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ORIGINAL ARTICLE

The study on rate of morbidity of fungal infections exiting in educational hospitals: Iran

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Abstract
Whereas hospitals have been assumed as the sites for spreading infection at level of world health, therefore, the current descriptive study has been conducted on 248 inpatients and outpatients who were suspected to fungal infection or disease. Samples were collected from several wards along with radiographic and endoscopic analyses in three hospitals, including urine, blood, skin, nail, wound (burning, surgery, eye and injury), lung, phlegm, ascites, bronchoaveolar lavage, (cerebrospinal, abdominal, and knee) fluids, peritoneum, fistula, ear tests and biopsy and sent to reference mycological center. The fungal species were identified by studying their macroscopic and microscopic and using PCR-RFLP technique. Among total studied patients, 180 cases had fungal elements; among which, there were 53 (29%) nosocomial infection and 127 (71%) community-acquired infection cases out of which inpatients and outpatients suffered from fungal diseases. The highest incidence of nosocomial infection belongs to intensive care units (ICU) ward in 16% of patients. The most common isolated fungi were *Candida* spp. The statistical results of this study suggest nosocomial fungal infections as the most important problems in the course of treatment among hospitalized patients who are more likely to be infected.

Keywords Nosocomial fungal infections · Fungal disease · *Candida* spp. · PCR-RFLP

Introduction

There are ten thousand fungal spores in every cubic meter in our surrounding ambience and this figure increases in some sites and centers further, e.g., in hospitals and ICUs where the above-said quantity may also reach to several hundred thousand. On the other hand, ever-increasing rise of patients with fungal infections and lack of access to antifungal efficient drugs have been led to creating concern for officials in healthcare and medical centers perse (George 2011; Tzar et al. 2013; Kordbacheh et al. 2005). Whereas fungal infections are assumed as the reason for rising mortality in inpatients at hospital, thus, the importance of review on epidemiology of fungal infections in adult patients has been considered in the instruction for control and prophylaxis of nosocomial fungal infections with focus on invasive candidiasis and recently aspergillosis (Pakshir et al. 2004; Tortorano et al. 2004; Nicolle et al. 2011). During the past decades, rising healthcare was related to fungal infections which have more likely been increased as a result of advancement in medicine and surgery and widely use of more invasive techniques in treatment, e.g., hematopoietic stem cells, organ transplantation, chemotherapy, and other factors. In addition to using invasive and accessorial devices which may lead to infections in blood circulation, candidoma, and metastatic candidiasis (Hinrichsen et al. 2008; Ahmed and Daad 2001; Tzar and Shamim 2009; Pagano et al. 2006), the patients with immunity system deficiency are exposed to risk of invasive fungal infections which act as susceptible agents to risk of suffering from opportunistic invasive fungal infections especially candidiasis in a host with cellular immunity deficiency in mucus

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(Takakura et al. 2004; Rangel-Frausto et al. 1999). The aim of this study is to determine how many and what kind of nosocomial fungal infections from hospitals in a developing country.

Materials and methods

Collection of samples

This descriptive-analytical study has been carried out on 248 cases suspicious of fungal infection received from inpatients and outpatient referents to three educational hospitals in Kerman during a year. Samples such as UTI, BI, skin, nail, wound (burning, surgery, eye and injury), lung, phlegm, ascites, BAL, (cerebrospinal, abdominal, and knee) fluid pseudocyst, peritoneum, fistula, ear infection and biopsy collected three educational hospitals in Kerman city during one year.

Culture

The received samples from patients (in oncological and infectious hospitalization ward) were entered directly by a syringe into a blood culture medium (BHI) and incubated at 37 °C for 2–3 weeks. All specimens were cultured in Sabouraud Dextrose Agar (SC), Sabouraud Dextrose Agar Chloramphenicol Cycloheximide (SCC), and dermatophyte test medium (DTM) (Seker and Dogan 2011). Cultures were incubated for 1 to 2 weeks at 25 and 27 °C and corn meal agar (tween-80) to form chlamydoconidia isolated from *Candida albicans*. Czapek Dox agar was utilized to identify aspergillus. For the observation of fungal elements, we squeezed the colonies on the lamina and stained it with lactophenol cotton blue (Karami Robati et al. 2014; Proverbio et al. 2014).

