* in the critical group of fungal priority pathogens [8].

Our knowledge of *C. auris*' basic biology has expanded rapidly and population genetic studies have shown that *C. auris* species is split into 6 clades originating from East Asia, the Indian sub-continent, austral Africa, the northern South America (Colombia, Venezuela), Singapore and Iran [9]. Whole Genome Sequencing has revealed minimal diversity between isolates within each clade but a significant genomic divergence between different clades, consistent with their nearly simultaneous and very recent emergence as human colonizers/pathogens in multiple geographic areas [3]. Index cases diagnosed in North America and Europe are mostly imported from these different geographical areas, but subsequent autochthonous transmission, primarily hospital-acquired, is now commonly reported [10,11].

To avoid local spread within hospital settings, it is strongly advised to screen patients for asymptomatic colonization and implement appropriate measures to limit transmission between patients and shedding into the environment [12,13]. Therefore, medical microbiologists need to know the most effective strategies for detecting and identifying *C. auris* in selected patients.

Until June 2023, France has been relatively spared from major epidemics, with only 24 cases of colonization/infection reported. Most of them involved single cases or series of fewer than 5 cases within the same center (data from the French National Reference Center for Invasive Mycoses and Antifungals (NRCMA), unpublished data). However, cases of cross-contamination between patients in certain centers highlight the need to strengthen the screening strategies and diagnostic methods recommended by health agencies, the National Center for Mycoses and Antifungals, or scientific societies like the French Society for Medical Mycology (SFMM).

In this context, we conducted a survey whose main objective was to describe the current knowledge and practices of French mycologists in terms of screening and diagnosis of *C. auris*.

Materials and methods

We set up this descriptive study by asking medical mycologists or microbiologists from large French university centers and general hospitals to fill out an online anonymous form focusing on their practices for

screening and diagnosing *C. auris*. The questionnaire was available for completion from February 20th to March 31st, 2023 (Supplementary Table 1).

Results and discussion

In 2019, general recommendations were published by the French High Council for Public Health (HCSP) regarding the management of patients infected or colonized with *C. auris* [14]. The most important recommendations focused on screening guidelines upon admission and during hospitalization: body sites to be sampled for, microbiological identification of *C. auris*, therapeutic management, and measures to limit the spread of *C. auris* in healthcare facilities. This study collected 36 responses from 31 university centers and 5 general hospitals. Among the participants, thirty-one (86.1 %) were aware of these national recommendations. This may be consecutive to messages from the SFMM and the NRCMA highlighting the emergence of *C. auris* and the need for mycology labs to establish reliable method(s) for its detection and identification. However, only 14 (38.9 %) reported *C. auris* screening on admission to their healthcare facility according to national recommendations. As *C. auris* can colonize patients without symptoms, the absence of testing on admission exposes the risk of subsequent cross-contamination and the development of low-profile outbreaks. Twelve centers reported an update of the national recommendations specific to their hospital, mainly regarding the country of hospitalization (expanded list) ($n = 9$) and the type of ward (not limited to ICU) ($n = 6$) and/or the duration of previous hospitalization (not only the previous year) ($n = 5$). Seven centers reported targeted screening distantly from the admission (Fig. 1). Overall, when screening was performed, axillae/groins ($n = 21$), nares ($n = 7$), rectum ($n = 9$), and mouth ($n = 6$) alone or in various combinations were the body sites the most frequently sampled (Fig. 2). The Centers for Disease Control and Prevention in the USA recommends using a composite swab of the patient's bilateral axilla and groins to optimize the detection of *C. auris* [15]. This is in line with the recommendations recently updated by the Assistance Publique-Hôpitaux de Paris, which also recommends swabbing the nares of any patient having stayed in any healthcare facility in the previous year, regardless of the country.

