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Original Article

Management of *Candida auris* outbreak in a tertiary-care setting in Saudi Arabia

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Abstract

Objective: To describe local experience in managing an outbreak of *Candida auris* in a tertiary-care setting.

Methods: In response to emerging *Candida auris*, an outbreak investigation was conducted at our hospital between March 2018 and June 2019. Once a patient was confirmed to have *Candida auris*, screening of exposed patients and healthcare workers (HCWs) was conducted. Postexposure screening included those who had had direct contact with or shared the same unit or ward with a laboratory-confirmed case. In response to the increasing number of cases, new infection control measures were implemented.

Results: In total, 23 primary patients were detected over 15 months. Postexposure screening identified 11 more cases, and all were patients. Furthermore, ~28.6% of patients probably caught infection in another hospital or in the community. Infection control measures were strictly implemented including hand hygiene, personal protective equipment, patient hygiene, environmental cleaning, cohorting of patients and HCWs, and avoiding the sharing of equipment. The wave reached a peak in April 2019, followed by a sharp decrease in May 2019 and complete clearance in June 2019. The case patients were equally distributed between intensive care units (51.4%) and wards (48.6%). More infections (62.9%) occurred than colonizations (37.1%). Urinary tract infection (42.9%) and candidemia (17.1%) were the main infections. In total, 7 patients (20.0%) died during hospitalization; among them, 6 (17.1%) died within 30 days of diagnosis.

Conclusions: Active screening of exposed patients followed by strict infection control measures, including environmental cleaning, was successful in ending the outbreak. Preventing future outbreaks is challenging due to outside sources of infection and environmental resistance.

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Candida auris is a resistant fungal pathogen that has been implicated in a number of outbreaks of healthcare-associated infections around the world.[1] *Candida auris* has emerged as a major healthcare challenge; it has received increasing attention over the past few years.[1] *Candida auris* frequently causes severe blood and other infections, largely among vulnerable patients.[2] Therefore, it has been associated with extremely high rates of morbidity and mortality.[2–4] Additionally, the high virulence and resistance to several antifungals may contribute to treatment failure.[5] Being highly resistant to routine environmental cleaning, it has high probability of hospital transmission and persistence.[6,7] These factors can make the management of a *Candida auris* outbreak in healthcare setting a real challenge.[8]

It has been a decade since the first *Candida auris* infection was described in 2009 in a Japanese man with an ear infection.[9] Since then, >3,500 cases have been described in 40 different reports covering the 6 continents.[3,10] The affected countries included at least 6 countries in the Middle East, ranked by number of cases reported: Kuwait, Israel, Oman, Saudi Arabia, United Arab Emirates (UAE), and Iran.[11] Although most reports of *Candida auris* have been case report or series,[10] a considerable number of cases were detected during an outbreak investigation in healthcare setting.[12–15]

In Saudi Arabia, 4 cases of *Candida auris* have been described in 2 isolated case reports from Dammam[16] and Makkah.[17] The common features in the reported cases were long complicated hospital stays that involved intensive care, antibiotic use, surgical procedures, and device insertion.[16,17] Giving the current challenges in laboratory confirmation of *Candida auris* in many hospitals,[18,19] these 2 reports probably represent the "tip of iceberg" of *Candida auris* problem in Saudi Arabia. In response to detection of *Candida auris* for the first time in our hospital, we conducted an outbreak investigation. Here, we describe our successful experience managing a *Candida auris* outbreak in our local tertiary-care setting at Riyadh, Saudi Arabia.

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Methods

Setting

The current investigation was conducted at King Abdulaziz Medical City–Riyadh (KAMC-R), a ~1,200-bed tertiary-care facility, including a 150-bed multisection emergency department and 185 beds dedicated to intensive care. KAMC-R is government-funded hospital that provides healthcare services for ~1,000,000 Saudi National Guard soldiers, employees, and their families. The care provided ranges from primary and preventive care to tertiary care. KAMC-R has ~52,000 admissions and provides 416,000 patient days of care each year. The average length of stay is 8.3 days. Notably, ~9,170 healthcare workers (HCWs) work for KAMC-R in jobs that involve direct patient care, including ~1,670 physicians, 4,660 nurses, and 2,840 other HCWs.

Design

We conducted an outbreak investigation included among patients with confirmed *Candida auris* and their exposed patients and HCWs at KAMC-R during the 15-month period from March 2018 to June 2019.

