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Concise Communication

An evaluation of outcomes and hospital readmissions among individuals with candidemia using statewide surveillance

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Abstract

Using statewide surveillance, we describe candidemia in Connecticut during 2019–2020. Mortality was high among individuals with candidemia, and the readmission rate was high among survivors. Mortality and readmission were associated with hospital-onset candidemia. Understanding risk factors for mortality and readmission can optimize prevention strategies to reduce mortality and readmissions.

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Introduction

In the United States, candidemia is a leading cause of sepsis with high morbidity and mortality rates.[1] More than one-third of patients with an admission for sepsis are readmitted to an acute care hospital.[2,3] A 2019 US study estimated the mean cost per readmission as $16,852, with an annual cost of over $3.5 billion.[4] Risk factors for readmission include medical comorbidities, prior antibiotic use, medical devices such as central venous catheters, diuretic use, and length of stay (LOS) of the index admission.[2,3,5]

Among individuals with sepsis who are readmitted, *Candida* is a frequently identified cause of the index sepsis case.[2] However, readmission rates following candidemia and risk factors for readmission following candidemia are unknown. Using data from candidemia surveillance and hospital readmissions, we describe the mortality rate and rate of readmission among individuals with candidemia and factors associated with readmission. Understanding risk factors is essential for designing interventions focused on preventing readmissions and improving outcomes.

Methods

In 2019, the Connecticut Department of Public Health (CT-DPH) made candidemia a laboratory-reportable condition and began statewide surveillance in conjunction with the CT Emerging Infections Program (EIP) with funding from the US Centers for Disease Control and Prevention (CDC). During January 2019–June 2020, adult candidemia cases (age ≥20 yr) were identified through statewide surveillance at all acute care hospitals in Connecticut. Information for standardized case report forms was abstracted from medical charts for all incident cases identified. Cases identified within 30 days of the initial positive blood culture were considered duplicates. The ChimeData database, maintained by the Connecticut Hospital Association, includes information on all hospital admissions in Connecticut and basic patient identifying information. Patients were matched using name, date of birth, and zip code, allowing longitudinal tracking of individuals with an index candidemia case with subsequent hospitalizations in Connecticut. Index candidemia cases were followed for 180 days after index infection.

Each candidemia case was examined to determine if the patient died on index admission, survived index admission and was not readmitted, or survived the index admission and was readmitted to a Connecticut hospital. Variables examined in univariate analysis included clinical and demographic variables, including an adaptation of an existing modified 5-point frailty index,[6] *Candida* species, intravenous drug use, and timing of infection. Time from admission to culture date ≥3 days was classified as hospital-onset infection. Coronavirus disease 2019 (COVID-19)-associated candidemia, defined as an individual with a positive severe acute respiratory coronavirus virus 2 test within 90 days prior to the incident candidemia case, was excluded.

Variables were evaluated in univariate analyses with χ^2 or Mann-Whitney tests, as appropriate. Multivariate logistic regression was performed to identify the association between age and location of infection onset and outcome variables of mortality during the index candidemia case and, among survivors, readmission within the study period. Analyses were performed using SPSS v.25 software (Armonk, NY: IBM Corp.). The study qualified as exempt by the Connecticut Department of Public Health Human Investigation Committee and University of Connecticut Institutional Review Board.

Results

During the study period, 347 candidemia cases met the inclusion criteria. Of these, 121 (34.9%) died during the index admission and 226 (65.1%) survived the index admission.

In univariate analysis, 54 (44.3%) individuals with cardiovascular disease died compared with 67 (29.8%) without cardiovascular disease ($P = .007$) (Table 1). Among those under

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Table 1. Description of clinical and healthcare-associated patient characteristics