It is commonly considered that a positive culture is required for a definitive diagnosis of *C. auris* infection or colonization. The macroscopic appearance of *C. auris* colonies on non-chromogenic media is identical to other *Candida* species. Culture at 40–42 °C may be valuable since *C. auris* is among the rare *Candida* species able to grow at this temperature [12,13]. Compared to other *Candida* species, the reduced growth rate previously reported for *C. auris* should extend the incubation time to at least 5 days [16]. In our survey, only three

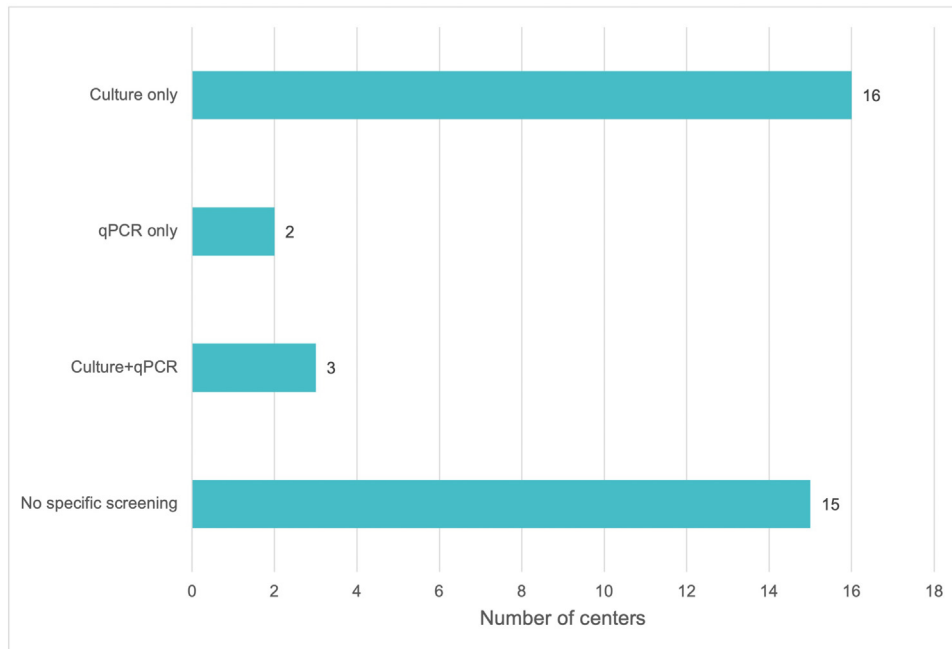


Fig. 1. Methodologies to screen for *Candida auris* in mycology labs in France 2023.

(8.3 %) participants reported using a commercially available plate (CHROMagar Candida Plus®) allowing the differentiation of *C. auris* colonies from that of other *Candida* species. Borman et al. showed that this medium promotes the rapid growth of *C. auris* with a distinctive color of the colonies (light blue with a blue halo) (Fig. 3) [17]. More recently, the specificity of this medium has been discussed, suggesting that adding fluconazole at 32 mg/ml to the “conventional” CHROMagar *Candida* medium could offer the best performances for *C. auris* identification [18]. It’s worth noting that this medium may be sub-optimal because, while rare, strains of *C. auris* susceptible to fluconazole have been reported, accounting for 7 % of the cases in the Lockard et al. study [3]. It should also be remembered that biochemical tests are inappropriate for identifying *C. auris* and may lead to erroneous identification [19]. Various PCR-based systems have been described to confirm the identification of *C. auris* [19]. Most French labs responsible for *Candida* species identification utilize MALDI-TOF mass spectrometry. Performances of this method are high but depend

on the proteomic profiles database associated with the spectrometer. Today, most commercial databases have been updated along these lines. Nevertheless, testing at least one quality control strain is advisable to ensure that a *C. auris* isolate cannot be overlooked. At date of the survey, only 17 (47.2 %) of the French labs have performed this test. Such quality control is important as misidentifications have been reported using certain commercial databases, notably with closely related species such as *Candida haemulonii* [20].

Specific qPCR offers the possibility to reduce the delay in obtaining results on the presence or absence of *C. auris* on various body sites [21]. The DNA extraction procedure before the PCR should be accounted for as it can significantly increase the turnaround of the technique. Several protocols have been described, and a few kits are commercially available [21–24]. At the time of our survey, five French laboratories (13.8 %) had implemented such a *C. auris*-specific qPCR. Three used an in-house protocol [21,22], while two utilized a commercial kit (Fungiplex *Candida auris*, Bruker). When used, qPCR

