



Study of the Prevalence and Pattern of Fungal Pneumonias in Respiratory ICUs

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قَالَ

سُبْحَانَكَ لَا عِلْمَ لَنَا
إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ
الْعَلِيمُ الْعَظِيمُ

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List of Abbreviations

Abb.	Full term
<i>ABPA</i>	<i>Allergic bronchopulmonary aspergillosis</i>
<i>AIDS</i>	<i>Acquired immunodeficiency syndrome</i>
<i>BAL</i>	<i>Bronchoalveolar lavage</i>
<i>BMI</i>	<i>Body mass index</i>
<i>BP</i>	<i>Blood pressure</i>
<i>BTS</i>	<i>British thoracic society</i>
<i>CBC</i>	<i>Complete Blood Count</i>
<i>CF</i>	<i>Cystic fibrosis</i>
<i>CMI</i>	<i>Cell mediated immunity</i>
<i>COPD</i>	<i>Chronic obstructive pulmonary disease</i>
<i>CT</i>	<i>Computed tomography</i>
<i>DM</i>	<i>Diabetes mellitus</i>
<i>ECG</i>	<i>Electrocardiogram</i>
<i>ELISA</i>	<i>Enzyme-linked immunosorbent assay</i>
<i>Hb</i>	<i>Hemoglobin</i>
<i>HBV</i>	<i>Hepatitis B virus</i>
<i>HIV</i>	<i>Human immunodeficiency virus</i>
<i>HRCT</i>	<i>High resolution computed tomography</i>
<i>HSCT</i>	<i>Hematopoietic stem cell transplantation</i>
<i>IA</i>	<i>Invasive aspergillosis</i>
<i>ICU</i>	<i>Intensive care units</i>
<i>IFI</i>	<i>Invasive fungal infections</i>
<i>IgE</i>	<i>Immunoglobulin E</i>
<i>IgG</i>	<i>Immunoglobulin G</i>

List of Abbreviations *cont...*

Abb.	Full term
<i>ILD.....</i>	<i>Interstitial lung disease</i>
<i>IPA.....</i>	<i>Invasive Pulmonary Aspergillosis</i>
<i>LOS.....</i>	<i>Length of stay</i>
<i>LPCB</i>	<i>Lacto-Phenol Cotton Blue</i>
<i>MV</i>	<i>Mechanical Ventilation</i>
<i>PCP.....</i>	<i>Pneumocystis carinii pneumonia</i>
<i>PCR.....</i>	<i>Polymerase chain reaction</i>
<i>PEF.....</i>	<i>Peak expiratory flow</i>
<i>PET.....</i>	<i>Positron emission tomography</i>
<i>RICU.....</i>	<i>Respiratory Intensive care unit</i>
<i>RML.....</i>	<i>Right middle lobe</i>
<i>SGA.....</i>	<i>Sabaroud glucose agar</i>
<i>TB</i>	<i>Tuberculosis</i>

INTRODUCTION

Infections have almost become an inseparable part of the intensive care units throughout the globe in spite of numerous advancements in diagnostic and therapeutic interventions. The presence of infection in critically ill patients poses unique challenges as it can directly influence the morbidity and mortality. Of the various infections prevalent in an intensive care unit, invasive fungal infection has always been considered to occur infrequently, but, over the past few years, with the surge in broad-spectrum antibiotic usage and improved knowledge of fungal diseases, the incidence has risen (*Bajwa et al., 2013*).

Pneumonia is the leading infectious cause of death in developed countries (*Restrepo et al., 2013*). Among the vast diversity of respiratory pathogens, fungi account for only a small portion of community-acquired and nosocomial pneumonias. However, fungal respiratory infections generate concern in the expanding population of immunosuppressed patients (*Lamoth et al., 2014*).

Fungal pneumonia is an infectious process in the lungs caused by one or more endemic or opportunistic fungi. Fungal infection occurs following the inhalation of spores, after the inhalation of conidia, or by the reactivation of a latent infection. Hematogenous dissemination frequently occurs, especially in an immunocompromised host (*Guarner et al., 2011*).

