



Candida Colonization and the Airway Microbiome of Patients with Cystic Fibrosis

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Background

- Isolation of *Candida* species from a pulmonary source in patients with cystic fibrosis (CF) is common, but its significance is unclear.
- In adults, chronic colonization with *C. albicans* has been associated with increased rate of FEV₁ decline, frequency of hospital-treated CF exacerbations, and pancreatic insufficiency.
- Both *C. albicans* and *C. dubliniensis* have been associated with *Pseudomonas aeruginosa* co-infection.
- Using a retrospective chart review, we sought to further characterize *Candida* colonization in patients with CF.

Methods

- We identified 273 subjects with CF who were followed for 938 patient years at six military CF centers across the United States.
- Candida* colonization was defined as an individual with *Candida* positivity in at least 50% of fungal respiratory cultures in any given year. Those patients with less than 2 annual fungal respiratory cultures were excluded.
- To determine whether prevalence was associated with different categorical variables, Fisher's exact tests were performed on 1000 random samples with the constraint that exactly one interval was selected from each individual to generate each sample.

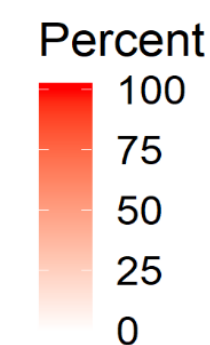
Results

Population Demographics at Enrollment

Location	Sex	N	Age (range) (p = 0.06)	Caucasian (%) (p = 0.17)	BMI (range) (p < 0.001)	Homozygous Delta F508 (%) (p = 0.15)	Diabetes (%) (p = 0.15)	FEV1 % (range) (p = 0.15)
Bethesda, MD	M	29	17 (1.8, 47.2)	62.1	20.6 (14, 28.8)	37.9	0	95.5 (69, 126)
	F	37	13 (0, 44.3)	67.6	17.9 (10.8, 29.7)	56.8	5.4	87.9 (47, 137)
Honolulu, HI	M	14	7.9 (0.1, 28.1)	64.3	17.5 (10.6, 25.2)	0	7.1	93 (70, 103)
	F	8	13.5 (3.6, 40.5)	75	16.9 (13.2, 25.9)	37.5	0	93.3 (66, 109)
Portsmouth, VA	M	31	9.1 (0, 27)	67.7	18 (12, 32.6)	58.1	9.7	79.1 (53, 104)
	F	34	17.8 (0, 50.4)	64.7	19.3 (10.6, 34.8)	35.3	23.5	77.1 (43, 120)
San Antonio, TX	M	27	20.5 (0.3, 45.9)	77.8	21.9 (14.3, 42.3)	29.6	22.2	80.2 (36, 116)
	F	24	18.5 (0.7, 59.1)	58.3	21.7 (14.9, 37.3)	62.5	8.3	86.7 (47, 119)
San Diego, CA	M	16	8 (0, 19.4)	75	17.9 (14.4, 22.1)	43.8	12.5	95 (55, 133)
	F	20	13.9 (0.1, 66.6)	80	17.2 (11.7, 24.4)	45	15	79.9 (39, 121)
Tacoma, WA	M	13	7.5 (0, 16.5)	38.5	16.9 (13.3, 19.9)	61.5	7.7	85.3 (56, 100)
	F	20	16.3 (0.1, 73)	50	18.5 (12.7, 24.9)	40	5	80.6 (47, 107)

Pathogen Colonization by *Candida* Status

Pathogen	None	Other	<i>C. albicans</i>
Aspergillus	26	19	5
MRSA	20	25	25
MSSA	57	66	70
NTM	14	0	0
<i>Pseudomonas</i>	41	50	51
<i>Stenotrophomonas</i>	10	25	9



Patients were classified as "colonized" with MRSA, MSSA, *Pseudomonas*, and/or *Stenotrophomonas* if these were isolated in at least 50% of all respiratory cultures; the same species of nontuberculous mycobacteria (NTM) and *Aspergillus* had to be isolated at least twice in a given year.

No differences were found between groups by colonization with MRSA, MSSA, or *Pseudomonas*. Significant differences were found between groups by colonization with *Stenotrophomonas* (p=0.014), *Aspergillus* (p<0.01), and NTM (p<0.01).

Candida Colonization Distribution

<i>Candida</i> Species	0-2	3-5	6-10	11-17	18+
<i>C. albicans</i>	40	85	95	82	86
<i>C. blankii</i>	0	0	0	0	0
<i>C. dubliniensis</i>	15	27	27	17	28
<i>C. famata</i>	0	0	0	0	1
<i>C. glabrata</i>	0	0	0	3	1
<i>C. guilliermondii</i>	8	0	0	1	0
<i>C. intermedia</i>	4	0	0	0	0
<i>C. krusei</i>	0	0	0	1	1
<i>C. lipolytica</i>	0	0	0	0	1
<i>C. lusitanae</i>	17	1	6	4	3
<i>C. parapsilosis</i>	39	17	21	24	9
<i>C. sp</i>	6	0	3	3	9
<i>C. tropicalis</i>	17	0	0	0	1
<i>C. zeylanoides</i>	0	0	0	0	0

Prevalence and distribution of colonizers differed by age group (p<0.01). *C. albicans* prevalence was lower in the 0-2 year old age group (p=0.031).

Conclusions

- Candida* colonization was not associated with degree of respiratory disease, exocrine pancreatic insufficiency, co-existing diabetes, or homozygous F508del CFTR mutation.
- Different species of *Candida* were more common in specific age categories.
- Patients with *Candida* colonization had significant differences in colonization with known pathogens, suggesting that *Candida* may play a role in influencing the CF airway microbiome.
- The absence of nontuberculous mycobacteria (NTM) colonization in our groups with *Candida* colonization is particularly interesting given the morbidity associated with these infections. To our knowledge, this association has not previously been reported.
- If *Candida* colonization decreases the rate of NTM colonization among those patients with CF then clinicians may elect to not aggressively treat *Candida* respiratory isolates with antifungals in this population.

References

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- Gileles-Hillel A, Shoseyov D, Polacheck I, Korem M, Kerem E, Cohen-Cymbarknoh M. Association of chronic *Candida albicans* respiratory infection with a more severe lung disease in patients with cystic fibrosis. *Pediatr Pulmonol*. 2015;50(11):1082-1089.