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# Isolation of *Aspergillus* in critically ill patients: a potential marker of poor outcome

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**Abstract**

**Objective:** Recent reports have suggested a rising incidence of pulmonary aspergillosis in intensive care unit (ICU) patients. The aim of this study was to determine the clinical significance of isolating *Aspergillus* from respiratory samples of critically ill patients.

**Design:** Retrospective review of medical records.

**Setting:** Tertiary medical center that has a large cancer center.

**Patients:** All patients admitted to the ICU between January 1998 and August 2004, in whom *Aspergillus* was isolated from respiratory samples or lung tissue.

**Intervention:** None.

**Results:** The charts of 104 patients were reviewed. *Aspergillus* was isolated for a mean of 6.6 days after ICU admission. Thirty-three percent of patients had hematological malignancy, 10% had absolute neutropenia, 14% had bone marrow transplant, 11% had HIV infection, and 22% had chronic obstructive pulmonary disease. Upon admission to ICU, 79%, 43%, and 19% were on antibiotics, corticosteroids, or immunosuppressive therapy, respectively. Ninety percent of patients required mechanical ventilation. The mean Acute Physiologic and Chronic Health Evaluation II score on ICU admission was 20.6, with predicted mortality of 35.5%. However, the actual ICU mortality rate for the cohort was 50%. Twenty-eight percent of patients were diagnosed with probable or definite invasive pulmonary aspergillosis, and 72% had *Aspergillus* colonization. On univariate analysis, the significant clinical differences between the 2 groups were the presence of neutropenia ($P < .05$), immunosuppressants ($P < .05$), antibiotics ($P < .05$), or bone marrow transplant ($P < .05$). The differences in Acute Physiologic and Chronic Health Evaluation II score, the need for mechanical ventilation, ICU length of stay, and ICU mortality were not statistically significant. On multivariate analysis, the following factors were independently associated with invasive diseases, bone marrow transplantation ($P < .01$), hematological malignancy ($P = .02$), and broad-spectrum antibiotics ($P = .02$).

**Conclusion:** Isolation of *Aspergillus* in critically ill patients is a poor prognostic marker and is associated with high mortality irrespective of invasion or colonization. Those who are neutropenic, on

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immunosuppressive therapy, on broad-spectrum antibiotics, or had bone marrow transplantation are more likely to have invasive pulmonary aspergillosis.


## 1. Introduction

*Aspergillus* is an ubiquitous fungus in the environment. It causes a wide spectrum of illnesses ranging from infection of pre-existent lung cavities to a disseminated disease that can infect almost any organ. It is being isolated from the clinical samples in tertiary care hospitals at an increasing frequency [1,2]. The invasive form of the disease most commonly affects the lungs. It is difficult to diagnose and carries a high mortality. Invasive pulmonary aspergillosis (IPA) was described as a disease of the immunocompromised, but now, it is being increasingly recognized as an emerging opportunistic infection in critically ill patients [3]. On the other hand, *Aspergillus* can colonize the airway, which is of unclear significance and always creates debate during clinical rounds. Because of the insidious onset of IPA and the lack of an easy and reliable method to diagnose it, differentiation between the 2 conditions is challenging, and confirmation is frequently only possible on autopsy [4,5].

The aim of this study was to describe the clinical characteristics of patients in whom *Aspergillus* was isolated from the respiratory tract in the ICU, to determine the predictors of invasive disease, and to determine the outcome of those patients.

## 2. Materials and methods

The study was conducted at the Detroit Medical Center hospitals, a tertiary care center of 1000 beds with more than 80 ICU beds, including medical, cardiac, and surgical ICUs. Between January 1998 and April 2004, critically ill patients in whom *Aspergillus* was isolated from the respiratory tract, by culture of sputum, bronchoalveolar lavage (BAL) or tissue sample after ICU admission were identified from the microbiology laboratory records. The respiratory samples were obtained as a part of workup of possible pneumonia. Patients who had *Aspergillus* isolated from the respiratory tract, or any other site, before ICU admission were not included in the study. Clinical charts were retrieved and reviewed for demographical characteristics, comorbidities, *Aspergillus* species isolated, ICU length of stay (LOS) before isolating *Aspergillus*, imaging and diagnostic studies performed, interventions taken including mechanical ventilation (MV), hemodialysis (HD), antibiotics and antifungal agents, ICU LOS, and mortality. The Acute Physiologic and Chronic Health Evaluation II (APACHE II) score on the time of ICU admission and the predicted mortality were calculated. The criteria for transfer to our ICU are in concordance with the published guidelines [6]. The usual indications for admission to the ICU in this cohort were similar to those previously reported by our group and included respiratory failure, hemodynamic instability, cardiac problems (such as pulmonary edema, arrhythmias, and pericardial tamponade), neurologic complications (such as seizures, intracranial bleeding, and strokes), and gastrointestinal bleeding [7]. There are no high-efficiency particulate air filters in our ICUs. However, patients are not cared for in areas of construction, and there have been no documented outbreaks of aspergillosis in our hospital.

The risk factors for IPA that were studied included neutropenia, hematological or solid organ malignancy, bone marrow transplantation (BMT), immunosuppressive therapy, corticosteroids, chronic obstructive pulmonary disease (COPD), HIV infection, and diabetes mellitus (DM). The dose of corticosteroids and the specific class of antibiotics used were not included in this analysis. The patients were divided into 2 groups: the first had patients with definite or probable IPA and the second had patients colonized with *Aspergillus*. Definite IPA was defined as the demonstration of the characteristic septate, acute branching hyphae, and/or positive culture for *Aspergillus* from lung tissue specimen obtained either by biopsy or autopsy. Probable IPA was defined as identification of *Aspergillus* species by culture from sputum samples or BAL with compatible clinical and radiological picture of IPA. Colonization was defined as identification of *Aspergillus* species by culture from sputum samples or BAL without compatible clinical and radiological picture of IPA. Risk factors, interventions and mortality in the 2 groups were compared using Fisher exact test. Age, APACHE II score, and ICU LOS were compared using Student *t* test. Multivariate analysis was done using logistic regression. A predicted risk of invasion was developed by use of composite risk score and an receiver operating characteristic (ROC) curve analysis to determine the best cutoff point.

## 3. Results

### 3.1. Clinical characteristics

One hundred twenty-four patients had *Aspergillus* species isolated from their respiratory tract after ICU admission during the study period. The charts of 104 patients (83.9%) were available for review. The ages of 65 men (62.5%) and 39 women (37.5%) ranged between 16 and 90 (mean, 50.8) years. *Aspergillus* was isolated for a mean of 6.6 days (range, 1-74 days) after ICU admission. None of the patients had *Aspergillus* isolated