Molecular test

Isolation of DNA molecules from yeast colonies by means of phenol-chloroform-isoamyl alcohol technique

Candida species were isolated from patients with superficial and deep candidiasis. All fungi were harvested by centrifuging in 5000 rpm and washed by sterile saline and frozen in − 25 °C until use. The fungal suspensions with predetermined concentrations were centrifuged at 5000×*g*, and then the pellet was frozen at − 20 °C for 1 h and incubated at 65 °C for 1 h in 0.5 ml of extraction buffer (50 mM Tris-HCl, 50 mM EDTA, 3% sodium dodecyl sulfate, 1% 2-mercaptoethanol) and 50 μl proteinase-K (20 mg/ml). The lysate was extracted with phenolchloroform-isoamyl alcohol (25:24:1, vol/vol/vol). Then, 65 μl of 3 M sodium acetate and 75 μl of 1 M NaCl were added to 350 μl of the supernatant and the resulting volume was incubated at 4 °C for 30 min. DNA was recovered by isopropanol precipitation and washed with 70% (vol/vol) ethanol (Haynes and Westerneng 1998).

PCR screening

The oligonucleotide primers based on the nucleotide sequences of interval transcribed spacers (ITSs) existing in ribosomal DNA in fungi (Iwen et al. 2002) were purchased from the Fanvaran Gene Company. The program for PCR was started with the first stage of 95 °C in 5 min, a cycle of initial denaturation in the second stage, with a temperature of 94 °C in 30 s, the third stage with a temperature of 50 °C for 1 min, and the fourth step with the temperature of 72 °C and in 1 min and 15 s, a total of 35 cycles for DNA replication, which took more than 2 h (Paganini et al. 2002).

PCR-RFLP

After the end of PCR, PCR products were exposed to the restricted effect MSP1 enzyme for enzymatic digestion. To this purpose, we added 5 μl of PCR product to 1.5 μl of buffer of the restricted effect enzyme and mixed well 0.5 μl of MSP1 enzyme with 8 μl of water (HPLC grade) and stored them at 37 °C for 2 h. To observe bands, 5 μl of digested products was treated with enzyme by electrophoresis (80–100 v) for 45 min. Agarose (1.5%) was used for PCR products and agarose (2%) was consumed for RFLP products (Fallahi et al. 2013).

Results

Out of the total 180 samples with positive culture in this study, UTI (36.5%), blood stream infection (BSI) (33.1%), ear infection (6.8%), endoscopic (5.5%), BAL sample (4.7%), and each of oral infections and in wound site with a rate of 2% were the most infectious samples (Fig. 1). The rate of nosocomial fungal infections from the three hospitals in this study was estimated (53/180) to be 29%. Among hospitalization wards, ICUs acquired nosocomial fungal infection (29/53) at the highest rate and in 16% of patients (29/180) (Table 1). The most common fungal infections were UTI (75%), BSI (4%), surgical site infection (SSI) (4%), x-ray chest, and respiratory tract infection (RTI) (13%) which are caused by *Candida* spp. (100%). *Candida albicans* is the most frequent species isolated from clinical specimens followed by *C. glabrata*, *C. parapsilosis*, *C. tropicalis*, *C. dubliniensis*, and *C. kefir* (Table 2). The highest rate of sample involved in fungal disease among hospitalized patient belonged to BSI (37.8%), and among outpatient referents, it is ear infection (26%). In this

