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Risk Factors Associated with Funguria in Nosocomial Septic Patients at Surgical Intensive Care Unit

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ABSTRACT

Background: Candida spp rarely encountered in urine is in healthy people with structurally normal urinary tract. However, It is of common occurrence in hospitalized patients.The current study to detect the risk factors of funguria in nosocomial septic patients in surgical ICU.**Patients and methods:**A Cross sectional study included nosocomial patients with septic criteria after 7 days of admission at surgical ICU.Presence and duration of risk factors of funguria (urinary bladder Catheter, central vein catheter, mechanical ventilation,total parenteral nutrition, diabetes mellitus, chemotherapy, surgical operation, burns, immunosuppression, trauma and organ transplantation) were recorded.**Results:**Diabetes mellitus was found in (35.5%), followed by hypertension and Ischemic heart disease in (32.3% & 19.4%) respectively, COPD and Hepatic disease were found in 9.7% and 3.2% of the studied patients respectively.There was a significant difference in age and sex in relation to occurrence of funguria that was statistically higher among females and older patients. There was a highly statistically significance funguria in DM, HTN and IHD respectively. No significance difference in COPD and Hepatic diseases**.**All patients were catheterized by UBC and CVC. Patients on mechanical ventilation, on parenteral nutrition, DM and Surgical operation were statistically more susceptible to funguria. **Conclusion**:Funguria commonly affected those above 40 years of age among surgical ICU patients. Females were more commonly affected than males. Pseudomonas aeruginosa was the most recurrent causative organism Urinary bladder catheter and central vein catheter were the most frequently detected risk factor, followed by parenteral nutrition and mechanical ventilation.

Keywords:Candiduria, Risk Factors; Funguria;ICU

INTRODUCTION

Nosocomial fungal infections had emerged as an increasing problem in the recent years. Fungal infection rarely encountered in urine is in healthy people with structurally normal urinary tract. However, it is of common occurrence in hospitalized patients **(1)**.Symptomatic candiduria is normally seen in the inpatients and asymptomatic candiduria is observed mostly in the outpatients and healthy people.

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The prevalence of candiduria and the rate of its mortality between ICU inpatients is absolutely higher **(2).**Funguria account for up to 40% of infections in hospitals and 23% of infections in ICU **(3).**

The prevalence of ICU-acquired infections is significantly higher in developing countries than in industrialized countries, varying between4.4% and 88.9% (**4**). Published World Health Organization (WHO) review revealed that "In low- and middle-income countries the frequency of ICU acquired infection is at least 2–3 higher than in high-income countries; device-associated infection densities are up to 13 times higher than in theUSA" (**5**).

Most cases of candiduria are nosocomial because of the use of catheters and antibiotic therapy. Women are more likely to develop candiduria. Advanced age, ICU hospitalization, surgery, and preexisting diabetes mellitus are other known risk factors for candiduria **(6).**Risk factors for candiduria, but not specifically for Candida UTI, include increased age, female gender, antibiotic use, urinary drainage devices, prior surgical procedures, and diabetes mellitus (**7**).Urinary tract infections (UTIs) are the most common nosocomial infections among the hospitalized patients and their incidence has considerably increased during the recent decades. Several microorganisms are associated with UTIs including, bacteria, viruses, filamentous and yeasts (**8**).

Principles of management are similar to those for Candida infections, namely, extended courses of antifungal, removal of macroscopic foci of infection, and reduction of predisposing risk factors (**9**). The current study to detect the risk factors of funguria in nosocomial septic patients in surgical ICU.

PATIENTS AND METHODS

A Cross sectional study included nosocomial patients with septic criteria after 7 days of admission at surgical ICU.

Inclusion and exclusion criteria:

Nosocomial septic patients (from 18-60 years)after 7 days of admission at surgical ICU who previously treated with 5 days of antibiotic and immunosuppressive agents. While, previous treatment with antifungals for 2 weeks and positive sepsis screen at admission were excluded.

