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Usefulness of screening for *Candida auris* colonisation in international patients admitted to a large university hospital

Judith Heindel[1] | Janine Zweigner[2] | Frieder Fuchs[1] | Axel Hamprecht[1,3,4]

[1]Institute for Medical Microbiology, Immunology and Hygiene,, University of Cologne, Medical Faculty and University Hospital of Cologne, Cologne, Germany

[2]Department of Infection Control and Hospital Hygiene, University Hospital Cologne, Cologne, Germany

[3]German Centre for Infection Research (DZIF), Partner Site Bonn-Cologne, Cologne, Germany

[4]Institute for Medical Microbiology and Virology, University of Oldenburg, Oldenburg, Germany

Correspondence
Axel Hamprecht, Institute for Medical Microbiology, Immunology and Hygiene, University of Cologne, Medical Faculty and University Hospital of Cologne, Cologne, Germany.
Email: axel.hamprecht@uol.de

Abstract

Introduction: *Candida auris* is an emerging pathogen in health care-associated infections. In contrast to many other countries with rising numbers of *C. auris*, only seven cases have been reported in Germany from 2015 to 2017, mostly from patients who received prior medical treatment abroad. We therefore established a mandatory screening for *C. auris* colonisation at our tertiary care centre for all patients who were admitted as international patients or previously hospitalised in a foreign country within the past 6 months.

Methods: Colonisation of patients was assessed using a previously established screening protocol for multidrug resistant bacteria. Since 2017, all screening samples were additionally analysed for *C. auris* using CHROMagar Candida (CHROMagar, Paris, France). Yeast isolates were identified using matrix-assisted laser ionisation time-of-flight (MALDI TOF), except for *C. albicans* (identified by the typical green colour on chromogenic agar). Data were analysed retrospectively.

Results: Our study cohort included 655 patients and an overall number of 1399 samples. Fifty-three patients were colonised with *Candida* species (*C. albicans*, $n = 37$; *C. glabrata*, $n = 14$; others $n = 9$). No case of *C. auris* was detected. *Candida* spp. were mainly detected from respiratory samples (5.4% positive) and gastrointestinal specimen (5.2%). Laboratory costs were 14,689 € and analyses resulted in 98.7 h of additional technician's work.

Conclusion: No colonisation with *C. auris* was detected among patients with previous hospitalisation abroad. Universal *C. auris* screening of patients with any contact to foreign health care does not seem to be cost-effective in our setting and more targeted screening strategies have to be developed.

KEYWORDS
C. auris, colonisation, foreign patients, Germany, screening, university hospital

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1 | INTRODUCTION

Candida auris is an emerging pathogen leading to a wide range of health care-associated infections mostly in severely ill patients. Prolonged hospital outbreaks have been reported, which were difficult to control despite advanced infection control measures.[1] *C. auris* is intrinsically resistant to fluconazole and shows elevated MICs to multiple antifungals, including other azoles, echinocandins and amphotericin B.[2] As the species is phylogenetically related to *C. haemulonii*, laboratory identification is challenging and the correct species identification of particular importance for infection control.[3]

Within a few years of its first identification in a case of otitis externa in Japan in 2009, *C. auris* cases have been detected on five continents, with outbreaks reported in South Korea, India, Italy, Pakistan, South Africa and Venezuela.[2,4,5] India, the United States and the United Kingdom (UK) report the highest number of *C. auris cases*[6]. In the European Union, 620 cases were reported from 2013 to 2017, mainly colonisations (75.2%) and bloodstream infections (17.7%).[7] The number of new cases in the European Union between 2018 and 2019 was comparable with 2016 and 2017.[8]

Only seven cases of *C. auris* were identified in Germany from 2015 to 2017 and six of the seven patients had previously been hospitalised abroad.[9] Additionally, two patients were identified in Germany, who were colonised with *C. auris* without contact to a foreign health system.[10]

In 2018, an update of the European Centre for Disease Prevention and Control outlined the increasing risk for spread of *C. auris* in European hospitals.[11] Data from the (UK) show that *C. auris* outbreaks can be prevented by early detection in combination with isolation, enhanced infection control measures and screening.[12,13]

Admission screening in Germany is still focused on multidrug-resistant (MDR) Gram-negative bacteria and methicillin-resistant *Staphylococcus aureus* (MRSA). Until now, there are no recommended screening protocols for *C. auris* in Germany. After the first *C. auris* case admitted to our hospital in 2017, we established a mandatory screening for *C. auris* colonisation for all patients with a previous history of medical treatment or stay abroad within the past 6 months. The aim of our study was to examine if *C. auris* screening is a cost-effective detection method to decrease the risk for further transmission and healthcare-related outbreaks in our medical centre.

