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Knowledge and Awareness of Orbital Mucormycosis in Post COVID-19 Recovered Patients in India

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Abstract

Background: The emergence of mucormycosis cases amid the COVID-19 pandemic and the fear associated with mucormycosis may turn out to be a terrifying public health issue. The current study aims to assess knowledge and awareness about orbital mucormycosis in post COVID-19 recovered patients.

Methods: A cross-sectional study was carried out among 242 COVID-19 recovered population from August 2021 to February 2022. A semi-structured online questionnaire was used for data collection using convenient and snow ball sampling methods.

Results: A total of 242 participants completed the questionnaire. Approximately 53.7% of participants were male and 46.3% were female. Most of the participants were working and were aware about mucormycosis through social media. Presenting symptoms and signs of COVID-19 were fever (87.6%), malaise (5.8%), weakness (72.3%), vertigo (5%), cough/cold (76.4%), shivering (22.3%), chills (23.1%), loss of taste (61.2%), rashes (25.6%) and rest were asymptomatic (5.8%) or presented with multiple signs and symptoms. A statistically significant association was found between reported history of mucor-mycosis and duration of steroid use (p value=0.003), being educated and aware about the disease (p value=0.000) and older age (p value=0.000).

Conclusion: Fungal infection and mucormycosis are not new phenomena but the emergence of mucormycosis associated with COVID-19 is a big concern. The current study highlighted the good awareness about mucor-mycosis among COVID-19 recovered patients in Indian population.

Keywords: Corticosteroid, COVID-19, Diabetes, Fungal co-infection, Mucormycosis, Rhino-orbito-cerebral mucormycosis, Steroid therapy

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Introduction

Coronavirus disease 2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome virus 2 (SARS-CoV-2), has affected more than 543 million people worldwide, accounting for over 6.3 million deaths as on 30th June 2022 [1]. The pandemic due to novel SARS Coronavirus-2 (COVID-19) continues to be a significant problem worldwide [2]. COVID-19-associated rhino-orbital-cerebral mucormycosis (ROCM) has reached epidemic proportion during India's second wave of COVID-19 pandemic, with several risk factors being implicated in its pathogenesis [3]. COVID-19 infection, its treatment, resultant immunosuppression, and pre-existing comorbidities have made patients vulnerable to secondary infections including mucormycosis [4].

The disease caused by the fungus has been reported all over the world and although associated with immunocompromised states like carcinomas or immunosuppressive therapy, it also affects a newer range of susceptible hosts like diabetics, neutropenics, patients on desferroxamine therapy, etc. [5]. The pandemic coronavirus disease 2019 (COVID-19) continues to be a significant problem

worldwide. While several treatment options have been evaluated, none except systemic glucocorticoids have been shown to improve survival in COVID-19 [6].

COVID-19 is a new disease condition caused by a novel coronavirus (SARS-CoV-2) first documented in Wuhan, China [7]. Mucormycosis is commonly associated with covid 19 disease in medically compromised individuals. Mucormycosis is an angio-invasive disease that is characterized by tissue infarction and necrosis. The mucormycosis are classified based on its anatomic location, such as rhino-orbital-cerebral (ROCM), pulmonary, gastrointestinal, cutaneous, renal and disseminated mucormycosis. ROCM mucormycosis is the commonest form (45-74%), followed by cutaneous (10-31%), pulmonary (3-22%), renal (0.5-9%), and gastrointestinal (2-8%) [8]. Higher risk of Mucormycosis is found in patients with diabetes mellitus, under chemotherapy, haematological malignancy, human immunodeficiency virus (HIV) infection, organ transplant recipients on immunosuppressive therapy. Globally, Rhizopus arrhizus is the commonest cause of mucormycosis [9]. The mortality rate of Mucormycosis in India is ranges from 28-52%, but there are limited studies in India on mucormycoisis [8].

Previous studies have documented the epidemiology, clinical profile, management, and outcome of COVID-19-associated RCOM after Covid-19 recovery [10,11]. Numerous studies have documented presenting symptoms and sign and outcome of management of post COVID-19 patients in India [11-15]. However, there exist a gap about the knowledge and awareness of orbital mucor-mycosis in literature specially among Indian population. The current study aimed at assessing knowledge about mucor-mycosis and associated risk factors of the disease among patients who had recovered from COVID-19 in Northern India.