Laboratory methods

The surveillance target was patients with laboratory-confirmed *Candida auris* according to CDC recommendations.[20] Traditional phenotypic methods (Vitek) were initially used identify isolates. In culture, *Candida auris* cannot form short pseudohyphae nor germ tubes. Supplemental matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) was performed to confirm *Candida auris* positivity. Antifungal susceptibility was determined using E-test (manually) and a Vitek system (automatically).

Contact tracing

Patients with suspected infection had specimens cultured for both bacterial and fungal pathogens. Starting July 2018, contact tracing was started by listing all exposed patients and/or HCWs once a patient with *Candida auris* was confirmed. Exposed patients and HCWs were then screened for *Candida auris* colonization according to CDC recommendations.[20] No active screening of specific group of patients was conducted; rather, postexposure screening was conducted for those who had had direct contact with or shared the ward/unit with a laboratory-confirmed case of *Candida auris*. Direct contact involved mainly HCWs with unprotected exposure during treatment, transport, or testing. Possible exposure was determined retrospectively based on the time and movements within KAMC-R. Screening specimens included swabs from the nares, axillae, and groins in both patients and HCWs, and from the rectums of patients only. Infection or colonization status was determined based on developing healthcare-associated infection at the time of diagnosis according to the standard National Healthcare Safety Network (NHSN) criteria.[21]

Infection control measures

Patients with clinical cultures were placed on contact isolation after the diagnosis was confirmed by the laboratory (usually after 3 days). Patients with screening cultures were placed on contact isolation on the same day until negative results were confirmed. Starting in March 2019, a new infection control policy was implemented. Positive patients were subjected to daily bathing using 2% chlorhexidine wipes. Infection control measures including hand hygiene, proper use of personal protective equipment, and environmental cleaning were strictly implemented. Additionally, cohorting of all positive patients in the same unit was done while limiting the rotation of HCWs caring for positive patients. Furthermore, assigning equipment (eg, blood-pressure machine, thermometer, and blood sugar measurement device) to a single patient was practiced to limit cross transmission. Sodium hypochlorite (1,000 ppm and 10,000 ppm, respectively) was used in regular daily and terminal cleaning. Hydrogen peroxide fumigation was added to terminal cleaning later in the outbreak.

Statistical methods

Categorical variables are presented as frequencies and percentages. Continuous variables are presented as means and standard deviations (SD) or median and interquartile range (IQR), as appropriate. The number of patients with *Candida auris* cases was plotted against the diagnosis time to create an epidemic curve. Additionally, the movements of patients with *Candida auris* within KAMC-R from admission to discharge or death were plotted against time. The patients were grouped based on clinical presentation (infection vs colonization). The χ^2 test or Fisher exact test, as appropriate, was used to test significant differences of categorical variables between the groups. The Student *t* test or Mann–Whitney U test, as appropriate, was used to test significant differences of continuous variables between the groups. All *P* values were 2-tailed. $P < .05$ was considered significant. SPSS version 25.0 software (IBM, Armonk, NY) was used for all statistical analyses.

Results

In total, 35 patients with laboratory-confirmed *Candida auris* were recorded at KAMC-R between January 2018 and June 2019. The epidemic curve shown in Figure 1 illustrates 4 sporadic cases between January and September 2018, preceding a large continuous epidemic wave between October 2018 and May 2019. The wave reached a peak in April 2019, followed by a sharp decrease in May 2019 and complete clearance in June 2019. Most patients (62.9%) were confirmed from clinical specimens (mainly urine and blood). The screening process included 253 exposed patients and 707 exposed HCWs, with an overall yield of 4.3% and 0.0% positive results, respectively. At the time of diagnosis, 22 patients (62.9%) had infections and 13 patients (37.1%) were colonized. In all patients, urinary tract infection (UTI, 42.9%) and candidemia (17.1%) were the main infections at the time of diagnosis. Additionally, 3 colonized patients developed infection after diagnosis.

Table 1 shows the demographic and clinical characteristics of the patients. The average age was 64.5±19.8 years and most (68.6%) were men. The most frequent primary diagnoses at admission were pneumonia (31.4%) and sepsis or other infection (15.8%). The possible sources of exposure were KAMC-R with identified exposures (37.1%), KAMC-R with unidentified exposures (34.3%), other hospitals (22.9%), and the community (5.7%). One-third of the case patients (34.3%) were transferred from other hospitals, including 1 from outside Saudi Arabia. Most patients (85.7%) were diagnosed with *Candida auris* >3 days from KAMC-R admission. Case patients were equally distributed between intensive care units (51.4%) and wards (48.6%) at the time of diagnosis. Case patients were isolated after a median 4 days from diagnosis of infection and after 1 day from diagnosis by screening. Most patients (91.4%) required intensive care (median, 32 days).