2 | METHODS

2.1 | Study setting and design

All international patients or patients with a history of medical treatment abroad who were admitted to the University Hospital of Cologne were regularly screened for multidrug-resistant pathogens according to the 'Kommission für Krankenhaushygiene und Infektionsprävention (KRINKO)' of the 'Robert-Koch-Institut (RKI)'.[14] Patients with a history of foreign health care treatment in six low prevalence countries (Sweden, Denmark, Norway, Austria, Switzerland and the Netherlands) were excluded from the screening. Screening sites comprised rectal swabs or stool, respiratory samples (nasal/throat swabs, tracheal secretion or sputa) plus skin or wound swabs if present. All samples submitted for screening were plated on selective agars for MDR Gram-negatives and from 2017 onwards additionally on a chromogenic *Candida* agar (CHROMagar Candida, CHROMagar). The samples were processed following the manufacturer's recommendations and incubated for 48 h at 37°C.

All yeast isolates were identified by MALDI TOF (Biotyper, Bruker Daltonics), except for *Candida albicans*, which was identified by the typical green colour on CHROMagar Candida. The same *Candida* species were counted separately if they were isolated from patients' different body sites, likewise different *Candida* species isolated from the same sample were counted separately. Data were retrieved from the laboratory information system and analysed using Microsoft Excel.

2.2 | Ethics

The authors confirm that the ethical policies of the journal, as noted on the journal's author guidelines page, have been adhered to. Patient data were obtained from the laboratory information system and documented in an anonymized form. The requirement for written informed consent was waived due to the observational, retrospective nature of this study.

3 | RESULTS

Overall, 655 patients were screened, yielding a total of 1399 samples that were analysed, including 480 respiratory specimen, 651 rectal swabs and stool samples, 68 skin/wound swabs, 171 urines and 29 unstratified swabs/biopsies, Table 1. Fifty-three patients (8.1%) were colonised with *Candida* species (*C. albicans*, $n = 37$; *C. glabrata*, $n = 14$; *C. tropicalis* $n = 3$, *C. krusei*, $n = 2$; *C. parapsilosis*, $n = 1$, *C. kefyr*, $n = 1$, *C. inconspicua*, $n = 1$, unspecified, $n = 1$), Table 2. Specimen from the rectal swabs and stool samples were positive for *Candida* spp. in 5.4% ($n = 35$) as compared to 5.2% ($n = 25$) from respiratory specimen and 1.5% ($n = 1$) from skin/wound swabs, Table 1. None of the patients screened was colonised with *C. auris*.

Of the 655 patients screened, 177 (27.0%) were colonised with multidrug-resistant bacteria (Table 3), underlining that the screened patients belonged to an at-risk population. Most patients ($n = 152$, 23.2%) were colonised with ESBL-producing Enterobacterales, 29 (4.4%) with carbapenem-resistant Gram-negatives (Enterobacterales, *Pseudomonas aeruginosa* or *Acinetobacter baumannii*) and 15 (2.3%) with MRSA.

We calculated the costs for the screening of *C. auris* for 1399 samples based on the current German Medical Fee Index (Gebührenordnung für Ärzte), amounting to a total of 14,689 € (only

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TABLE 1 *Candida* spp. isolated from 655 patients

