

The Impact of Portable High Efficiency Hepa Filters on the Incidence of Invasive Fungal Infection in COVID 19 Inpatients in a Tertiary Care Hospital: A Retrospective Analysis from Pakistan

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ABSTRACT

Objective: To identify impact of air filtration on incidence of Invasive fungal infections in COVID-19 patients after restructuring of COVID-19 wards.

Study Design: Cross-sectional observational study

Place and Duration of Study: This study was conducted at the Department of Clinical Microbiology and Infectious Disease at the COVID-19 ward from June 2021 to November 2021.

Materials and Methods: All COVID-19 patients >18 years (non-severe, severe and/or critical) admitted at the tertiary care center were included. Even COVID-19 patients with suspected IPA, based on isolation of fungal species from one or more respiratory samples were included. Two time frames were used for inclusion of patients, one three months prior to and second three months after installation of HEPA filters in COVID wards. Patients with underlying respiratory disease, previous history of invasive pulmonary aspergillosis, on chronic steroid use (>3 months), on broad-spectrum antibiotics and with hematological malignancies were excluded. SPSS version 23.0 was used for data analysis.

Results: From 187 patients, 97 enrolled before installation of HEPA filters while 90 after installation of HEPA filters. Overall the mean age of patients was 62.7 ± 14.6 years. A significant difference of $p=0.04$ was observed in terms of length of stay in-between before installation of HEPA filter group (13.1 ± 11.2 days) and in after installation of HEPA filter group (10.2 ± 8.2 days). Beta-D-Glucan test with HEPA filter was positive in 17 (17.5%) of patients while in 28 (31.1%) of patients without HEPA filter ($p=0.03$). Treatment with Azoles was found to have significant difference in-between both groups ($p=0.002$). Overall, treatment was successful in 16 (16.5%) patients in without HEPA filter group while in 38 (42.2%) of patients with HEPA filter ($p<0.001$)

Conclusion: Substantial decrease in incidence of invasive fungal infections among COVID-19 patients was reported in terms of age, length of stay, Beta-D-Glucan, treatment with azoles and overall treatment in favor of HEPA filters.

Key Words: HEPA filters, SARS-CoV-2, Invasive Fungal Infections.

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INTRODUCTION

The primary spread of the global coronavirus (COVID-19) pandemic was due to airborne droplets.

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To control the acquisition and/or transmission of such respiratory droplet infections is of prime importance, especially within indoor environments, where people remain in close contacts.¹ Reduction in airborne microbes can help in reducing not only respiratory but other systemic infections that can be transmitted through fomite or hand contamination and close contacts, through decrease in number of microbes which land on surfaces.²

In such circumstances, high specification filters are observed to cleanse air of droplets and aerosols.³ Filtration of air is a commonly employed method for reducing infections especially in high-risk health care environments as in operation theatres and in hospital rooms for immune-compromised patients.⁴ Even portable air filtration units, were made initially for trapping vehicle emission particulates and pollen >0.02 micrometer, being more than sufficient for capturing

droplets and aerosolized pathogens.⁵ SARS-CoV 2 is around 0.1 micrometer in diameter.⁶ A few products that are available commercially especially for domestic use include high efficiency particulate air (HEPA) filters, being capable of removing >99 % of aerosolized particles within a short amount of time.⁷

Various techniques have been used for preventing fungal infections especially in immune-compromised patients but have yielded limited effects; reducing environmental exposure through air-handling system specialized in being able to exclude fungal (*Aspergillus* specie).⁸ For instance, by using HEPA filters either with or without ventilation (laminar air flow) it has been regarded as being highly efficacious, by augmenting natural defense mechanism of hosts through recombinant growth factors.⁹

Outbreaks of nosocomial invasive fungal infections such as aspergillosis have been reported within last couple of decades, being correlated with increase in air counts of *Aspergillus* specie.¹⁰ To minimize such outbreaks, it is pivotal to control and manage the aerosolized environment for preventing contamination.¹¹ The mechanism by which filtration of aerosol particles take place in gas phase has been extensively studied, however the combined action of all such filtration mechanisms by using HEPA filters tends to show their high efficiency of filtering across the spectrum of aerosols.¹²

Despite advances and use of air filtration in healthcare environments as in operation theatres, yet it remains unresolved as to whether the effect of air filtration when deployed in other setting such as in wards will have the same effect or not.^{13,14}

The objective of this study was to determine the impact of air filtration on incidence of fungal infections among COVID-19 patients after restructuring of COVID-19 wards using HEPA filters. A secondary objective was to identify incidence of invasive aspergillosis in COVID-19 patients prior to restructuring with air filtration, therefore evaluating the environmental effect on nosocomial fungal infection's incidence at a tertiary care center.

