Fungal Urinary Tract Infection in Burn Patients

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Abstract

Background: Urinary tract infection is the most common hospital-acquired infection. Fungal species are unusual causes of urinary tract infection in healthy individuals, but common in the hospital setting or among patients with predisposing diseases and structural abnormalities of the kidney and collecting system. Burn patients are susceptible to nosocomial infections owing to the immunocompromising effects of burn injury, cutaneous and respiratory tract injury, prolonged intensive care unit stays and broad-spectrum antibiotic therapy. **Objective:** The study population includes adult patients of both genders who presented with different percentages of body burns. Urine sample was collected from each patient at the time of admission and weekly thereafter for 6 weeks and sent for general urine examination and urine culture to test for the possibility of fungal growth. Those who found to develop fungal UTI by urine culture during their hospitalization and had no infection at the time of admission were selected as subjects for our study. **Results**: 28 (18.6%) patients had positive fungal culture during their hospitalization, 11 of them were males and 17 were females, the most common age of presentation was 41-50 years and the mean age ± SD was (44.4 ± 10.7) years. The most common isolated fungi were *Candida albicans* (64.3%), followed by *Candida glabrata* (21.4%) and *Candida tropicalis* (7.1%). The majority of patients developed infection within the 2nd and 3rd weeks of hospitalization, however, those who presented with total body surface area burned > 40% developed an earlier infection within the 1st week. Female gender, urethral catheterization and diabetes mellitus were significantly associated with higher risk of infection as the P values were 0.03, 0.005 and 0.004 respectively. **Conclusion:** Fungal urinary tract infection occurred in 18.6% of burn patients. The most common causative fungi are *candida species*. Advanced age, female gender, high percentage of body burn, urethral catheterization and diabetes mellitus were identified as the most common risk factors of such infection.

Keywords: fungal urinary tract infection, candiduria.

الخلاصة

المقدمة: ان التهاب المسالك البولية هو اكثر انواع الالتهابات المكتسبة من المستشفيات شيوعاً. تعتبر الفطريات سبب غير تقليدي لحدوث التهاب المسالك البولية في الاشخاص الاصحاء, لكنها تكون سبب رئيسي لدى المرضى الراقدين في المستشفيات او في المرضى المصابين بامراض مهيئة للالتهاب او المصابين بالشذوذ الهيكلي للكلى والمسالك البولية. ان المرضى المصابين بالحروق يكونون عرضة للاصابة بعدوى المستشفيات بسبب نقص المناعة الناجم عن الحرق, اصابة الجلد والقناة التنفسية, طول فترة البقاء في وحدة العناية المركزة واستعمال المضادات الحيوية الواسعة الطيف. **المواد والطرائق:** تضمنت الدراسة عدد من المرضى البالغين من كلا الجنسين المصابين بدرجات مختلفة من حروق الجسم. تم تجميع الادرار لكل مريض في وقت الدخول الى المستشفى ومن ثم اسبوعياً لمدة 6 اسابيع وارساله الى فحص تحليل الادرار العام وزرع الادرار لاختبار نمو الفطريات. تم اعتبار المرضى الذين اصيبوا بالتهاب المسالك البولية الفطري خلال فترة رقودهم في المستشفى والذين هم بالاصل غير مصابين بهذا الالتهاب وقت الدخول الى المستشفى على انهم العينة الاساسية التي استخلصت منها نتائج الدراسة الحالية. **النتائج:** 28 (18.6%) مريض ظهرت لديهم نتائج زرع الفطريات موجبة خلال فترة رقودهم في المستشفى, منهم 17 انثى و 11 ذكر. غالبية اعمار المرضى كانت تتراوح بين 41–50 سنة وكان معدل الاعمار ± الانحراف المعياري (44.4 ± 10.7 سنة). اكثر انواع الفطريات المسببة للالتهاب كان *Candida albicans* بنسبة 64.3%, يليه *Candida glabrata* بنسبة 21.4% ثم *Candida tropicalis* بنسبة 7.1%. حدث الالتهاب عند غالبية المرضى في الاسبوعين الثاني والثالث خلال فترة رقودهم, على الرغم من ذلك فان بعض المرضى الذين كانت لديهم نسبة حروق الجسم اكثر من 40% اصيبوا بالالتهاب في وقت مبكر وذلك خلال الاسبوع الاول من الرقود. في هذه الدراسة وجد أن الجنس الانثوي, قسطرة الاحليل و داء السكري هي اكثر عوامل الخطر المؤدية الى زيادة نسبة الالتهاب حيث كانت قيمة **P** 0.03, 0.005

و 0.004 على التوالي. **الاستنتاج:** ان التهاب المسالك البولية الفطري يحدث بنسبة 18.6% لدى المرضى المصابين بالحروق. اكثر انواع الفطريات المسببة للالتهاب هو *candida species*. يعتبر تقدم العمر, الجنس الانثوي, النسب العالية من حروق الجسم, قسطرة الاحليل و داء السكري اكثر عوامل الخطر المسببة لهذا الالتهاب.