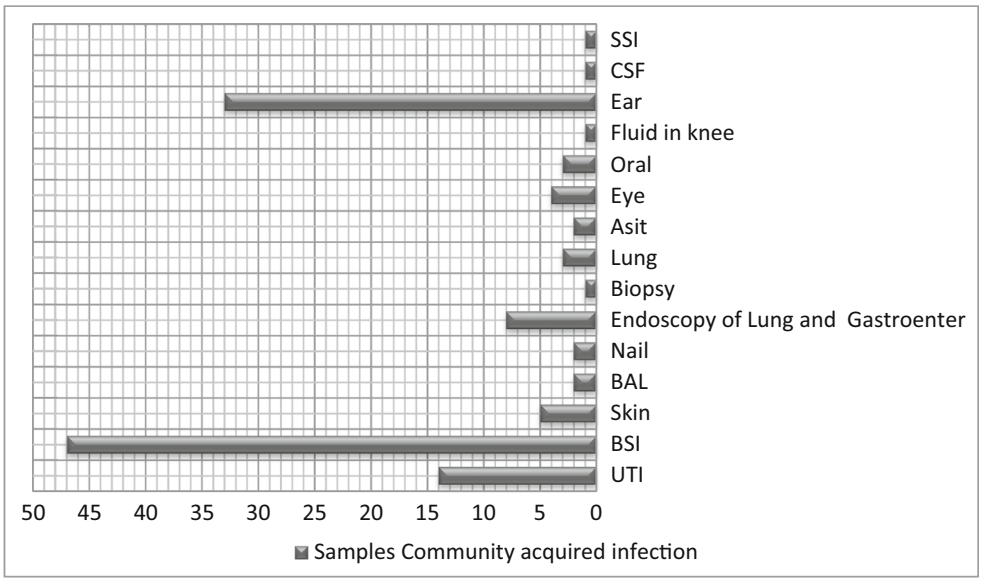

Fig. 1 Distribution of community-acquired infection cases by site of infection

study, 180 different genus and species of fungi were identified based on microscopic observations, macroscopic examination, and PCR-RFLP. The most common isolated fungi were *Candida* spp. (71 cases of *C. albicans*, 3 cases of *C. glabrata*, and 1 case of each of *C. parapsilosis*, *C. tropicalis*, *C. dubliniensis*, and *C. kefir*), *Aspergillus* spp. (4 cases *of A. fumigatus*, 2 cases of *A. niger*, and 1 case of rhinocerebral mycosis), and dermatophyte species (1 case of *Trichophyton mentagrophytes*), respectively (Table 3) and the remaining positive samples of the fungal disease were diagnosed as *Candidiasis*. The fungal agent of rhinocerebral mucormycosis was identified as one of the isolated fungal agents from a biopsy sample in the suborbital zone on the face of a 72-year-old man who suffered from chronic diabetes and hospitalized in the infection ward. The onychomycosis was caused by *A. fumigatus* was reported, the pleural infection case with aspergilloma, and the involved species are *A. fumigatus*, *A. niger*, and *C. parapsilosis* in aural infection, and the case of foot wound in a diabetic patient is caused by *C. albicans.*

Table 1 Patients ($n = 180$) with nosocomial infection and community-acquired infection: ward of referral

Ward of referral	Community-acquired infection ($n = 127$) %	Nosocomial infection ($n = 53$) %
Intensive care units (ICUs)	6	55
Oncology	21	6
Infectious	15	6
Urology and nephrology	2	0.0
Neonatal intensive care unit	2	6
ENT	26	0.0
Eye	3	0.0
Obstetrics and gynecology	0.0	6
Gastroenterology	5	0.0
Dermatology	4	0.0
Lungs	5	4
Repair the jaw face	0.0	4
Nephrology rheumatoid	1	4
Neurology	2	8
Emergency	8	0.0
Hemodialysis	0.0	1

Results of PCR-RFLP

Candida albicans, *C. glabrata*, *C. parapsilosis*, and *C. kafier* were identified by the method PCR-RFLP (Fig. 2).

