



Published in final edited form as:

Am J Infect Control. 2025 December ; 53(12): 1354–1358. doi:10.1016/j.ajic.2025.08.032.

Progression from *Candida (Candidozyma) auris* colonization to bloodstream infection, New York State (NYS) and Chicago

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Abstract

In 2 cohorts of patients colonized with *Candida auris* in New York State and Chicago, those who progressed to *C. auris* bloodstream infection had comorbidities, including respiratory failure and mechanical ventilation, cocolonization with multidrug-resistant organisms, and extensive health care facility admissions, devices, and procedures. Fewer had traditional risk factors for candidemia (e.g. hematological malignancy, immunosuppression). Secondary prevention efforts are essential, including avoiding unnecessary device use and ensuring meticulous device maintenance and equipment cleaning and disinfection.

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Conflicts of interest: None to report.

Previous presentation: A preliminary version of the work was presented as a poster at the 2018 ID Week meeting, October 6, 2018, San Francisco, CA. (https://academic.oup.com/ofid/article/5/suppl_1/S594/5206786?searchresult=1).

Keywords

Candida auris ; Progression to clinical infection; Candidemia; Invasive Candidiasis

Candida (Candidozyma) auris is a serious global health threat. It is often multidrug-resistant, can be difficult to identify, and can be associated with health care facility (HCF) outbreaks.¹ Patients can be colonized with *C auris* for prolonged periods; *C auris* can contaminate the environment, equipment, and health care workers' hands and be passed to other patients.¹ Individuals colonized with *C auris* may be at risk of progression to infection, including *C auris* bloodstream infection (BSI).¹

New York State (NYS) and Chicago were early epicenters of *C auris* emergence in the United States in 2016 and 2017 and continue to identify cases.¹⁻³ Our objective was to characterize patients with *C auris* colonization who developed *C auris* BSI.

The study period began on April 1, 2016 (NYS) and May 1, 2016 (Chicago), coinciding with the month of the initial detection of *C auris* in each jurisdiction,⁴ and ended on December 31, 2018 for both jurisdictions.²⁻⁴ Cases were included if they developed *C auris* BSI 1 calendar day or more after obtaining positive *C auris* surveillance cultures. These patients are referred to as "progression patients." Commercial and hospital laboratories and infection prevention and control programs in acute care hospitals (ACHs) and skilled nursing facilities (SNFs) reported *C auris* BSIs to the respective health department as part of public health reporting. Chicago patients colonized with *C auris* were identified through point prevalence surveys in ACHs, SNFs, and long-term acute care hospitals (LTACHs). NYS patients colonized with *C auris*, mainly from the New York City metropolitan area, were identified 1 of 3 ways: screening upon admission to an ACH or SNF,⁵ contact investigation of patients with *C auris* infection or colonization, or point prevalence surveys in ACHs or SNFs. Local protocols for colonization screening varied. NYS body sites included nares, axillae, and groin; Chicago included only axillae and groin.^{1,6}

Lists of patients with new onset of *C auris* BSI were compared to lists of patients with surveillance test results positive for *C auris* to identify individuals who progressed from colonization to BSI; in this project these patients are referred to as "progression patients." Only each patient's first positive *C auris* surveillance test was used in this project. HCFs used standardized forms to inform health departments about progression patients' demographics, clinical histories, ACH and SNF admissions, procedures, and outcome data. Investigators reviewed medical records for antimicrobial use. NYS used progression patients' medical records for multidrug-resistant organism (MDRO) history. Chicago used a preexisting extensively drug-resistant organisms registry as referenced.⁷

Patient days at risk for *C auris* BSI infection were defined as the number of days between date of the first positive surveillance specimen obtained and the date of clinical BSI infection, death, or end of study, whichever came first. The incidence of BSI was calculated as number of surveillance cases that developed BSI divided by the number of patient days at risk.

The NYS and Chicago institutional review boards reviewed this project and deemed it as exempt research. This activity was reviewed by CDC, determined not to be research, and was conducted consistent with applicable federal law and CDC policy. Deidentified, patient-specific data about progression patients from both study sites were combined, and analysis was performed using SAS version 9.4 (SAS Institute Inc). HCFs involved were identified only as ACHs, LTACHs (Chicago only), and SNFs. Basic descriptive analyses were performed for the entire cohort of progression patients.

