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**COMPARISON BETWEEN CULTURE AND NON-
CULTURE-BASED METHODS FOR DETECTION OF
NOSOCOMIAL FUNGAL INFECTIONS IN INTENSIVE
CARE UNIT PATIENTS**

A thesis

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Microbiology**

By

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Declaration

This thesis has not previously been submitted for any other university. The references were being checked whenever possible ;show the extent to which I have availed myself of the work of other authors.

Lamia Mohamed Rady

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Introduction:

It is apparent that nosocomial fungal infections are becoming more prominent. They are increasingly isolated from immunocompromised patients and patients receiving a broader range of antimicrobial agents. Consequently, infections due to previously obscure fungi are being seen more commonly in hospitalized patients. In addition, standards for susceptibility testing are currently being developed and should help in guiding clinicians and hospital epidemiologists in the management of nosocomial fungal infections. However, continued epidemiological and laboratory research is needed to better characterize these pathogens, allowing for improved diagnostic and therapeutic strategies in the future (Findik and Tuncer, 2002).

The incidence of fungal infections, particularly those caused by *Candida* spp., has considerably increased in hospitalized patients. Usually it affects severely ill and immunocompromised patients. However, there has been an increase of this type of infection in non-neutropenic patients, including surgical patients (Luzzati et al., 2000; Leon et al., 2009), which implies a higher morbidity and mortality, as well as an increase in the use of resources (Olaechea, et al., 2004; Zaoutis et al., 2005).

Candida spp. are part of the normal flora on the skin and on the mucosal membranes of the oral cavity and gastrointestinal tract. *Candida* spp. can be recovered from sputum in 20% of

health care personnel and 55% of hospitalized patients receiving antibiotics (Baum, 1960).

The evolution of fungi of the genus *Candida* from infrequent pathogens to among the most common agents of nosocomial infection has been both dynamic and interesting. The past three decades have witnessed major changes in the incidence of nosocomial infections due to these yeasts. Earlier it was seen that the majority of cases of candidemia and disseminated candidiasis were due to *Candida albicans*. But in the recent years, a distinct increase has been noted in the proportion of cases resulting from infection with non-albicans *Candida* species (Rumpa *et al.*, 2008).

1. Nosocomial Fungal Infections:

Infections acquired during a hospital stay are called nosocomial infections. These infections can be bacterial, viral, and fungal or even parasitic (Kordbacheh *et al.*, 2005).

In the mid-1980s, many institutions, including cancer research, university, and community hospitals, reported that fungi were becoming common pathogens in nosocomial infections (Harvey & Myers, 1987; Anaissie & Bodey, 1989; Bodey, 1988).

In addition, during 1980 to 1990, hospitals reporting data to the Centers for Disease Control and Prevention (CDC) National Nosocomial Infections Surveillance (NNIS) system reported a steady increase in the rate of nosocomial fungal infections, from 2.0 to 3.8 per 1,000 discharges (Beck-Sague *et al.*, 1993; Scott & William, 1996).

It is apparent that nosocomial fungal infections are becoming more prominent. They are increasingly isolated from immunocompromised patients and patients receiving a broader range of antimicrobial agents. Consequently, infections due to previously obscure fungi are being seen more commonly in hospitalized patients (Findik & Tuncer, 2002).

Advances in medicine by use of newer technologies and therapies have helped to treat patients suffering from previously

devastating or fatal diseases but these successes have resulted in proliferation of a severely ill immunocompromised, hospitalized patient population. Furthermore, the AIDS epidemic has added to this growing population of immunocompromised individuals (Fridkin & Jarvis, 1996; Bolignano & Criseo, 2003).

These immunocompromised patients are highly susceptible to nosocomial infections caused by organisms such as fungi that were previously considered to be of low virulence or non-pathogenic (Fridkin & Jarvis, 1996).

Fungal infections in these patients are often severe, rapidly progressive, and difficult to diagnose or treat (Edwards, 1991).

Therefore, during the past two decades fungi have become increasingly important causes of nosocomial infections and have emerged as a frequent cause of mortality and morbidity in hospital patients (Walsh & Pizzo, 1988; Fridkin & Jarvis, 1996; Nucci *et al.*, 2001).

Since nosocomial fungal infections (NFI) are often severe, rapidly progressive and difficult to diagnose or treat, there is a critical need for more efforts to be directed toward prevention, early diagnosis and aggressive treatment of these infections (Kordbacheh *et al.*, 2005).

In addition, standards for susceptibility testing are developed and are helpful in guiding clinicians and hospital epidemiologists in the management of nosocomial fungal infections. However, continued epidemiological and laboratory research is needed to better characterize these pathogens, allowing for improved diagnostic and therapeutic strategies in the future (Fridkin & Jarwis, 1996; Moran *et al.*, 2002).

Fungi are increasingly recognized as major pathogens in critically ill patients. *Candida* spp. and *Cryptococcus* spp. are the yeasts most frequently isolated in clinical practice. The most frequent filamentous fungi (moulds) isolated are *Aspergillus* spp., but *Fusarium* spp., *Scedosporium* spp., *Penicillium* spp. and Zygomycetes are increasingly seen (Marr *et al.*, 2002; Husain *et al.*, 2003; Meersseman *et al.*, 2009).

Several reasons have been proposed for the increase in invasive fungal infections, including the use of antineoplastic and immunosuppressive agents, broad-spectrum antibiotics, and prosthetic devices and grafts, and more aggressive surgery. Patients with burns, neutropenia, HIV infection and pancreatitis are also predisposed to fungal infection (Eggimann *et al.*, 2003).

2. Candida:

Candida spp are ubiquitous dimorphic yeasts that can exist as 2- to 5-µm round-oval cells called blastospores, which reproduce