

Acknowledgements

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Candida auris outbreak report from Pakistan: a success story of infection control in ICUs of a tertiary care hospital



Sir,

Over the past few years, *Candida auris* has emerged as a deadly nosocomial multi-drug-resistant (MDR) pathogen around the globe [1]. There is a danger of *C. auris* transmission in hospitals of developing countries due to their limited facilities for fungal identification and antifungal susceptibility testing [2]. Excessive use of fluconazole empirically has made a shift of invasive candida infections from *albicans* to non-*albicans Candida* spp. It has also contributed to the emergence of MDR yeasts in hospital environments [3].

We encountered a cluster of *C. auris* cases from July 2018 to October 2018. The outbreak investigation was carried out in 45-bedded intensive care units (ICU) (medical and surgical) at the Combined Military Hospital, Rawalpindi, Pakistan. All cases were confirmed by Vitek 2 Version 8.01 (bioMérieux, Marcy l'Etoile, France) at the Department of Microbiology, Armed Forces Institute of Pathology. The bedside Leon scoring system was used to identify risk groups [4]. A case was defined, based on the Leon scoring system, as a patient with persistently raised C-reactive protein, and microbiological criteria of positive *C. auris* cultures with similar phenotypic profiles as that of the index case. Colonization was defined as a positive culture from a central venous catheter (CVC) tip, skin and/or urine in the absence of clinical findings, or treatment given. A positive culture from urine or a CVC tip with negative blood culture but treated with an antifungal drug was deemed to be a possible *C. auris* infection. Candidaemia was defined as clinical and laboratory evidence of sepsis, including positive blood cultures.

To investigate the source of spread, active surveillance and environmental screening were carried out in September 2018. Sterile swabs were taken from various surfaces, including

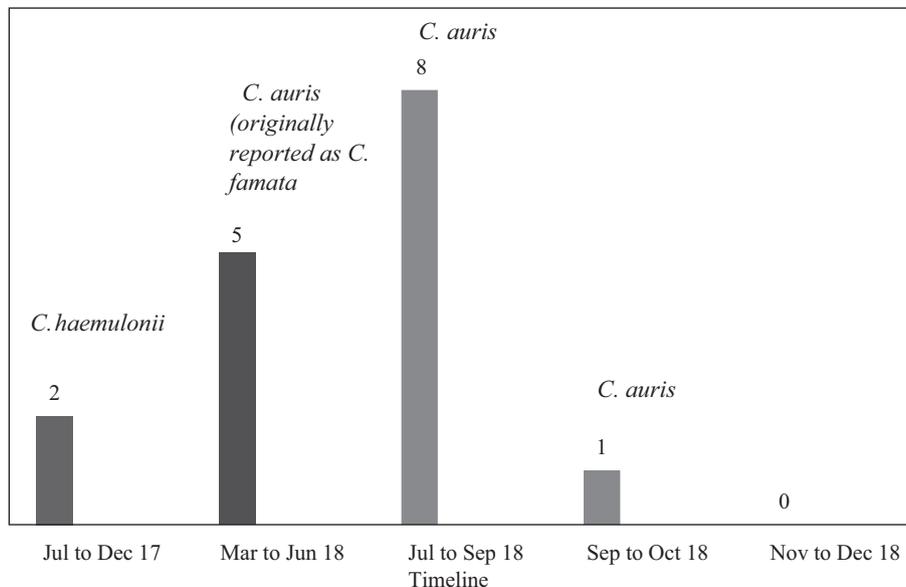


Figure 1. Occurrence of clinical isolates identified as *Candida auris*, including isolates that were, or may have been, misidentified as other *Candida* species.

ventilators, CVC lines, nasogastric tubes and nursing stations. Blood and urine samples were drawn from all patients admitted to the ICU during that time period, and all CVC tips removed from patients were cultured. Nasal and finger web swabs from healthcare workers (HCWs) were also collected for culture. All specimens were processed as per standard laboratory protocols. Further confirmation and minimum inhibitory concentrations of antifungal drugs were performed by Vitek 2 YST card and Vitek 2 AST–YS08, respectively.

The index case was a critically ill 58-year-old female patient, admitted with stomach carcinoma, who had undergone repeated laparotomies. She developed sepsis during her ICU stay, and was treated with multiple antibiotics and fluconazole. *C. auris* was isolated from blood cultures in July 2018. Subsequently, *C. auris* was cultured from eight more patients over a period of almost 4 months until October 2018.

Retrospective analysis of isolates over the previous year revealed two cases of candidaemia reportedly caused by *C. haemulonii* during November and December 2017, and five cases reportedly caused by *C. famata* from March to June 2017. All *C. famata* isolates were later confirmed as *C. auris*, and may represent the beginning of the 2018 outbreak reported here (Figure 1). Unfortunately, the *C. haemulonii* isolates were no longer available for retrospective investigation. Overall, amongst the 14 patients confirmed to have *C. auris*, nine had candidemia. Eight patients responded well to antifungal treatment and were discharged after 2 weeks; the other six patients died.

On environmental screening, *C. auris* was isolated from patients' surroundings and the nursing station. Only one HCW was found to be colonized with a fluconazole-resistant *Candida* sp. However, that isolate was identified as *C. parasilosis*.

