

Species Distribution and Antifungal Susceptibility Pattern of Candiduria in a Tertiary Care Hospital of Western Uttar Pradesh

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Abstract

Background: Urinary tract infection (UTI) is one of the most common infections encountered in clinical practice. Bacteria and fungus are the common microorganisms associated with UTI. This study was carried out with the aim to identify the species distribution and anti-fungal susceptibility pattern of candiduria in a tertiary care Hospital of Western Uttar Pradesh.

Methods: This prospective hospital-based study was conducted over a period of one year. A total of 6250 urine samples were subjected for isolation and identification of microorganisms as per standard microbiological method. The antifungal susceptibility testing was performed for fungal isolates as per Clinical and Laboratory Standards Institute (CLSI) M44-A document recommendations.

Result: The culture positivity rate was 58.43%. Among the culture positive, *Candida* species was isolated from 141 (3.86%). There was predominance of Non-albicans *Candida* (NAC) species 131 (92.91%) as compared to *Candida albicans* 10 (7.09%). The positivity was more in the females in the age group of >60 years. *C. tropicalis*, was the predominant NAC species isolated. The isolates showed good susceptibility towards azoles such as fluconazole and voriconazole. However, high level of resistance was seen towards clotrimazole.

Conclusion: Predominance of NAC species in cases of candiduria and emerging resistance towards azoles over the years is a matter of concern. Knowledge regarding the species distribution and its antifungal susceptibility tests will help the clinicians in empirical therapy for better patient outcome.

Keywords: Urinary tract infection, Candiduria, NAC, anti-fungal, azoles.

Introduction

Urinary tract infection (UTI) is one of the commonest infections encountered in clinical practice both in the community and as part of healthcare-associated infection (HCAI). The latter are most often caused by the placement or presence of a catheter in the urinary

tract¹. Infections of urinary tract can be caused by a range of pathogens such as bacteria, fungi, parasites, and viruses.^{2,3}

Candiduria is the presence of *Candida* in urine and it is an increasingly common finding in patients admitted in intensive care units (ICUs), patients on

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immunosuppressive agents, and patients on broad spectrum antibiotic therapy.⁴ Diabetes mellitus, genitourinary tuberculosis, prior use of antifungals and extreme of age are other risk factors associated with candiduria.⁵

Identifying *Candida* upto species level is clinically important due to the fact that they differ in virulence and susceptibility to antifungal agents.⁶ *Candida* pyelonephritis is a severe nosocomial upper UTI which may lead to candidemia and sepsis⁷. Early identification of Candidal infection in clinical sample helps in early initiation of antifungal therapy. This study was planned to know the species distribution and anti-fungal susceptibility pattern of *Candida* species isolated from urine samples of patients suffering from UTI.

Materials and Method

This prospective hospital-based study was conducted in a tertiary care Hospital of Meerut, Uttar Pradesh for a period of one year. A total of 6250 urine samples received in Clinical Microbiology Lab from various IPDs & OPDs were subjected to culture to isolate various microorganisms causing UTI as per standard microbiological methods.^{3,4} The urine samples were cultured on Cysteine lactose electrolyte deficient agar (CLED) plates and incubated at 37°C overnight. The growth on the culture plates were identified by Gram stain, colony morphology and biochemical tests.^{3,4}

Isolation and identification of *Candida* species:

Only the yeast like colonies resembling *Candida* species was included in this study and further processed for identification. Gram's stain was prepared from the yeast like colonies to look for the morphological arrangement of yeast cells followed by urease test. Germ-tube test (GTT) was performed for presumptive identification of *C. albicans* in urease negative isolates. Further, the *Candida* species were sub-cultured on cornmeal agar (CMA) (Dalmau technique) and Hi-chrome agar plates (Hi-Media) [Fig.1] for further identification of species on the basis of morphology and colour production respectively⁴. The acid & gas production in sugar fermentation tests using Glucose, Maltose, Sucrose and Lactose in 2% concentration with Andred's indicator and Durham's

tube and sugar assimilation tests were also performed to identify the species.^{4,9} [Fig 2]

Antifungal susceptibility test (AST):

AST for all the isolates of *Candida* was performed using disc diffusion method on Mueller.