Discussion

Invasive fungal infections are increasingly common in the nosocomial setting (Perlroth et al. 2007). Concerning statistical results from the rate of morbidity of nosocomial infection, the rate of hospital-acquired fungal infection has been totally approximated to be 29% in the given studied hospitals, which

Table 2 Distribution of commonly reported *Candida* spp. (100%) by site of nosocomial infection

Candida spp.	UTI ($N = 40$) %	RTI ($N = 7$) %	BSI ($N = 2$) %	SSI ($N = 2$) %	Others ($N = 2$) %
C. albicans	90	72	100	100	100
C. glabrata	5	14	0.0	0.0	0.0
C. tropicalis	0.0	14	0.0	0.0	0.0
C. dableninsis	2.5	0.0	0.0	0.0	0.0
C. kafier	2.5	0.0	0.0	0.0	0.0

Table 3 Identification of the fungal species isolated ($n = 86$) from 180 patients

Fungal species	Fungal agents		
	Candidia ($n = 78$) %	*Saprophyte* ($n = 7$) %	*Dermatophyte* ($n = 1$) %
C. albicans	91		
C. glabrata	5		
C. parapsilosis	1		
C. tropicalis	1		
C. dableninsis	1		
C. kafier	1		
Aspergillus fumigatus		57	
Aspergillus niger		29	
Rhinocerbral mucormycosis		14	
T. mentagrophytes			100

is consistent with the values mentioned in reference books of infection diseases as 5–20% and agreed with the results of a study as 11.4% (Ferrer et al. 2001). The study conducted in Iran suggests morbidity rate of 25% of infectious diseases in the studied patients (Lotfi and shokohi 2014). Among the studied wards, six ICU wards in hospitals were reported with a rate of 54.7% of nosocomial infection; this rate has been reported to be 17.69% based on the conducted studies in ICU of hospitalization wards (Mythri and Kashinath 2014). A large cohort multicentric international study has reported at least one ICU-acquired infection in 18.9% of patients, with an incidence ranging from 2.3 to 49.2% across the centers (Alberti et al. 2002). In the EPIC II study (Vincent et al. 2009), the most frequently reported sites for ICU-acquired infections were the lungs followed by the abdomen and bloodstream. Data from the US National Nosocomial Infections Surveillance System showed the nosocomial pneumonia, UTI, and BSI (Richards et al. 2000). The world statistical figures about morbidity of fungal agent of infectious type including epidemiological and microbiological analysis on nosocomial infection done in At-Taif in Saudi Arabia have reported community-acquired (51.7%) and hospital-acquired (48.3%) rates during the studied period (Sherifa and Moataz 2012), and the studied nosocomial infections included RTI with an average rate of 32.3%, UTI 25.3%, BSI 18.2%, and SSI 12.9% in which the isolated fungal species constituted 2% of total isolated samples, similar to the record statement of UTI (11.3%), BI (8.32%), SSI (12.9%), and BAL (12.9%) in which the isolated fungal species were *Candida* sp. (Pfaller and Diekema 2007). Patients with urinary tract catheters were reported with a rate of 77% of nosocomial UTIs (Richards et al. 1999). Candidiasis now is the most frequent nosocomial infection in hospitals in the USA and worldwide (Wisplinghoff et al. 2014; Pakshir et al. 2004). In our study too, the most commonly isolated organisms were *Candida* sp. *Candida* spp. were the second most common pathogen causing 21% of catheter-associated UTIs (Craven et al. 1988). More than 95% of all *Candida* BSI worldwide are caused by five species: *C. albicans*, *C. glabrata*, *C. parapsilosis*, *C. tropicalis*, *and C. krusei* (Takakura et al. 2004). The detection of *Candida* species in 15% of the isolates in the present study is also consistent to some extent with the studies of Pittet and Wenzel (Pittet and Wenzel 1995) and Edgeworth et al. (Edgeworth et al. 1999) who have reported that fungal pathogens are also becoming increasingly common among patients with nosocomial bloodstream infections. Some of fungal and yeast species are etiological agents for foot infection in diabetic patients. The involved fungus in a diabetic foot wound is mainly of *Candida* species including foremost ones like *C. albicans*, *C. tropicalis*, *C. parapsilosis*, *and C. glabrata* (Kafaie and Taghi Noorbala 2010), with *C. albicans* as the second frequent agent of onychomycosis after dermatophyte (Gerami shoar et al. 2002). Epidemiological study done in Ahwaz City (Iran) on opportunistic fungi which could treat otomycosis, the isolated fungi from external ear infection have been reported in about 26.7% of cases, where in other studies done in Iran, this suggests the aforesaid fungus is the agent for external ear infection in 38–74% of cases (Mahmoudabadi et al. 2010). *Aspergillus* spp. (38–74%) were isolated from out ear infection (Nicolle et al. 2011). A study performed in a Turkish university hospital during 2001–2002 found the prevalence of dermatophytoses to be 7.34% (68 out of 926)

