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Research Article

Postoperative Hepatobiliary Surgeries' Fungal Infections Epidemiology (Prevalence and Risk Factors)

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Abstract

Background: Candidemia and disseminated candidiasis are major causes of morbidity and mortality in hospitalized patients especially in ICU, the incidence of invasive candidiasis is on a steady rise because of increasing use of multiple antibiotics and invasive procedures carried out in the ICUs. Risk factors for invasive candidiasis and candidaemia include prior antimicrobial therapy, central venous catheters, urinary catheters, ICU admission, parenteral nutrition, major surgery and immunosuppressive therapies. Candida species were the most frequently isolated organism from any sites and comprise 85% of total number of cultures.

Aim of the Study: Assessing the rate of fungal infections after hepatobiliary surgery and identification of the risk factors associated with the development of fungal infections in such patients.

Patients and Methods: A prospective cohort hospital based study was carried out at National Liver Institute. The studied group consisted of 210 patients All of them were examined thoroughly, their data were registered and sampled at two times, one at day of admission to be sure that they are free of fungal infection and the second was after hepatobiliary surgery pre-designed questionnaire was used which include data about personal history, medical history and suggested risk factors for fungal infections according to literature review and a pilot study of 40 cases excluded from the study sample.

Results: In the present study the incidence rate of fungal infection among patients undergone hepatobiliary surgeries in NLI is (45.2%) and the main predictors of fungal infection were Age (p value 0.001), Antibiotic use (p value 0.05), liver disease (p value 0.006), CVC (p value 0.043), urinary catheter (p value 0.05), and ICU hospitalization more than 48 hours (p value 0.000008).

Conclusions: High incidence of fungal infection after hepatobiliary surgeries may reach 45% due to type of patient doing such surgeries. The great prevalence of fungal colonization inside ICU which is easily transmissible emphasizes very strongly on the importance of infection- control guidelines.

Recommendations: Aggressive antibiotics shouldn't be used outside ICU and only antibiotics according to culture and sensitivity should be used to lessen down emergence of resistant strains and fungal flourishment.

Keywords: *Intensive Care Unit; Central Venous Catheter; National Liver Institute*

Introduction

Fungal diseases pose an important threat to public health. Opportunistic infections such as cryptococcosis and aspergillosis are becoming increasingly problematic as the number of people with weakened immune systems rises. This group includes cancer patients, transplant recipients, other people taking medications that weaken the immune system, and people with HIV/AIDS. Hospital-associated infections such as candidemia are the leading cause of bloodstream infections in the United States. Advancements and changes in healthcare practices can provide opportunities for new and drug-resistant fungi to emerge in hospital settings [1].

Community-acquired infections such as coccidioidomycosis (Valley fever), blastomycosis, and histoplasmosis, are caused by fungi that live in the environment in specific geographic areas. These fungi are sensitive to changes in temperature and moisture [1].

Candidemia and disseminated candidiasis are major causes of morbidity and mortality in hospitalized patients especially in the Intensive care units (ICU), the incidence of invasive candidiasis is on a steady rise because of increasing use of multiple antibiotics and invasive procedures carried out in the ICUs. Worldwide there is a shifting trend from *C. albicans* towards non albicans species, with an associated increase in mortality and antifungal resistance [2].

Candida species were the most frequently isolated organism from any sites and comprise 85% of total number of cultures [3].

Risk factors for invasive candidiasis and candidaemia include prior antimicrobial therapy, central venous catheters, urinary catheters, ICU admission, parenteral nutrition, major surgery and immunosuppressive therapies. Candidemia in ICUs is associated with a considerable increase in hospital costs and length of hospital stay, so once fungal infection is confirmed, species identification is in most cases an effective method for prediction of antifungal susceptibility [4].

Patients and Methods

A Prospective cohort hospital based study which was conducted at National Liver Institute (NLI) during the period from the first of May 2014 to the end of December 2015. Number of patients included in this study was 210 undergo hepatobiliary surgeries of both sex and any age during the period from the first of august 2014 to august of 2015 who were eligible to be included in the study according to inclusion criteria children or adults of both gender and undergo hepatobiliary major surgery with negative blood culture for fungal infection before surgery while any patient who took antifungal therapy during surgery or with positive blood culture before surgery were excluded from the study. All participants were examined thoroughly, their data were registered and sampled at two times, one at day of admission to be sure that they are free of fungal infection and the second was after hepatobiliary surgery, then sample identification; Conventional methods for yeast and yeast-like isolates (Corn meal agar description, Germ tube formation, Urease test, finally cultured on HiCrome™ *Candida* Differential Media) and Morphological methods for filamentous isolates identification (Slide culture technique and cultured on *Candida* Differential Media). Data were collected and statistically analyzed using SPSS (Statistical Package of Social Science) version 20 and Epi Info 2000 programs applying both student's t test and Mann-Whitney for quantitative variables, Chi squared test for qualitative variables with a significance level of $P \leq 0.05$. Logistic regression model was used to give adjusted odds ratio at 95% confidence interval of the effect of the different risk factors for the subject under the study.