Hinton agar supplemented with 2% glucose and 0.5 µg/ml of methylene blue as per CLSI guidelines⁹. The standard disks used and their disk concentration are: voriconazole (1 µg), fluconazole (10 µg), ketoconazole (10 µg), Clotrimazole (10 µg). (HiMedia, Mumbai, India).

Results

The overall culture positivity rate in urine was 58.43%. Among the culture positives, candiduria was present in 141 (3.86%) samples. *Candida* species were isolated predominantly from urine samples received from indoor patients (92.2%) as compared to those from outdoor patients (7.80%). The positivity rate was more in elderly females >60 years of age (31.9%) followed by in the age group of 21-30 years (16.3%). However, candiduria was uncommon in children in the age group of 1-10 years (1.4%). Overall, in our study the youngest patient was a neonate 1 day old and the oldest patient was 92 years old showing that candiduria is prevalent in extremes of ages with the average mean age of 51.7 years. There was a female predominance in cases of candiduria 77 (54.61%) followed by males 64 (45.39). The female: male ratio was 1:1.2.

There was predominance of Non-albicans *Candida* (NAC) species 131 (93%) as compared to *C. albicans* 10 (7.09%). [Table 1] *C. tropicalis* 83 (58.86%) was the predominant NAC species isolated followed by *C. parapsilosis* 18 (12.76%), *C. guilliermondii* 13 (9.21%), *C. krusei* 7 (4.96%), *C. glabrata* 4 (2.86%), *C. kefyr* 2 (1.42%) and *C. cerevisiae* 2 (1.42%). Out of 12 GTT positive *Candida* species, 2 (1.42%) isolates were *C. dubliniensis* and the remaining 10 (7.09%) were *C. albicans*.

Resistance to various antifungal agents was observed. Out of 141 *Candida* isolates total 18 (12.76%) isolates were resistant to fluconazole, 27 (19.14%) were resistant to ketoconazole and 10 (7.09%) isolates were resistant to voriconazole. Highest level of resistance was seen against clotrimazole in 106 (75.17%) isolates of *Candida* species.

Table 1: Species distribution of candida species isolated in candiduria (n=141)

Species	No. of cases	Percentage (%)	
Non albicans Candida (NAC) species	<i>C. tropicalis</i>	83	58.86
	<i>C. parapsilosis</i>	18	12.76
	<i>C. guillirimonidii</i>	13	9.21
	<i>C. krusei</i>	07	4.96
	<i>C. glabrata</i>	04	2.86
	<i>C. kefyfyr</i>	02	1.42
	<i>C. dubliniensis</i>	02	1.42
<i>C. cerevisiae</i>	02	1.42	
<i>Candida albicans</i>	10	7.09	

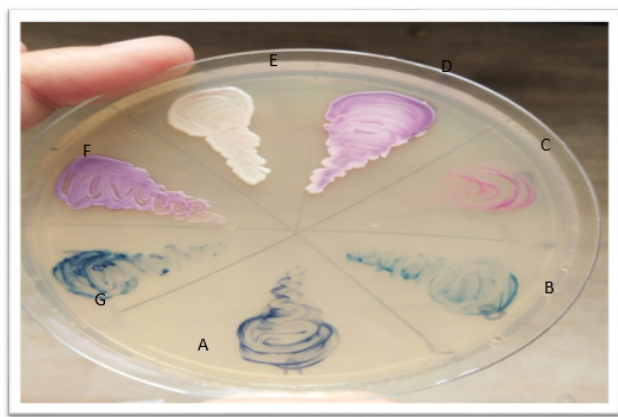


Fig 1: CHROMAgar: A) *C. albicans* B) *C. dubliniensis* C) *C. krusei* D) *C. kefyfyr* E) *C. glabrata* F) *C. parapsilosis* G) *C. tropicalis*

