

Prevalence of *Candida* infection in Covid-19 pandemic: A study from a tertiary care center in Central India



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Submission: 23-06-2021

Revision: 07-09-2021

Publication: 01-10-2021

ABSTRACT

Background: Corona virus disease 2019 (COVID-19) infections may be associated with a wide range of bacterial and fungal co-infections. *Candida* and mucor are the common fungus encountered during this pandemic. *Candida* is one of the commonly encountered opportunistic fungi that cause superficial mucosal infections usually, but can invade tissue and produce life threatening infections. *Candida* species recognized as one of the major agent of hospital Acquired (nosocomial) fungal infections. Keeping this in background the current study was conducted. **Aims and Objective:** To estimate the prevalence of *candida* infection in tertiary care hospital of Indore. **Materials and Methods:** The present study was done in the period of one and half year. During this period all received clinical specimens like urine, sputum; high vaginal swab and pus suspected for fungal infection from Covid as well as non-Covid patients were processed according to standard protocol. The specimen was subjected to preliminary tests like wet mount, Gram's stain, culture on sabourads dextrose agar (SDA) and Hichrome agar, germ tube test, sugar assimilation test and culture on Cornmeal agar (dalmau technique) for *candida* species were done. For statistical analysis Chi-square test was performed and $p \leq 0.05$ was considered statistically significant. **Results:** The prevalence of Candidiasis was 0.86%. Non-*albicans candida* (65.9%) isolates was more than *Candida albicans* (34.07%). Among non-*albicans species*, *C. tropicalis* was 27.4% followed by *C. glabrata* 16.29%, *C. krusei* 15.55%, *C. parapsilosis* 5.92% and *C. lusitania* 0.74% were the major isolates. Males were affected more than the females. In both the genders maximum patients were from the age group of > 60 years. Maximum number of *Candida* isolates was from blood followed by urine, pus, sputum, vaginal swab and aural swab. Most common risk factors for candidiasis noted in this study was diabetes mellitus in both Covid as well as non-Covid patients. **Conclusion:** Non *albicans candida* are gradually increasing in India. Speciation of *candida* play an important role in preliminary treatment because different species is intrinsically resistant to different antifungal drugs and have different antifungal susceptibility pattern.

Keywords: Covid19; *Candida albicans*; Nosocomial; Non-*albicans candida*; Candidiasis

INTRODUCTION

Corona virus disease 2019 (COVID-19) infections may be associated with a wide range of bacterial and fungal co-infections. *Candida* and mucor are the common fungus encountered during this pandemic. *Candida* is one of the

commonly encountered opportunistic fungi that cause superficial mucosal infections usually, but can invade tissue and can be a source of life threatening infections.¹ The incidence of fungal infection has increased significantly, contributing to mortality and morbidity. The increasing frequency can be attributed to factors such as the use

Access this article online

Website:

<http://nepjol.info/index.php/AJMS>

DOI: 10.3126/ajms.v12i10.38528

E-ISSN: 2091-0576

P-ISSN: 2467-9100

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of potent chemotherapeutic agents that alter the host's immune response, the advent of HIV/AIDS, intravenous drug abuse and the success of intensive care unit in prolonging the survival of highly compromised patients.² *Candida albicans* is the most common cause of candidiasis, and affect almost all the systems of the body starting from skin to Central nervous system.³ Common predisposing factors for Candidiasis are diabetes, malignancy and prolonged use of antibiotics.⁴ *Candida* also occurs as commensal flora in healthy individuals on mucosal oral cavity, Gastro intestinal tract, vagina etc. With changes in environmental and host conditions this commensal can act as endogenous opportunistic pathogen. The emergence of non-albicans *Candida spp.* becomes a challenge for clinicians. *C.glabrata* is less susceptible and *Candida krusei* is intrinsically resistant to Fluconazole.⁵ *C.tropicalis* has the highest adherence rate to inanimate materials such as urinary and vascular catheters, and is often involved in biofilm formation, that is more resistant to Antifungal agents.⁵⁻⁷ So it becomes an immense important to identify the species of *Candida*. Speciation of *candida* play an important role in preliminary treatment because different species is intrinsically resistant to different antifungal drugs and have different antifungal susceptibility pattern which vary from area to area (geographical distribution).⁶ Keeping this in mind, the current study was done to estimate the prevalence of *candida* infection as well as speciation of *candida* isolates and to bring out the various risk factors associated with candidiasis.