Results

The study included 210 patients admitted to surgery department from august 2014 to august 2015, their mean ages was 39.2 ± 22.7 years ranging from 0.15 -73y. Most of the studied cases (79%) were above 18 years of age and also it was noted that 56.7% of the total number of patients studied was male and 43.3% was female, 83.1% of patients above age of 18 were educated, 53.6% of patients above age of 18 were not working, 92.3% of patients above age of 18 were married and 62.9% of the all studied patients were from urban areas (Table 1). Incidence rate of fungal infection among patients undergone major hepatobiliary surgeries in national liver institute is (45.2%) (Figure 1). Nearly 98% of positive cultures were of *Candida* species only 2.1% non-*candida* (*Aspergillus*) as 47.4% had *C. glabrata* infection, 41.1% had *Candida albican* infection, 4.2% *C. tropicalis*, 3.1% mixed tropicalis and C. non albican, 21% mixed *C. albican* and C. non albican and 2.1% *A. nigra* (Figure 2).

Socio-demographic risk factor	Fungal infection				Chi square test P value	OR (95%CI)
	Positive (N = 95)		Negative (N = 115)			
	No	%	No	%		
Age group						
≤ 18 year	9	20.5	35	79.5	0.0002	4.18 (1.89 - 9.24)
> 18 years	86	51.8	80	48.2		
Mean ± SD	43.7 ± 19.0		35.4 ± 24.6		0.029*	
Gender						
Male	57	47.9	62	52.1	0.376	0.78 (0.45 - 1.35)
Female	38	41.8	53	52.2		
Education (> 18yr., N = 166)						
Lower	15	53.6	13	46.4	0.838	0.918 (0.41 - 2.1)
Higher	71	51.4	67	48.6		
Occupation (> 18yr., N = 166)						
Non worker	43	48.3	46	51.7	0.333	1.353 (0.73 - 2.49)
worker	43	55.8	34	44.2		
Residence						
Urban	55	41.7	77	55.3	0.176	1.47 (0.84 - 2.59)
rural	40	51.3	38	48.7		
Marital status (> 18yr., N = 166)						
Single	8	66.7	4	33.3	0.285	0.513 (0.15 - 1.78)
Married	78	50.6	76	49.4		
Special habits smoking						
Smoker	41	55.4	33	46.6	0.03	1.89 (1.02 - 3.49)
Non smoker	54	39.7	82	60.3		

Table 1: *Socio-demographic risk factor in relation to fungal infection among patients undergoing hepatobiliary surgeries.*
** t- test p- value; OR: Odds Ratio; CI: Confidence Interval.*