	Total population (N = 347)	Died (n = 121)	Survived (n = 226)	*P* value[a]	Readmitted (n = 128)	Not readmitted (n = 98)	*P* value[a]
Any healthcare exposure within 90 days prior to date of index surveillance culture (DISC)							
Yes	201	70 (34.8)	131 (65.2)	0.984	76 (58.0)	55 (42.0)	0.623
No	146	51 (34.9)	95 (65.1)		52 (54.7)	43 (45.3)	
Central venous catheter within 2 days prior to DISC							
Yes	183	69 (37.7)	114 (62.3)	0.258	68 (59.6)	46 (40.4)	0.419
No	161	50 (31.1)	111 (68.9)		59 (53.2)	52 (46.8)	
Mean length of stay prior to DISC (days)[b]							
	8.92	11.32	7.62	0.015*	8.18	6.89	0.204
Hospitalized within 90 days prior to DISC							
Yes	183	64 (35.0)	119 (65.0)	0.999	70 (58.8)	49 (41.2)	0.446
No	163	57 (35.0)	106 (65.0)		57 (53.8)	49 (46.2)	
Mean frailty score[c]							
	1.22	1.30	1.18	0.284	1.15	1.22	0.670
Chronic lung disease[d]							
No	286	94 (32.9)	162 (56.6)	0.090	109 (67.3)	83 (51.2)	0.923
Yes	61	27 (44.2)	34 (55.7)		19 (55.9)	15 (44.1)	
Diabetes mellitus							
Yes	132	44 (33.3)	88 (66.7)	0.638	50 (56.8)	38 (43.2)	0.965
No	215	77 (35.8)	138 (64.2)		78 (56.5)	60 (43.5)	
Cardiovascular disease[e]							
Yes	122	54 (44.3)	68 (55.7)	0.007*	42 (61.8)	26 (38.2)	0.308
No	225	67 (29.8)	158 (70.2)		86 (54.4)	72 (45.6)	
Gastrointestinal disease[e,f]							
Yes	22	8 (36.4)	14 (63.6)		10 (71.4)	4 (28.6)	
No	325	113 (34.8)	212 (65.2)		118 (55.7)	94 (44.3)	
Immunocompromised condition[g]							
Yes	20	4 (20.0)	16 (80.0)		12 (75.0)	4 (25.0)	
No	327	117 (35.8)	210 (64.2)		116 (55.2)	94 (44.8)	
Cirrhosis							
Yes	36	10 (27.8)	26 (72.2)		16 (61.5)	10 (38.5)	
No	311	111 (35.7)	200 (64.3)		112 (56.0)	88 (44.0)	
Hematological malignant tumor							
Yes	24	8 (33.3)	16 (66.7)		10 (62.5)	6 (37.5)	
No	320	114 (35.6)	206 (64.4)		118 (57.3)	88 (42.7)	
Solid malignant tumor with metastasis							
Yes	37	9 (24.3)	28 (75.7)		15 (53.6)	13 (46.4)	0.705
No	310	112 (36.1)	198 (63.9)		113 (57.1)	85 (42.9)	
Solid malignant tumor without metastasis							
Yes	42	11 (26.2)	31 (73.8)	0.194	15 (48.4)	16 (51.6)	0.303
No	305	110 (36.1)	195 (63.9)		113 (57.9)	82 (42.1)	
Neurologic condition[h]							
Yes	72	26 (36.1)	46 (63.9)	0.804	25 (54.3)	21 (45.7)	0.726
No	275	95 (34.5)	180 (65.5)		103 (57.2)	77 (42.8)	
Chronic kidney disease							
Yes	78	30 (38.5)	48 (61.5)	0.450	29 (60.4)	19 (39.6)	0.552
No	269	91 (33.8)	178 (66.2)		99 (55.6)	79 (44.4)	

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Table 1. (*Continued*)

	Total population (N = 347)	Died (n = 121)	Survived (n = 226)	*P* value[a]	Readmitted (n = 128)	Not readmitted (n = 98)	*P* value[a]
Skin condition[i]							
Yes	70	22 (31.4)	48 (61.5)	0.499	24 (50.0)	24 (50.0)	0.296
No	277	99 (35.7)	178 (64.3)		104 (58.4)	78 (41.6)	
Chronic dialysis							
Yes	39	22 (56.4)	17 (43.6)	0.003*	13 (76.5)	4 (23.5)	
No	306	99 (32.4)	207 (67.6)		114 (55.1)	93 (54.9)	
Abdominal surgery within 90 days prior to DISC							
Yes	44	16 (36.4)	28 (63.6)	0.824	16 (57.1)	12 (42.9)	0.954
No	303	105 (34.7)	198 (65.3)		112 (56.6)	86 (43.4)	
Non-abdominal surgery within 90 days prior to DISC							
Yes	61	22 (36.1)	39 (63.9)	0.829	22 (56.4)	17 (43.6)	0.975
No	286	99 (34.6)	187 (65.4)		106 (56.7)	81 (43.3)	
Pancreatitis within 90 days prior to DISC							
Yes	14	5 (35.7)	9 (64.3)		4 (80.0)	5 (20.0)	
No	331	116 (35.0)	215 (65.0)		123 (57.2)	92 (42.8)	
Urinary tract procedure within 90 days prior to DISC							
Yes	44	7 (15.9)	37 (84.1)		17 (45.9)	20 (54.1)	0.311
No	51	11 (21.6)	40 (78.4)		23 (57.5)	17 (42.5)	

