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Prevalence of Candiduria in Diabetic Patients Attending Gondar University Hospital, Gondar, Ethiopia

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Original Paper

Introduction. About 10% to 15% of in-hospital urinary tract infections (UTIs) are due to *Candida* species, and the prevalence is still increasing. A cross-sectional study was conducted to determine fungal causative agents of UTI in asymptomatic and symptomatic diabetic patients and associated risk factors.
Materials and Methods. Between May and June 2010, a total of 422 diabetic patients with asymptomatic UTI (n = 387) and symptomatic UTI (n = 35) were investigated for UTI at Gondar University Hospital. Clean-catch midstream urine specimens were collected from each participant. Fungal urine culture and identification were done using standard microbiologic procedure.
Results. The age range of the participants was 20 to 84 years (mean, 42.3 years). Significant candiduria was detected in 7.5% and 17.1% of asymptomatic and symptomatic diabetic patients, respectively. The overall prevalence of significant candiduria in both groups was 8.3%. *Candida* species were isolated in 38 urine samples. Of these, 84.2% were from the asymptomatic diabetic patients and the remaining 15.8% were from the symptomatic patients. The most common species were *C albicans* (42.0%), *C glabrata* (34.2%), and *C tropicalis* (15.8%). Significant candiduria was strongly associated with being female.
Conclusions. The presence of candiduria in diabetic patients should not be neglected. Although *C albicans* is the organism most often associated with serious fungal infection, other *Candida* species are also isolated as clinically important opportunistic pathogens in type 2 diabetic patients.

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INTRODUCTION

Candiduria refers to the presence of *Candida* species in urine. It is an increasingly common finding in hospitalized patients.[1,2] Since 1980s, there has been a marked increase in opportunistic fungal infections involving the urinary tract, of which *Candida* species are the most prevalent.[1,3]

According to some authors, candiduria is a marker for hematogenous seeding in the kidney. In the vast majority of patients, however, candiduria most likely reflects colonization or infection of the lower urinary tract or the collecting systems of the kidneys. *Candida* colonization of the urinary tract is common in patients with diabetes mellitus. In patients receiving broad-spectrum antibiotics or immunosuppressants, or those with long-term urinary catheters, the clinical course of fungal urinary tract infection (UTI) vary from being an asymptomatic and self-limiting disorder to fungal septicemia, which can be fatal.[4]

All *Candida* species are capable of causing UTIs, and in many centers worldwide, non-*C albicans* species now predominate. Among *Candida* species, *C albicans* is the most common isolated species according to epidemiological studies of fungal UTI.[5] The newly emerging non-*C albicans*, including *C glabrata*, *C krusei*, and *C parapsilosis* are also implicated as causative agents. However, these strains show more resistance to antifungal drugs, especially to the first-line treatments. Some previous studies showed an increase in the incidence of *C glabrata* infection which might be due to the extensive and long-term utilization of antifungal drugs such as azoles.[5,6] Thus, the differentiation of diverse species of *Candida* in the laboratory seems imperative.

Among the various culture methods employed, chromogenic agar medium is nowadays widely used for isolation of and identification of different *Candida* species in clinical specimens, based on their colony color and morphology.[7] The agar contains chromogenic substrates which are cleaved by enzymes possessed by certain *Candida* species, hexosaminidase and alkaline phosphatase. The action of the enzymes on the chromogens results in a build-up of color within the colony. The color produced depends on which enzymes the organisms possess.

Different studies in Ethiopia showed that the prevalence rates of UTIs are increasing. In most studies, the prevalence of significant bacteriuria is in between 10.5 to 39.5%.[8-11] There are no data regarding fungal etiologies of UTI. Therefore, this study was done with the aim of isolation and identification of different *Candida* species and the associated risk factors in diabetic patients with UTI.