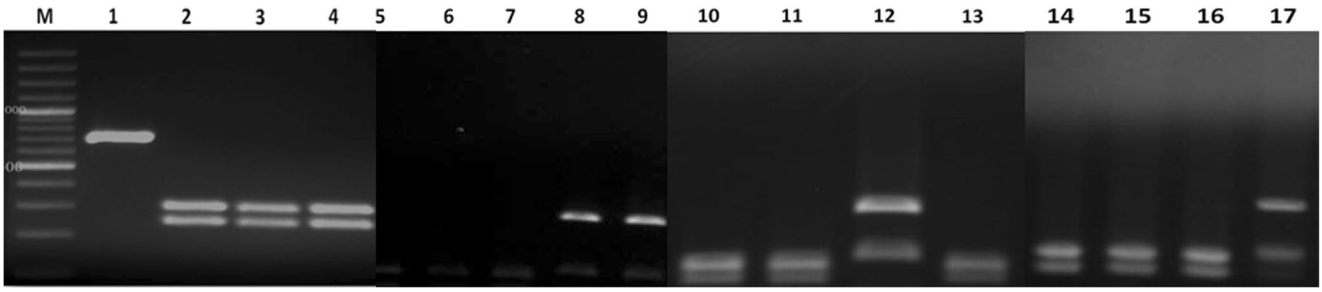

Fig. 2 Product electrophoresis PCR. Molecular marker 100 bp. M: *Candida kefir* 1; *Candida albicans* 2, 3, 4, 5, 6, 10, 11, 13, 14, 15, 16, and 7; *C. glabrata* 8 and 9; *C. glabrata* 12; *C. parapsilosis* 17 wells

(Ozkutuk et al. 2007). In our study, *Candida* spp. are the most common fungal pathogens causing nosocomial fungal infections of patients admitted to the ICU. It seems that increased length of hospital stay, prior antimicrobial therapy, and urinary catheterization were associated with the acquisition of nosocomial infections. The objectives of the current study were to define how many and what kind of nosocomial fungal infections are there in education hospitals as a model of hospitals from a developing country.

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Authors' contributions Seyyed Amin Ayatollahi Mousavi, Sanaz Hadizadeh and Azadeh karami Robati conceived and designed research. Azadeh karami Robati collected samples and clinical data. Seyyed Amin Ayatollahi Mousavi, Sanaz Hadizadeh, mahboobeh madani, Azadeh karami Robati performed research. Azadeh Karami Robati and Mahshid lalvand, analyzed data and wrote the paper. All authors read and approved the final manuscript.

Compliance with ethical standards

Conflict of interests The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

References

Ahmed T, Daad H (2001) Candidemia at a university hospital: epidemiology, risk factors and predictors of mortality. Ann Saudi Med 21(3–4):178–182

Alberti C, Brun-Buisson C, Burchardi H, Martin C, Goodman S, Artigas A, Sicignano A, Palazzo M, Moreno R, Boulmé R, Lepage E, le Gall J (2002) Epidemiology of sepsis and infection in ICU patients from an international multicentre cohort study. Intensive Care Med 28(2): 108–121. https://doi.org/10.1007/s00134-001-1143-z

Craven DE, Kunches LM, Lichtenberg DA, Kollisch NR, Barry MA, Heeren TC, McCabe WR (1988) Nosocomial infection and fatality in medical and surgical intensive care unit patients. Arch Intern Med 148(5):1161–1168. https://doi.org/10.1001/archinte.1988.00380050165024