الكلمات المفتاحية: التهاب المسالك البولية الفطري, بيلة المبيضات.

Introduction

Urinary tract infection is the most common hospital-acquired infection (Schaberg et al. 1991). Fungal species are unusual causes of urinary tract infection (UTI) in healthy individuals, but common in the hospital setting or among patients with predisposing diseases and structural abnormalities of the kidney and collecting system (Fisher et al. 2011). Although an increase of candiduria among hospitalized patients has been reported, the significance of the presence of yeasts in the urine of patients is not clearly understood (Nucci 2000). The urinary tract may be invaded in either an antegrade fashion from the bloodstream or retrograde via the urethra and bladder (Fisher et al. 2011). A common clinical problem is to decide whether candiduria represents urinary tract infections or merely bladder colonization or contamination (Akalm et al. 2004). It has been observed that nosocomial urinary tract infections have increased in the last two decades, probably due to many predisposing factors associated with occurrence of candiduria. Several risk factors such as use of indwelling urinary devices, diabetes mellitus, antibiotic use, immunosuppressive therapy, extended hospitalization, extremes of age and female sex have been identified as associated with increase of *Candida* growth in urine (Sobel 2002). Catheter acquired urinary tract infection is one of the most common health care acquired infections (Magill et al. 2014). Even with preventive administration of antibiotics and the most careful hygiene of the urethra and catheter, urinary tract infection (UTI) occurs quite frequently in patients with long-term urethral catheterization (Kim et al. 2011). The most frequently occurring organism is *Candida albicans,* followed by *Candida glabrata, Candida tropicalis,* and *Candida krusei* (Lundstrom et al. 2001). However, non-albicans *Candida* species and non-candidal yeasts are increasingly being reported as the etiological cause of fungal UTI (Sobel 1999). Burn patients are susceptible to nosocomial infections owing to the immunocompromising effects of burn injury, cutaneous and respiratory tract injury, prolonged intensive care unit stays (which may involve endotracheal intubation and catheterization of blood vessels and bladder), and broad-spectrum antibiotic therapy (Kim et al. 2011).

The aim of the study is to determine the prevalence of fungal urinary tract infection, the most common fungal species and possible risk factors that may increase occurrence of infection in burn patients.

Materials And Methods

1. Patients:

A prospective study of 150 selected burn patients attending Medical City Burn Center in Baghdad from February 2015 to January 2017 was conducted. The study included adult patients of both genders who presented with different percentages of body burns; from them, urine samples were collected at regular intervals and investigated for fungal infection. Informed consent was obtained from each participant prior to sample collection. Data on patient demographics, underlying diseases, previous and concurrent infections, antibiotic and immunosuppressive therapy, urinalysis results,

urinary tract instrumentation and duration of hospitalization were collected from patients. All patients were receiving intravenous antibiotics from the time of admission or oral forms later. Intravenous antibiotics were given until the patients were able to tolerate oral intake (Kim *et al.,* 2011).

2. **Urine collection:**

Urine sample was collected from each patient at the time of admission and sent for general urine examination and urine culture to confirm that none of the patients had any form of UTI. Positive results were excluded from our study. Silicon-coated latex Foley catheters, 16 to 20 French, were inserted aseptically (in some patients as indicated) after lubrication by a team of trained health professionals following various procedures.

Then, Urine samples were aspirated again weekly for 6 weeks either directly or from the needleless sampling port of Foley catheter with a sterile syringe after cleansing the port with a disinfectant and were immediately sent to the microbiology laboratory for urine cultures and urinalysis to test for the possibility of fungal growth.

3. **Fungus culture**:

The urine samples were spread by calibrated loop (0.01 ml) onto Sabouraud dextrose agar plates supplemented with 100 µg/ml of chloramphenicol. Plates were incubated aerobically at 37ºC and read within 24 h. The detection level for quantitative cultures used in this study was greater than 10^4 CFU/ml, represented by a single colony of yeast on a plate (Platt *et al.,* 1983). The yeast like colonies were identified using Biochemical and Physiological tests viz. Germ tube production, chlamydospore formation on cornmeal agar, sugar fermentation and assimilation tests (Passos et al. 2005).