MATERIALS AND METHODS

The present study was a prospective cross sectional study done in a tertiary care hospital of Indore (M.P.) from January 2020 to June 2021. This study was pre-approved by the Institutional Ethics Committee (IEC) for the final permission. During this period all received clinical specimens like urine, sputum, high vaginal swab, and pus suspected for fungal infection were processed according to standard protocol. The specimen was subjected to preliminary tests like wet mount, Gram's stain, culture on sabourads dextrose agar (SDA) and Hichrome agar, germ tube test, sugar assimilation test and culture on Cornmeal agar (dalmau technique) for *candida* species were done.⁵ Gram stain was performed from direct samples and inoculated onto SDA slopes and incubated at 25°C and 37°C for 24-48 hours. White to cream-colored, pasty and smooth colonies appeared in within 24 hours to 48 hours. These colonies morphologically resembling the members of genus *candida* were subjected to Gram staining. On microscopic examination they appeared as Gram-positive budding yeast cells with or without pseudohyphae. Germ tube test was done and the positives were identified as

either *C.albicans* or *C.dubliniensis*. *C.albicans* was further identified by growth at 45°C and chlamyospore formation on corn meal agar. All the isolates were subjected to sugar fermentation and sugar assimilation tests for final confirmation of the species. Simultaneously the *Candida spp.* were inoculated onto Hichrom *Candida* agar (Hi Media Pvt. Ltd, Mumbai) and incubated at 37°C for 24 hrs and the species were identified by type and color of the colonies on Hichrom *Candida* agar as per manufacturer's instructions (Figure-1). Hichrom *Candida* agar is a novel, differential culture medium that is claimed to facilitate the isolation by colorimetric presumptive identification.⁸ Statistical analysis was carried out for 135 *Candida* isolates associated with various risk factors including Covid. The association was analyzed using Chi-square test. P value ≤ 0.05 was considered statistically significant. Microsoft Excel 2000 (version 9) and SPSS (Statistical Package for Social Sciences) Version 22.0 software was used for data entry and analysis.

RESULTS

In this study total no of 15559 various clinical specimens were processed and total *candida* species isolated were 135. The prevalence of Candidiasis was 0.86% (Table-1).

Non-albicans *candida* (65.9%) isolates was more than *Candida albicans* (34.07%), (Table-2). Among non-albicans species, *C. tropicalis* was 27.4% followed by *C. glabrata* 16.29%, *C. krusei* 15.55%, *C. parapsilosis* 5.92% and *C. lusitania* 0.74% were the major isolates (Table-2).

Maximum number of *Candida* isolates was from blood followed by urine, pus, sputum, vaginal swab and aural swab (Table-3). *C.albicans* and *C.krusei* was the major isolates from blood while *C.tropicalis* and *C. glabrata* was the major isolates from urine. *C.parapsilosis* was the major isolate from aural swab while single isolate of *C.lusitania* isolated from oral thrush (Table-3). However, statistical analysis with

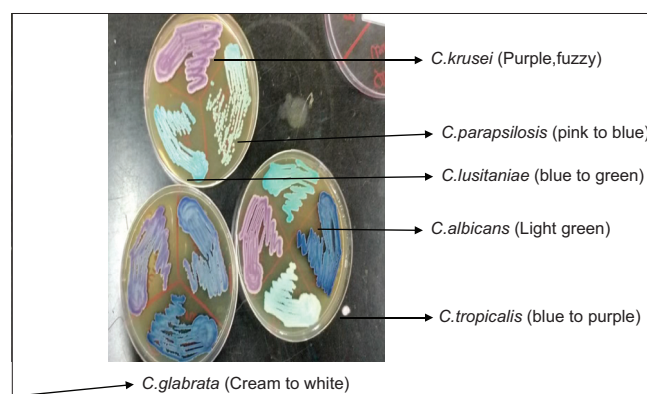


Figure-1: Appearance of different species of candida on Hichrome candida agar

Chi square test does not reveal any significant trend in distribution with $P > 0.05$ ($P=0.125$).

