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Research Article

Comparison the Prevalence of Candiduria in Diabetes and non-diabetic Patient's: A case study

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ABSTRACT

The prevalence of opportunistic fungal infections has increased in the past few decades. Opportunistic fungal infection is one of the most common causes of death and complications in immunocompromised patients. Candiduria is a general term for the presence of *Candida* spp. in urine. Diabetes Mellitus (DM) is considered one of the predisposing factors for *Candida* urinary tract infections. The aimed of this study was to compare the prevalence of Candiduria in diabetes and non-diabetic patient's referent to Amir Al-Momenin Hospital. By designing a case-control study, 90 diabetic patients referred to the clinic of Amir al-Momenin hospital during six months period were included in the case group and 90 non-diabetic patient's was placed in the control group. A midstream urine (MSU) sample was taken from each patient, after confirming the presence of yeast agents from all patient samples using the direct examination, culture was done on CROMagar candida medium. Out of 90 patients in the case group, 17 were diagnosed with candiduria. The frequency of candiduria in this group was reported to be 18.9%, the highest frequency was *Candida albicans* (12.2%), followed *by C. glabrata* (5.6) and *C. parapseliosis* (1.1). Also, in the control group, 2 people were diagnosed with candiduria. The surveys displayed that the prevalence of candiduria in diabetic patients was significantly higher compare to non-diabetics. In addition, there was a significant relationship between the prevalence of candiduria with *C. albicans* and non-*albicans Candida* in diabetic patients with predisposing factors such as uncontrolled blood sugar, and use of broad-spectrum antibiotics were observed. In conclusion candiduiria significantly more common in diabetic patients with uncontrolled Blood sugar and broad-spectrum antibiotic usage.

1. Introduction

Candiduria is a general term for the presence of *Candida* spp. in urine and defined as the presence of more than 10^4 CFU/ml of *Candida* spp. in urinary tract system. Its appearance may be asymptomatic to clinical sepsis (Lestari & Zulkarnain, 2021). Although, during the last decades the guidelines for the diagnosis and management of candiduria have changed significantly Nevertheless, Candiduria were considered as one of the controversial issues in

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patients management whose diagnosis and treatment options are probably not standardized(Alfouzan & Dhar, 2017; He et al., 2021). On the other hand, the statistics published by the International Diabetes Federation indicate that more than 537 million adults in universal have diabetes and will reach more than 600 million people in the next 25 years(International Diabetes Federation, 2021; Lin et al., 2020). Further evidence from the Global Action Fund states that more than 300 million people suffer from Life-threatening fungal infections every year(Global Action Fund for Fungal Infections, 2024). Diabetes Mellitus (DM) is known to increase urinary tract infections and is one of the predisposing factors for candiduria. Various factors such as diabetes mellitus, immunosuppression, gender, age, usage of broad-spectrum antibiotics, and organ transplantation have been considered in occurrence of urinary tract candiduria (Akinjogunla, Divine-Anthony, Ajayi, Etukudo, & Etok, 2020). Research has shown that chronic fungal infections in the group of diabetic patients suffering from immune disorders; has led to death rate growing (Pandya, 2020). The presence of *Candida* in the urine serves as a marker for hematogenous implantation into the kidneys. Candiduria reflects colonization or infection of the lower urinary tract or kidneys. *Candida* spp. is the fifth most common urinary tract pathogen in some countries (Rishi, Jain, & Ruchi, 2020). *Candida* spp. can colonize in the lower or upper urinary system and cause pyelonephritis, cystitis, urethritis and prostatitis. They may even appear through the bloodstream in the upper urinary tract or ascend the urinary tract from the focus of *Candida* colonization in the urethra (Lai et al., 2023). According to epidemiological studies, *C. albicans* is the most common species isolated from candiduric patients in Iran. However, in recent years, due to the increase in resistance to antifungal drugs, non-albicans *Candida* species, including *C. glabrata*, *C. krusei*, *C. parapsilosis*, and *C. tropicalis*, have also been implicated. To date, the average prevalence of candiduria among Iranian patients is lower than the global ratio, and men are more affected than women: M:F, 1.2:1, as in other countries, *C. albicans* has been the most common infectious agent, followed by non-*albicans candida*, including *C. glabrata*, *tropicalis*, and *krusei*, are more common(Gharaghani, Taghipour, Halvaeezadeh, & Mahmoudabadi, 2018). Evidences indicates that Akinjogunla et al investigated asymptomatic candiduria in type 1 and type 2 diabetic patients. Their results showed out of 51 MSU samples, more than 31.4% of the samples contained yeast cells and leukocytes. Furthermore, the prevalence of candiduria among people was not significantly related to age, types and duration of diabetes, gender, smoking, and alcohol consumption(Akinjogunla et al., 2020). Ghasemi et al analyzed the isolated species of candiduria and antifungal sensitivity trends in hospitalized patients. The rate of candiduria among patients was 11.5%. According to CROMagar candida and PCR-RFLP, the most common isolated species was *C. albicans* (74%), followed by *C. glabrata* (26%)(Ghasemi, Rabiei, Lotfali, Abolghasemi, & Ansari, 2020). The evaluation of *Candida* spp. in diabetic patients showed that there was a significant relationship between candiduria and female gender, high FBS and positive urine glucose test, uncontrolled diabetes (HbA1c $\geq$8)($P<0.05$). The predisposing factor and causal relationship between diabetes and candiduria should be highlighted(Falahati et al., 2016). Considering the significant prevalence of these conditions in today's society, if candiduria and diabetes are found to be related to other risk factors, it can be used as a cost-effective and accessible test for screening vulnerable persons. The present study were applied an endeavor to examine the relationship between candiduria and diabetes. The prevalence rate of *Candida* infection in people with diabetes and non-diabetic patients who referred to Amir Al-Momenin Hospital in Zabol city, Iran was evaluated.