MATERIALS AND METHODS

Patients and Setting

A cross-sectional study was conducted during the period from May to July 2010 at Gondar University Hospital, Gondar. The research project proposal was approved by the Institutional Review Board, Faculty of Medicine, Addis Ababa University. Official permission from the study site was obtained. All diabetic patients coming for their diabetic checkup during the study period were informed about the purpose of the study and their consent was sought for the study. After obtaining informed consent, diabetic patients with and without symptoms of UTI coming for their diabetic checkup at the diabetic clinic of Gondar University Hospital were investigated for UTI. Diabetic patients on antibiotics for the past 2 weeks were excluded. All study participants were interviewed during the study period to collect baseline sociodemographic and clinical data.

Collection of Specimens

Each diabetic patient was instructed to collect a clean-catch midstream urine specimen. About 10 mL to 20 mL urine specimen was collected in a sterile screw-capped wide-mouth container from each diabetic patient. The bottle was labeled with a unique sample number and date and time of collection, and was immediately delivered to the microbiology laboratory of Gondar University Hospital.

Culture and Identification of *Candida* Species

Urine specimens were inoculated on Brilliance Candida agar (Oxoid, Hampshire, UK) supplemented with chloramphenicol and incubated at 36°C for up to 72 hours. Brilliance Candida agar is a selective differential medium. With the inclusion of chromogenic substrates in the medium, the colonies of *C albicans*, *C tropicalis*, and *C krusei* produce different colors, thus allowing the direct detection of these yeast species on the isolation plate. Colonies of *C albicans* appear light to medium green, *C tropicalis* colonies appear dark blue to metallic-blue, and *C krusei* colonies appear light mauve to mauve flat colonies with a whitish border. Other yeasts may appear light to dark mauve (eg, *C glabrata* and other species).

Significant candiduria was defined as urine culture which grows 10^4 colony-forming unit/mL midstream urine or greater. All significant candiduria were identified microscopically for their morphological characteristics and further identified by sugar assimilation, sugar fermentation, urea hydrolysis, and enzymatic tests using API *Candida* strips (API BioMerieux, Marcy-l'Etoile, France).

Data Analysis

The data were analyzed using the SPSS software (Statistical Package for the Social Sciences, version 16.0, SPSS Inc, Chicago, Ill, USA). Percentage for proportions and odds ratios for categorical variables were reported, where appropriate. The

chi-square test and Fisher exact test were used for comparisons between groups. A *P* value less than .05 was considered significant.

RESULTS

Study Population

The sociodemographic characteristics of study subjects are presented in Table 1. Of the 422 diabetic patients investigated, 387 (91.7%) had no symptoms of UTI (asymptomatic) and the remaining 35 (8.3%) presented with symptoms of UTI (symptomatic). Types 1 and 2 diabetes mellitus were observed in 249 (59.0%) and 173 (41.0%) of the patients, respectively. The mean age of the study participants was 42.3 years (range, 20 to 84 years), and 38.2% of the patients were in the age range of 20 to 35 years. Of the 422 diabetic patients, 200 (47.4%) were men and 222 (54.6%) were women (male-female ratio of 0.9:1).

Significant Candiduria

Significant candiduria was detected in 29 of 387 (7.5%) and 6 of 35 (17.1%) asymptomatic and symptomatic diabetic patients, respectively (P = .047). The overall prevalence of significant candiduria was 35 of 422 (8.3%).

Candida Species

A total of 38 *Candida* species were isolated from 35 diabetic patients investigated for UTI. Of these, 32 (84.2%) were from asymptomatic diabetic patients and the remaining 6 (15.8%) were from symptomatic diabetic patients (P = .06; Table 2). Of the 38 *Candida* species isolated, *C albicans* accounted for 42% of the cases, followed by *C glabrata* (34.2%), *C tropicalis* (15.8%), *C famata* (5.3%) and *C kefyr* (2.6%).

Risk Factors

Risk factors associated with candiduria are listed in Table 3. Significant candiduria was strongly associated with being female as shown in Table 3.