Thirty-three patients (21 in NYS and 12 in Chicago) met the definition for BSI progression patients and were included in the analysis (Table 1A). Patients colonized with *C auris* (NYS and Chicago, respectively) were followed for 69,216 and 51,744 patient days. Incidence of *C auris* BSI following colonization was 3.0 and 2.3 per 10,000 observed patient days. Table 1B summarizes demographic, comorbidity, and exposure data for the 33 *C auris* BSI progression patients. Crude mortality rate at 30 days was 33% (333 per 1,000) and 25% (250 per 1,000), for the progression patients from NYS and Chicago, respectively).

Progression patients often had multiple comorbidities, including respiratory failure and mechanical ventilation, prior cocolonization with other MDROs, and extensive health care exposures, including HCF admissions, devices, and invasive procedures. Typically, progression patients received prolonged courses (mean 15 days, range 2-30 days) of antibiotics within 30 days before BSI (Table 1C). Twenty-seven percent received systemic antifungal medications within 30 days before BSI. The majority of progression patients with *C auris* received systemic antifungal treatment upon BSI diagnosis (documented in 79% overall, 76% NYS, 83% Chicago; 88% of patients treated with antifungals in NY and 80% of patients treated with antifungals in Chicago received echinocandins.) (Tables 1B and 1C). None were known to have BSIs with an echinocandin- or pan-resistant *C auris* strain.

The progression patients from NYS and Chicago were similar with a few exceptions (Tables 1B and 1C). NYS surveillance cases included specimen collection from the nares (due to local screening protocols). NYS has very few LTACHs, and differences in facility type designation between the 2 jurisdictions resulted in more NYS patients found to be colonized in SNF ventilator units compared to Chicago, where more were in LTACHs. Most NYS progression patients were diagnosed with BSI in an ACH in contrast to Chicago, where infections were diagnosed in both ACH and LTACHs. Progression patients in Chicago were in more HCFs and had more admissions than in NYS. The NYS progression patients were more frequently mechanically ventilated and had a higher proportion of tracheostomies. For additional context, overall, *C auris* BSIs represented approximately half of the clinical cases in NYS in the study period (Table 1A).

Many *C auris* progression patients had devices (eg, central lines) placed or replaced or had other invasive procedures shortly before the BSI (Table 1B). This highlights the importance of secondary prevention in those colonized, including avoiding unnecessary invasive devices, ensuring aseptic device insertion and maintenance practices, routinely assessing the need for invasive devices and discontinuing as soon as possible, giving “holidays” from invasive devices when possible, and routine cleaning and disinfection of medical equipment while in use. CDC also underscores the role of environmental cleaning and disinfection,

surgical skin preparation, and antimicrobial stewardship to prevent colonized individuals from developing infections.^{8,9}

Our report has some limitations. NYS cases were clade 1, the South Asian clade, and the Chicago cases were clade 4, the South American clade.¹⁰ Colonization rates are likely underestimated. The number of patients identified as colonized is dependent on intensity of screening. Although both jurisdictions had aggressive initiatives for *C. auris* colonization testing in high-risk settings, they did not have programs in place for universal surveillance, and screening strategies were different. Even for patients with *C. auris* colonization detected, it is unknown when patients were exposed or colonized. Another limitation was that we did not censor all the data for the patient days in the denominator for patients who may have died but never developed BSI. Although our report covers 2 large cohorts during a 2-year period, a modest number of patients colonized with *C. auris* progressed to BSI. Of note, subsequent national^{11,12} and local public health surveillance (Table 1A, footnote 11)¹³ continue to identify individuals colonized with *C. auris* who progress to BSI in a manner consistent with the cohort described in this report. This report complements these national and local publications by providing much more descriptive clinical and exposure data for these BSI progression patients. It was not feasible as part of routine public health surveillance to collect this level of detail for the patients who did not progress to BSI; it is a limitation to this study that we do not have a comparison group. These rates of progression from colonization to BSI are only applicable in locations in which frequency and volume of screening is comparable to those in Chicago and NYS. Rates from the 2 jurisdictions should not be compared.

In 2 large, early cohorts of patients colonized with *C. auris*, those who progressed to a *C. auris* BSI (progression patients) often had multiple comorbidities, prior cocolonization with other MDROs, and extensive health care exposures, including respiratory failure and mechanical ventilation. Fewer had traditional risk factors for candidemia, including hematologic malignancy or immunosuppression. These findings reinforce preliminary findings from the early NYS experience with individuals colonized with *C. auris*.¹⁴ Further analysis is ongoing to examine the longer timeframe in NYS and compare those who progress from colonization to infection to those who do not.

