Postepy Hig Med Dosw (online), 2014; 68: 1036-1039
e-ISSN 1732-2693

www.phmd.pl
Original Article

Received: 2013.09.30
Accepted: 2014.06.04
Published: 2014.08.29

The problems of urinary tract infections with *Candida* spp. aetiology in women

Problematyka zakażeń układu moczowego (ZUM) o etiologii *Candida* spp. u kobiet

Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

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Summary

Urinary tract infections (UTIs) in women are a growing clinical concern. The most frequent risk factors of UTIs with fungal aetiology in women are: antibiotic therapy (especially broad-spectrum antibiotics), immunosuppressive therapy, diabetes, malnutrition, pregnancy, and frequent intercourse. The aim of the study was to analyse urinary tract infections with *Candida* spp. aetiology in women hospitalised at the Clinical Hospital in Poznań, Poland, between 2009 and 2011. The investigations revealed that as many as 71% of positive urine cultures with *Candida* fungi came from women. The following fungi were most frequently isolated from the patients under analysis: *C. albicans* (47%), *C. glabrata* (31%), *C. tropicalis* (6%), *C. krusei* (3%). In order to diagnose a UTI the diagnosis cannot be based on a single result of a urine culture. Due to the small number of antifungal drugs and high costs of treatment, antifungal drugs should be applied with due consideration and care.

Key words: **Candida • urinary tract infections • women**

Full-text PDF: http://www.phmd.pl/fulltxt.php?ICID=1118989

Word count: 1705
Tables: –
Figures: –
References: 22

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Introduction

Urinary tract infections (UTIs) are one of the most frequent causes of doctor's visits [11,22], and in recent years their number has grown significantly [1,3]. The UTI is an inflammatory reaction with bacterial, fungal or viral aetiology [20], proved by the presence of microbes in urine [17].

Candida fungi are a frequent and common factor responsible for infections in the urinary tract (about 10-30%) [8, 13]. This is due to the closeness of the urethra and anus. The region of the vulvar vestibule may be periodically colonised by microbes from the alimentary tract, including yeast-like fungi [15, 19]. The ascending pathway may be the route of urinary tract infections [1]. UTIs are more often diagnosed in women than in men, as a consequence of their anatomical structure (a short urethra and the closeness of the vagina and anus) [3,20]. As many studies have shown, 3-8% of the female population develop a UTI at least once in their lifetime [1]. Urinary tract infections can be observed both in healthy and hospitalised patients [9].

Candida fungi are very often cultured in urine. However, this does not always mean that the urinary tract is infected and it is necessary to start an antifungal therapy. This situation may have been caused by vaginal mycosis or fungal colonisation of the perineum rather than a urinary tract infection. An antifungal therapy should not be initiated upon a single result of an investigation where *Candida* spp. fungi were cultured. The infection should not be confused with colonisation and the urine test must be repeated.

The most important moment in the diagnostic process of UTI is appropriate collection of urine for culture, which should be done after the night, after careful washing, without wiping the scrotal region, from the midstream, into a sterile container. The sample needs to be delivered to a laboratory as soon as possible and stored in a refrigerator if necessary. Only this procedure of urine collection guarantees reliability of the test result [21].

The urinary catheter is a frequent cause of UTIs, especially in diabetics. It may even cause urosepsis [7,10]. UTIs make up 30-40% of hospital infections, but 90% of them are infections of patients with a urinary catheter [2,7,14].

The most frequent risk factors of fungal infections of the urinary tract and/or vaginal mycosis are: antibiotic therapy (especially broad-spectrum), immunosuppressive therapy, diabetes, malnutrition, pregnancy, and frequent intercourse. The woman may also be infected by a partner who is an asymptomatic carrier of *Candida* spp. fungi [1,15,18,19,20]. Infections are usually caused by microbes which colonise the vulvar vestibule and microorganisms which are under the man's foreskin [20]. Mycosis may also develop as a result of poor intimate hygiene. In spite of the application of local and/or general treatment, there are frequent infection relapses [18]. It is possible to prevent infection relapses by due care of the urethral outlet region [1]. UTI relapses, which usually result from vaginal mycosis, are a serious problem, especially in pregnant women [22]. *Candida albicans* is the most frequent aetiological factor of those infections in this group of patients [16].