Methods:

All patients were conducted to full history taking, clinical examination and radiological investigation at surgical ICU of during a period of 6 months. Also, the demographic features,concomitant infections and underlying disease.

The studied risk factors of funguria included: urinary bladder Catheter, central vein catheter, mechanical ventilation ,total parenteral nutrition, diabetes mellitus, chemotherapy, surgical operation, burns, immunosuppression, trauma and organ transplantation.Urine culture for identification of funguria in nosocomial septic patients after 7 day of stay in ICU. If there was funguria, blood culture was done for fungi.

Statistical analysis:

The collected data were analyzed by computer using Statistical Package of

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Social Services version 24 (SPSS),Data were represented in tables and graphs, Continuous Quantitative variables e.g. age were expressed as the mean ± SD & median, and categorical qualitative variables were expressed as absolute frequencies & relative frequencies. Suitable statistical tests of significance were used after checked for normality. The results were considered statistically significant when the significant probability was less than (P <0.05) asinsignificant (NS).P-value < 0.001 was considered highly statistically significant (HS).

RESULTS

The presents study demonstrates that 21 out of 31 patients (67.7%) of the studied patients were males and (32.3%) were females**(Figure 1)**.Diabetes mellitus was found in (35.5%), followed by hypertension and Ischemic heart disease in (32.3% & 19.4%) respectively, COPD and Hepatic disease were found in 9.7% and 3.2% of the studied patients respectively**(Figure 2)**.

All patients were catheterized by UBC and CVC. Parenteral nutrition was found in (48.4 %) of studied patients, other risk factors were in the form of mechanical ventilation, trauma, DM and surgical operation in (41.9%,41.9%,29% &29%) respectively, immunosuppression was found in only (3.2%) of the studied group**(Table 1)**.About 13 out of 31 patients (41.9%) of the studied patients had positive Funguriain culture**(Figure 3)**.Pseudomonas aeruginosa was (58.1%) of theincluded cases, acinetobacterbaumannii (41.9%) and Klebsiella pneumonia in (29%) of cases**(Table 2)**.

Regarding antibiotic sensitivity, ciprofloxacin and gentamycin were the commonest antibiotic sensitivity results of culture in (29%), Followed by Vancomycin or Colistin in (9.7%) of cases**(Table 3)**.

There was a significant difference in age and sex in relation to occurrence of funguria that was statistically higher among females and older patients**(Table 4)**. There was a highly statistically significance funguria in DM, HTN and IHD respectively. No significance difference in COPD and Hepatic diseases**(Table 5)**.

All patients were catheterized by UBC and CVC. Patients on mechanical ventilation, on parenteral nutrition, DM and Surgical operation were statistically more susceptible to funguria**(Table 6)**.

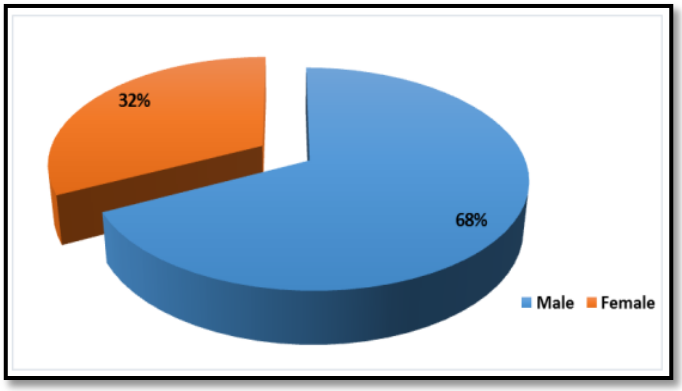

Figure (1): Pie diagram showing sex distribution among the studied patients.