	Species					
Specimen (n = 1399)	***C. albicans* n = 44**	***C. glabrata* n = 15**	***C. tropicalis* n = 3**	***C. krusei* n = 3**	***others* n = 4**	Total positive in %
Respiratory specimen (*n* = 480)						25 (5.2)
Nasal/throat swab (*n* = 441)	15	3	2		*C. parapsilosis* (*n* = 1) *C. kefyr* (*n* = 1)	22 (5.0)
Tracheal aspirate (*n* = 34)	2			1		3 (0.9)
Sputa (*n* = 5)						0
Gastrointestinal samples (*n* = 651)						35 (5.4)
Stool (*n* = 327)	12	3			*C. inconspicua* (*n* = 1) Unidentified (*n* = 1)	17 (5.2)
Rectal swab (*n* = 324)	10	6	1	1		18 (5.6)
Skin/ wound swabs (*n* = 68)						1 (1.5)
Groin (*n* = 45)	1					1 (2.2)
Wound swab (*n* = 16)						0
Axilla (*n* = 4)						0
Skin swab (*n* = 3)						0
Others (*n* = 200)						8 (4.0)
Urine (*n* = 171)	1	2				3 (1.8)
Unstratified swab or biopsy (*n* = 29)	3	1		1		5 (17.2)

TABLE 2 Overall number of patients colonised with *Candida* species

***Candida* species (*n* = 69)**	**Number of patients colonised with *Candida* species (*n* = 53 patients)**
C. albicans	37
C. glabrata	14
C. tropicalis	3
C. krusei	2
C. parapsilosis	1
C. kefyr	1
C. inconspicua	1
Unidentified *Candida* species	1

Note: Different *Candida* species isolated from the same patient were counted separately.

TABLE 3 Overall number of patients colonised with multidrug-resistant organisms

Number of patients colonised with multidrug-resistant organisms	
Multidrug-resistant bacteria	
ESBL-producing Enterobacterales	152 (23.2%)
Carbapenem-resistant Gram-negatives	29 (4.4%)
MRSA	15 (2.3%)
Multidrug-resistant yeasts	
Candida auris	0 (0%)

for laboratory analyses, excluding patient screening). We calculated 4.2 min working time per sample for the medical assistant technician to culture the sample, if necessary subculture it, conduct MALDI TOF and document the results, resulting in 98.7 h. For sampling of patients on the wards, we calculated 1.5 min working time per sample, resulting in 35.0 working hours.

4 | DISCUSSION

According to the recommendations of KRINKO, all patients admitted to German hospitals with high risk of colonisation by MDR Gram-negative bacteria should be screened.[14] Since there is considerable overlap between regions of high prevalence for MDR Gram-negatives and *C. auris*, screening protocols, which include both pathogen groups could be useful. Additionally, it has been shown that co-colonisation of *C. auris* with MDR Gram-negative bacteria is common especially in critically ill patients.[15] To the best of our knowledge, there is only limited data about the prevalence of *C. auris*

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in European hospitals at admission and no clear screening strategies have been established so far.[10,16]

Among 655 patients with a history of previous stay or medical treatment abroad who were screened at our institution upon admission for *C. auris*, no colonisation was detected; however, the laboratory analyses amounted to 14,689 € which would be even higher if the swabbing of patients was included. In contrast to zero cases of *C. auris*, 27.0% of patients were colonised with multidrug-resistant bacteria.

In a study from London from 2016, 0.04% (1/2246 screened patients) were colonised with *C. auris* at admission, though these data were recorded during a *C. auris* outbreak and the patients were either exposed to *C. auris* or have stayed in an environment with previously positive patients.[1] In another study from England, 921 patients admitted to eight ICUs in three major cities were screened for *C. auris* between 2017 and 2018.[12] The aim of this study was to assess genuine introduction of *C. auris*, therefore hospitals that shared patient populations with hospitals with ongoing outbreaks of *C. auris* were excluded. Additionally, the authors hypothesized that communities with high rates of travel to risk countries for *C. auris* would have a higher prevalence and were thus preferably selected as study sites. However, comparable with our results, no *C. auris* isolate could be detected. It was concluded that widespread screening for patients in ICUs in England is not recommended, but all hospitals should establish a *C. auris* screening policy after local risk assessment of patients likely to be colonised.[12]

In a European study between January 2018 and May 2019, only 5% of *C. auris* isolates were classified as imported, whereas six out of seven cases in Germany were previously hospitalised abroad.[8,9] Eighty-five per cent of 233 participating German laboratories correctly identified *C. auris*[8]. Due to the large number of international patients in European hospitals *C. auris* could be frequently imported and pose a relevant threat to healthcare systems, as evidenced by outbreaks in Spain[17,18] or the UK.[1,19]