*Indicates a result with a significant *P* value of <0.05.
[a]Statistical analysis was not performed if a sample size (n) was ≤10. The percentage of unknown values is not included in the table.
[b]Length of stay prior to DISC was calculated for cases with hospital-onset candidemia by subtracting the admission date from the date of the positive *Candida* blood culture.
[c]Variables included (1) congestive heart failure, (2) diabetes mellitus, (3) chronic obstructive pulmonary disease, (4) partially dependent or totally dependent functional health status based on a presentation to the hospital from a long-term care facility or short-term rehabilitation, and (5) heart disease including stroke, myocardial infarction, or peripheral vascular disease (1 point for each variable).
[d]Chronic lung disease includes cystic fibrosis and chronic pulmonary disease.
[e]Cardiovascular disease includes cerebrovascular accident/stroke/transient ischemic attack, congenital heart disease, congestive heart failure, myocardial infarction, and peripheral vascular disease.
[f]Gastrointestinal disease includes diverticular disease, inflammatory bowel disease, peptic ulcer disease, and short gut syndrome.
[g]Immunocompromised condition includes human immunodeficiency virus infection, primary immunodeficiency, hematopoietic stem cell transplant, and solid organ transplant.
[h]Neurologic condition includes cerebral palsy, chronic cognitive deficit, dementia, epilepsy/seizure/seizure disorder, multiple sclerosis, neuropathy, and Parkinson's disease.
[i]Skin condition includes burn, decubitus/pressure ulcer, surgical wound, and other chronic ulcer or chronic wound.

65 years of age, 51 individuals (29.5%) died during the index admission, and among those over 65 years of age, 70 individuals (40.2%) died ($P = .036$). Mortality was associated with hospital-onset infection (n = 94, 52.8%) compared with community-onset infection (n = 26, 15.6%; $P < .001$), *albicans* species (n = 60, 43.5%) compared with non-*albicans* species (n = 61, 29.2%; $P = .006$) (Table 2), and mean LOS prior to date of index surveillance culture (DISC) (11.32 vs 7.62 days; $P = .015$). In multivariate regression, mortality was associated with hospital-onset infection (OR 6.866; CI 4.009–11.760). The mean LOS after DISC for the index candidemia case for all survivors was 21.98 days.

Of the 226 individuals who survived the candidemia case, 128 (56.6%) were readmitted during the follow-up period. Among those readmitted, 96 (75%) were readmitted within 30 days post-discharge from the index admission. The mean index admission LOS for readmitted cases was 23.12 days, while the mean LOS for non-readmitted cases was 20.49 days. In univariate analysis, individuals who were readmitted were more likely younger than 65 years (n = 78, 63.9%) compared with those older than 65 years (n = 58, 48.5%; $P = 0.017$) and have hospital-onset candidemia (n = 56, 66.7%) compared with community-onset infection (n = 71, 50.4%; $P = 0.017$) (Table 1). In multivariate regression, readmission was associated with hospital-onset infection (OR = 1.791; CI = 1.008–3.184).

Discussion

Our study found a high mortality (34.9%) among individuals with candidemia and frequent readmission (56.6%) among those who survived the index infection. The overall mortality rate in our study was consistent with prior studies documenting a mortality range of 27.7%–58%.[4,7–9] Our study demonstrated that older age and hospital-onset infection are associated with increased mortality. These findings support previous studies identifying risk factors for mortality among individuals with candidemia.[7–9]

To date, no studies have specifically evaluated readmissions among patients with candidemia using population-based surveillance data. In our study, the proportion of patients readmitted was higher than that reported in prior studies of patients with sepsis with 30-day readmission rates ranging from 17.5% to 32.0%.[2,3] Our higher readmission rate may have reflected improved capture of readmissions using statewide data including readmissions outside the hospital where the index infection occurred. Additionally, our study followed patients for a longer period after the index admission. Our findings of an increased risk of

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Table 2. Description of demographics and infection characteristics