Results and Discussion

In burn patient's management, infection with systemic sepsis is the most important consideration. This systemic sepsis resulting from invasive infection remains the most common cause of high mortality rates among patients with major body burns. One of these is urosepsis. Multiple studies of nosocomial infections showed an increase in fungal isolates, particularly *Candida* species. Despite its prevalence, the significance of funguria remains uncertain. This disorder lacks consistant diagnostic criteria, such as the presence of pyuria or a colony count above which predicts the presence, location or severity of infection.

In our study, the results showed that 28 (18.6%) patients had positive fungal culture during their hospitalization. Variable results obtained by other studies (Passos *et al.,* 2005, Alvarez *et al.,* 2003, Kim *et al.,* 2011 and Febre *et al.,* 1999) showed that the prevalence of fungal urinary tract infections was 44.4%, 22%, 19.7% and 18.6% respectively.

There were 86 (57.3%) males and 64 (42.7%) females, among them 11 males and 17 females had positive fungal culture and this finding was significantly higher in females as the P value was 0.03, as shown in table 1. This incidence in females may reflect vaginal candidiasis. Yeasts may ascend from the genital tract to the urinary tract, explaining a higher candiduria incidence in women. A similar conclusion was achieved by (Sobel 2002, Febre et al. 1999 and Alvarez et al. 2003) as female sex have been identified to be associated with an increase of *Candida* growth in urine. Passos et al. 2005 also found that candiduria was higher in females (61.6%) than in males ($p = 0.001$).

Table 1: Gender of the patients and its relation to fungal culture results

Gender	No.	%	Positive culture	%	Negative culture	%	P value
Males	86	57.3	11	12.8	75	87.2	0.03
Females	64	42.7	17	26.6	47	73.4	
Total	150	100	28	---	122	---	

Patients age was ranging from 21 to 68 years, among those who presented with positive fungal cultures (28 patients) the most common age of presentation was 41-50 years and the mean age ± SD was (44.4 ± 10.7) years. Their age distribution is shown in figure 1. Other studies performed by (Carvalho et al. 2001, Passos et al. 2005, Kauffman et al. 2000 and Febre et al. 1999) also found advanced age of presentation as the mean age was (50.74 ± 3.13), (53 ± 19), (64.5 ± 18.2) and (65) respectively.

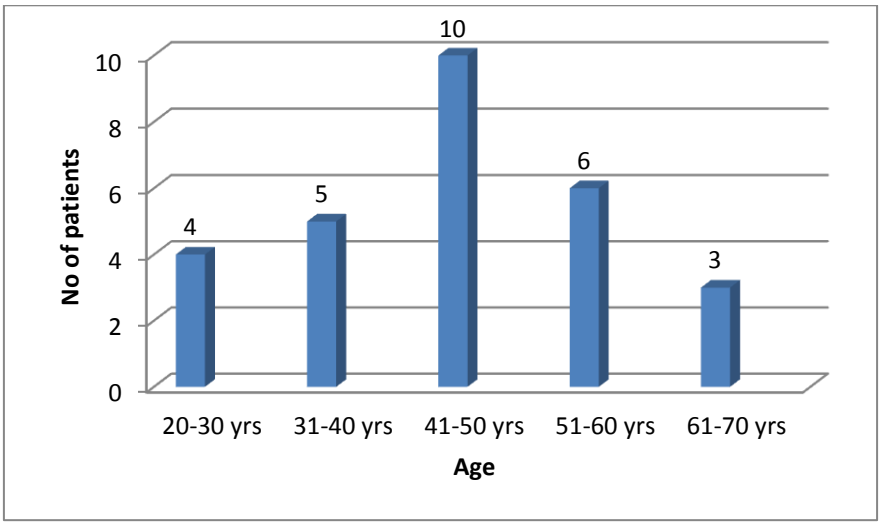

Fig. 1: Age distribution of patients who had positive fungal culture.

It was previously reported that the main pathogenic fungal types are candidal, aspergilli, and cryptococcal (Atiyeh *et al.*, 2005, Singh *et al.*, 2007). In this study, the most common isolated fungi were *Candida albicans* in 18 (64.3%) patients, followed by *Candida glabrata* in 6 (21.4%) and *Candida tropicalis* in 2 (7.1%). The distribution of different types of isolated fungi is shown in table 2. The emergence of non-*albicans* species may indicate selection of less susceptible species by antifungal agents especially fluconazole. Some *Candida* species as *C. glabrata* and *C. krusei* are less susceptible to fluconazole than *C. albicans* (Hoppe *et al.*, 1994, Nenoff *et al.*, 1999). Similar results were obtained by (Passos *et al.*, 2005, Alvarez *et al.*, 2003, Rezende *et al.*, 2002).

