PAHO

Pan American Health Organization

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Epidemiological Alert

Candida auris outbreaks in health care services in the context of the COVID-19 pandemic

6 February 2021

In view of the increase of healthcare-associated Candida auris outbreaks in the Region of the Americas and in the context of the COVID-19 pandemic, the Pan American Health Organization/World Health Organization (PAHO/WHO) recommends that Member States build capacity for early detection and effective reporting, with the goal of implementing public health measures to prevent and control its spread in health services.

Introduction

Since it was first isolated in 2009, in the external ear canal of a Japanese patient,[1] the yeast *Candida auris* (*C. auris*) has been identified as a colonizing organism and cause of infection in humans in healthcare services in several countries around the world. In most reported cases, isolates were obtained from blood cultures or cultures from deep anatomical sites. Invasive medical devices, mechanical ventilation, extended stay in intensive care units, and prior exposure to broad-spectrum antibiotics were risk factors associated with these infections.[2]

Candida auris poses a public health problem, because, unlike the other species of the genus *Candida*, it is difficult to identify, is multi-drug-resistant to antifungals (see **Box 1** for further details) and can persist in the hospital environment and spread easily among patients. These characteristics are responsible for high mortality and underscore the importance of constant clinical and microbiological suspicion, for early detection and immediate infection prevention and control measures. This requires health workers to keep their knowledge fully up to date and ensure fluid communication among the different health workers involved.

Whole genome sequencing suggests that *C. auris* arose simultaneously and independently in four regions of the world. Through phylogenetic analysis, isolates were grouped geographically into four main clades: clade I (Southern Asia), clade II (Eastern Asia), clade III (Africa), and clade IV (South America).[3] A single isolate belonging to a potential clade V has been identified in Iran.[4] It is now known that there is phylogeographic mixing of the clades, with the exception of clade IV, which presents a more defined phylogeographic substructure, with isolates mainly from South America.[5]

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Commercial methods available in standard clinical laboratories incorrectly identify *C. auris*, primarily as *C. haemulonii*, *C. famata*, *C. kefyr*, *C. duabushaemulonii, C. pseudohaemulonii*, among others. Consequently, the incidence or prevalence of infections caused by this yeast may be underestimated and its management could be inappropriate. It is important to point out that the most widely used conventional methods and automated devices in the Region of the Americas have shown limited capacity to correctly identify *C. auris.* However, the general performance of one of the automated devices with its up-to-date database seems to differ according to genetic clade, with South American isolates (clade IV) yielding the most accurate results.[6]

Protein analysis, using MALDI-TOF, with its up-to-date database, as well as molecular biology techniques (PCR) have shown to be the most reliable methods for correctly identifying this microorganism.[7-8]