Endemic fungal pathogens (eg, *Histoplasma capsulatum*, *Coccidioides immitis*, *Blastomyces dermatitidis*, *Paracoccidioides brasiliensis*, *Sporothrix schenckii*, *Cryptococcus neoformans*) cause infection in healthy hosts and in immunocompromised persons (**Ellen Jo Baron et al., 2013**).

Opportunistic fungal organisms (eg, *Candida* species, *Aspergillus* species, *Mucor* species) tend to cause pneumonia in patients with congenital or acquired defects in the host immune defenses (**Ellen Jo Baron et al., 2013**).

Among yeasts and molds, *Candida* and *Aspergillus* species are the most frequent nosocomial fungal pathogens including in the critical care setting (**Dimopoulos et al., 2012**).

Risk factors of the development of invasive fungal infections in ICUs patients have been analyzed in numerous retrospective studies with a heterogeneous patient population. Various conditions including patient's age, prolonged length of stay, administration of broad-spectrum antibiotics, central vascular catheters, diabetes mellitus, parenteral nutrition, mechanical ventilation, renal insufficiency, hemodialysis, colonization, antifungal prophylaxis, surgery, pancreatitis, and treatment with corticosteroids and chemotherapy were the most frequently identified risk factors. Prior to surgery, *Candida* colonization, acute renal failure., hemofiltration, use of parenteral nutrition, presence of triple lumen catheter, and ICU

length of stay were factors also identified in prospective studies (*Delaloye and Calandra, 2013*).

The diagnosis of fungal pneumonias is difficult to prove and is often made on a presumptive basis. It relies on a combination of clinical, radiologic, and microbiological factors (*Limper et al., 2010*).

The individual prognosis is often linked to the severity and outcome of the underlying disease and to whether a reversal of factors affecting the patient's immune status is possible (*Bateman et al., 2016*).

AIM OF THE WORK

In this study we will put a hand on the prevalence of fungal pneumonias in a group of respiratory ICUs and their pattern.

Chapter (1)

FUNGAL PNEUMONIA

An overview

Definition:

Fungal pneumonia is an infection of the lungs by fungi. It can be caused by either endemic or opportunistic fungi or a combination of both.

Fungi are one of the five kingdoms of life. A fungus is any member of the group of eukaryotic organisms that includes microorganisms such as yeasts and molds, as well as the more familiar mushrooms. Many fungi are good and useful (edible mushrooms would be an example of these) while some cause problems (some fungi can injure plants and people) (**Baron et al., 1996**). Of the approximately 100,000 recognized species of fungi, about 300 are known to cause human infections. Fungal diseases of healthy humans tend to be relatively benign, but the few life-threatening fungal diseases are extremely important (**Vartivarian et al., 1993**).

Morphology of fungi:

Yeasts are single-celled forms that reproduce by budding, whereas molds form multicellular hyphae (**Baron et al., 1996**).

Yeasts:

Yeast taxa are distinguished on the basis of the presence or absence of capsules, the size and shape of the yeast cells, the mechanism of daughter cell formation (conidiogenesis), and the presence of sexual spores (**Matsumoto et al., 1994**).

Yeasts include the *Candida* spp., *Cryptococcus* spp., and *Pneumocystis jiroveci*. *Candida* species grow by forming pseudohyphae. The pathogenic species of *Candida* include *C.albicans*, *C.krusei*, *C.parapsilosis*, *C.tropicalis*, *C.lusitaniae*, *C.glabrata*, *C.guilliermondii*, *C.pseudotropicalis*, and *C.dubliniensis* (**Bellmann et al., 2008**).

Molds:

Molds are characterized by the development of hyphae which result in the colony characteristics seen in the laboratory.

Molds include *Aspergillus* spp. and the agents of mucormycosis. *Aspergillus fumigatus* is the most pathogenic of the molds and the most common of that species to cause invasive disease. Other species of *Aspergillus* include *A. flavus*, *A. terreus*, and *A. niger* (**Richardson et al., 2008**).

Structure of fungi

Fungi are eukaryotes. They possess a nucleus enclosed by a nuclear membrane, a rigid cell wall, endoplasmic reticulum, and mitochondria like plant and animal cells (**Baron**