Acknowledgments

We want to thank Jiankun Kuang and Ronald Jean-Denis of the New York State Health Department Bureau of Healthcare Associated Infections for their surveillance work; Dr Sudha Chaturvedi and YanChun Zhu of the Department of Mycology of Wadsworth Public Health Laboratory; Hira Adil, Stephanie Black, and Massimo Pacilli of the Chicago Department of Public Health and the Wisconsin State Laboratory of Hygiene which are the regional laboratories of the Antibiotic Resistance Laboratory Network for testing the majority of Chicago specimens. We also thank Dr Snigdha Vallabhaneni from CDC.

Funding/support:

Elements of this work (including case surveillance and screening activities) were supported by Cooperative Agreement Number NU50CK000423, funded by the Centers for Disease Control and Prevention. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the Centers for Disease Control and Prevention, the Department of Health and Human Services, or the New York State or Chicago Departments of Health.

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Table 1A
Candida auris clinical and surveillance cases, including surveillance cases that progressed to BSIs, during the study period, by jurisdiction (New York State [NYS] and Chicago) *

Location	New York	Chicago
Study timeframes	April 1, 2016-December 31, 2018 n (%) [†]	May 1, 2016-December 31, 2018 n (%) [†]
Total clinical <i>C. auris</i> cases	283	72
Total overall BSIs [‡]	145 (51%)	31 (43%)
Total surveillance <i>C. auris</i> cases	393	241
Subset of surveillance cases that subsequently became clinical cases [§]	32 (8%)	16 (7%)
Subset of surveillance cases that subsequently became clinical BSIs [¶] ("Progression BSI patients")	21 (5%) ^{//}	12 (5%)

BSI, bloodstream infection.

* Study period began on April 1, 2016, (NYS) and May 1, 2016, (Chicago) and ended on December 31, 2018.

[†] Variable distributions are reported as (n%) unless otherwise specified.

[‡] Includes any *C. auris* case that has had a BSI. These include cases where a BSI was the first detection of *C. auris*, cases where BSI occurred following *C. auris* detection at another clinical site as well as BSI detected following positive *C. auris* colonization screening.

[§] Includes any *C. auris* case that was diagnosed initially by surveillance swab and at least 1 calendar day later, had a positive culture collected from any body site in the process of clinical care.

[¶] Includes any case that was diagnosed initially by surveillance swab and later had a blood culture positive (these are a subset of all patients with *C. auris* BSIs).

^{//} Between December 31, 2018 and March 31, 2023, 11 more progression to BSI NY cases were identified from the total number of 372 surveillance case identified during the study time frame.

Table 1B

Summary of demographics and exposures for *Candida auris* screening cases with subsequent *C. auris* bloodstream infection (BSI), “progression patients” by jurisdiction (New York State [NYS] and Chicago) *

Demographic/Exposure [†]	Categories [*]	NYS (n = 21) (%) [‡]	Chicago (n = 12) (%) [‡]	Combined (n = 33) (%) [‡]
Sex	Male	15 (71%)	9 (75%)	24 (73%)
	Female	6 (29%)	3 (25%)	9 (27%)
Race	Black	8 (38%)	9 (75%)	17 (52%)
	White	10 (48%)	2 (17%)	12 (36%)
	Other/unknown	3 (14%)	1 (8%)	4 (12%)
Ethnicity	Hispanic	1 (5%)	2 (17%)	3 (9%)
	Non-Hispanic	15 (71%)	10 (83%)	25 (76%)
	Unknown	5 (24%)	0 (0%)	5 (15%)
Age (years)	Mean (range)	69 (61,77)	57 (47,68)	63 (47, 77)
Days colonized to infection	Mean (95% CI)	85 (38, 132)	119 (59, 179)	101 (38, 179)
Colonized site(s) [§]	Axillae only	1 (5%)	1 (8%)	2 (6%)
	Axillae and groin [§]	2 (10%)	11 (92%)	13 (39%)
	Axillae, groin, and nares [§]	15 (71%)	0 (0%)	15 (45%)
	Nares only	2 (10%)	0 (0%)	2 (6%)
	Unknown swab	1 (5%)	0 (0%)	1 (3%)
Health care facility (HCF) type where colonization detected	Acute Care Hospital (ACH)	8 (38%)	2 (17%)	10 (30%)
	Long-term acute care hospital (LTACH)	0 (0%)	5 (42%)	5 (15%)
	Skilled nursing facility (SNF)	13 (62%)	5 (42%)	18 (55%)
HCF unit where colonization detected	ACH-ICU	3 (14%)	1 (8%)	4 (12%)
	ACH-medical-surgical unit	1 (5%)	0 (0%)	1 (3%)
	ACH-ventilator unit, non-ICU	4 (19%)	1 (8%)	5 (15%)
	LTACH	0 (0%)	5 (42%)	5 (15%)
	SNF ventilator unit	11 (52%)	5 (42%)	16 (48%)
	SNF unit not specified	2 (10%)	0 (0%)	2 (6%)
Underlying conditions	Diabetes	12 (57%)	6 (50%)	18 (55%)
	Cancer—solid tumor	5 (24%)	1 (8%)	6 (18%)
	Cancer—hematologic malignancy	0 (0%)	0 (0%)	0 (0%)