Box 1. *Candida auris* antifungal resistance

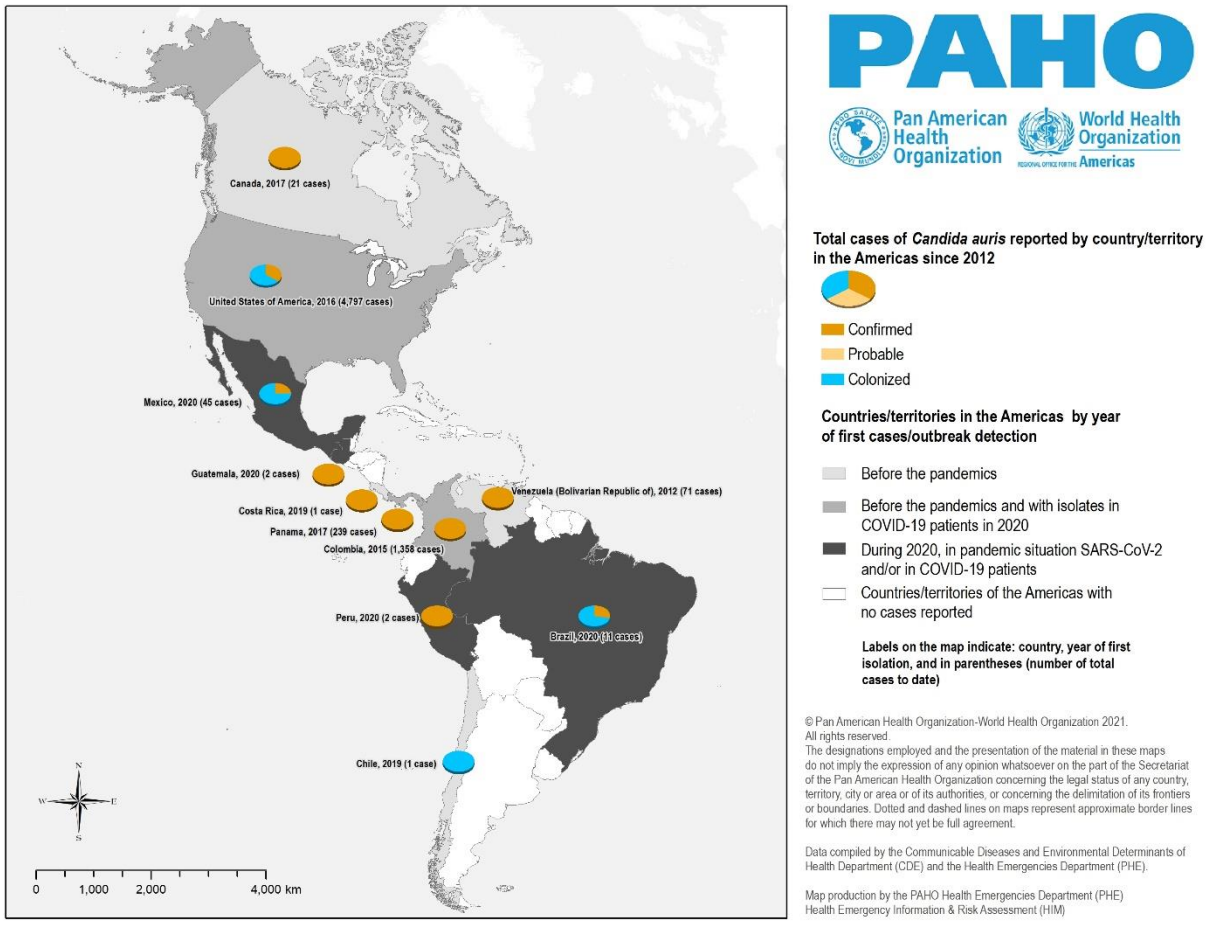
Reference institutes—the Clinical and Laboratory Standards Institute (CLSI) and the European Committee on Antimicrobial Susceptibility Testing (EUCAST)—have not yet established minimum inhibitory concentration (MIC) thresholds for different antifungals. However, using the tentative values proposed by the United States Centers for Disease Control and Prevention (CDC),[9] the South American clade presents the following resistance percentages: fluconazole (59%), amphotericin B (11%), micafungin (9 %), and 10% multi-drug resistance (MDR). It is important to point out that these percentages tend to vary according to the clade studied.[5]

Epidemiological Situation in the Region of the Americas

The first outbreak of *C. auris* in the Region of the Americas was reported in **Venezuela** in March 2012**.**[10,11] Since then, different countries have reported outbreaks and isolated cases in the Americas. Among them, in **Colombia in 2015**,[12,13] in the **United States of America** in 2016,[14] in **Panama**[15] and **Canada**[16,17] in 2017, and in **Chile**[18] and **Costa Rica**[14] in 2019. (**Figura 1**)

Both in Colombia (2016)[19] and the United States of America (2018), *C. auris* is a notifiable microorganism. This has made it possible to obtain statistical data on infection/colonization, occurrence and spread, learning about trends, and tracking and controlling outbreaks. In this regard, the CDC reported that cases in 2018 increased by 318% compared to the average number of reported cases from 2015 to 2017.[20]

Figure 1. Countries and territories of the Region of the Americas with confirmed, probable, and colonized *C. auris* cases, by year of first finding, 2012-2020.



Source: Scientific publications and reports from National IHR (International Health Regulations) focal points, as of January 2021.

Update in the context of the COVID-19 pandemic: *Candida auris* and SARS-CoV-2

The appearance and subsequent worldwide spread of the SARS-CoV-2 virus has presented a great challenge for health systems, overloading their capacity. Intensive care unit, with patients who have the greatest risk factors for *C. auris* infection, have been the most affected. In the second semester of 2020, seven countries documented cases of *C. auris*, for the most part, in patients with a history of COVID-19 infection: **Brazil**, **Guatemala**, **Mexico, Peru, Panama, Colombia, and the United States.** It is noteworthy that in the first four of these countries, no isolates of this yeast had been reported prior to this period.