Edgeworth JD, Treacher DF, Eykyn SJ (1999) A 25-year study of nosocomial bacteremia in an adult intensive care unit. Crit Care Med 27(8):1421–1428. https://doi.org/10.1097/00003246-199908000-00002

Fallahi AA, Korbacheh P, Zaini F, Mirhendi H, Zeraati H, Noorbakhsh F et al (2013) Candida species in cutaneous candidiasis patients in the Guilan province in Iran; identified by PCR-RFLP method. Acta Med Iran 51:799–804

Ferrer C, Colom F, Frasés S, Mulet E, Abad J, Alió J (2001) Detection and identification of fungal pathogens by PCR and by ITS2 and 5.8S ribosomal DNA typing in ocular infections. J Clin Microbiol 39(8): 2873–2879

George J (2011) Nosocomial fungal infections: epidemiology, infection control, and prevention. Infect Dis Clin 25(2011):201–225

Gerami shoar M, Zomorodian K, Emami M, Tarazoei B, Saadat F (2002) Study and identification of the etiological agents of onychomycosis in Tehran, capital of Iran. Iran J Publ Health 31(3–4):100–104

Haynes KA, Westerneng TJ (1998) Rapid identification of Candida albicans, C. glabrata, C. parapsilosis and C. krusei by species-specific PCR of large subunit ribosomal DNA. J Med Microbiol 44(5):390–396

Hinrichsen SL, Falcao E, Vilella TA, Colombo AL, Nucci M, Mouram L, Rêgo L, Lira C, Almeida L (2008) Candidemia in a tertiary hospital in northeastern Brazil [in Spanish]. Rev Soc BrasMed Trop 41(4): 394–398. https://doi.org/10.1590/S0037-86822008000400014

Iwen PC, Hinrichs SH, Rupp ME (2002) Utilization of the internal transcribed spacer regions as molecular targets to detect and identify human fungal pathogens. Med Mycol 40(1):87–109. https://doi.org/10.1080/mmy.40.1.87.109

Kafaie P, Taghi Noorbala M (2010) Evaluation of onychomycosis among diabetic patients of Yazd diabetic center. J Pak Assoc Dermatol 20: 217–221

Karami Robati A, Ayatollahi Mousavi SA, Madani M (2014) Study of nosocomial fungal infections acquired from three Kerman educational hospitals. JRUMS 13(2):151–162

Kordbacheh P, Zaini F, Kamali P, Ansari K, Safara M (2005) Study on the sources of nosocomial fungal infections at intensive care unit and transplant wards at a teaching hospital in Tehran. Iran J Publ Health 34(2):1–8

Lotfi N, Shokohi T (2014) A review on fungal infection in burn patients, diagnosis and treatment. J Mazand Univ Med Sci 23(108):151–165

Mahmoudabadi AZ, Abdoulhosien Masoomi S, Mohammadi H (2010) Clinical and mycological studies of otomycosis. Pak J Med Sci 26(1):187–190

Mythri H, Kashinath K (2014) Nosocomial infections in patients admitted in intensive care unit of a tertiary health center, India. Ann Med Health Sci Res 4(5):738–741. https://doi.org/10.4103/2141-9248.141540

Nicolle MC, Benet T, Vanhems P (2011) Aspergillosis: nosocomial or community-acquired. Med Mycol 49(1):S24–S29

Ozkutuk A, Ergon C, Yulug N (2007) Species distribution and antifungal susceptibilities of dermatophytes during a one year period at a university hospital in Turkey. Mycos 50(2):125–129. https://doi.org/10.1111/j.1439-0507.2006.01333.x

Paganini H, Rodriguez BT, Santos P, Seu S, Rosanova MT (2002) Risk factors for nosocomial candidaemia: a case-control study in children. J Hosp Infect 50(4):304–308. https://doi.org/10.1053/jhin.2002.1169