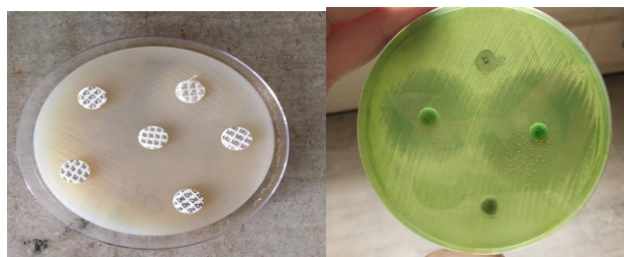


Fig 2: Sugar assimilation test for Candida species

Fig 3: Anti-fungal susceptibility test by disk diffusion method MHA supplemented with 2% glucose and 0.5 µg/ml of methylene blue

Discussion

The culture positivity rate in our study was 58.43%. Among the culture positive, *Candida* species was isolated from 141 (3.86%) urine samples. Similar study done by Yashavanth *et al*¹⁰ and Ragini *et al*¹¹

showed candiduria in 2.27% and in 1.37% cases respectively, which is slightly lower than our observation.

The positivity rate was more in elderly females >60 years (31.9%) of age followed by age group of 21-30, which is concordant to study done by Wanjare *et al*.¹² On the contrary Abishek *et al*.¹³ reported candiduria to be more prevalent in age group of 21-40 years (46%) followed by in the elderly age group of 50-60 years (18%). Our study showed candiduria in the youngest patient, a neonate and the oldest in 92 years old proving the fact that candiduria is prevalent in extremes of ages. Candiduria was more prevalent in female patients 77 (54.61%) in our study. Similar findings were reported by other workers in the past¹⁴.

Candida species were isolated predominantly from urine received from indoor (IPD) patients (92.2%) which is concordant with the study carried out by Rengaraj *et al*.¹⁵ where they also found 40 (66%) isolates were from IPD samples.

There was predominance of Non-albicans *Candida* (NAC) species 131 (93 %) as compared to *Candida albicans* 10 (7.09%). Similar findings of predominance of NAC species was reported by other workers Gharanfoli *et al*.¹⁴ and Yashavanth *et al*.¹⁰ Among the NAC species, *C. tropicalis* 83 (58.86%) was the predominant species isolated followed by *C. parapsilosis* 18 (12.76%), *C. guillirimonidii* 13 (9.21%), *C. krusei* 7 (4.96%), *C. glabrata* 4 (2.86%), *C. kefyfyr* 2 (1.42%) and *C. cerevisiae* 2 (1.42%). This finding is concordant to the studies done by Adhikary *et al*¹⁶, Chakrabarti *et al*¹⁷ and Rani *et al*.¹⁸ Out of 12 GTT positive *Candida* species, 2 (1.42%) were *C. dubliniensis* and the remaining 10 (7.09%) were *Candida albicans*.

We evaluated the antifungal susceptibility pattern by using disk diffusion method according to CLSIM44 guidelines⁹. Resistance to various antifungal agents was observed in our study. A total of 18 (12.76%) isolates were resistant to fluconazole, 27(19.14%) were resistant to ketoconazole and 10 (7.09%) isolates were resistant to voriconazole. Highest resistant pattern was seen against clotrimazole as 106 (75.17%). Similar study done by Sumana *et al.*¹⁹ found 14% of candida species showing resistance to fluconazole, 8% showed resistance to Voriconazole and 4% showed resistance to Ketoconazole. However, a study by Rengaraj *et al.*,¹⁵ found 100% susceptibility to fluconazole and voriconazole in all species except *C. albicans* and *C. glabrata*. Singh *et al.*²⁰, observed overall sensitivity of 95.6% and 100% among Candida isolates to fluconazole and voriconazole respectively. As compared to our study, in the above studies resistance against clotrimazole was not evaluated and reported.

Conclusion

The present study shows a changing trend in patients of candiduria with predominance of NAC species from Meerut city in Uttar Pradesh. As NAC species are more resistant to antifungal agents, knowledge regarding the species distribution and its antifungal susceptibility tests will help the clinicians in empirical therapy for better patient outcome.

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Conflict of Interest: Nil

Ethical Clearance: Approval from the University Ethics Committee (Medical) of Swami Vivekanand Subharti University Meerut was taken via letter No: SMC/IEC/2019/98/09, dated: 18/02/2019.

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