Candida isolates was found to be higher in male patients (52.5%) as compared to female patients (47.4%) (Table-4).

Maximum no of isolation of *Candida* species was in the age group above 60 years (39.2%) (Table-5).

Covid was an important risk factor to acquire the opportunistic *candida* infection. Patients with diabetes (includes both Covid and non-Covid) had prevalence rate of 31.8% while only Covid along with diabetes had

prevalence rate of 32.6%. Diabetes mellitus followed by use of broad-spectrum antibiotics and steroids were the common risk factor associated with candidiasis in both Covid as well as non-Covid patients. Patients on chemotherapy, indwelling Foleys catheter, Pregnancy and long term ICU stay were the other risk factors associated with candidiasis in non-Covid patients only (Table-6).

Statistical analysis with Chi square test reveal significant association of risk factors like diabetes mellitus, use of broad spectrum antibiotics, patient on chemotherapy, urinary catheterization and vaginitis/pregnancy with $P < 0.05$. That is the results were found to be highly significant.

Table 1: Prevalence of *Candida* species in various clinical specimens

Clinical specimen	Total no sample screened	No of <i>candida</i> species Isolated
Blood	3474	26
Urine	3126	23
Pus	2713	19
Sputum	1287	15
Vaginal swab	1254	15
Aural swab	1646	13
Endotracheal aspirate	555	9
Oral thrush	45	5
Throat swab	1350	6
Juglar tip	54	1
Corneal scrappings	55	3
Total	15559	135

Table 2: Distribution of candida species in clinical specimens

Different Species	Total isolates	Percentage (%)
<i>C.Albicans</i>	46	34.07
<i>C.Tropicalis</i>	37	27.40
<i>C.Glabrata</i>	22	16.29
<i>C.Krusei</i>	21	15.55
<i>C.Parapsilosis</i>	8	5.92
<i>C.Lusitania</i>	1	0.74
Total	135	100

Table 3: Distribution of different species of *Candida* in various clinical specimens

Isolated <i>candida</i> species	Clinical specimens						Total
	<i>Candida tropicalis</i>	<i>Candida albicans</i>	<i>Candida parapsilosis</i>	<i>Candia krusei</i>	<i>Candida glabrata</i>	<i>Candida lusitanea</i>	
Blood	6	10	1	7	2	0	26
Urine	6	9	0	4	4	0	23
Pus	4	10	1	2	2	0	19
Sputum	6	3	1	3	2	0	15
Vaginal swab	6	3	0	2	4	0	15
Aural swab	3	3	3	1	3	0	13
Entotracheal secretion	2	4	2	0	1	0	9
Oral thrush	2	1	0	0	1	1	5
Throat swab	1	2	0	1	2	0	6
Jugular tip	0	1	0	0	0	0	1
Corneal scrapping	1	0	0	1	1	0	3
Total	37	46	8	21	22	1	135

DISCUSSION

Studies over the years have shown that there is a considerable increase in the prevalence non-*candida albicans* (NAC) species. In this study NAC in all clinical specimens were 65.9% which were frequently encountered than *C. albicans* (34.7%), which was in agreement with the findings by Shivanand et al., Ragini et al., Manchanda et al. and Vijaya et al., who also showed the NAC incidence to be higher than that of *C. albicans*.⁹⁻¹² In our study non-albicans, *Candida tropicalis* were 27% which was similar to study conducted by Ragini et al., and Chakrabarthy et al.^{10,13}

In our study *candida* isolates was found to be higher in male patients (52.5%) as compared to female patients (47.4%). This correlates with the study done by R A Kashid et al.,¹⁸ males 55.10% while females 44.8% and Arasi Samyuktha A et al.,¹⁴ male 51.2% while female 48.8%. But differed from Amar C S et al., who isolated *Candida* species more from female (60.2%) than male (39.8%) patients.¹⁹ In our study maximum number of isolation of *Candida* species was in the age group above 60 years (39.2%) which was similar to