2. Materials and Methods

The current research was performed through a descriptive analytical study. The research population consisted of all people between 17 to 75 ages with type I, type II diabetes, pregnancy and juvenile diabetes, who were selected through random sampling. Nineteen persons participated in case and control groups respectively. A researcher-made checklist was used to collect data, and various variables such as age, education level, *C. albicans*, and type of antibiotic used, diabetes, HbA1c, predisposing factors, and non-*C. albicans* were extracted from

the patients' files. After recording the patient's information referring to Amir Al-Momenin Hospital and obtaining informed consent, the first morning urine sample was collected from the patients using a midstream urine (MSU) sample method. Subsequently the presence of yeast agents from all patient samples using direct examination and culture methods were approved. Samples were cultured on Sabouraud Chloramphenicol Agar (Manufactured by Europeen Division QUELAB/ UK) medium (65.5 g/L) for 48 hours in 35°C. In the next phase, phenotypic tests such as germ tube, chlamydospore and CHROMagar candida media (*C. albicans*: green; *C. glabrata*: purple, *C. tropicalis*: royal blue…) were used to detect of fungi. The obtained data were analyzed using chi-square and t-test.

3. Results

According to the table1, the average age of the studied patients in case group and control was group 55.43 and 49.57 respectively. The average Hba1c in the case and control group was 8.32 and 5.48 and lastly the average FBS in the case group was 130.68 and in the control group is 100.15(Table 1). In terms of gender, in the case group, 41 people (45.6%) were male and 49 people (54.4%) were female. In the control group, out of 90 patients studied, 42 (46.7%) were male and 48 (53.3%) were female.

The frequency distribution of Candiduria according to the causative species, in 90 diabetic patients studied in the case group; candiduria with *C. albicans* 12.2%, *C. glabrata* 5.6%, and *C. parapseliosis* 1.1% were observed. In addition, in the control group, out of a total of 90 patients, 2 patients had *C. glabrata* (Table 2).

The occurrence of Candiduria in the diabetic and non-diabetic patients also show that among the 90 diabetic patients in the case group, 17 people had Candiduria and in the control group, only 2.2% of the total number of non-diabetic patients had Candiduria. Based on the results of statistical analysis, there was a significant relationship between the prevalence of Candiduria in diabetic and non-diabetic persons (Table 3).

Other findings exhibited that candiduria with *C. albicans* agent in patients using the phenotypic method of candiduria with agent 12% of *C. albicans* and 6.7% of non-albicans were positive, while in the control group, only 2.2% of non-*albicans* were observed. Based on the results a significant difference was observed in the prevalence of *C. albicans* between the case and control groups (Table 4).

According to table 5; from the total number of patients suffering Candiduria with a non-*albicans* agent in the case group, 5 people had a Predisposing factors (at least one history of hypertension, kidney failure, or hematological disorders). Also, in the control group, none of the 2 patients with Candiduria had a Predisposing factors. Furthermore a significant difference was observed between the prevalence of Candiduria with a non-*albicans* factor and predisposing factors in the case and control groups.