MATERIALS AND METHODS

This cross sectional observational study was carried out for a period of 6 months, from June 2021 to November 2021 at the COVID-19 ward, Department of Clinical

Microbiology and Infectious Disease where maintenance of surveillance and registry of fungal infections and an anti-fungal stewardship programme is done. This was a single-centered study with over 1500 beds in the hospital. Patients, above the age of 18 years, admitted due to COVID-19 (severe, non-severe and/or critical) were included in the study. In addition, COVID-19 patients with suspected invasive pulmonary aspergillosis (IPA) based on isolation of *Aspergillus* species from one or more respiratory sample were also included in the study. Patients with underlying lung disease, on chronic steroid use (>3 months) and with use of broad-spectrum of antibiotic (< 3 months) and with any hematological malignancy were excluded from the study.

RESULTS

From the total of 187 patients included in the study, 97 were enrolled before installation of HEPA filters while 90 after installation of HEPA filters. Overall, the mean age of patients was 62.7 ± 14.6 years. In patients before installation of HEPA filters, the mean age was 60.5 ± 14.2 years while in patients admitted after HEPA filter installation, the mean age was 65.2 ± 14.7 years. A significant difference of $p=0.03$ was observed between the two groups. Overall, 100 (58.8%) patients were males while 77 (41.2%) females, in without HEPA filter group, 60 (61.9%) patients were male while 37 (38.1%) females whereas in HEPA filter group, 50 (55.6%) were males while 40 (44.4%) were females, having an insignificant difference of $p=0.38$ between them. A significant difference of $p=0.04$ was observed in terms of length of stay in-between before installation of HEPA filter group (13.1 ± 11.2 days) and in after installation of HEPA filter group (10.2 ± 8.2 days).

The Beta-D-Glucan test in before installation of HEPA filter group was positive in 17 (17.5%) of patients while in 28 (31.1%) of patients after installation of HEPA filter, with a significant difference of $p=0.03$. A significant difference of $p=0.04$ was reported in terms of malignancy in-between patients included in both groups. Treatment with Azoles was found to have significant difference in-between both the groups ($p=0.002$). Overall, treatment was successful in 16 (16.5%) of patients in before installation of HEPA filter group while in 38 (42.2%) of patients after installation of HEPA filter ($p<0.001$) Table No. 1.

Table No. 1: Cross tabulation of variables with versus without Hepa-Filter (n=187)

	Total (n=187)	Without Hepa-filter (n=97)	With Hepa-filter (n=90)	p-value
Age	62.7 ± 14.6	60.5 ± 14.2	65.2 ± 14.7	0.03
Gender				
Male	110 (58.8)	60 (61.9)	50 (55.6)	0.38
Female	77 (41.2)	37 (38.1)	40 (44.4)	
Ward				