In **Brazil,** on 7 December 2020, the National Health Surveillance Agency (ANVISA per its acronym in Portuguese) issued an alert due to the first *C. auris* isolate in the country, in a healthcare facility in the state of Bahia. The isolate was recovered from the catheter tip of a hospitalized intensive care unit (ICU) patient with complications from COVID-19.[21] As of 30

December 2020, two other cases had been confirmed in hospitalized patients (one positive for *C. auris* on the catheter tip and the other positive for *C. auris* in blood culture). The outbreak investigation subsequently found extensive colonization of patients and environmental contamination by *C. auris*.[22]

In **Guatemala**, in December 2020, *C. auris* was isolated in soft tissue and bone biopsies from a patient diagnosed with acute osteomyelitis of the right tibia. In addition, a second case, from the same general surgery service, was recovered from a leg tissue biopsy of a multiple trauma patient with a surgical site infection.[23]

In **Mexico**, the first *C. auris* isolate was identified in May 2020 in the state of Nuevo León, in the blood cultures of a non-COVID patient with severe endometriosis.[24] Three months later, while the hospital was transitioning from general care to exclusively caring for COVID-19 patients, 34 colonizations[25] and an outbreak of *C. auris* were identified, involving 10 ICU patients. These isolates were obtained from the bloodstream and urine. All infected patients had a history of COVID-19 pneumonia, ICU hospitalization, mechanical ventilation, urinary catheter, central venous catheter, prolonged stay, and antibiotic therapy.[26]

In **Peru**, in epidemiological week 47 of 2020, the National Institute of Health reported identification and confirmation of *C. auris* in two patients at a public hospital in Lima, both with respiratory ailments (latent tuberculosis in the first and COVID-19 in the second). While hospitalized, they were exposed to risk factors, including a central venous catheter, indwelling urinary catheter, and mechanical ventilation; furthermore, they had health care-associated infections from carbapenem-resistant *Pseudomonas aeruginosa*. Antifungal susceptibility testing found that the isolates were resistant to fluconazole.[27,28]

In **Panama**, since the beginning of the pandemic, 124 *C. auris* isolates have been identified, of which 108 correspond to patients diagnosed with COVID-19. All isolates were identified by PCR or MALDI-TOF.[29]

In **Colombia**, during the year 2020, 585 cases of *C. auris* were reported, of which 37 occurred in patients hospitalized with SARS-CoV-2 infections. These latter cases were identified in hospitals in the states of Atlántico, Bogotá, Cesar, Huila, Magdalena, and Valle.[30,31]

In the **United States**, in July 2020, the Health Department of the State of Florida, **United States**, was alerted to a *C. auris* outbreak that involved three bloodstream infections and one urinary tract infection, in four hospitalized COVID-19 patients. An investigation was then carried out to identify colonized patients. Of the 67 patients admitted to the COVID-19 unit and tested, 35 (52%) had positive cultures. The average age of the colonized patients was 69 years (range = 38-101 years) and 60% were male. Six (17%) colonized patients subsequently developed *C. auris* infection.[32]

Guidance for national authorities

The Pan American Health Organization / World Health Organization (PAHO/WHO) reminds Member States that the guidance published in the 3 October 2016 Epidemiological Alert for *Candida auris* outbreaks in health care services[33] (available at: https://bit.ly/3cAOZlM), continues to be in effect, with the addition of the following recommendations:

Case definition

Any person with a *C. auris* isolate in any samples from epidemiological screening (colonization) and/or with a demonstrated clinical infection from *C. auris*.

Epidemiological surveillance and investigation

- Raise awareness on early detection and recognition of C. auris suspect cases for health workers (physicians, nurses and auxiliary nurses) and cleaning personnel that attend to affected patients.

- In health services where a confirmed case is identified it is recommended to conduct a retrospective search for yeast isolates with an atypical resistance pattern or identification compatible with species with which *C. auris* is misidentified, in order to confirm or rule out prior presence of *C. auris* in the facility.

- All patients colonized or infected by *C. auris* who are discharged from the hospital should be flagged with a computer alert (traceability) to facilitate their identification in future hospital admissions. Furthermore, they should be microbiologically screened upon re-entry into the health system and treated as a "suspected case" until colonization by *C. auris* is ruled out.[34]

- When the epidemiological evidence points to the existence of concrete links among environmental sources, or transmission of *C. auris* persists despite strict adherence to recommendations and intervention measures, consider environmental studies, for example: swabbing of medication pumps, computer keyboards, patients' tray tables, sphygmomanometers, beds and railings, among others.[35]

Laboratory diagnosis

- C. *auris* should be suspected when conventional or automated methods isolate the microorganisms listed in **Table 1**. It is recommended to contact the national reference laboratory and relevant public health authorities in order to assess the need to remit the isolate or perform specific tests (MALDI-TOF, molecular methods) for detection of *C. auris*.

Table 1. Microorganisms for which misidentification of *Candida auris* should be suspected

Agent
C. haemulonii, C. pseudohaemulonii, and *C. duobushaemulonii,* regardless of type of sample.
Other species of the genus *Candida,* such as *C. guilliermondii*, *C. famata*, *C. sake*, *C. lusitaniae*.
Other yeast genera, such as *Rodothorula glutinis* and *Saccharomyces cerevisiae*.
C. albicans without production of germ tubes and with high MICs to azoles or to amphotericin B.

