

Factors Associated with Outcome in Patients Managed for Invasive Fungal Infections at the Infectious Diseases Department of a Tertiary Care Hospital

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ABSTRACT

Objective: To look for the factors associated with outcomes in patients managed for invasive fungal infections at the Infectious Diseases Department of a Tertiary Care Hospital

Study Design: Comparative cross-sectional study

Place and Duration of Study: Department of Infectious Diseases, Pak Emirates Military Hospital, Rawalpindi Pakistan, from Apr 2021 to Sep 2022.

Methodology: A total of 90 patients with a different types of invasive fungal infections diagnosed by consultant infectious diseases were recruited. First, they were given standard treatment for fungal infection; they were diagnosed as per guidelines. Then, they were followed up for one month to look for an outcome.

Results: Out of 90 patients with invasive fungal infections included in the study, 62(68.8%) had a good outcome, while 28(31.2%) had a poor outcome. The mean age of the patients recruited in our study was 39.54±6.27 years. Of all the participants, 65(72.2%) patients were male, while 25(27.8%) were female. Statistical analysis revealed that poorly controlled diabetes, COVID-19 infection and HIV positive were statistically significantly associated with poor outcomes in our study participants (p -value<0.05).

Conclusion: The Considerable number of patients with invasive fungal infections had a poor outcome in our study. The presence of poorly controlled diabetes, COVID-19 infection and being HIV positive were the factors associated with poor outcomes in our study participants.

Keywords: Infectious diseases, Invasive fungal infections, Outcome.

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INTRODUCTION

Infectious diseases (ID) are an emerging speciality in our part of the world with the evolving curriculum. Still, only a few trained professionals are available for a population of over 20 million.^{1,2} Fungal diseases usually get treated by the organ involved. ID experts are involved in cases of serious or invasive disease or if the infection is not responding to standard antifungal treatment.³ It becomes very important for clinical teams to look for factors associated with the outcome of severe or invasive fungal infections in order to triage high-risk cases early.⁴

Several studies have been published in developed countries to look into factors related to poor outcomes in patients with invasive fungal infections.^{5,6} Five-year retrospective data was published from China in 2022 regarding deep fungal infections. It was revealed that these cases were on the rise, and poor prognosis was

seen in many patients. Patients with renal diseases, tumours or neurological disorders were more at risk of poor prognosis in their study participants.⁷

Doctors commonly treat fungal infections of various specialities in different settings in our country.^{8,9} A local study published in 2017 discussed the basic epidemiological data regarding various fungal diseases in our country, especially invasive fungal infections.¹⁰ Limited local data has been generated on invasive fungal infections, their management and outcome in our part the world. We did not study the impact of different medications on the outcome. However, we planned this study to look for the factors associated with outcomes in patients managed for invasive fungal infections at the infectious diseases department of a tertiary care hospital in Rawalpindi.

METHODOLOGY

The comparative cross-sectional study was conducted at the Department of Infectious Diseases in Pak Emirates Military Hospital Rawalpindi from April 2021 to September 2022. The Ethical Review Board

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Committee of the Hospital approved the study (A/28/EC/460/2022). The sample size was calculated by WHO Sample Size Calculator taking population proportion of poor outcomes in invasive fungal infections at 18%.¹¹ Non-probability Consecutive sampling technique was used to gather the cases for this study.

Inclusion Criteria: Patients of either gender, aged 15 to 60 years, with invasive fungal infections diagnosed by a consultant medical specialist or infectious diseases expert were included in the study.

Exclusion Criteria: Patients with the unclear diagnosis who were managed empirically on antifungal drugs were not included. Pregnant and lactating women and patients refusing consent to participate were also excluded from the study. Patients who stopped treatment during treatment or were discharged against medical advice were also excluded from the study.

Written informed consent was taken from all the potential participants of this study before the start after a complete description of the study. Diagnosis of invasive fungal infection was made by a consultant infectious diseases specialist or medical specialist on clinical findings and relevant investigations.

Blood or other relevant cultures were sent to the microbiology section of the laboratory affiliated with our hospital, and an infectious diseases expert, along with a micro-biologist, ascertained the type of fungus involved in each patient. According to recent guidelines, the team put patients on standard antifungal treatment depending on the type of fungus involved.^{12,13}

Outcome was defined as good if the patient's condition improved. The patient was discharged from the hospital within four weeks of diagnosis. It was defined as poor if the condition did not improve and the patient had more than one month stay in the ward, required critical care admission, or died within four weeks of diagnosis. Relevant baseline and specific investigations were carried out on all the patients, especially COVID-19, control of diabetes and HIV. They have been carried out in the laboratory of our hospital through standard protocols.

Statistical Package for Social Sciences (SPSS) version 23.0 was used for the data analysis. Quantitative variables were expressed as Mean±SD and qualitative variables were expressed as frequency and percentages. Chi-square test was applied to find out the association. The *p*-value lower than or up to 0.05 was considered as significant.

RESULTS

Out of 90 patients with invasive fungal infections included in the study, 62(68.8%) had good outcomes, while 28(31.2%) had poor outcomes. The mean age of the patients recruited in our study was 39.54 ±6.27 years. Of all the participants, 65(72.2%) patients were male, while 25(27.8%) were female. Out of the total patients included in the study, 16(17.8%) had controlled DM, 15(16.7%) had poorly controlled DM, 14(15.5%) had hypertension, 06(6.7%) had HIV, while 14(15.5%) had COVID 19 (Table-I).

