COMPARISON OF CANDIDA COLONIZATION IN INTENSIVE CARE UNIT PATIENTS WITH AND WITHOUT COVID-19: FIRST PROSPECTIVE COHORT STUDY FROM TURKEY

Çaklovica Küçükkaya İ [1] , Orhun G [2] , Çağatay A [3] , Kalaycı S [4] , Esen F [2] , Şahin F [4] , Ağaçfidan A [1] , Erturan Z [1]

[1] Istanbul University, Istanbul Faculty of Medicine, Department of Medical Microbiology, Istanbul, Turkey
[2] Istanbul University, Istanbul Faculty of Medicine, Department of Anaesthesiology and Reanimation, Istanbul, Turkey
[3] Istanbul University, Istanbul Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, Istanbul, Turkey
[4] Yeditepe University, Faculty of Engineering, Genetics and Bioengineering Department, Istanbul, Turkey

20-24 September 2022
WWW.ISHAM2022.ORG

OBJECTIVES

Candida **species, as the main component of human mycobiome, are the most common cause of fungal infections in intensive care units. ICU patients with COVID-19 are more prone to fungal infections, due to various causes like mechanical ventilation, use of steroids or long-term hospitalization. There is yet no extended prospective study examining *Candida* colonization rates, epidemiology of species and predisposing factors in this population. This is the first prospective cohort study comparing the time-varying colonization features of *Candida* species in ICU patients with and without COVID-19.**

METHODS

This study was performed between March 2021-December 2021 in intensive care units of Istanbul University, Istanbul Faculty of Medicine, Department of Anaesthesiology and Reanimation. COVID-19 and non-COVID-19 ICU patients who were ≥18 years and expected to stay in the ICU for at least 7 days were included in the study.
Samples were taken at certain time intervals from different body parts of the patients [mouth, skin (axilla), rectal and urine] (Table 1) and evaluated in Istanbul University, Istanbul Faculty of Medicine, Department of Medical Microbiology, Mycology Laboratory. All specimens were inoculated on CHROMagar *Candida* media (CHROMagar *Candida*, France) to detect mixed growth and CHROMagar *Candida* Plus media (CHROMagar *Candida* Plus, France) to avoid missing *Candida auris.*

Cultures were incubated at 35-37°C for 48 hours and phenotypically different colonies on primary media were subcultured on corn meal-tween-80 agar for determining their morphology. All strains were identified to the species level using MALDI-TOF MS (Version 4.1.80; Biotyper Bruker) in Yeditepe University, Faculty of Engineering, Genetics and Bioengineering Department. Patient groups were compared statistically in terms of isolated *Candida* species and distribution according to regions.

RESULTS

The study consisted of 122 ICU patients including 62 COVID-19 (25 female; 37 male; mean age: 63.29) and 60 non-COVID-19 (24 female ; 36 male; mean age: 63.9). A total of 1464 samples (756 COVID-19 and 708 non-COVID-19 patients) were taken (Table 1) and fungi grew in 340 (23.2%). Mixed growth was observed in 108 cultures; was more frequently in COVID-19 patients ($p<0.05$) and significantly higher in oral specimens ($p<0.05$).

Out of a total of 471 strains which were obtained from fungal cultures, *Candida albicans* (42.25%) and *Candida glabrata* (24.2%) were most frequently isolated. *Candida auris* was not observed in this period (Table 2).

Patients with COVID-19 were found more frequently colonized in oral ($p<0.001$), rectal ($p<0.05$) regions and urine ($p<0.001$) compared to non-COVID-19 patients. There was no growth in the axilla region in any of the patients. Non-albicans *Candida* strains were found significantly more frequent in patients with COVID-19 in oral ($p<0.001$) and rectal regions ($p<0.05$).

Table 1: Sampling times and numbers of specimens taken from COVID-19 (+) and COVID-19 (-) patients

COVID STATUS	REGIONS	SAMPLES					
		1st Samples[a] (n)	2nd Samples[b] (n)	3rd Samples[c] (n)	4th Samples[d] (n)	5th Samples[e] (n)	Total Samples
Positive Patients (n:62)	Oral	62	62	60	4	1	189
	Skin (Axilla)	62	62	60	4	1	189
	Rectal	62	62	60	4	1	189
	Urine	62	62	60	4	1	189
Negative Patients (n:60)	Oral	60	60	56	1	0	177
	Skin (Axilla)	60	60	56	1	0	177
	Rectal	60	60	56	1	0	177
	Urine	60	60	56	1	0	177
Total Samples		488	488	464	20	4	**1464**

n: Numbers of the patients

a: 1st samples were taken on the 1st day at ICU

b: 2nd samples were taken on the 7th day at ICU

c: 3rd samples were taken on the last day at ICU [(COVID-19 (+): mean 16.06, days (8-42); COVID-19 (-): mean 12.56, days (8-32)]

d: 4th samples were taken on the 30th day (for patients stayed ≥30 days)

e: 5th samples were taken on the 42nd day

Table 2: Distribution of the fungi isolated from different samples / regions of COVID-19 (+) and COVID-19 (-) patients

	SAMPLES / REGIONS						
	ORAL		RECTAL		URINE		TOTAL (n)
FUNGI	COVID-19 (+) (n)	COVID-19 (-) (n)	COVID-19 (+) (n)	COVID-19 (-) (n)	COVID-19 (+) (n)	COVID-19 (-) (n)	
Candida albicans	35	21	57	40	22	24	**199**
Non-albicans *Candida*	81	25	80	42	25	13	**266**
Candida glabrata	30	7	38	22	12	5	**114**
Candida kefyr	23	9	15	6	3	0	**56**
Candida tropicalis	12	9	13	8	8	3	**53**
Candida krusei	4	0	5	2	0	2	**13**
Candida lusitaniae	2	0	2	3	0	3	**10**
Candida parapsilosis	1	0	3	1	0	0	**5**
Candaida inconspicua	3	0	1	0	1	0	**5**
Candida guilliermondii	4	0	0	0	0	0	**4**
Candida lambica	1	0	2	0	0	0	**3**
Pichia norvegensis	1	0	1	0	1	0	**3**
Saccharomyces cerevisiae	0	0	0	3	0	0	**3**
Mold*	2	1	0	0	0	0	**3**
TOTAL (n)	118	47	137	85	47	37	**471**

n: Numbers of the isolates

*: *Aspergillus niger* (2), *Aspergillus flavus* (1)

CONCLUSION

In this study we found significantly higher oral, rectal and urine *Candida* colonization rates in COVID-19 ICU patients compared to non-COVID-19 individuals. Increased oral *Candida* colonization can be the result of insufficient oral care application to these patients in the ICUs due to infection control anxiety, and also mechanic ventilation.
Because non-albicans *Candida* strains were found significantly more frequent in COVID-19 patients, intrinsically resistant isolates should be kept in mind before administering antifungals.
The high mixed growth rate detected in all individuals and especially in COVID-19 patients will affect the antifungal therapy and therefore emphasized the importance of using chromogenic media for routine evaluation. In addition, a new medium, Chromagar *Candida* Plus, will help in rapid identification in hospitals where infections due to *C. auris* are seen.