Materials and Methods

The aim of the research was to analyse urinary tract infections with *Candida* spp. aetiology in women hospitalised at the Clinical Hospital in Poznań, Poland, between 2009 and 2011.

All urine samples were analysed for bacteria and fungi. Each sample was quantitatively cultured on ready-to-use solid growth media on Columbia Agar plates with 5% sheep blood, on a CPS chromogenic medium for urine culture and on a Sabouraud medium. The media were manufactured by bioMerieux. Each urine sample underwent a Gould test to indicate the possible presence of the antimicrobial agent in the patient's urine. The test enables appropriate interpretation of the test result.

The Columbia Agar plates with 5% sheep blood and the CPS chromogenic medium were incubated for 24 hours at 37°C, whereas the Sabouraud plates were incubated at 37°C for 24 hours and at 30°C for another 24 hours (the growth of fungi after 48 hours). After the incubation the growth of microbes was assessed for quantity. There was further identification of the species and the VITEK 2 system from bioMerieux with appropriate cards for microbial data was used to make the antibiogram.

Results

From 2009 to 2011, 7272 microbiological urine tests were performed at the Central Microbiological Laboratory, H. Święcicki Clinical Hospital, University of Medical Sciences,

Table 1. The number of urine tests with fungi cultured from patients from 2009 to 2011

Year	Number of urine tests	Number of positive urine tests	Number of positive urine tests with fungi	Number of tests with fungi in women (%)	Number of tests with fungi in men (%)
2009	2887	1096	104	84 (81%)	20 (19%)
2010	2345	1065	121	91(75%)	30 (25%)
2011	2040	948	121	68 (56%)	53 (44%)
Total	7272	3109	346	243 (70%)	103 (30%)

Table 2. The number of urine tests with individual species of Candida fungi from 2009 to 2011

Species	Number of strains						Total (%)
	2009		2010		2011		
	I	II	I	II	I	II	
C.albicans	16	23	19	19	15	22	114 (46.5%)
C.glabrata	15	13	16	17	10	4	75 (30.6%)
C.tropicalis	1	2	3	1	7	0	14 (5.7%)
C.krusei	0	0	1	3	0	3	7 (2.9%)
C.non-albicans	6	7	7	6	1	8	35 (14.3%)
Candida (total)	38	45	46	46	33	37	245 (100%)

I – firsthalf-year; II - secondhalf-year

Poznań, Poland. The material was analysed both for bacteria and yeast-like fungi.

Table 1 shows detailed data for the period under analysis.

There was a total of 3109 (42.7%) 'positive' tests, i.e. those where pathogenic microbes were cultured.

The negative results were 'sterile culture', 'no significant bacteriuria diagnosed' or 'unsterile urine collection, another test necessary'.

The positive results, i.e. those where pathogens were cultured, were usually the tests of nephrological patients (more than 40% of all positive tests), both outpatients (671 – 21.6%), and hospitalised patients (659 – 21.2%).

Fungi were cultured in 346 cases, including 243 cases of cultures from women patients (70.2%). The tests where fungi were cultured came from 193 patients. Table 2 shows detailed data.

In a situation when there were few fungi – individual colonies, i.e. the number implied it was colonisation rather than infection – in each case the result included information about the need to have gynaecological consultation which would facilitate diagnosis. The comment was given in 89 out of 243 tests with *Candida* fungi cultured from women. In reply to the suggestion urine was tested again in 39 cases. As a result fungi were cultured again in as many as 27 tests, which proved infection with fungal aetiology in the urinary tract.

The following fungi were cultured most often: *C. albicans*, *C. glabrata*, *C. tropicalis* and *C. krusei*. Other *Candida* non-*albicans* species were cultured in individual cases – *C. lusitaniae* (6), *C. kefyr* (4), *C. inconspicua*/*C. norvegensis* (3), *C. parapsilosis* (2), *C. guilliermondii* (1), *C. holmii* (1) and *C. rugosa* (1) and other *C.* non-*albicans* without the possibility of further identification of the species, because the strains did not exhibit further growth in laboratory conditions (17). 255 strains of individual species were cultured from women in 243 tests. In 12 tests two different species or strains of *Candida* fungi were cultured.