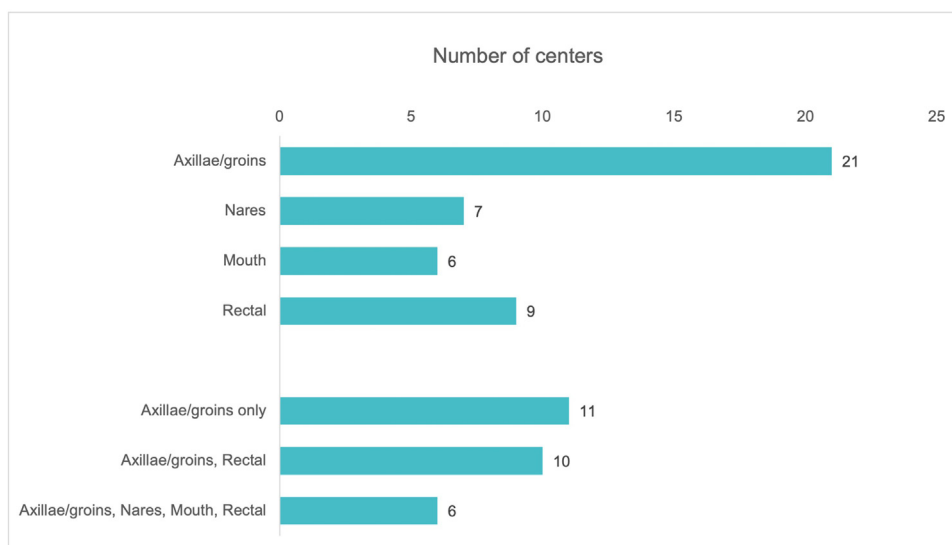


Fig. 2. Preferential body sites and combinations of sampling for *C. auris* screening on admission in France 2023.

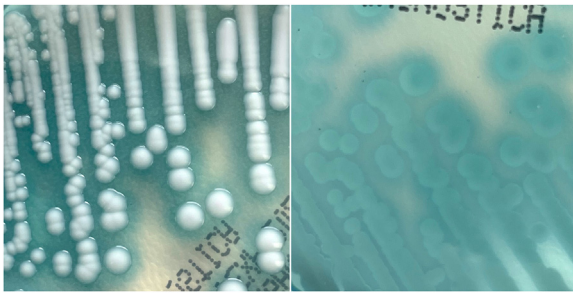


Fig. 3. Macroscopic appearance of *C. auris* colonies grown on CHROMagar *Candida* Plus medium. On the left: recto white colonies surrounded by a blue halo. On the right: verso pale blue colonies with blue halo.

was included in the screening strategy either alone ($n = 2$) or combined with culture ($n = 3$), while 16 (44.4 %) labs performed screening only by culture (Fig. 3). Currently, it is not possible to state with certainty these strategies, but including qPCR may become advisable as it has been shown that turnaround time for positive results can dramatically decrease from 141 h (5.8 days) for culture to nearly 24 h for qPCR [25]. However, a positive result only for qPCR should be interpreted with caution and attempts to isolate the strain are mandatory by adding supplementary body sites to be sampled (skin, mouth stool, hands) for culture [25].

Finally, 8 labs (22.2 %) reported isolation of at least one *C. auris* strain, all in the context of systematic screening. Recently the NRCMA released a note reporting 24 cases of *C. auris* colonization/infection (positive culture) diagnosed in France (unpublished data). In most cases, the strains were isolated from patients with a history of hospitalization in countries known to be hyperendemic for *C. auris*, but autochthonous cross-contamination has already been documented [21].

In conclusion, *C. auris* has become a major public health problem, both in the countries where it initially appeared and now worldwide. Given its propensity to trigger large outbreaks and its natural or acquired resistance to various antifungal classes, systematic screening on admission is mandatory. Whether culture should be combined with qPCR for detecting *C. auris* during screening remains debated. In any case, clinicians must be aware of this serious threat that represents a *C. auris* outbreak, with all direct and indirect consequences they may have on the care of all patients, and not just those infected with *C. auris*, admitted or to be admitted in their healthcare facility. Successful management for preventing these epidemics relies on the systematic screening of patients to identify those who are colonized and, with the help of an infection prevention team, on isolation or cohorting of colonized/infected patients to prevent the further spread of the pathogen in the healthcare facility.

The authors thank S. Jolivet, S. Fournier, A. Alanio, E. Leroux, F. Lanternier, and M. Desnos-Ollivier for fruitful discussions.

Declaration of competing interest

The authors declared no conflict of interest

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.mycmed.2024.101490.

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