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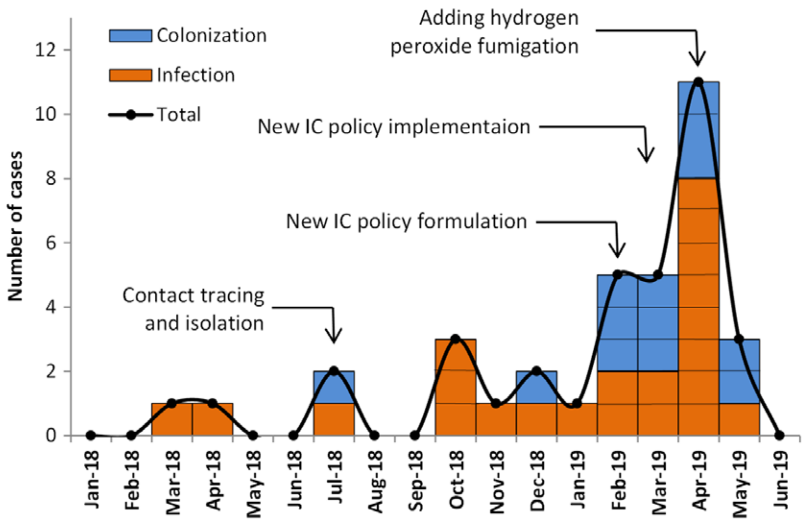

Fig. 1. Epidemic curve of the patients diagnosed with *Candida auris* between January 2018 and June 2019 at MNGHA, Riyadh, Saudi Arabia. Note. IC policy, infection control policy as described in the Methods section.

Table 1. Demographic and Clinical Characteristics of the Patients Diagnosed With *Candida auris*

Characteristic	Infection (N=22), No. (%)	Colonization (N=13), No. (%)	Total (N=35), No. (%)	*P* Value
Age groups, mean ±SD	65.8±19.1	62.2±21.4	64.5±19.8	.603
Gender				
Male	14 (63.6)	10 (76.9)	24 (68.6)	.478
Female	8 (36.4)	3 (23.1)	11 (31.4)	
Primary admission diagnosis				
Pneumonia	4 (18.2)	7 (53.8)	11 (31.4)	.057
Sepsis/other infections	3 (13.6)	3 (23.1)	6 (15.8)	.648
Other respiratory disease	2 (9.1)	1 (7.7)	3 (8.6)	>.99
Altered level of consciousness	3 (13.6)	0 (0.0)	3 (8.6)	.279
Renal disease	2 (9.1)	1 (7.7)	3 (8.6)	>.99
Others	9 (40.9)	3 (23.1)	12 (34.3)	.463
Type of infection at time of diagnosis				
Urinary tract infection	15 (68.2)	. . .	15 (42.9)	. . .
Candidemia	6 (27.3)	. . .	6 (17.1)	. . .
Ventilator-associated pneumonia	2 (9.1)	. . .	2 (5.7)	. . .
Possible place of responsible exposure				
KAMC-R, identified exposures	3 (13.6)	10 (76.9)	13 (37.1)	.002
KAMC-R, unidentified exposures	10 (45.5)	2 (15.4)	12 (34.3)	
Other hospital	7 (31.8)	1 (7.7)	8 (22.9)	
Community	2 (9.1)	0 (0.0)	2 (5.7)	
Source of admission				
Emergency department	15 (68.2)	8 (61.5)	23 (65.7)	.726
Other hospitals	7 (31.8)	5 (38.5)	12 (34.3)	
Time of *Candida auris* diagnosis				
At admission (≤3 d)	4 (18.2)	1 (7.7)	5 (14.3)	.630
During admission (>3 d)	18 (81.8)	12 (92.3)	30 (85.7)	
Location at the time of diagnosis				
Intensive care units	9 (40.9)	9 (69.2)	18 (51.4)	.164

(*Continued*)

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Table 1. (*Continued*)