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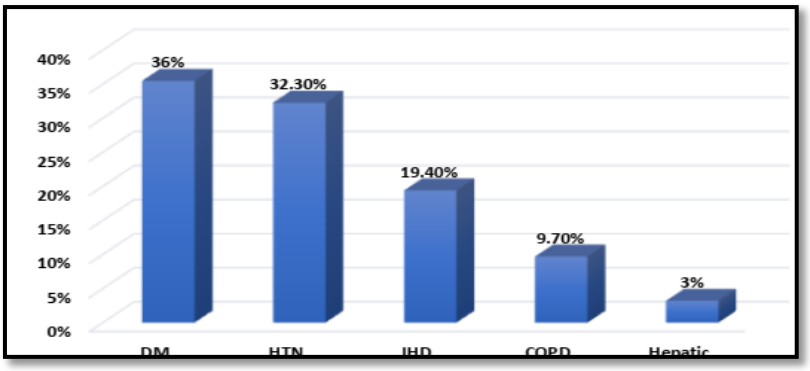

Figure (2): Bar chart showing concomitant disease among the studied patients.

Table (2): Risk factors among the studied patients

‡Risk factors	Studied patients(N=31)	
	No.	%
Urinary bladder catheter	31	100.0
Central vein catheter	31	100.0
Parenteral nutrition	15	48.4
Mechanical ventilation	13	41.9
Trauma	13	41.9
DM	9	29.0
Surgical operation	9	29.0
Immunosuppression	1	3.2

‡Multiple risk factors were found

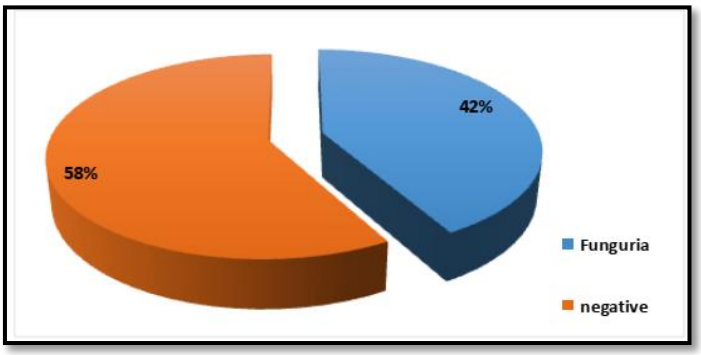

Figure (3): Pie diagram showing prevalence of funguria among the studied patients.

Table (2): Organism detected after culture among the studied patients

Organism	Studied patients (N=31)	
	No.	%
Pseudomonas aeruginosa	18	58
Acinetobacter baumannii	13	41.9
Klebsiella pneumonia	9	29
Staphylococcus aureus	8	25.8
Streptococcus pyogenes	5	9.7

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Table (3): Antibiotic sensitivity results of culture among the studied patients

‡Antibiotic	Studied patients(N=31)	
	No.	%
Ciprofloxacin	9	29.0
Gentamycin	9	29.0
Vancomycin	3	9.7
Colistin	3	9.7
Linzolid	2	6.5
Piperacillin \ Tazobactam	2	6.5
Meropnem	2	6.5
Rifampicin	1	3.2

Table (4): Funguria in relation to demographic data of the studied patients

Demographic data	Funguria (No=31)				p-value
	Negative (N=18)		Positive (N=13)		
	No.	%	No.	%	
Sex					
Female	2	11.1	8	61.5	0.006*
Male	16	88.9	5	38.5	
Age (years)					
Mean ± SD	31.67 ± 7.004		63.23 ±12.47		0.000**
(Range)	(19-43)		(47-88)		

Table (5): Occurrence of funguria in relation to concomitant disease among the studied patients

‡Concomitant disease	Funguria				p-value
	Negative (N=18)		Positive (N=13)		
	No.	%	No.	%	
Diabetes mellitus	0	0.0	11	84.6	0.000*
Hypertension	0	0.0	10	76.9	0.000*
Ischemic heart disease	0	0.0	6	46.2	0.002*
COPD	0	0.0	3	23.1	0.064
Hepatic disease	0	0.0	1	7.7	0.419