Table 1. Mean and standard deviation of quantitative variables in case and control groups

Groups/ variables	Case Groups			Control Groups		
	Number	Mean	standard deviation	Number	Mean	standard deviation
Age	90	55.43	12.47	90	49.57	14.54
Hba1c	90	8.32	1.40	90	5.48	0.27
FBS	90	130.68	24.78	90	100.15	9.87

Table 2. Frequency of predisposing factor of Candiduria in case and control groups

Groups/ variables		Case Groups		Control Groups	
		Number	percent	Number	percent
The causative factor of Candiduria	*C. albicans*	11	12.2	0	0
	C. glabrata	5	5.6	2	2.2
	C. parapsoriasis	1	1.1	0	0
	Negative	73	81.1	88	97.8
	Total	90	100	90	100

Table 3. Frequency of Candiduria in the diabetic and non-diabetic patients

Groups/ variables		Group				p-value
		Case Groups		Control Groups		
		Number	percent	Number	percent	
Candiduria	Positive	17	18.9	2	2.2	0.000
	Negative	73	81.1	88	97.8	
	Total	90	100	90	100	

Table 4. Frequency of candiduria with *C. albicans* agent in patients with diabetes and non-diabetic group using phenotypic method

Groups/ variables		Group				p-value
		Case Groups		Control Groups		
		Number	percent	Number	percent	
Candiduria with the *C. albicans* agents	Positive	11	12.2	0	0	0.001
	Negative	79	87.7	90	100	
	Total	90	100	90	100	
Candiduria with the none *C. albicans* agents	Positive	6	6.7	2	2.2	0.14
	Negative	84	93.3	88	97.8	
	Total	90	100	90	100	

Table 5. Frequency of Candiduria with albicans and non-*albicans* in diabetic and non-diabetic patients according to predisposing factors

Groups/ variables		Predisposing factors	Group				p-value
			Case Groups		Control Groups		
			Number	percent	Number	percent	
Candiduria with the *C. albicans* agents	Positive	yes	11	100	0	0	0.000
	Negative	no	0	0	0	0	
	Total		11	100	0	0	
Candiduria with the none *C. albicans* agents	Positive	yes	73	92.4	14	15.6	0.14
	Negative	no	6	7.6	76	84.4	
	Total		79	100	90	100	

4. Discussion

Although candiduria has been observed in hospitalized patients, it can lead to cystitis, pyelonephritis, prostatitis, epididymitis, and invasive candidiasis in people with predisposing factors such as Diabetes mellitus, indwelling urinary catheters, use of broad-spectrum antibiotics, urinary obstruction and hospitalization in the intensive care unit (Odabasi & Mert, 2020). In our study, we compared the prevalence of *Candida* infection in people with diabetes and non-diabetic people who referred to Amir al-Mominin Hospital in Zabol city, Iran. This study was conducted on 180 people, including 90 people in the control group consisting of non-diabetic people and 90 people of the case group consisting of diabetic patients were performed. In the case group, 45.6% were men and 54.4% were women. In the control group, 46.7% of the study people were men and 53.3% were women. The average age of the case group was 55 and the average age of the control group was 49 years.

According to the results, out of 90 diabetic patients in the case group, 17 cases had

Candiduria in control group, 2 non-diabetic patients had candiduria. There was a statistically significant relationship between non-diabetics, so that the prevalence of candiduria was higher in diabetic people. This finding was in agreement with the consequences of Haghigi Pour et al. and Akinjogunla et al (Akinjogunla et al., 2020; Haghighipour, Pourahmad, Noorbakhsh, & Mohammadi, 2019).The results of Haghigi Pour et al study showed that Candida albicans was the most common species among clinical isolates (94%), followed by Candida tropicalis (4%), Candida glabrata (1%) and Candida parapsilosis (1%). In terms of age, most of the patients are between 71 and 80 years old, and diabetes mellitus and neutropenia are the main risk factors among patients (Haghighipour et al., 2019). The results of Akinjogunla et al research also showed that patients with diabetes were more sensitive to Candida sp. (Akinjogunla et al., 2020).