Characteristic	Infection (N=22), No. (%)	Colonization (N=13), No. (%)	Total (N=35), No. (%)	*P* Value
Wards	13 (59.1)	4 (30.8)	17 (48.6)	
ICU stay during current hospitalization				
No	3 (13.6)	0 (0.0)	3 (8.6)	.279
Yes	19 (86.4)	13 (100.0)	32 (91.4)	
Transmission-related numbers				
No. of movements within facility, median (IQR)	3 (2–3)	3 (3–4)	3 (3–4)	.101
No. of exposures to others	33 (1–78)	0 (0–3)	7 (0–55)	.003
Length of stay, median d (IQR)				
Hospital	105 (46–155)	103 (56–146)	103 (52–151)	.746
Intensive care unit	17 (11–79)	60 (21–73)	32 (12–73)	.227
Before diagnosis	28 (11–61)	46 (19–97)	31 (13–73)	.322
Between diagnosis and isolation	4 (2–6)	1 (0–4)	3 (0–5)	.061

Note. SD, standard deviation; IQR, interquartile range; KAMC-R, King Abdulaziz Medical City–Riyadh.

As shown in Figure 2, the patients generally had long hospital stays (median, 103 days; IQR, 52–151), and ~60.0% of diagnosed patients were between February and April 2019. On average, patients moved between a median of 3 locations (IQR, 3–4), including 2 ICUs (IQR, 1–3) and 1 ward (IQR, 1–2). On average, patients were diagnosed after a median of 31 days (IQR, 13–73). On average, patients were discharged after a median of 53 days (IQR, 28–109) from diagnosis or died after a median of 8 days (IQR, 6–18) from diagnosis. On average, a single patient with confirmed *Candida auris* caused a median of 7 exposures (IQR, 0–55), mainly among HCWs. As shown in Table 1, infected patients were more likely to expose more individuals to infection (median 33 [IQR, 1–78] vs median 0 [IQR, 0–3]; $P = .003$) but less likely to have within-hospital exposure (13.6% vs 76.9%; $P = .002$) compared with colonized patients.

As shown in Table 2, most patients (65.7%) were treated with antifungal medications, especially caspofungin (43.5%) and amphotericin B (39.1%). All specimens were resistant to