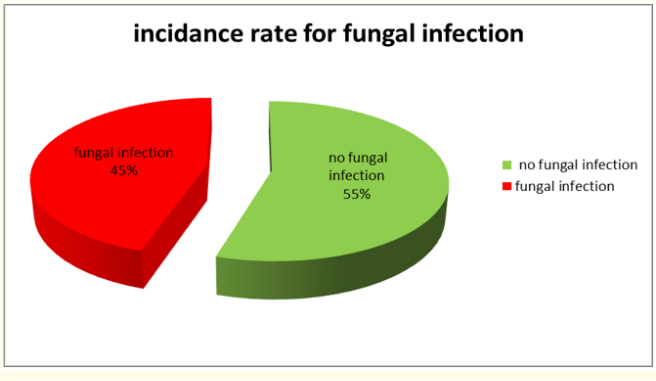

Figure 1: *Incidence rate for fungal infection.*

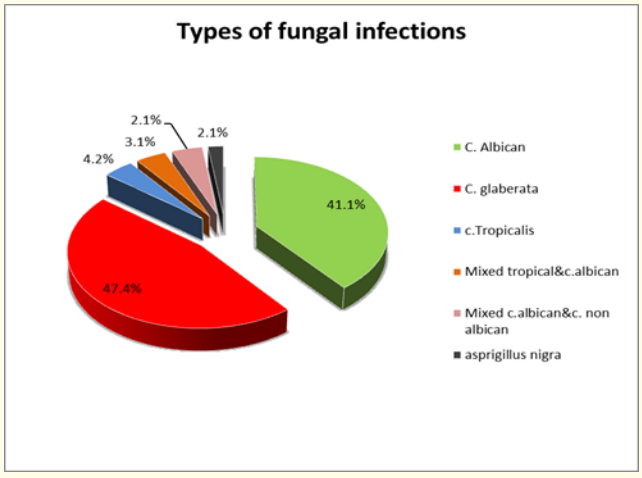

Figure 2: *Types of fungal infections.*

Discussion

In this study the incidence rate of fungal infection among patients undergone major hepatobiliary surgeries in national liver institute is (45.2%) (Figure 1) which is consistent with study of Magalhães., *et al.* 2015 at three different hospitals were (39%), (29.6%) and C (31.4%) [5]. The Singh., *et al.* 1997 study who found fungal infection rate was only 11% out of the 130 liver transplanted patients [6]. In this study 45.2% of the patients were positive culture for fungal infection, nearly 98% of positive culture were of *Candida* species only (Figure 2) this was in agreement with Magalhães., *et al.* 2015 study which showed that 89.8% of all the isolates (97 isolates) belonged to the *Candida* genus [5]. In this study age, antibiotic use, liver disease, Central Venous Catheter, urinary catheter, and ICU hospitalization more than 48 hours were the independent predictors of fungal infection (Table 4), however in the study of Wang., *et al.* 2014 the distribution of *Candida* species did not differ between elderly (above 60) and younger patients (below 60) which is against the result of the current study [7]. In this study long term use of antibiotics; Long-term aminoglycosides, penicillins, cephalosporins, imipenem, fluoroquinolones, clindamycin, metronidazole and erythromycin any combinations of these powerful antibiotics more than 2 weeks with cumulative antibiotics dosages adverse effects, of hepatobiliary surgery patients' was two times risky to acquire fungal infection than others (Table 2). This was consistent with Cornely., *et al.* 2008 study which stated that the risk of fungal infection also increased in patients who received a high number of antibiotics (P value 0.019) or long term using [9] however it was in contrast to study of Blumberg., *et al.* 2001 study where there was no increased risk of developing fungal infection associated with the individual use of some antibiotic agents [8]. In the current study positive HBV and/or HCV infection was four times risky to acquire fungal infection than others (Table 2), this result was compatible with the study of Singh., *et al.* 1997 which sated that histopathological document of recurrent hepatitis C virus hepatitis was a significant factor associated with late fungal infections in liver transplant patients (P = 0.006) [6]. In this study central venous catheter usage more than 7 days with multiple CVC insertion was three times risky to acquire fungal infection than others (Table 3) where this result was similar to result of Blumberg., *et al.* 2001 study which stated that patients who underwent a surgical procedure or had a CVC were 11 times more likely to develop candidemia [8]. In this study urinary catheter usage more than 14 days was two times risky to acquire fungal infection than others (Table 3) which was in consistent with Tambyah and Maki 2013 concluded that 14.9% of newly catheterized patients developed catheter associated urinary tract infections [10]. The current study stated that hospitalization intensive care unit more than 48 hour was six times risky to acquire fungal infection than others (Table 3) which was compatible with Blumberg., *et al.* 2001 study in which 76.0% of CBSI cases occurred within the first 3 weeks of admission to a surgical intensive care unit [8]. Also Wade., *et al.* 1995 study noticed that patients with early fungal infections had prolonged ICU admissions more than 48 hours p-value was 0.002 [11].

