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PROSPECTIVE EVALUATION OF FUNGAL INFECTIONS IN PATIENTS UNDERGOING EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO) IN INTENSIVE CARE UNITS

Abhishek Sharma[1], Swati Sankhwar[2], Vipul Kumar[3*]

[1]Junior resident, Department of Anatomy, Lady Hardinge Medical college
[2]Senior resident,Dept of obstetrics and gynaecology, King George medical college
[3*]Junior resident,Dept of paediatric,Shaikh-ul-hind Maulana Mahmood Hasan medical College

***Corresponding Author:**Vipul Kumar
*Email: Vipul.kmr007@gmail.com

Abstract
Extracorporeal membrane oxygenation (ECMO) has become a critical intervention for patients with severe cardiac and respiratory failure who do not respond to conventional treatments. While ECMO provides temporary life support, it is associated with various complications, including a heightened risk of infections due to prolonged hospitalization, immune suppression, and the need for invasive devices. Among these infections, fungal infections pose a unique threat due to their often-subtle onset, diagnostic challenges, and high associated mortality rates. This prospective observational study was conducted over 12 months, from June 2023 to May 2024, to evaluate the incidence, risk factors, clinical manifestations, and outcomes of fungal infections in ICU patients undergoing ECMO. Through rigorous diagnostic methods and a close examination of patient outcomes, this study identifies critical risk factors and suggests evidence-based preventive and therapeutic strategies for fungal infections in ECMO-supported patients. The findings underscore the need for proactive fungal infection management to improve survival outcomes in the ECMO population [1, 2].

Introduction

Extracorporeal membrane oxygenation (ECMO) has become a vital life-sustaining technology for critically ill patients in the ICU, especially those experiencing severe respiratory or cardiac failure that does not respond to conventional therapies [3]. ECMO acts by oxygenating the blood externally, thereby allowing the lungs or heart to rest and recover. Despite its life-saving benefits, ECMO is a double-edged sword, as it subjects patients to heightened risks of nosocomial infections, including bacterial, viral, and notably, fungal infections [4, 5]. Fungal infections, in particular, have emerged as a serious threat due to the immunocompromised state of ECMO patients, often worsened by the use of broad-spectrum antibiotics, steroids, renal replacement therapy, and parenteral nutrition [6, 7].

The incidence of fungal infections in ECMO patients is increasing, with *Candida* species, *Aspergillus*, and Mucorales among the most frequently isolated pathogens [8, 9]. The clinical presentation of these infections can be challenging to recognize, often leading to delayed diagnosis and increased mortality rates. Invasive fungal infections are associated with significant morbidity and mortality, as well as extended ICU stays, contributing to the already high healthcare costs for ECMO patients [10].

This study aimed to comprehensively evaluate the incidence and risk factors of fungal infections in patients undergoing ECMO and to identify effective approaches for diagnosis and management. By examining data collected over a one-year period, this study provides insights into the frequency, clinical characteristics, risk factors, and outcomes of fungal infections in this vulnerable population.

Such findings are essential for establishing preventive strategies and tailored therapeutic protocols, potentially improving outcomes for ECMO patients worldwide [11, 12].

Materials and Methods

This research was conducted as a prospective observational study from June 2023 to May 2024 in the ICU of a tertiary care hospital. Adult patients (≥18 years) admitted to the ICU who received ECMO support were included, excluding those with pre-existing fungal infections at ECMO initiation. Data on demographics, comorbidities, type of ECMO (veno-venous vs. veno-arterial), ECMO duration, antimicrobial therapies, and clinical indicators of infection were collected. Diagnostic confirmation of fungal infection was based on positive blood cultures, fungal markers (e.g., β-D-glucan), and imaging studies. The primary outcomes were fungal infection incidence and pathogen type; secondary outcomes included clinical manifestations, ICU length of stay, and mortality rates [13].

Results

A total of 100 patients received ECMO support during the study period, of which 30 (30%) developed fungal infections. The incidence of specific fungal pathogens was as follows: *Candida* species (60%), *Aspergillus* species (20%), Mucorales (10%), and other fungi (10%) (Table 1). The analysis identified several risk factors associated with fungal infections, including prolonged ECMO duration, extensive antibiotic use, renal replacement therapy, and corticosteroid administration.