Additionally, from 90 diabetic patients studied in the case group, candiduria with *C. albicans (*11 cases), *C. glabrata (*5 case), and 1 case parapseliosis were observed. As well as in 2 patient *C. glabrata* agent were identified and 88 people did not have candiduria. Thus, the most common causative agent of candiduria among diabetic patients was *C. albicans*, which is consistent with the results of the study performed by Ghasemi et al and Rodrigues et al(Ghasemi et al., 2020; Rodrigues, Rodrigues, & Henriques, 2019).Besides in the non-diabetic group, the most common causative agent was *C. glabrata*, which is consistent with the results of Falahati et al.'s study (Falahati et al., 2016). The results showed that in the case and control groups, 6 and 2 patients had candiduria with a non-albicans agent, respectively. The analysis of the research shows that there was no significant difference in the prevalence of candidiasis with a non-albicans agent between the case and control groups. The findings was not consistent with the results of Falahati et al.'s study (Falahati et al., 2016). In terms of gender, there were 5 males and 6 females in the group of patients with candidiasis caused by *C. albicans*, while in the control group, candiduria caused by *C. albicans* was not observed. In the group of patients with non-*albicans* candiduria, there were 3 men and 3 women, respectively. Also, all subjects in the control group of candiduria with a non-albicans agent were male. The relationship between candiduria with *C. albicans* and non-*albicans* agents according to gender in the group of diabetic and non-diabetic patients were not significant, which was consistent with the results of Akinjogunla et al.'s study and the results of Yashavanth et al.'s research were different(Akinjogunla et al., 2020; Yashavanth, Shiju, Bhaskar, Ronald, & Anita, 2013). In Akinjogunla et al.'s research, the prevalence of candidiasis in subjects was not significant in terms of age, type and duration of diabetes and gender ($P \geq 0.005$)(Akinjogunla et al., 2020).whereas Yashavanth et al.'s finding showed that The isolation rate of Candida species among men group was 41 cases (62.12%) more than 25 cases of women (37.87%) (Yashavanth et al., 2013).

The results exhibited that there was a significant relationship between candiduria with albicans and non-*albicans* agents and the average age among the diabetic patients studied. This finding were in accordance with Ismail et al results (Ismail, El-Haliem, Farouk, & Aboelmagd, 2020). So the average age was higher in positive cases. In the group of non-diabetic patients, there was no candiduria with albicans factor, and there was no significant relationship between candiduria with non-albicans factor and the average age in this group. In the present study, all patients with candiduria caused by *C. albicans* in the case group had a diabetic disease, but no candiduria caused by *C. albicans* was observed in the control group. The results of data analysis indicated that there was a significant relationship between candiduria with *C. albicans* and predisposing factors. In the group of patients with candiduria with non-albicans agents, 5 cases had high blood pressure, heart failure, kidney or hematological disorders. It should be mentioned that a significant difference was detected between the prevalence of candiduria with non-*albicans* agent and predisposing factors in the case and control groups. This finding was contrast with the study results of Ghasemi et al and Rodrigues et al (Ghasemi et al., 2020; Rodrigues et al., 2019). The evidence of another investigation indicated that in the case group, patients with candidiasis with albicans agent, 7 people had taken antibiotics; but it was not observed in the control group. Therefore, there was a significant relationship between candiduria with *C. albicans* and antibiotic usage. These findings were

aligned with the results of Gajdacs et al study (Gajdács, Dóczi, Ábrók, Lázár, & Burián, 2019).

Among the limitations of the research, the lack of cooperation of the hospital personnel to collect information, the lack of provision of the study subjects with the entry and exit criteria; and also the patient's lack of satisfaction with diagnostic procedures such as urine sample and blood test to determine HbA1c level occurred. The research team tried to give the necessary explanations to the people studied in this subject. Also, considering the small number of studies conducted, similar studies with a larger sample size are recommended.

Conclusion

Our finding showed that candiduiria significantly more common in diabetic patients with uncontrolled Blood sugar, and broad-spectrum antibiotic usage. In fact, each of these factors such as: indwelling urinary catheters, use of broad-spectrum antibiotics, urinary obstruction and hospitalization in the intensive care unit, kidney or hematological disorders can be a risk factor for the prevalence of Candiduria in diabetic patients. Furthermore, considering the significant relationship between the prevalence of candidiasis with albicans and non-albicans agents in diabetic patients with various factors such as fasting blood sugar level, Hba1c, background factors and antibiotic use; Health care policymakers should pay special attention to the risk factors in diabetics peoples.

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Refereces

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