Demographic/Exposure [†]	Categories [*]	NYS (n = 21) (%) [‡]	Chicago (n = 12) (%) [‡]	Combined (n = 33) (%) [‡]
# Underlying conditions reported	Transplant—bone marrow	2 (10%)	0 (0%)	2 (6%)
	Transplant—solid organ	0 (0%)	0 (0%)	0 (0%)
	Liver disease	1 (5%)	0 (0%)	1 (3%)
	Wounds	17 (81%)	7 (58%)	24 (73%)
	Respiratory disease	17 (81%)	2 (17%)	19 (58%)
Current or history of MDRO (90 d before colonization) [§]	Neurologic disease	15 (71%)	9 (75%)	24 (73%)
	Immunosuppressed	3 (14%)	1 (8%)	4 (12%)
	Median (range)	4 (2, 7)	3 (1, 5)	4 (1, 7)
	Yes	14 (67%)	8 (67%)	22 (67%)
	No	2 (10%)	4 (33%)	6 (18%)
Current or history of MDRO (90 d before BSI) [§]	Unknown	5 (24%)	0 (0%)	5 (15%)
	Yes	17 (81%)	8 (67%)	25 (76%)
	No	1 (5%)	4 (33%)	5 (15%)
	Unknown	3 (14%)	0 (0%)	3 (9%)
	ACH	18 (86%)	8 (67%)	26 (79%)
# HCFs between C and I	LTACH	0 (0%)	4 (33%)	4 (12%)
	SNF	3 (14%)	0 (0%)	3 (9%)
	Mean (95% CI)	1.9 (1.5, 2.3)	2.8 (2.3, 3.4)	2.4 (1.5, 3.4)
	Mean (95% CI)	3.4 (2.3, 5.0)	5.5 (2.6, 8.4)	4.5 (2.3, 8.4)
	Invasive devices present 14 d before BSI	15 (71%)	8 (67%)	23 (70%)
Invasive device placed or replaced within 30 d of BSI ^{***}	Arterial line	1 (5%)	0 (0%)	1 (3%)
	Indwelling urinary catheter	8 (38%)	1 (8%)	9 (27%)
	Percutaneous feeding tube	17 (81%)	8 (67%)	25 (76%)
	Endotracheal/nasotracheal tube	6 (29%)	1 (8%)	7 (21%)
	Tracheostomy	20 (95%)	7 (58%)	27 (82%)
Central line	Intra-abdominal drain	2 (10%)	1 (8%)	3 (9%)
	Other invasive device	7 (33%)	5 (42%)	12 (36%)
	Y	11 (52%)	2 (17%)	13 (39%)
	N	9 (43%)	9 (75%)	18 (55%)

Demographic/Exposure [†]	Categories*	NYs (n = 21) (%) [‡]	Chicago (n = 12) (%) [‡]	Combined (n = 33) (%) [‡]
	Unknown	1 (5%)	1 (8%)	2 (6%)
Mechanical ventilation	Y	20 (95%)	8 (67%)	28 (85%)
	N	1 (5%)	3 (25%)	4 (12%)
	Unknown	0 (0%)	1 (8%)	1 (3%)
Surgery	Y	4 (19%)	0 (0%)	4 (12%)
	N	12 (57%)	12 (100%)	24 (73%)
	Unknown	5 (24%)	0 (0%)	5 (15%)
Nonsurgical invasive procedure	Y	9 (43%)	4 (33%)	13 (39%)
	N	8 (38%)	8 (67%)	16 (48%)
	Unknown	4 (19%)	0 (0%)	4 (12%)
Dialysis	Y	6 (29%)	1 (8%)	7 (21%)
	No/Unknown	15 (71%)	11 (92%)	26 (79%)
Antibiotics 30 d before BSI	Y	20 (95%)	12 (100%)	32 (97%)
	No/Unknown	1 (5%)	0 (0%)	1 (3%)
Systemic antifungal 30 d before BSI	Y	5 (24%)	4 (33%)	9 (27%)
	N	14 (66%)	8 (67%)	22 (67%)
	Unknown	2 (10%)	0 (0%)	2 (6%)
CHG bath within 48 h before clinical culture	Y	8 (38%)	6 (50%)	14 (42%)
	N	7 (33%)	0 (0%)	7 (21%)
	Unknown	6 (29%)	6 (50%)	12 (36%)
Systemic antifungal receipt for BSI (documented)	Y	16 (76%)	10 (83%)	26 (79%)
	N	0 (0%)	2 (17%)	2 (6%)
	Unknown	5 (24%)	0 (0%)	5 (15%)
Patient outcome at 30 d post BSI (n = deaths/1,000 patients)	Died	7 (33/1,000)	3 (250/1,000)	10 (300/1,000)
# Patient days at risk ^{††}	Days colonized	69,216	51,744	120,960
Rate of identified colonization to BSI (progression patients)	Average per 10,000 patient days	3.0 per 10,000 patient days	2.3 per 10,000 patient days	N/A ^{##}