Table 4: Gender wise distribution of candida isolates

Gender	Number of candida isolated	Percent (%)
Male	71	52.5
Female	64	47.4
Total	135	100

Table 5: Age wise distribution of the study population

Age (years)	Number of cases	Percent(%)
0-10	11	8.1
10-20	05	3.7
20-30	03	2.2
30-40	12	8.8
40-50	17	12.5
50-60	34	25.1
>60	53	39.2
Total	135	100

Table 6: Association of Candida isolates with various risk factors

Predisposing factor	Number of candida isolates			Percentage	P value	Association
	Covidpositive (n=38)	Covidnegative (n=97)	Total (n=135)			
Diabetes mellitus	14	29	43	31.85	0.02	Significant
Broad spectrum antibiotics	10	22	32	23.70	0.03	Significant
Steroids	14	10	24	17.77	0.41	Insignificant
Patient on chemotherapy	00	17	17	12.59	0.00003	Significant
Urinary catheterization	00	12	12	8.88	0.0005	Significant
Vaginitis/pregnancy	00	05	05	3.70	0.03	Significant
ICU stay and intravenous juglar tip	00	02	02	1.48	0.15	Insignificant

the report from the studies conducted by Arasi Samyuktha A et al.,¹⁴ and Kashid et al.¹⁸ who also reported highest incidence in the age group above 60 years (24.4%). In our study we found that diabetes mellitus was most important risk factor associated with candida infection (31.8 %) which was similar to the study of Arasi Samyuktha A et al.¹⁴ In our study highest prevalence rate of candida was maximum from blood samples (19.2%). A New Delhi based study gave a prevalence rate of candida from blood sample were 18% while a study in South India reported an prevalence rate of 5.7%.^{15,16} Study conducted by Sahni et al. from Maulana Azad Medical College, New Delhi, found an prevalence rate of 6.9% for *Candida* species in BSI.¹⁷ These studies suggest wide variations in the prevalence of candidemia in different geographical location of India. In our study we found that the candida infection in ear discharge were 9.62%, In a clinical study done by Ram Kumar et al.,⁸ the incidence of tympanic membrane perforation especially in immunocompromised patients was found to be 11% which was similar to our study. In our study 3.70% women with vaginitis/pregnancy affected with candidiasis In other study conducted by Vijaya D et al.,¹² reported 10% pregnant women with candidiasis. The increased incidence of vaginal candidiasis in pregnant women may be due to elevated levels of progesterone and estrogen. In the present study

patients with diabetes had prevalence rate of 31.8%, which was noted to be higher than the study reported by Kamali et al., (17%).⁴ In this study Covid along with diabetes have a high prevalence rate of 32.6% which was similar to the study of J. Katz.²⁰ Covid play as game changer role because it interfere with T cells causing decreased immunity leading to opportunistic candida infection.²⁰ Analyses have reported vulnerability of immune-compromised patients with pre-existing comorbidities e.g. diabetes, excessive use of broad spectrum antibiotics and steroids towards candidiasis. Diabetes and uncontrolled glycaemia were reported as significant predictors of severity in Covid patients.²⁰

CONCLUSION

The prevalence of Candidiasis was 0.86%. Non-*albicans candida* (65.9%) isolates was more than *Candida albicans* (34.07%). Among non-*albicans* species, *C. tropicalis* was 27.4% followed by *C. glabrata* 16.29%, *C. krusei* 15.55%, *C. parapsilosis* 5.92% and *C. lusitania* 0.74% were the major isolates. Males were affected more than the females. In both genders maximum patients belong to the age group of >60 years. Maximum number of *Candida* isolates was from blood followed by urine, pus, sputum, vaginal swab and aural swab. Most common risk factors for candidiasis

noted in this study was diabetes mellitus in both Covid as well as non-Covid patients.

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Author's Contribution:

SJ, KP-Concept and design of the study, prepared first draft of manuscript; PP, AV, RD- coordination; reviewed the literature and manuscript preparation; BS- Concept, coordination, Interpretation of results, preparation of manuscript and revision of the manuscript.

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Source of Funding: None, Conflicting Interest: None.