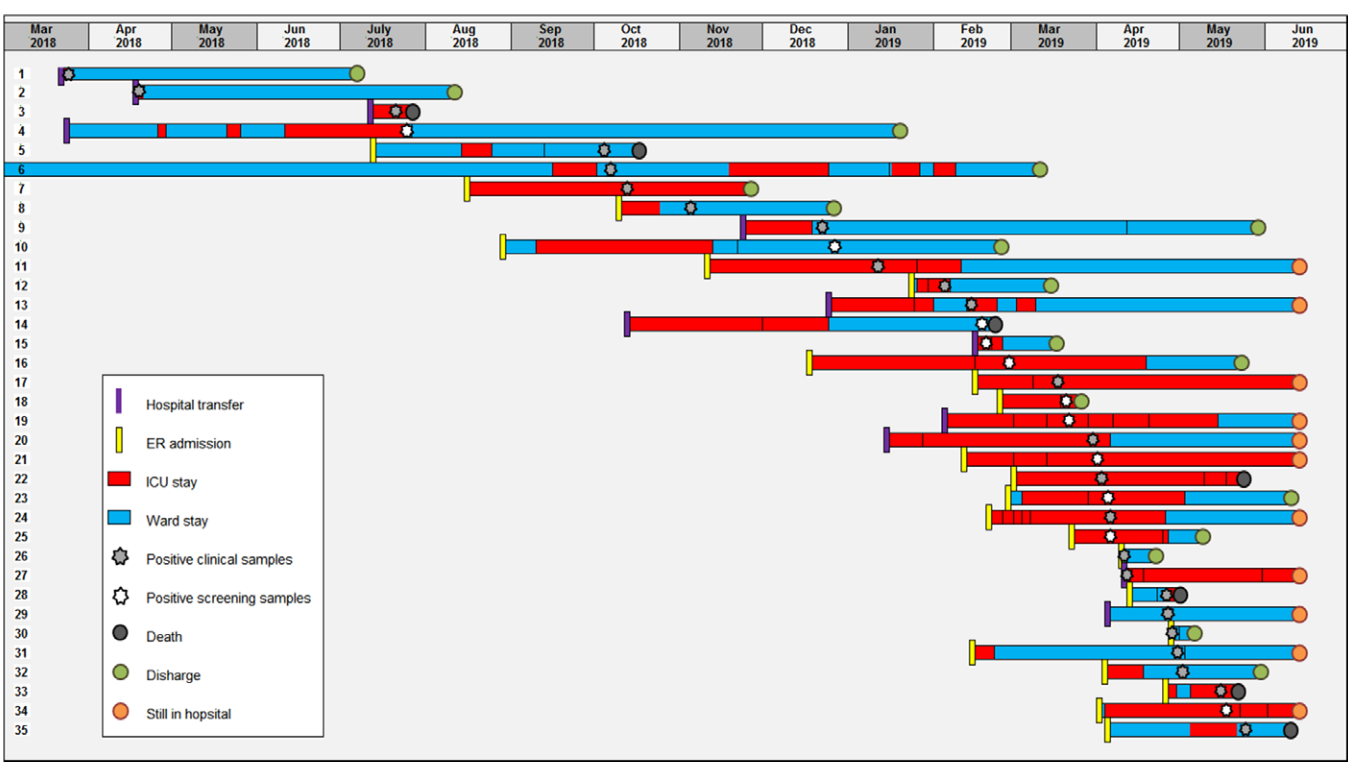

Fig. 2. Within-hospital movements and outcomes of the patients diagnosed with *Candida auris* between January 2018 and June 2019 at MNGHA, Riyadh, Saudi Arabia.

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Table 2. Risk Factors and Outcomes of the Patients Diagnosed With *Candida auris*[a]

	Infection (N=22), No. (%)	Colonization (N=13), No. (%)	Total (N=35), No. (%)	*P* Value
Possible Risk Factor				
Antimicrobial therapy for at least a week during the month before diagnosis[a]	21 (95.5)	12 (92.3)	33 (94.3)	>.99
Antifungal therapy for at least a week during the month before diagnosis	7 (31.8)	6 (46.2)	13 (37.1)	.480
Previous hospitalization during the three months before diagnosis	11 (50.0)	3 (23.1)	14 (40.0)	.116
Prolonged hospital stay (>2 weeks)	18 (81.8)	10 (76.9)	28 (80.0)	>.99
Immunosuppressive conditions[b]	11 (50.0)	7 (53.8)	18 (51.4)	.826
Central line use	17 (77.3)	12 (92.3)	29 (82.9)	.377
Urinary catheter use	22 (100.0)	13 (100.0)	35 (100.0)	. . .
Mechanical ventilation	11 (50.0)	10 (76.9)	21 (60.0)	.116
Endoscopy	4 (18.2)	3 (23.1)	7 (20.0)	>.99
Blood transfusion	13 (59.1)	9 (69.2)	22 (62.9)	.721
Total parenteral nutrition	1 (4.5)	0 (0.0)	1 (2.9)	>.99
Surgery during the 3 mo before diagnosis	9 (40.9)	4 (30.8)	13 (37.1)	.721
Burns	1 (4.5)	0 (0.0)	1 (2.9)	>.99
Trauma	1 (4.5)	1 (7.7)	2 (5.7)	>.99
Staying with a patient diagnosed with *Candida auris* in the same unit	7 (31.8)	12 (92.3)	19 (54.3)	.001
Antifungal used				
No	5 (22.7)	7 (53.8)	12 (34.3)	.079
Yes	17 (77.3)	6 (46.2)	23 (65.7)	. . .
Caspofungin	8 (47.1)	2 (33.3)	10 (43.5)	.660
Amphotericin B	6 (35.3)	3 (50.0)	9 (39.1)	.643
Anidulafungin	5 (29.4)	1 (16.7)	6 (26.1)	>.99
Fluconazole	3 (17.6)	3 (50.0)	6 (26.1)	.279
Mortality				
Hospitalization death	5 (22.7)	2 (15.4)	7 (20.0)	.689
Hospitalization death within 30 d of diagnosis	4 (18.2)	2 (15.4)	6 (17.1)	>.99

[a]Diagnosis refers to the first positive culture.
[b]Immunosuppressive conditions included cancer, hemodialysis, systemic autoimmune disease, human immunodeficiency virus, organ transplantation, corticosteroid use, chemotherapy, and neutropenia.

fluconazole, voriconazole, itraconazole, and flucytosine but were sensitive to caspofungin and anidulafungin. In total, 7 (20.0%) patients died during their hospitalization; of these, 6 (17.1%) died with 30 days of diagnosis. Compared with infected patients, colonized patients were more likely to stay in the same unit with a patient diagnosed with *Candida auris* at the time of diagnosis (92.3% vs 31.8%; $P = .001$). We detected a trend of greater antifungal use among infected patients than colonized patients (77.3% vs 46.2%; $P = .079$).