Risk factors and past history of diseases	Fungal infection				Chi square test P value	OR (95%CI)
	Positive (N = 95)		Negative (N = 115)			
	No	%	No	%		
Long-term use of antibiotic						
Yes	85	53.1	75	46.9	0.00004	4.53 (2.12 - 9.69)
No	10	20.0	40	80.0		
Chemotherapy						
Yes	4	66.7	2	33.3	0.41	2.48 (0.38 - 20.0)
No	91	44.6	113	55.4		
Steroids						
Yes	13	72.2	5	27.8	0.016	3.49 (1.2 - 10.17)
No	82	42.7	110	57.3		
Immunosuppressive drugs						
Yes	6	85.7	1	14.3	0.04	7.69 (0.89 - 172.49)
No	89	43.8	114	56.2		
HBV and/ or HCV						
Positive	84	50.9	81	49.1	0.002	3.21 (1.52 - 6.75)
Negative	11	24.4	34	75.6		
Diabetes						
Yes	30	66.7	15	33.3	0.001	3.08 (1.53 - 6.16)
No	65	39.4	100	60.6		
History of cancer						
Yes	29	78.4	8	21.6	0.00008	5.88 (2.54 - 13.62)
No	66	38.2	107	61.8		
CMV infection						
Yes	5	83.3	1	16.7	0.093	6.33 (0.7 - 145.85)
No	90	44.1	114	55.9		
Anemia						
Yes	73	49.7	74	50.3	0.049	1.84 (1.00 - 3.39)
No	22	34.9	41	65.1		
Organ transplantation						
Yes	11	84.6	2	15.4	0.003	7.4 (1.60 - 34.27)
No	84	42.6	113	57.4		
Past Operations						
Yes	78	59.1	54	40.9	0.0002	5.18 (2.73 - 9.82)
No	17	21.8	61	78.2		

Table 2: *Risk factors associated with fungal infection among patients undergoing hepatobiliary surgeries. OR: Odds Ratio; CI: Confidence Interval.*

Invasive techniques	Fungal infection				Chi square test P value	OR (CI 95%)
	Positive (N = 95)		Negative (N = 115)			
	No	%	No	%		
Blood transfusion						
Yes	55	66.3	28	33.7	0.0000007	4.27 (2.37 - 7.70)
No	40	31.5	87	68.5		
CVC						
Yes	80	65	43	35	0.0000001	8.93 (4.58 - 17.43)
No	15	17.2	72	82.8		
intravenous catheter						
Yes	94	45	115	55	0.452	0.00 (0.00 - 14.39)
No	1	100	0	0.0		
Abdominal Drain						
Yes	89	48.9	93	51.1	0.007	3.51 (1.36 - 9.06)
No	6	21.4	22	78.6		
Urinary catheter						
Yes	71	66.4	36	33.6	0.0000001	6.49 (3.54 - 11.92)
No	24	23.3	79	76.7		
Parenteral nutrition						
Yes	32	65.3	17	34.7	0.001	2.93 (1.50 - 5.71)
No	63	39.1	98	60.9		
Hospitalization ICU > 48h						
Yes	83	61.5	52	38.5	0.0000001	8.38 (4.12 - 17.01)
No	12	16.0	63	84.0		

Table 3: *Invasive techniques risk factor in relation to fungal infection among patients undergoing hepatobiliary surgeries.*

Logistic regression	β	S.E.	Wald test	p- value	OR (CI 95%)
	β constant = -7.17				
Age category	1.594	0.485	10.80	0.001	4.924 (1.903 - 12.739)
Antibiotic use	0.913	0.485	3.55	0.05	2.491 (0.964 - 6.437)
HBV and/ or HCV infection	1.376	0.496	7.70	0.006	3.958 (1.498 - 10.457)
Central Venous Catheter using	0.949	0.469	4.09	0.043	2.583 (1.030 - 6.476)
Urinary catheter	0.831	0.433	3.68	0.05	2.295 (0.983 - 5.358)
Hospitalization ICU > 48 hr.	1.770	0.456	15.09	0.000008	5.874 (2.405 - 14.347)

Table 4: *Logistic regression for the most relevant factors associated for developing fungal infection among patients undergoing hepatobiliary surgeries.*

Conclusions and Recommendations

Based on the findings of the present study, we can conclude that, high incidence of fungal infection after major hepatobiliary surgeries may reach 45% due to type of patient doing such surgeries. The great prevalence of fungal colonization inside ICU which is easily transmissible emphasizes very strongly on the importance of infection- control guidelines. Aggressive antibiotics shouldn't be used outside ICU and only antibiotics according to culture and sensitivity should be used to lessen down emergence of resistant strains and fungal flourishment. Using of antifungal prophylaxis only to high risk patients as a routine use of antifungal prophylaxis may cause resistance of fungal pathogens and selection of more hostile and less susceptible fungal species. A great attention must be paid in Egyptian hospitals for patients who undergoing major hepatobiliary surgeries in order to prevent and treat the fungal infections. Continued epidemiologic and laboratory investigations is needed to better characterize the ever-increasing array of endemic and opportunistic fungal pathogens, allowing for improved diagnostic, therapeutic and preventive strategies in the future.

Funding

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Conflicts of Interest

None.

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