Table 2. Candida Species Isolated From Urine of Asymptomatic and Symptomatic Diabetic Patients

Candida Species	Diabetic Patients		Total (%)
	Asymptomatic (%)	Symptomatic (%)	
Candida albicans	15 (46.9)	1 (16.7)	16 (42.0)
Candida glabrata	9 (28.1)	4 (66.7)	13 (34.2)
Candida tropicalis	6 (18.8)	0	6 (15.8)
Candida famata	1 (3.1)	1 (16.7)	2 (5.3)
Candida kefyr	1 (3.1)	0	1 (2.6)
Total	32 (84.2)	6 (10.5)	38 (100)

Table 1. Characteristics of diabetic Patients Investigated for Candiduria

Characteristics	Total (%) (n = 422)	Asymptomatic Diabetic Patients (%) (n = 387)	Symptomatic Diabetic Patients (%) (n = 35)
Age, y			
20 to 35	161 (38.2)	157 (40.6)	4 (11.4)
36 to 45	81 (19.2)	75 (19.4)	6 (17.1)
46 to 55	93 (22.0)	83 (21.4)	10 (28.6)
> 56	87 (20.6)	72 (18.6)	15 (42.9)
Sex			
Male	200 (47.4)	193 (49.9)	7 (20.0)
Female	222 (52.6)	194 (50.1)	28 (80.0)
Living area			
Urban	254 (60.2)	224 (57.9)	30 (85.7)
Rural	167 (39.8)	163 (42.1)	5 (14.3)
Diabetes type			
1	249 (59.0)	241 (62.3)	8 (22.9)
2	173 (41.0)	146 (37.7)	27 (77.1)
Duration of diabetes			
< 5 years	256 (60.7)	245 (63.3)	11 (34.4)
≥ 5 years	166 (39.3)	142 (36.7)	24 (68.6)
Blood glucose level			
< 126	87 (20.6)	86 (22.2)	1 (2.9)
≥ 126	335 (79.4)	301 (77.7)	34 (97.1)
History of urinary tract infection	63 (14.9)	37 (9.6)	26 (74.3)
History of antibiotics use	31 (7.3)	16 (4.1)	15 (42.9)

Table 3. Variables Associated With Significant Candiduria in Urine of Asymptomatic and Symptomatic Diabetic Patients

Characteristics	Patients With Candiduria (%)			Univariable Data	Adjusted data	
	Symptomatic	Asymptomatic	Total	Odds Ratio (95% CI)	Odds Ratio (95% CI)	*P*
Age, y						
20 to 35	0	13 (100)	13 (37.1)	referent	referent	
36 to 45	1 (20.0)	4 (80.0)	5 (14.3)	1.614 (0.518 to 5.030)	1.335 (0.459 to 3.884)	.60
46 to 55	1 (11.1)	8 (88.9)	9 (25.7)	1.247 (0.411 to 3.781)	0.820 (0.336 to 1.999)	.66
> 56	4 (50.0)	4 (50.0)	8 (22.9)	1.178 (0.363 to 3.815)	0.867 (0.345 to 2.181)	.76
Sex						
Male	0	9 (100)	9 (25.7)	referent	referent	
Female	6 (23.1)	20 (76.9)	26 (74.3)	0.355 (0.157 to 0.804)	0.355 (0.162 to .778)	.01
Diabetes type						
1	0	19 (100)	19 (54.3)			
2	6 (37.5)	10 (62.5)	16 (45.7)	0.881 (0.374 to 2.077)	0.811 (0.404 to 1.625)	.55
Duration of diabetes						
< 5 years	2 (10.5)	17 (89.5)	19 (54.3)	referent	referent	
≥ 5 years	4 (25.0)	12 (75.0)	16 (45.7)	0.848 (0.385 to 1.871)	0.752 (0.375 to 21.507)	.42
Blood glucose level						
< 126	0	3 (100)	3 (8.6)	referent	referent	
≥ 126	6 (18.8)	26 (81.2)	32 (91.4)	0.390 (0.110 to 1.375)	2.957 (0.884_9.895)	.08
History of urinary tract infection						
Yes	5 (55.6)	4 (44.4)	9 (25.7)	referent	referent	
No	1 (3.8)	25 (96.2)	26 (74.3)	1.619 (0.534 to 4.911)	2.135 (0.949 to 4.802)	.07
History of antibiotics use						
Yes	2 (40.0)	3 (60.0)	5 (14.3)	referent	referent	
No	4 (13.3)	26 (86.7)	30 (85.7)	1.220 (0.318 to 4.674)	0.432 (0.155 to 1.207)	.11