Considering the known potential of *C. auris* to cause hospital outbreaks, strict infection control measures were implemented from October 2018. These included strict adherence to contact precautions and environmental disinfection. Routine use of quaternary ammonium compounds for disinfection was stopped

in the ICU, and replaced with hypochlorite solution (1000 ppm) for daily and terminal cleaning of surfaces. Shared equipment (e.g. stethoscopes, blood pressure apparatus etc.) was disinfected before use with hypochlorite swabs. Rooms vacated by patients were fumigated with hydrogen peroxide. Decolonization of carriers was attempted by bathing with 2% chlorhexidine and application of nystatin ointment for 5 days. Following implementation of these measures, there was a steep decline in the number of cases, and no cases were found on monthly screening from November 2018 onwards (Figure 1). We have since implemented periodic re-assessment by screening colonized patients and infected patients every 3 months [5].

In our study, the majority of infections were in patients who had undergone major surgery (43%), had CVCs (71%) or had urinary catheters (64%). Around half of the cases had a history of prior fluconazole therapy. Similar findings were reported by Lockhart *et al.* [6]. The majority (71%) of infected patients were male, and all strains were resistant to fluconazole and amphotericin; these results are in contrast to the findings of Calvo *et al.* [7]. Unfortunately, we were unable to perform molecular typing of isolates, in contrast to other recent reports [7,8].

In conclusion, our study shows that outbreaks of *C. auris* can occur unrecognized for some time in developing countries. Ideally, all *Candida* spp. from clinically important sites should be identified to species level, and this is particularly important where antifungal resistance is demonstrated by in-vitro testing or is suspected because of poor clinical response. Strict infection control practices along with antibiotic and antifungal stewardship, especially in ICUs, is also required to manage the risk.

Conflict of interest statement

None declared.

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The impact of dispatching infectious diseases physicians for infection control. Interrupted time-series analysis on carbapenem use and blood cultures



The overuse of broad-spectrum antimicrobials is associated with multidrug-resistant organisms. Whereas infectious disease

(ID) specialists and their consultation services are associated with successful antimicrobial stewardship, there is a shortage of ID specialists in Japan and many hospitals do not have them [1–6]. Some hospitals rely on ID physicians dispatched on a part-time basis for consultations and antimicrobial stewardship programmes. To evaluate the effectiveness of such part-time ID physicians, we conducted an interrupted time-series analysis (ITSA) on broad-spectrum antibiotic, carbapenem, and blood culture use to evaluate the effectiveness of ID physicians dispatched on a weekly basis.

ITSA was conducted at Kakogawa Medical Center, a 300-bed tertiary care hospital in Hyogo prefecture, Japan. The study period was from April 2012 to April 2017. The hospital did not have trained full-time ID specialists. As the first intervention (intervention 1), an ID fellow from the division of infectious diseases at Kobe University Hospital, Hyogo, Japan was dispatched weekly to provide ID services and antimicrobial stewardship in April 2015. He was replaced by an ID attending physician from the same division in April 2016 (intervention 2). Their work included providing a consultation service for hospitalized patients, aiming specifically at appropriate use of antibiotics, as well as multiple lectures for staff regarding management of infectious diseases.

By defining the time of commencement of these two physicians (interventions 1 and 2), and assuming that there was no time lag for their interventions to be effective, the intervention efficacy was assessed using segmented regression analysis of an interrupted time-series using the Newey model [7]. Both the changes following commencement, and the post-intervention trend, were evaluated monthly, using moving-average methods to adjust autocorrelation. Monthly carbapenem use was measured using defined daily dose, or DDD per 1000 patient-days. The number of blood cultures taken, the number of multiple sets of blood cultures, and the multiple sets of blood culture rate were also measured monthly per 1000 days. We also compared in-hospital mortality rates during the pre- and post-intervention periods to see whether there was no increase in in-hospital mortality after decreasing broad-spectrum antibiotic use. All comparisons were performed using Stata version 15.1 (StataCorp, College Station, TX, USA). The ethics committee at Kakogawa Medical Center approved this study.

Carbapenems other than meropenem were not approved or rarely used at the hospital, and only data on meropenem were used for analysis. Meropenem use significantly decreased after commencement of intervention 1 ($P < 0.001$), as well as for post-intervention trend ($P = 0.006$). Intervention 2 also led to a significant further decrease in meropenem use ($P < 0.001$ for intercept and $P < 0.001$ for trend) (Figure 1).

For blood cultures, there was already an increase in numbers before any intervention ($P < 0.001$). Both interventions 1 and 2 were associated with a significantly increased trend ($P < 0.001$); similar patterns were observed for both the number of multiple sets of blood cultures and multiple sets rate.

In-hospital mortality during the study period increased significantly after intervention 1 (for trend, $P = 0.001$). However, intervention 2 led to a significant decrease in mortality ($P = 0.002$ for intercept, and $P < 0.001$ for trend).

Our investigation revealed that intervention by weekly assigned ID physicians significantly affected the use of the broad-spectrum antibiotic, meropenem. Likewise, both interventions somewhat contributed to boosting blood cultures.