	Total population (N = 347)	Died (n = 121)	Survived (n = 226)	*P* value[a]	Readmitted (n = 128)	Not readmitted (n = 98)	*P* value[a]
Age							
19–34	35	2 (5.7)	33 (94.3)		18 (54.5)	15 (45.5)	
35–49	51	13 (25.5)	38 (74.5)		27 (71.1)	11 (28.9)	
50–64	87	36 (41.4)	51 (58.6)		33 (64.7)	18 (35.3)	
65–79	126	48 (38.1)	78 (61.9)		36 (46.2)	42 (53.8)	
80 +	48	22 (45.8)	26 (54.2)		14 (53.8)	12 (46.2)	
Over 65 versus under 65							
Under 65	173	51 (29.5)	122 (70.5)	0.036*	78 (63.9)	44 (36.1)	0.017*
Over 65	174	70 (40.2)	103 (59.2)		50 (48.5)	54 (52.4)	
Race/ethnicity							
Hispanic	43	12 (27.9)	31 (72.1)		15 (48.4)	16 (51.6)	
Non-Hispanic Asian or Pacific Islander	2	2 (100.0)	0		0	0	
Non-Hispanic black	48	18 (37.5)	30 (62.5)		22 (73.3)	8 (26.7)	
Non-Hispanic white	248	85 (34.3)	163 (65.7)		91 (55.8)	72 (44.2)	
Non-Hispanic unknown	6	4 (66.7)	2 (33.3)		0	2 (100.0)	
Stratified Race/ethnicity							
Non-Hispanic white	248	85 (34.3)	163 (65.7)	0.712	91 (55.8)	72 (44.2)	0.693
All other race/ethnicity	99	36 (36.4)	63 (63.6)		37 (58.7)	26 (41.3)	
Sex							
Male	206	72 (35.0)	134 (65.0)	0.969	76 (56.7)	58 (43.3)	0.977
Female	141	49 (34.8)	92 (65.2)		52 (56.5)	40 (43.5)	
Intravenous drug use							
Yes	48	2 (4.2)	46 (95.8)		25 (54.3)	21 (45.7)	0.726
No	299	119 (39.8)	180 (60.2)		103 (57.2)	77 (42.8)	
Location of infection onset							
Community-onset	167	26 (15.6)	141 (84.4)	<0.001*	71 (50.4)	70 (49.6)	0.017*
Hospital-onset	178	94 (52.8)	84 (47.2)		56 (66.7)	28 (33.3)	
***Candida* species**							
Albicans	138	60 (43.5)	78 (56.5)		46 (59.0)	32 (41.0)	
Glabrata	108	35 (32.4)	73 (67.6)		39 (53.4)	34 (46.6)	
Parapsilosis	45	6 (13.3)	39 (86.7)		22 (56.4)	17 (43.6)	
Tropicalis	19	4 (21.1)	15 (78.9)		9 (60.0)	6 (40.0)	
Other	10	2 (20.0)	8 (80.0)		4 (100.0)	4 (100.0)	
Multi	8	3 (37.5)	5 (62.5)		5 (100.0)	0	
Krusei	7	4 (57.1)	3 (42.9)		1 (33.3)	2 (66.7)	
Lusitaniae	7	5 (71.4)	2 (28.6)		1 (50.0)	1 (50.0)	
Dubliniensis	5	2 (40.0)	3 (60.0)		1 (33.3)	2 (66.7)	
Candida albicans* versus non-*albicans							
Albicans	138	60 (43.5)	78 (56.5)	0.006*	46 (59.0)	32 (41.0)	0.607
Non-*albicans*	209	61 (29.2)	148 (70.8)		82 (55.4)	66 (44.6)	
Candida glabrata* versus non-*glabrata							
Glabrata	108	35 (32.4)	73 (67.6)	0.518	39 (53.4)	34 (46.6)	0.501
Non-*glabrata*	239	86 (36.0)	153 (64.0)		89 (58.2)	64 (41.8)	

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Table 2. (*Continued*)

	Total population (N = 347)	Died (n = 121)	Survived (n = 226)	*P* value[a]	Readmitted (n = 128)	Not readmitted (n = 98)	*P* value[a]
Candida parapsilosis* versus non-*parapsilosis							
Parapsilosis	45	6 (13.3)	39 (86.7)		22 (56.4)	17 (43.6)	0.975
Non-*parapsilosis*	302	115 (38.1)	187 (61.9)		106 (56.7)	81 (43.3)	

*Indicates a result with a significant *P* value of <0.05.
[a]Statistical analysis was not performed if a sample size (n) was ≤10.

readmissions associated with hospital-onset infection underscores the importance of infection prevention activities to prevent hospital-onset candidemia.

Study strengths include our use of statewide surveillance data and statewide readmission data, allowing for longitudinal tracking of patients with candidemia and a unique analysis of readmissions. The study captured a broad, statewide population as opposed to prior studies limited to a single institution.

The study had several limitations. Individuals readmitted to facilities outside of Connecticut would not have been captured in ChimeData. Although we explored age and location of infection onset in multivariate analysis, the relatively small sample size precluded our ability to explore many variables, including subcategories of comorbidities and healthcare-related factors that may have limited the statistical power to detect differences among included variables. This study was limited to variables included in the EIP surveillance which may have excluded factors that could affect candidemia-associated morbidity and mortality.

The study period included the early phase of the COVID-19 pandemic, potentially limiting generalizability to candidemia outside this period. COVID-19-associated candidemia demonstrated an atypical epidemiology, particularly during the initial phase of the pandemic.[10] To account for the unique clinical presentation and management of individuals with COVID-19 during this period, we removed COVID-19-associated cases from our analysis.

Mortality was high among patients with candidemia and was associated with hospital-onset infection. The readmission rate was higher in survivors of candidemia compared to overall survivors of sepsis, and readmission was associated with hospital-onset infection. Understanding risk factors for candidemia-associated mortality and readmission can guide clinical management and prevention strategies to reduce mortality and readmissions.

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Competing interests. The authors report no conflicts of interest relevant to this article.

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