DISCUSSION

Candiduria is common, and generally speaking, is not an indication of any problem. However, in isolated cases, candiduria may indicate the presence of UTI.[12] Candiduria is a common nosocomial infection afflicting the urinary tract. About 10% of UTIs acquired in hospital are due to *Candida* species. Some recent studies have shown that the rate of *Candida* UTI has increased from 0.9 to 2.0 per 1000 patients.[13] The most frequent organism causing *Candida* UTI is *C albicans* followed by *C* (*Torulopsis*) *glabrata*, *C tropicalis*, and *C krusei*.[14, 15] Non-*C* albicans and non-*Candida* yeasts are steadily increasing as the ethological cause of fungal UTI.[15]

In this study, the overall prevalence of candiduria in diabetic patients was 8.3%. Similar findings have been reported in Pakistan (10.2%)[16] and Saudi Arabia (8%).[17] However, a higher rate of isolation (30%) was reported in Brazil from diabetic patients.[18] A high proportion of significant candiduria was observed in women (74.3%) than in men (25.7%) in the present study. This is in agreement with studies conducted elsewhere.[19, 20] The high prevalence in women may indicate the presence of vaginal candidiasis or just colonization since *Candida* is a normal flora of the genitourinary tract in women.

In the present study, *C albicans* accounted for about 42% of all candiduria isolates, followed by *C glabrata* (34.2%) and *C tropicalis* (15.8%). *Candida famata* (5.3 %) and *C kefyr* (2.6%) were the least frequently isolated *Candida* species (Table 2). Similar findings have been reported in studies conducted elsewhere.[21, 22] Other investigators also showed that *C albicans* accounts for 50% to 70% of all *Candida*-related urinary isolates, followed by *C glabrata*, which comprises 20% of isolates, and *C tropicalis*, which is the third most common species. There has been a steady increase in the incidence of non-albicans strains producing nosocomial infections. Notably, *C glabrata* candiduria has increased in frequency following the widespread and increased use of immunosuppressive agents and broad-spectrum antifungal agents. This is of special importance since *C glabrata* has increased resistance to fluconazole.[1,23]

In the present study, the prevalence of asymptomatic and symptomatic candiduria was 7.5% and 17.1%, respectively. Most infections by *Candida* species are asymptomatic. Regarding *Candida* infections, the mere presence of asymptomatic

candiduria usually does not require specific treatment. Correcting risk factors, such as glycemic control and removal of urinary catheters, can result in remission of candiduria. Diabetic patients are under the risk of developing fungal UTI and symptomatic candiduria is an indication for treatment and may signal diverse pathological states. Local complications are not frequent; however, they can be potentially severe in diabetic patients and include pneumaturia, fungal ball formation, calyceal invasion, perinephric abscess, and papillary necrosis.[24]

Diabetes mellitus, indwelling bladder catheter, female sex, and the use of antibacterial agents have been risk factors identified for both *C glabrata* and *C albicans* candiduria.[5] In this study, a significant association was observed for candiduria and being female (Table 3), which is in agreement with other similar studies.[24, 25]

CONCLUSIONS

Both *Candida albicans* and non-*albicans* species were identified in both asymptomatic and symptomatic diabetes patients with UTI. Brilliance *Candida* agar can be used as rapid identification of *Candida* species. The presence of candiduria in diabetic patients should not be neglected and although *C albicans* is the organism most often associated with serious fungal infection, other *Candida* species also have isolated as clinically important opportunistic pathogens in type 2 diabetic patients. Follow-up studies are required to supplement the present findings for appropriate management of asymptomatic UTIs in diabetic patients.

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CONFLICT OF INTEREST

None declared.

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