Note: The laboratory technique and database used to identify the microorganism should be taken into account.

- Regarding isolation of the *Candida* species mentioned in **Table 1**, susceptibility testing should be carried out for azoles, amphotericin B, and echinocandins using commercial methods. This should be confirmed by the broth microdilution reference method, because an unusual resistance pattern raises suspicion of *C. auris*.

- Notification of health authorities is recommended for any positive *C. auris* isolate confirmed by validated methods (MALDI-TOF whenever the species is included in the device's reference database, or molecular methods).

- For epidemiological surveillance cultures and for seeding environmental samples, modified Sabouraud broth (dulcitol as a replacement carbohydrate for glucose) with 10% NaCl can be used; this broth should be incubated at 42° C (*C. auris* is capable of growing at that temperature and salinity). Other alternatives include CHROMagar™ Candida Plus or CHROMagar™ *Candida* with added fluconazole (64 mg/L). The use of at least two different culture media is recommended.

Infection prevention and control measures

- Reinforce hand hygiene before, during, and after provision of care.

Patient isolation

- Maintain and reinforce standard precautions and contact precautions in the care of patients colonized or infected by *C. auris*.

- Single isolation of cases in individual rooms is recommended. When more than one case is identified, and single rooms are not available, cohort isolation is recommended, ensuring that beds are at least one meter apart and standard and transmission-based precautions are followed.

Screening

When a case of *C. auris* is confirmed in a health facility:

- Screen all patients who are in the same hospital ward, especially patients with: a) a confirmed case of COVID-19; b) atypical pneumonia; c) risk factors (diabetes, immunosuppression, chronic kidney disease, recent surgery, etc.); d) prolonged hospitalization in ICUs; e) invasive methods, such as hemodialysis, parenteral feeding, or mechanical ventilation; or f) use of broad-spectrum antibiotics; and g) direct case contacts.

- For screening, sampling from the axilla, oropharynx, nostrils, groin, urine, and rectum is recommended. If collecting samples from all these sites is not feasible, at least sample from the groin or axilla (pooling sample analysis can be carried out).

Environmental cleaning and disinfection

- Monitor cleaners and other health professionals use the correct personal protective equipments for contact precautions.[36]

- Clean and disinfect the patient area and surfaces (walls, floors, tray tables, beds, among others) using a disinfectant effective against *C. auris* at least daily, especially on frequently touched surfaces, including those in close contact with the patient (e.g., chairs, beds, patient tables, monitors, infusion pumps, cables, keyboards, respirator, among others). Consider the type of surface material to be cleaned and select the best disinfectant. Recommended compounds are summarized in **Table 2**.

- If the patient is isolated, clean twice a day. To monitor cleaning, the use of a log including date and time of cleaning is recommended.

- When the patient is discharged, perform terminal cleaning of the room. This should be done three times, allowing surfaces to dry between each cleaning. The health facility should use – if available – audit mechanisms (e.g., fluorescence) to evaluate the cleaning process.

- Comply with disinfectant preparation and storage standards, check the use of active components and their concentrations, and follow the manufacturer's recommended contact times for each product. Quaternary ammonium compounds are to be avoided since they are not effective.

- For more information on infection prevention and control of measures for *C. auris* colonization and infection in patients in health facilities, please refer to the aide-memoire available at: https://iris.paho.org/handle/10665.2/53247.

Table 2. Hospital disinfectant activity against *Candida auris*

Agent	Concentration*	Activity
Sodium hypochlorite	≥1000 ppm, 0.39-0.65%, 10%	High
Vaporized hydrogen peroxide	8 g peroxide/m^3	High
Peracetic acid and hydrogen peroxide <1%	1200 ppm	High
Hydrogen peroxide	0.5-1.4%	High
Ethyl alcohol	29.4 %	Moderate
Acetic acid	>5% pH 2.0	Moderate
Ultraviolet light	515 J/m^2	Moderate
Quaternary ammonium		Low

(*) Concentration based on product used. **Source:** Alastruey-Izquierdo et al., 2019.[34]

Case management

- To date, there is insufficient evidence on appropriate antifungal treatment, but the use of combination antifungal therapy as the first option or initial option is not advised, although clinicians should make case-by-case decisions.

- The first line of treatment are the echinocandins, which are used while waiting for susceptibility test results. There is data that suggest rapid development of resistance to this family of antifungals, demonstrating the importance of local resistance surveillance to guide treatment recommendations.

- Treatment of *C. auris* colonization is not recommended, although it is advisable to consider prophylaxis, according to local recommendations, in high-risk colonized patients, prior to surgery or certain invasive procedures (cardiac catheterization, percutaneous drainage, stent placement, shunt implant, solid organ transplantation, etc.).

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