‡Multiple comorbidities were found *Chi-square test *p-value is significant

Table (6): Occurrence of funguria in relation to presence of risk factors among the studied patients

Risk factors	Funguria				p-value
	Negative (N=18)		Positive (N=13)		
	No.	%	No.	%	
Urinary bladder catheter	18	100.0	13	100.0	---
Central vein catheter	18	100.0	13	100.0	---
Mechanical ventilation	0	0.0	13	100.0	0.000*
Parenteral nutrition	3	16.7	12	92.3	0.000*
DM	0	0.0	11	84.6	0.000*
Surgical operation	0	0.0	9	69.2	0.000*
Trauma	0	0.0	1	7.7	0.419
Immunosuppression	0	0.0	1	7.7	0.419

*Chi-square test *p-value is significant

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DISCUSSION

Fungal diseases mostly are opportunistic mycoflora found frequently in genitourinary tract of humans especially in the immunocompromised, diabetics or pregnant women. If left untreated, this may lead to systemic candidiasis, multiple organ failure or death (**10)**.

In our study there was significant difference in age and sex in relation to occurrence of funguria, where funguria was statistically higher among females (8 cases vs. 2 cases; p=0.006), and older patients as mean age in funguria positive cases was 63.23 ±12.47 years versus 31.67 ± 7.004 years in funguria negative cases (table 9). Funguria was more frequent in females because they are more liable to develop ascending infection. Some reasons for higher prevalence of candiduria in females compared with males may be their shorter urethral length, transmission from the genital tract to the urinary tract, and the anti-*Candida* activity of prostatic fluid in male **(11)**.

Our finding was in agreement with **Alkilani et al. (12)** reported that; candiduria was more common in female (52.6%) than male patients (47.4%). On the other hand, candiduria was found more common in males (61.4%) as compared to the females (38.6%) in study of **Jain et al. (13)**.this difference may be due to small sample size of our study. In **Alkilani et al. (12)** study, candiduria was proved in 38 out of 200intensive care patients' urine samples (19%), other fungi were 2(1%), while 75 (37.5 %) showed no growth. Total no. of *Candida* was 38 as detected by API, 18(47.3%) of them was *Candida albicans*, 19(50%) of them was *Candida* tropicalis, and 1 (2.6%) of them was *candida* kruzi.

In the current study the most considerable concomitant disease was diabetes mellitus in (35.5%) of the studied patients, followed by hypertension and Ischemic heart disease in (32.3% &19.4%) respectively, other Concomitant diseases as COPD and Hepatic disease were found in 9.7% and 3.2% of the studied patients respectively, this came in agreement with previous studies that showed that chronic diseases like DM were associated with increased incidence of funguria (**12).** Also, **Rodrigues et al. (14)** found that diabetes mellitus (DM) is a metabolic disorder that predisposes individuals to fungal infections, including those related to Candida sp., due to immunosuppressive effect on the patient.

In our study in septic patient, with presence of multiple risk factors, as all patients were catheterized by UBC and CVC, parenteral nutrition was found in (48.4 %) of studied patients, other risk factors were in the form of mechanical ventilation, surgical operation and DM in (41.9%, 29%&29%) respectively, immunosuppression was found in only 3.2% of the studied group. All patients received antibiotics for at least 5.

Antibiotic therapy is one of the most important risk factors contributed to the pathogenesis of nosocomial candiduria by suppressing susceptible endogenous bacterial flora in the gastrointestinal and lower genital tracts. Antibiotic favors epithelial surface fungal colonization of the urinary tract especially in the presence of

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indwelling bladder catheter through impairing phagocytic activity and antibody synthesis **(15**).

In accordance with our results, **Ghahri (16)** found that indwelling urinary catheter is one of the most imperative risk factor contributing to the overgrowth of *Candida* spp. **Alkilani et al. (12)** reported that 78.9% among the investigated patients with candiduria, were urinary catheterized.

