



A retrospective study of the epidemiology and clinical manifestation of invasive aspergillosis in a major tertiary care hospital in Bahrain

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Summary Limited data are available on the epidemiology, clinical manifestations and outcomes of patients with invasive aspergillosis in Bahrain. This study was conducted retrospectively to determine the epidemiology of invasive aspergillosis and its risk factors, clinical presentation, underlying conditions, and outcomes over the past five years in a major hospital.

The medical records of patients with positive *Aspergillus* cultures admitted to a major tertiary care hospital in Bahrain during 2009–2013 were reviewed. Cases were classified according to (1) the European Organization for the Research and Treatment of Cancer/Mycoses Study Group (MSG) criteria (proven, probable, possible IA or not classifiable) and (2) “validated” criteria to distinguish *Aspergillus* colonization from IA (putative or proven IA). Demographic, microbiologic and diagnostic data were collected, and outcomes were recorded.

A total of 60 patients were included, of whom 44 were colonized (73.3%), and 16 had probable IA (26.7%); no proven or possible IA cases were identified according to the EORTC/Mycoses Study Group (MSG) criteria. In comparison, with the alternative “validated” criteria, 32 were colonized (53.3%), 28 had putative IA (46.7%), and none had proven IA (0%). The lung was the most common site of infection,

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and *Aspergillus fumigatus* was the most commonly isolated species (53%). Mortality was 25% among colonized patients, 44% in probable cases and 32% in those with putative IA. All patients were immunocompromised or had one or more predisposing factors. Independent risk factors for death among patients with IA included older age, history of mechanical ventilation, renal replacement therapy and higher sequential organ failure assessment scores at diagnosis.

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Introduction

Aspergillosis refers to a wide variety of diseases caused by members of the genus *Aspergillus* [1]. *Aspergillus* species are ubiquitous organisms commonly found in soil, water and decaying vegetation [2]. There are approximately 200 species of *Aspergillus* [3]. However, *A. fumigatus* is the most frequently encountered species in human disease, followed by *A. flavus*, *A. terreus* and *A. niger* [4,5].

There are several types of aspergillosis: the most common are allergic aspergillosis, aspergilloma and invasive aspergillosis [6].

Allergic bronchopulmonary aspergillosis (ABPA) is a hypersensitivity reaction to the fungus, mostly due to *A. fumigatus*. It is commonly seen in patients with longstanding asthma or cystic fibrosis [7].

Aspergilloma is the most common form of pulmonary involvement by *Aspergillus* species. The aspergilloma (fungal ball) consists of a mass of fungal hyphae, inflammatory cells, fibrin, mucus and tissue debris and usually develops in a pre-existing lung cavity [8].

Invasive aspergillosis (IA) is a serious opportunistic infection that commonly affects immunocompromised patients, such as those with prolonged neutropenia and cancer [9]. Patients with immune suppression as a result of solid organ or bone marrow transplantation and patients with AIDS are also at high risk [10,11].

In clinical practice, a diagnosis of IA is often suspected when *Aspergillus* is isolated from non-sterile body sites, particularly tracheal and bronchial aspirates [12]. However, because *Aspergillus* spp. are ubiquitous, one must be cautious in attributing a pathogenic role to fungus isolated from these samples [13].

This study was therefore conducted to collect data from patients with either *Aspergillus* colonization or invasive disease in order to investigate the epidemiology of invasive aspergillosis and determine the risk factors for *Aspergillus* infections along with the associated clinical presentation, underlying conditions and outcomes.

Materials and methods

Patients and settings

The Salmaniya Medical Complex is the largest public hospital located in the Salmaniya district of Manama, in the Kingdom of Bahrain. Established in 1979, the hospital has approximately 1200 beds. The hospital receives an average of 900–1000 patients a day and employs

more than 2000 physicians, nurses and workers. It is a multi-specialty tertiary hospital. It includes specialties in cardiology, dermatology, diabetes, endocrine glands, the digestive system, hematology, infectious diseases, internal diseases, kidney and lung diseases, rheumatic diseases and oncology; it also provides outpatient services.

In this retrospective study, the medical records of all patients with a positive *Aspergillus* culture admitted to the Salmaniya Medical Complex, a major tertiary care hospital in Bahrain, between January 2009 and December 2013 were reviewed. All consecutive adult (>14 years) patients with a culture, direct examination and/or histopathologic sample positive for *Aspergillus* spp. at any site were eligible for inclusion. The study was approved by the local ethics and research committees.

Data collection and outcomes

Outpatients were excluded from the study, which includes only hospitalized patients. Unfortunately, it was not possible to report the number of outpatients with a positive *Aspergillus* culture.

Collected patient data included demographics (i.e., age, sex, and nationality), risk factors, underlying diseases and clinical presentation, including signs and symptoms compatible with invasive fungal disease (that is, refractory or recrudescing fever, pleuritic chest pain or rub, dyspnea, hemoptysis or worsening lung function). The organs which were affected by *Aspergillus* and the isolated species were recorded. The date of the first positive *Aspergillus* culture was considered the date of diagnosis of IA.

Although *Aspergillus* species are well recognized as common environmental airborne contaminants, the detection of *Aspergillus*, especially *A. fumigatus* and *A. flavus* in sputum cultures from patients with appropriate predisposing conditions, is likely to be of diagnostic importance, and empiric antifungal therapy should be considered.

In our study, the microbiological diagnosis of aspergillosis from sputum depends on the Gram stain. To evaluate whether the sample is acceptable, the presence or absence of squamous epithelial cells, polymorphonuclear leukocytes and microorganisms was evaluated. Filamentous hyphae are usually seen in aspergillosis. A direct sputum smear using a wet preparation of 10% potassium hydroxide was performed in suspected cases or if hyphae were seen in the Gram stain. The presence of hyaline, branching, septate hyphae consistent

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