P1	48 (25.7)	27 (27.8)	21 (23.3)	0.45
P2	29 (15.5)	17 (17.5)	12 (13.3)	
P3	92 (49.2)	42 (43.3)	50 (55.6)	
ACU	10 (5.4)	7 (7.2)	3 (3.3)	
ER	8 (4.3)	4 (4.1)	4 (4.4)	
Length of stay	11.7 ± 9.9	13.1 ± 11.2	10.2 ± 8.2	0.04
Beta-D-Glucan				0.03
Negative	112 (59.9)	67 (69.1)	45 (50.0)	
Positive	45 (24.1)	17 (17.5)	28 (31.1)	
Not done	30 (16.0)	13 (13.4)	17 (18.9)	
GM				0.61
Negative	112 (60.5)	60 (63.2)	52 (57.8)	
Positive	43 (23.3)	22 (23.2)	21 (23.2)	
Not done	17 (18.9)	13 (13.7)	17 (18.9)	
Diabetes mellitus	115 (61.5)	58 (59.8)	57 (63.3)	0.61
Chronic kidney disease	21 (11.2)	8 (8.2)	13 (14.4)	0.18
Hypertension	100 (53.5)	49 (50.5)	51 (56.7)	0.40
Ischemic heart disease	39 (20.9)	15 (15.5)	24 (26.7)	0.06
Malignancy	11 (5.9)	9 (9.3)	2 (2.2)	0.04
CVA	12 (6.4)	4 (4.1)	8 (8.9)	0.18
Connective tissue disease	7 (3.7)	6 (6.2)	1 (1.1)	0.07
Chronic pulmonary disease	26 (13.9)	17 (17.5)	9 (10.0)	0.14
Azoles	128 (68.4)	76 (78.3)	47 (52.2)	0.002
Ecchinocandins	9 (4.8)	7 (7.2)	2 (2.2)	0.11*
AmphotericinB	29 (15.5)	16 (16.5)	13 (14.4)	0.70
Treatment	54 (28.9)	16 (16.5)	38 (42.2)	<0.001
Duration of development of infection	4	4	3	0.35
Toci	46 (24.6)	30 (30.9)	16 (17.8)	0.04
Clinical symptoms	126 (67.4)	69 (71.1)	57 (63.3)	0.26
Radiological change	93 (49.7)	45 (46.4)	48 (53.3)	0.34
Mortality	74 (39.6)	34 (35.1)	40 (44.4)	0.19

DISCUSSION

According to the results of this study of 187 patients with 97 admitted before installation of HEPA filters and 90 patients admitted after HEPA filters installation, it was observed that a significant reduction in the length of stay, positivity of Beta-D-Glucan test, treatment with Azoles, overall success after treatment and Tocilizumab with positive results in favor of HEPA filters. Even though clinical symptoms decreased from 71 % to 63 % after installation of HEPA filters, yet the mortality increased from 35 % in the pre-HEPA filter installation group to 44 % in the post-HEPA filter installation group. Positivity of Beta-D-Glucan decreased from 69 % in pre-HEPA filter group to 50 % in post-HEPA filter group. Likewise, the duration of infection development was although not significantly but slightly lesser in the HEPA filter group as compared to the without filter group.

Paucity of data persists in the published literature with regards to effectiveness of portable HEPA filters in being able to reduce incidences of infections of respiratory tract, including SARS-CoV-2 especially in indoor environments (15-17). In one of the research projects, it was observed that in comparing use of HEPA filter in immune-compromised patients, the frequency of respiratory fungal infections in patients with HEPA filter was reported to be 07 % (18/254) while 17 % (6/35) in the without filter groups. However, there was no difference in terms of 100-days mortality in-between the two groups (14 % vs. 17 %).¹⁸ In yet another study aimed at determining the incidence of IPA after installation of HEPA filters, it was reported that in the group without HEPA filters, the average *Aspergillus* specie were observed at 15 spores/m³ while in HEPA filter group, the average count of *Aspergillus* specie was reported at around 0.18 spores/m³. This showed that HEPA filters lead to substantial decrease in the air counts of fungal organisms, a finding also observed in our study as well.¹⁹

From the above, it is evident that intervention that are based on filtration of air by using adequate equipment's must be widely implemented for reduction of spread of SARS-CoV-2 via aerosol phase as well as for preventing spread of invasive fungal infections.²⁰

Although this study evaluated the factors associated with incidence of IPA with or without HEPA filters, yet this study was not free from limitations. Since this study was a single centered study with limited sample size of 187 and was divided in two groups with variable demographics, the study was also not free from selection and observer bias. Further, multi-centered studies with greater sample size would be enlightening to generalize the findings reported in this study.

CONCLUSION

According to the findings of this study, a substantial decrease in the incidence of invasive fungal infections among COVID-19 patients was reported in terms of age, length of stay, Beta-D-Glucan, treatment with azoles and overall, in favor of HEPA filters. Nonetheless mortality was found to have insignificant difference between both groups.

Author's Contribution:

Concept & Design of Study: Aneera Ahmed
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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