In contrast a very low incidence of catheter associated candiduria was reported by **Deorukhkar et al. (17)** aimed to determine the rate of catheter associated urinary tract *Candida* infections in medical intensive care unit patients. The rate of candiduria was 0.7% device days. This difference may be due to small sample size of our study or their good infection control bundle for urinary bladder catheter.

we found all patients positive for funguria in our study had central vein catheter, there was no cases of fungemia after blood culture was obtained from all patients to determine the risk of developing fungemia in patients presenting with funguriawhich is in disagreement with other researchers who observed lowered risk of candidemia following candiduria.**Jain et al. (13)**reported that the definite risk of developing invasive fungal disease is the presence of associated risk factors, and the mortality in these patients is very high. Hence, in critically ill patients having other associated risk factors and admitted in the ICUs, candiduria should not be ignored**.**

All positive funguria cases in our study were under mechanical ventilation. This came in agreement with **Abdeljaleel et al. (18)** found that in critically ill patients admitted to intensive care units, risk factors for candiduria were mechanical ventilation and length of hospital stay.

We found that parenteral nutrition was significantly associated with funguria as it was found in 12 patients (92.3%) of positive funguria cases $p<0.001$. This was similar to finding of **Ghiasian et al. (1)** as 56% of their patients used feeding tubes and of interest, the obtained results showed that there was a difference between candiduria and using feeding tubes in patients admitted to Iranian ICUs. Moreover **Wang et al. (19)** found that total parenteral nutrition is associated with candiduria.

Diabetic patients are at increased threat of funguria by predisposition to fungi colonization/infections via increase of fungal growth in the urinary tract and by impairment of phagocytic activity of macrophages as a result of lowered host resistance and fungal invasion **Ghiasian et al. (1)**.

In our study 84% of cases were positive for funguria had diabetes which was statistically significant $p<0.001$. Other studies have investigated diabetes mellitus as a risk factor for candiduria, **Alkilani et al. (12)** results showed that diabetes mellitus was seen in 31.5% of *Candida* infected patients. Also, **Jain et al. (13)** showed that diabetes mellitus was seen in 38.6% of patients with candiduria. However, **Ghiasian et al. (1)** study, reported that only 10% of patients with UTI had diabetes mellitus. **Bukhary (20)** upon conducting a literature review on candiduria management during a 37-year period, stated that the risk to develop candiduria was increased by two folds in the presence of diabetes mellitus. Therefore, control of this risk factor can be one of the most common approaches to manage candiduria in diabetic patients**.**

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Our results revealed that 9 cases (69.2) of positive funguria had a surgical procedure and it was significantly associated with funguria $p<0.001$, this was in agreement with **Gharaghaniet al. (8)** who found that candiduria is relatively more common among patients with specific predisposing factors such as surgery that was one of the invasive therapy that has important roles in the prevalence and increasing rate of candiduria in patients.

Trauma and immunosuppression were not significantly associated with positive funguria in our results. This was against previous studies who revealed that the increased incidence of nosocomial candiduria has also been associated with immune suppressive corticosteroid treatment (**8)**. In **Ghiasian et al. (1)** study, cortico therapy was the third most common risk factor (84%) contributed to UTIs. Similar results were found by **Marottaet al. (21)** showing that the Corticosteroid therapy may contribute to the development of candiduria among patients. In addition, **Youssef et al. (22)** reported that use of Corticosteroid and immunosuppressive agents was associated with increased risk of nosocomial infection. This difference may be due to small sample size of our study.

CONCLUSION

Funguria commonly affected those above 40 years of age among surgical ICU patients. Females were more commonly affected than males. Pseudomonas aeruginosa was the most recurrent causative organism Urinary bladder catheter and central vein catheter were the most frequently detected risk factor, followed by parenteral nutrition and mechanical ventilation.

No Conflict of interest.

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