Table 2: distribution of isolated fungi

Fungal species	No of patients	Percentage
Candida albicans	18	64.3%
Candida glabrata	6	21.4%
Candida tropicalis	2	7.1%
Cryptococcus neoformans	1	3.6%
Trichosporon beigelii	1	3.6%
Total number	28	100

The time intervals from admission to the occurrence of infection were classified into 6 groups on a weekly basis. The distribution of patients who developed a fungal infection according to time of occurrence is shown in figure 2.

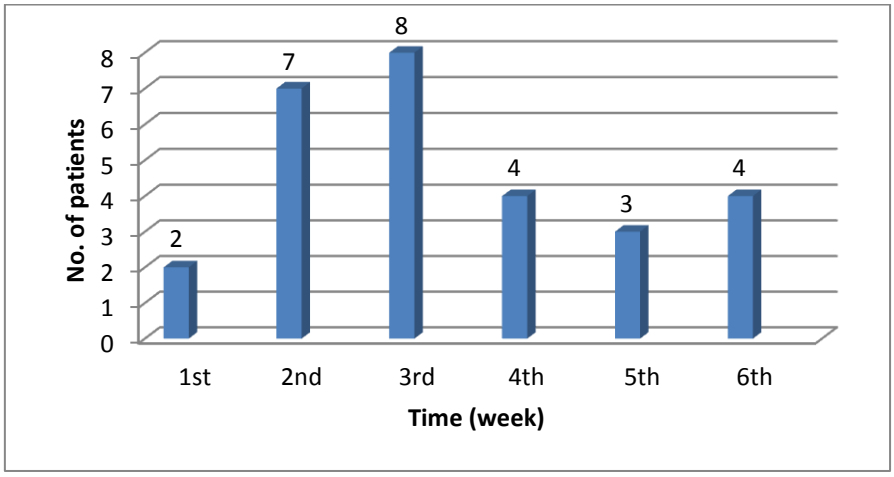

Fig. 2: Time intervals of infection development

Patients were classified into 3 groups according to the percentage of the total body surface area burned: ＜30%, 30% to 40%, and > 40%, body surface area burned was estimated by using the Lund and Browder chart (Neaman et al. 2011). The relation between the time intervals for development of infection and percentage of body burn is shown in table 3.

Table 3: Time of occurrence of fungal infection in relation to body surface area burned

Time of occurrence of infection	No. of patients who developed infection classified according to body surface area burned		
	＜30%	30% to 40%	> 40%
1st week	-	-	2
2nd week	2	2	3
3rd week	2	3	3
4th week	1	2	1
5th week	1	1	1
6th week	2	1	1
Total	8	9	11

So, majority of patients developed fungal UTI within the 2nd and 3rd weeks of admission, a possible explanation for this might be that a 2-week period is necessary for exogenous fungal colonization on wounds or other sites or from the patient's own gastrointestinal or upper respiratory tract flora (Luo G et al. 2011); however those who presented with high percentage of body surface area burned (> 40%) developed earlier infection (within the first week). Kim et al. 2011 also found an association between high percentage of body surface area burned (> 45%) and earlier development of infection.

Established predisposing factors for candidal urinary tract infections are diabetes mellitus, female gender, prolonged catheter drainage, and corticosteroid use (Wise GJ et al. 1993, Wainstein MA et al. 1995). Regarding other possible risk factors, it has been found that urethral catheterization and diabetes mellitus significantly increased the risk of fungal urinary tract infection as the P values were 0.005 and 0.004

respectively. Although fungal infection in patients with urethral catheterization has not been well defined, the use of invasive procedures has been shown to be as an important factor for fungal infection development (Alvarez *et al.,* 2003). Kim et al. 2011, Febre et al. 1999, Kobayashi et al. 2004 and Kauffman *et al.,*. 2000 also found that urinary catheterization is one of the most common predisposing and risk factors for development of fungal UTI. DM was demonstrated as the most common underlying disease by (Alvarez *et al.,* 2003, Carvalho *et al.,* 2001; Kauffman *et al.,* 2000).

Table 4: Significance of urethral cath. and DM in development of infection

	Catheterized	+ve culture	Non-catheterized	+ve culture	P value
No. of patients	88	23	62	5	0.005
	Diabetic	+ve culture	Non-diabetic	+ve culture	P value
No. of patients	56	17	94	11	0.004

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