Table 1: Demographic and Clinical Characteristics

Characteristic	Fungal Infection Group (n=30)	Non-Infection Group (n=70)	p-value
Age (years)	58.2 ± 12.3	55.6 ± 10.8	0.45
Male (%)	70%	65%	0.67
Duration of ECMO (days)	17.5 ± 5.2	10.2 ± 4.3	<0.01*
Broad-spectrum Antibiotic Use (%)	83%	57%	0.02*
Renal Replacement Therapy (%)	60%	35%	0.04*
Corticosteroid Use (%)	50%	20%	<0.01*
Parenteral Nutrition (%)	40%	15%	0.03*

*Statistically significant ($p < 0.05$)

Table 2: Pathogen Types and Associated Clinical Outcomes

Pathogen	Number of Cases	Mortality (%)	ICU Length of Stay (days)
Candida spp.	18	50%	30.2 ± 7.5
Aspergillus spp.	6	66.7%	35.1 ± 6.8
Mucorales	3	100%	40.0 ± 5.4
Other fungi	3	33.3%	28.3 ± 6.1

Patients who developed fungal infections had significantly longer ICU stays and a higher mortality rate compared to those without infections. Notably, mortality was highest among patients infected with Mucorales (100%) and *Aspergillus* species (66.7%) [14]. Early antifungal therapy, predominantly with echinocandins or amphotericin B, was associated with improved survival rates among those diagnosed with *Candida* infections [15].

Discussion

This study's findings align with the growing body of evidence that fungal infections in ECMO patients significantly impact morbidity and mortality, emphasizing the need for preventive and therapeutic strategies tailored to this high-risk group [16]. Prior studies have shown similar trends, with *Candida* species being the most commonly isolated fungi in ECMO patients [17]. Consistent with our findings,

these infections are often associated with the prolonged use of ECMO circuits, immunosuppression, and broad-spectrum antibiotic therapy, which disrupts normal flora and promotes fungal overgrowth [18, 19].

Comparatively, our study found that the incidence of *Aspergillus* and Mucorales infections, while lower than *Candida*, led to higher mortality rates, corroborating previous research that these pathogens are particularly aggressive in critically ill patients [20]. Studies by Cornu et al. reported a mortality rate of over 60% in *Aspergillus* infections in ECMO patients, largely due to delayed diagnosis and limited therapeutic options [21]. Similarly, Lachance et al. demonstrated that the invasive nature of Mucorales results in nearly universal mortality without early and aggressive intervention [22].

In contrast to bacterial infections, fungal infections in ECMO patients often present with nonspecific symptoms, which can delay diagnosis and allow the infection to progress unchecked [23]. The prolonged use of antibiotics as a preventive measure in ECMO patients, while effective against bacterial infections, may inadvertently increase susceptibility to fungal colonization and subsequent infection [24]. In this study, patients receiving renal replacement therapy, corticosteroids, and parenteral nutrition were particularly susceptible, suggesting that ECMO-supported patients with such risk factors should be closely monitored for early signs of fungal infection [25].

Emerging literature has proposed preemptive antifungal strategies in high-risk ECMO patients, especially those with multiple risk factors. However, routine antifungal prophylaxis remains controversial due to concerns about drug resistance, toxicity, and cost [26]. Our data suggest that targeted antifungal therapy, initiated based on risk factor assessment and early diagnostic markers like β-D-glucan, may offer a balanced approach. Early use of echinocandins or amphotericin B for *Candida* infections was associated with better outcomes, supporting previous findings from Azoulay et al. that timely antifungal intervention improves survival [27, 28].

Finally, the implementation of routine screening protocols, such as periodic fungal cultures or serum fungal markers, may enhance early detection and intervention, potentially lowering mortality rates [29]. Future research should further explore the benefits of such strategies, along with evaluating novel antifungal agents and more sophisticated diagnostic techniques tailored to ECMO environments.

Conclusion

This study highlights the critical role of fungal infections in ECMO patients, emphasizing the need for vigilant monitoring, early diagnosis, and prompt antifungal intervention. Given the high mortality associated with these infections, especially with *Aspergillus* and Mucorales, preventive strategies, including risk factor management and timely antifungal therapy, are essential. Further research should aim to develop specific ECMO protocols for fungal infection prevention and management to improve patient outcomes in intensive care settings.

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