Table-I: Characteristics of Study Participants with Invasive Fungal Infections (n=90)

Study Parameters	n (%)
Age (years)	
Mean±SD	39.54±6.27 years
Range (min-max)	18 years-59 years
Gender	
Male	65(72.2%)
Female	25(27.8%)
Types of Fungus	
Histoplasmosis	02(2.2%)
Mucormycosis	56(62.2%)
Aspergillosis	16(17.8%)
Candida	0(6.7%)
Cryptococcus	0(7.7%)
Others	03 (3.3%)
Outcome	
Good	62(68.9%)
Poor	28(31.1%)
Comorbidities	
Controlled Diabetes Mellitus	16(17.8%)
Poorly controlled Diabetes mellitus	15(16.7%)
Hypertension	14(15.5%)
HIV	06(6.7%)
COVID-19	14(15.5%)
Others	01(1.1%)

Table-II summarizes the results of the statistical analysis.

Table-II: Factors Associated with Outcome of Treatment in Patients of Invasive Fungal Infections (n=90)

Factors Studied	Good Outcome n=62	Poor Outcome n=28	<i>p</i> -value
Poorly Controlled Diabetes Mellitus			
No	58(93.6%)	17(60.7%)	<0.001
Yes	04(6.4%)	11(39.3%)	
COVID-19 Positive			
No	57(91.9%)	19(67.8%)	0.005
Yes	05(8.1%)	09(32.2%)	
Steroid Use			
No	53(85.5%)	22(78.5%)	0.423
Yes	09(14.5%)	06(21.5%)	
HIV Positive			
No	61(98.3%)	23(82.1%)	0.006
Yes	01(1.7%)	05(17.9%)	

It was revealed that the presence of poorly controlled diabetes (p -value <0.001), COVID-19 infection (p -value-0.005) and HIV positive (p -value-0.006) were the factors statistically significantly associated with the presence of poor outcomes in our study participants. At the same time, the use of steroids had no such relationship found in our study (p -value-0.423).

DISCUSSION

Uncontrolled DM, the presence of COVID-19 and being HIV positive was associated with poor outcome in patients with invasive fungal infection included in our study. Invasive fungal infections have been a great challenge for treating teams.¹⁴ Most of these patients have complex clinical pictures, and the decline in condition is sometimes rapid and irreversible. Researchers have been trying hard to identify the risk factors associated with poor response to treatment in these difficult patients, so an aggressive strategy should have been opted for right from the start of management. It is believed that in COVID times, treatment strategies have been affected grossly and patients have suffered a lot due to many diseases-related and service-related reasons.

A French study was conducted in multiple centres regarding outcomes and factors related to invasive fungal infections in patients suffering from burn injuries. They revealed that very few patients had invasive fungal infections, but those who suffered usually did not have a good outcome. Furthermore, bacterial co-infection was associated particularly with poor outcomes.¹⁵ We did not restrict to burn patients only. We included all patients with invasive fungal infections in our hospital for 1.5 years. We discovered that many patients had poor outcomes, and co-infection with viruses like HIV or COVID-19 was particularly associated with poor outcomes.

Li et al. They studied more than 500 patients with invasive fungal infections. They concluded that low neutrophil count, bilirubin levels, length of CCU stay, renal failure and use of immunosuppressant agents within the last month predicted poor outcomes in their study participants.¹⁶ We studied around 90 patients and concluded that uncontrolled DM, HIV infection, and COVID-19 were predictors of poor outcomes in our patients suffering from invasive fungal infections. Gao et al. concluded that serum creatinine and bilirubin levels, presence of endotoxic shock and a long stay in ICU and hospital were factors associated with poor outcome.¹⁷ We only studied patients with invasive fungal infections and found out that many

patients had poor outcomes in our study. The presence of poorly controlled diabetes, COVID-19 infection and systemic steroid use were the factors associated with poor outcomes in our study participants.

A study published in North India in 2019 revealed that 110 cases of invasive fungal infections were seen in 2 years. Of those 110, most patients with cryptococcosis had a human immunodeficiency virus infection. Overall mortality was observed in 73% of the patients.¹⁸ 31.1% of our patients had a poor outcome, and 6(6.7%) patients had HIV. HIV was also related to poor outcomes in our study participants.

STUDY LIMITATIONS

Outcome parameters were not very specific and were only related to overall betterment or worsening of clinical condition. Fungal illness and systemic treatments sometimes cause reversible or irreversible end-organ damage to various body organs, and the impact may be long-lasting. Future studies with more sample sizes and long-term follow-up may generate results that can be used as local guidelines.

CONCLUSION

Many patients with invasive fungal infections had poor outcomes in our study. The presence of poorly controlled diabetes, COVID-19 infection and systemic steroid use were the factors associated with poor outcomes in our study participants.

Conflict of Interest: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

FSZ & UQ: Data acquisition, data analysis, drafting the manuscript, critical review, approval of the final version to be published.

SN & SWA: Study design, data interpretation, critical review, approval of the final version to be published.

FAS & SM: Conception, study design, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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