Discussion

The current report outlines our a the successful management of an outbreak of *Candida auris* at a tertiary-care hospital in Riyadh, Saudi Arabia, where ~60% of the patients had either documented in-hospital exposure or admission to another hospital before confirmation. These findings demonstrate a high risk of cross transmission of *Candida auris* infection among patients (but not HCWs) within and between healthcare facilities. It is well known that contaminated surfaces and equipment are the main source of *Candida auris* transmission in the healthcare setting.[22,23] Similar to our findings, transmission between patients within and between healthcare facilities were the main contributors to a large New York outbreak of *Candida auris*, with a minor role of community exposure.[14] Additionally, colonization of HCWs (<1%) and community exposure (<1 per 1,000) were not suggested as a source of transmission during a large outbreak of *Candida auris* in London, despite high environmental contamination and patient involvement.[15] The role of HCWs is believed to be mainly cross transmission between patients through temporary contaminated hands not actual colonization.[23] However, the possibility of transmission from colonized HCWs should not be dropped, as shown in the report of a small outbreak in Colombia.[24]

Furthermore, ~37% of the patients in the current outbreak were detected by screening exposed patients. This finding highlights the importance of contact screening in detecting colonized patients during the time of outbreak, which may detect between 22% and 89% of the total outbreak cases.[12,14,23,25] Interestingly,

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colonized patients in this report who probably caught *Candida auris* by staying with infected patients in the same unit resulted in fewer exposures than infected patients. This was probably due to earlier pre-emptive isolation with screening cultures compared with clinical cultures. This finding may further highlight the importance of contact screening and early isolation in limiting hospital exposures. Consistent with the screening yield among patients in the current outbreak (4.3%), previous studies showed that 0.04% to 9.3% of individuals screened during outbreak investigations were actually colonized.[12,15] The lack of any colonization among >700 HCWs presumably exposed in the current outbreak may indicate that routine screening of HCWs at the time of the outbreak is not recommended.[14,26]

Most patients in the current outbreak were treated with antifungal medications, especially caspofungin and amphotericin B. Echinocandins, including caspofungin and anidulafungin, have been shown to be very effective against *Candida auris*, with overall resistance ranging between 0% and 7% in different studies.[2,10] Amphotericin resistance ranged between 8% and 35% in different studies.[2,10] On the other hand, *Candida auris* has shown almost full resistance to triazoles, especially fluconazole in our experience and in previous studies.[10] In the current outbreak, ~20% of the patients died during their hospitalization. This rate was better than the crude-hospital mortality rate (29.8%) reported in a systematic review of studies covering outbreak and sporadic cases.[2] However, crude hospital mortality during an outbreak situation varied considerably among studies, ranging from 0% in London[15] to 39% in New York[14] to 43% in Colombia[27] and 53% in Oman.[25]

Active screening of exposed individuals followed by strict infection control measures were successful in ending the outbreak in our hospital. In response to the increasing number of cases, a new hospital infection control policy (based on CDC and other institutional recommendations)[10,20] was formulated late in February 2019 for immediate implementation. In addition to contact tracing and isolation, which began earlier, the plan (described in the methods) focused on preventing transmission through strict implementation and recording hand hygiene, use of personal protective equipment, patient hygiene, environmental cleaning, cohorting of patients and HCWs, and limiting shared equipment. The addition of hydrogen peroxide fumigation to terminal cleaning coincided with a rapid drop in new cases. The contact tracing and isolation were supported by our up-to-date laboratory confirmation methods, which may not be available in many hospitals.[18,19] Although these measures were able to end this outbreak, there is no guarantee regarding similar outbreaks in the future. These can be challenging given the high possibility of new cases from other hospitals, virulence and environmental persistence of the organism, and patient colonization.[8,28]

In conclusion, we are sharing our successful experience in managing an outbreak of *Candida auris* in a tertiary-care setting. Active screening of exposed patients followed by strict infection control measures were successful in ending the outbreak observed in our hospital. These findings could be useful in similar healthcare settings where *Candida auris* transmission is ongoing or is expected.

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