Discussion

The growing number of UTIs with *Candida.* spp. aetiology in hospitalised patients is a significant clinical problem. It is difficult for the doctor to distinguish between colonisation and infection and to implement an appropriate therapy [10].

When fungi are cultured in women's urine at the Central Microbiological Laboratory, H. Święcicki Clinical Hospital, University of Medical Sciences, Poznań, Poland, there is an extra note that gynaecological consultation should be taken into consideration in order to exclude the possibility of vaginal mycosis. Another collection of urine for microbiological tests is recommended. No antifungal therapy should be started on the basis of a single test result. It is particularly important for women. The tests showed that as many as 71% of positive urine cultures with *Candida* fungi came from women. The following fungi were most frequently isolated from the patients under analysis: *C. albicans* (47%), *C. glabrata* (31%), *C. tropicalis* (6%), *C. krusei* (3%). Other *Candida* non-*albicans* species were diagnosed in individual cases (*C. lusitaniae*, *C. kefyr*, *C. inconspicua*/*C. norvegensis*, *C. parapsilosis*, *C. guilliermondii*, *C. holmii* and *C. rugosa*).

If vaginal mycosis is diagnosed in a gynaecological examination, urine needs to be collected for tests after prior application of local treatment (clotrimazole vaginal tablets for 6 days before sleep, and simultaneously, clotrimazole cream) [6]. After this treatment urine needs to be collected for culture by means of vaginal tamponade. If fungi appear in the culture again, this is probably urinary tract mycosis.

In order to diagnose a UTI, it is not enough to rely on the urine culture only [1]. The result of the microbiological test always needs to be assessed in reference to the clinical situation on the basis of PCT, CRP, leucocytosis as well as a measurement of the temperature and general urine test. It is very important to make a distinction between a urinary

tract infection and a general infection. It is always necessary to determine which part of the urinary tract is infected, e.g. the urethra, bladder or kidneys. It is important for the choice of an appropriate therapy as it is related to drug penetration.

It is difficult to treat fungal infections. There are very few antifungal drugs, so they should be applied with due consideration. In view of the fact that antifungal drugs are usually toxic, it is necessary to carefully consider the application of appropriate drugs in a particular clinical situation. The problem becomes even more serious when pregnant women are infected [9]. Voriconazole and flucytosine belong to category D. Echinocandins and azoles are not recommended, either (category C) [12].

It is very important, especially in patients with lower immunity, to exclude systemic mycosis deriving from the urinary tract. In such cases antifungal therapies should be started immediately.

Fluconazole is a preferable drug for the treatment of urinary tract infections caused by *Candida* spp. due to its favourable safety profile, high concentration in urine and the possibility of oral and intravenous administration [13]. The optimal dosage of fluconazole in UTIs with *Candida* spp. aetiology without systemic mycosis in patients without acute renal failure is a saturation dose of 200 mg a day, followed by 100 mg a day for at least 4 days [4]. Other sources recommend that fluconazole be administered at a dose of 200 mg a day for 7-14 days [18].

There is a special problem with *Candida* non-*albicans* fungi in the therapy of UTIs. The fungi often colonise the vulva and vagina, and they are usually resistant to fluconazole, which is commonly applied [15].

There are four groups of drugs that can be used in an antifungal therapy: polyenes, azoles, echinocandins and nucleosides. The choice of an appropriate antifungal therapy should be made upon the identification, assessment of sensitivity and clinical state of the patient, the concomitant diseases, organ failure and toxicity of antifungal drugs [5].

According to many sources, it is possible to reduce the number of fungal infections of the urinary tract by limiting the application of urinary catheters, reducing the time of broad-spectrum antibiotic therapy and optimisation of the hypoglycaemic therapy in diabetic patients [8,13].

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The authors have no potential conflicts of interest to declare.