CHG, chlorhexidine gluconate.

* Study period began on April 1, 2016 (NYs) and May 1, 2016 (Chicago) and ended on December 31, 2018.

† Statistically significant *P*-value < .05 between jurisdictions is written in bold print. Chi-square or Fisher exact (categorical) or t-test (continuous) using SAS or stat calculator (<https://www.socscistatistics.com/tests/fisher/default2.aspx>).

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[‡]Variable distributions are reported as (n%) unless otherwise specified.

[§]Colonized site: Axillae and groin = separate axillae and groin swabs OR composite axillae/groin swab; Axillae, groin, and nares = separate axillae, groin, and nares swabs OR some combination of composite swabs nares/axillae/groin. Swab protocol varied over time.

[¶]MDRO = multidrug-resistant organism, excludes *C. auris*.

^{//}Between C and I = in the time between colonization and infection.

^{**}Patient had an invasive procedure or device placed or replaced between the day they were first found to be colonized and the day clinical *C. auris* culture was obtained (or during the 30 days before clinical *C. auris* culture was obtained if time between colonization and clinical case was > 30 days).

^{††}Patient days at risk = number of days between the date of the first positive surveillance specimen to the date of clinical infection, death date, or end of study, whichever came first.

^{##}Comparison of rates between jurisdiction is not applicable, see text.

Table 1C

Summary of antimicrobial exposures for *Candida auris* screening cases with subsequent *C. auris* bloodstream infections (“progression patients”) by jurisdiction (New York State [NYS] and Chicago)^{*,†,‡,§}

Antimicrobials (Documented in 30 d before infection)	NYS (n = 21)	Chicago (n = 12)	Combined (n = 33)
Antibacterials (mean, range in day)	19 (3-30 d)	11 (2-30 d)	15 (2-30 d)
Antifungals (mean, range in days)	4 (1-13 d)	9 (2-16 d)	9 (1-16 d)
Specific antimicrobials	n (%)¶	n (%)¶	n (%)¶
Antibacterials			
Carbapenems	9 (43%)	5 (42%)	14 (42%)
Third/Fourth generation cephalosporins	11 (52%)	9 (75%)	20 (61%)
Aminoglycosides	3 (14%)	3 (25%)	6 (18%)
Vancomycin	12 (57%)	3 (25%)	15 (45%)
Quinolones	1 (4%)	3 (25%)	4 (12%)
Extended spectrum beta lactams/Beta lactam-beta lactam inhibitors	4 (19%)	6 (50%)	10 (30%)
Antibiotic of last resort¶¶	5 (24%)	1 (8%)	6 (18%)
Antifungals			
Azoles	2 (10%)	0 (0%)	2 (6%)
Echinocandins	3 (14%)	4 (33%)	7 (21%)
Polyenes	0 (0%)	0 (0%)	0 (0%)
Antiparasitic	6 (29%)	0 (0%)	6 (18%)

* Chi-square or Fisher exact (categorical) or t-test (continuous) using SAS or stat calculator (<https://www.socscistatistics.com/tests/fisher/default2.aspx>).

† Antibiotics of last resort include: colistin and polymyxin, etc.

‡ Exposures in the 30 days prior to the bloodstream infections.

§ Study period began on April 1, 2016 (New York State) and May 1, 2016 (Chicago) and ended on December 31, 2018.

¶ No statistically significant differences of *P*-value < .05 were identified between the 2 jurisdictions.

¶¶ Drugs last resort = antibiotics kept in reserve as the last resort in infections due to multidrug antibiotic resistance.