Pagano L, Caira M, Candoni A, Offidani M, Fianchi L, Martino B et al (2006) The epidemiology of fungal infections in patients with hematologic malignancies: the SEIFEM-2004 study. Haematol J 91: 1068–1075

Pakshir K, Mogadami M, Emmami M, Kordbacheh P (2004) Prevalence and identification of etiological agents of funguria in Foley catheterized patients. J Med Reser 2(3):33–41

Perlroth J, Choi B, Spellberg B (2007) Nosocomial fungal infections: epidemiology, diagnosis, and treatment. Med Mycol 45(4):321–346

Pfaller MA, Diekema DJ (2007) Epidemiology of invasive candidiasis: a persistent public health 293 problem. Clin Microbiol Rev 20(1): 133–163. https://doi.org/10.1128/CMR.00029-06

Pittet D, Wenzel RP (1995) Nosocomial bloodstream infections. Secular trends in rates, mortality, and contribution to total hospital deaths. Arch Intern Med 155(11):1177–1184. https://doi.org/10.1001/archinte.1995.00430110089009

Proverbio D, Perego R, Spada E, Bagnagatti de Giorgi G, Della Pepa A, Ferro E (2014) Survey of dermatophytes in stray cats with and without skin lesions in northern Italy. Veterin Medic Intern 2014(1):1–4

Rangel-Frausto MS, Wiblin T, Blumberg HM (1999) National Epidemiology of Mycoses Survey (NEMIS): Variations in rates of

blood stream infections due to Candida species in seven surgical intensive care units and six neonatal intensive care units. Clin Infect Dis 29:253–258.

Richards MB, Jonathan R, Edwards MS, David H, Robert P, Gaynes MD (1999) Nosocomial infections in pediatric intensive care units in the United States. National Nosocomial Infections Surveillance System. Pediatr 103(4):e39

Richards MJ, Edwards JR, Culver DH, Gaynes RP (2000) Nosocomial infections in combined medical-surgical intensive care units in the United States. Infect Control Hosp Epidemiol 21(08):510–515. https://doi.org/10.1086/501795

Seker E, Dogan N (2011) Isolation of dermatophytes from dogs and cats with suspected dermatophytosis in western Turkey. Preven Veterin Medic 98(1):46–51. https://doi.org/10.1016/j.prevetmed.2010.11.003

Sherifa M, Moataz M (2012) Epidemiological and microbiological profile of nosocomial infection in Taif hospitals, KSA (2010-2011). World. J Med Sci 7(1):01–09

Takakura S, Fujihara N, Saito T, Kudo T, Iinuma Y, Ichiyama S (2004) National surveillance of species distribution in blood isolates of Candida species in Japan and their susceptibility to six antifungal agents including voriconazole and micafungin. J Antimicrob Chemother 53(2):283–289. https://doi.org/10.1093/jac/dkh053

Tortorano AM, Peman J, Bernhardt H (2004) Epidemiology of candidaemia in Europe: results of 28-month European Confederation of Medical Mycology (ECMM) hospital-based surveillance study. Eur J Clin Microbiol Infect Dis 23(4):317–322

Tzar MN, Shamim AS (2009) Candidaemia and antifungal susceptibility testing in a teaching hospital. Med J Malaysia 64(1):61–64

Tzar MN, Suhaila B, Shamsul AS, Azizah M (2013) Epidemiology of fungal infections at an infectious disease reference centre in Malaysia. Int Medic Malay 12(1):39

Vincent JL, Rello J, Marshall J, Siva E, Anzueto A, Martin CD et al (2009) The extended prevalence of infection in the ICU study: EPIC II. JAMA 302(21):2323–2329. https://doi.org/10.1001/jama.2009.1754

Wisplinghoff H, Ebbers J, Geurtz L, Stefanik D, Major Y, Edmond MB, Wenzel RP, Seifert H (2014) Nosocomial bloodstream infections due to candida spp. in the USA: species distribution, clinical features and antifungal susceptibilities. Int J Antimicrob Agents 43(1):78–81. https://doi.org/10.1016/j.ijantimicag.2013.09.005