However, since the first published report more than 25 cases have been documented by the National Reference Center for Invasive Fungal Infections (NRZMyk) in Germany and only one single case of nosocomial transmission has been reported[20]. Consequently, based on our data and the current prevalence, routine *C. auris* screening for patients admitted with a history of previous hospitalisation abroad cannot be recommended in Germany. However, it might be useful for all institutions to establish screening protocols which can be quickly initiated in cases of outbreaks or for patients with specific risk factors (e.g. previous colonisation). Previous studies determined possible risk factors for developing *C. auris* infections or colonisation. Risk factors identified included the presence of tracheostomies and ventilators, percutaneous endoscopic gastrostomy tube, prior antibiotic medication, intensive care unit stay and comorbidities such as diabetes mellitus, chronic kidney disease and lung disease[21,6].

In regions with high prevalence of *C. auris* or in outbreak situations the implementation of a rapid and automated molecular surveillance admission screening may prevent the spread of *C. auris*[22]. This is in line with the recent recommendations of an expert panel developed as a joint effort of the German National Reference Centers for Invasive Fungal Infections and Surveillance of Nosocomial Infections[23]. Due to the low *C. auris* prevalence a generalised admission screening is not recommended, whereas identification of *Candida* species from clinical samples in high-risk patients should be performed to the species level by MALDI-TOF, especially for non-albicans species[24].

When screening for *C. auris*, it is not yet clearly defined which body sites should be included in the screening. In our study, screening for MDR bacteria was conducted from different body sites, mainly from stool samples or rectal swabs ($n = 651$), followed by respiratory specimen ($n = 480$). The Centers for Disease Control and Prevention (CDC) in the US classify the patients' bilateral axilla and groin as the most common and consistent sites of colonisation,[24] whereas the European Centre for Disease Prevention and Control (ECDC) states that other sites should be considered for sampling such as nose/throat, axilla, groin, rectum, insertion sites of venous catheters, urine, faeces, wound drain fluid and respiratory material.[25] However, there are no studies investigating *C. auris* colonisation sites in detail. In a study from the neurosciences intensive care unit of the Oxford University Hospitals, a high percentage of patients was first colonised in the axilla, but these results can probably not be generalised as the outbreak observed in this hospital might have been linked to reusable axillary temperature probes.[19] In this study, it was also concluded that a single screen was not sensitive enough to detect colonisation with *C. auris*[19]. More studies are needed to assess the optimal number and sampling sites to reliably detect *C. auris*.

Our study has several strengths and limitations. As far as we know, our study is the first study investigating *C. auris* colonisation in a German hospital upon admission. One major strength is the large study cohort which could only be achieved at a university hospital treating many international patients. Limitations include that screening was not performed at the same body sites for all patients. Between 2020 and 2021, less international patients were admitted to the University Hospital of Cologne due to the COVID-19 pandemic and we had no data including the patient's country of origin. Additionally, a regular chromogenic agar was used and not an agar specific for *C. auris*, which has recently been developed.[26] This could have improved detection in case of a colonisation with different *Candida* species. Furthermore, molecular assays for *C. auris* screening have become available and have demonstrated higher sensitivity compared with culture-based screening.[22,27] Nevertheless, no *C. auris* outbreak and no detection of *C. auris* in any clinical sample was observed between 2017 and 2021 at the University hospital of Cologne.

In conclusion, our study demonstrates that *C. auris* colonisation among international patients admitted to our hospital is rare. We cannot recommend to implement general screening in this patient group based on the current prevalence. Our results might not be transferable to other centres, in particular those treating many patients from regions of high endemicity of *C. auris*. In our setting,

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C. auris screening of patients with any contact to foreign health care does not seem to be cost-effective. More targeted strategies and risk scores for *C. auris* colonisation have to be developed and validated in future studies.

AUTHOR CONTRIBUTIONS

JH formal analysis, investigation, project administration, writing—original draft preparation and writing-review and editing. JZ investigation and writing—review and editing. FF formal analysis, investigation and writing—original draft preparation. AH conceptualization, formal analysis, methodology, supervision, funding acquisition and writing—review and editing.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ORCID

Judith Heindel https://orcid.org/0000-0002-5520-3038
Janine Zweigner https://orcid.org/0000-0002-0360-434X
Frieder Fuchs https://orcid.org/0000-0001-7075-5378
Axel Hamprecht https://orcid.org/0000-0003-1449-5780

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