Methodology

A cross-sectional online study was conducted to assess knowledge and awareness about orbital mucor-mycosis in post COVID-19 patients. The participants were interviewed, using an online questionnaire that was developed specifically for this study. The inclusion criteria were all persons who had recovered from COVID-19 and gave informed consent for participation in the study. The study population comprised of all the COVID-19 recovered adults in India. The sample size of 242 was calculated using 4.3% prevalence of mucor-mycosis from previous studies, absolute precision of 2.5%, confidence level of 95% and a population size of 5000 [12]. The sampling technique was non-probability sampling comprising of convenience and snowball sampling methods. For data collection, a semi-structured online questionnaire (in "Google Form") was created and shared widely in social media platforms like WhatsApp™, (Facebook Inc, Cambridge, MA, USA) by text messages for data collection. Google forms is one of the online data collection tools that is commonly used for surveys [16,17]. If any participant did not install WhatsApp™ on his phone, they were requested to provide an alternative mobile number with WhatsApp™ installed. This was done to enhance the participation rate.

WhatsApp™ is a popular medium for communication and has been used in many studies as an electronic platform for communication [18,19]. Once the survey link was forwarded, the participants were requested to save the sender number first and then to activate the survey link. Prior to inclusion in the survey, the participants were required to offer informed e-consent. A total of three reminders at a gap of one to two days were sent to participants who did respond to the survey link sent earlier. The study was approved by the Institute Ethics Committee of the institution.

A nominal group technique was used to develop the questionnaire. One researcher developed first draft of the study tool after extensive review of the relevant published papers to ensure all possible ocular symptoms. The questionnaire was revised based on the feedback received from optometrists during the group discussions (in person and online). The questionnaire included demographic information and possible risk factors of mucormycosis. Pre-testing of the questionnaire was done among ten non study persons who had recovered from COVID-19 for standardization purpose. The English language questionnaire was translated into local language Hindi by a translator and back translated into English to ensure the accuracy of the translation.

By clicking on the link, the participants could see the study's aims and objectives and the patient information sheet. The study questionnaire comprised of socio-demographic information of the participants, COVID-19 Reverse Transcriptase Polymerase Chain Reaction (RTPCR) positivity date and presenting symptoms. Pre and post COVID-19 health status was recorded including co-morbidities like diabetes mellitus, hypertension and duration of steroid usage along with awareness about mucormycosis was also recorded.

Study definitions

Post COVID-19 symptoms: Symptom(s) that persisted beyond four weeks from the date of SARS-CoV-2 positive test conducted using either RTPCR or Cartridge Based Nucleic Acid Amplification Test (CBNAAT). Further, according to timeframe, ocular COVID-19 symptoms were classified as short-term COVID-19 symptoms: symptoms present beyond four weeks after the SARS-CoV-2 positive test and lasting less than or up to twelve weeks; and long-term ocular COVID-19 symptoms: symptoms present beyond twelve weeks after SARS-CoV-2 positive test.

Statistical analysis

Descriptive statistics were performed for the background characteristics of the participants. A multivariate linear regression model was fitted to find the association between mucormycosis knowledge and awareness status with other predictors. Regression models were fitted to investigate the contributory role of the studied variables on mucor-mycosis knowledge and awareness. The p-value < 0.05 was considered statistically significant at 95% confidence interval. Data were analyzed by using statistical software STATA-16. Since it was web-based survey, the CHERRIES checklist guidelines were followed while reporting the data [20].

Results

A total of 242 participants out of 427 completed the study questionnaire, giving a response rate of 56.7%. Approximately 53.7% of participants were male and 46.3% were females (Table 1 and Figure 1).

Most of the participants were working. Among males, the most common occupation was private job (34.6%) and among females the most common occupation was house-wife (65.2%) (Figure 2).

Awareness about mucormycosis was high, especially through through social media. A total of 173 (71.2%) of the respondents had heard about black fungus (mucormycosis) (Figure 3).

Around 10.7% were post graduate, 33.5% were graduate, 14.0% were undergraduate and 41.7% were educated up to 10th class or

Table 1: Age and gender distribution of the study participants (N=242).

Age Groups (in years)	Male (%)	Female (%)	Total
0-19	3 (2.3)	5 (4.5)	8 (3.3)
20-29	25 (19.2)	23 (20.5)	48 (19.8)
30-39	20 (15.4)	15 (13.4)	35 (14.5)
40-49	32 (24.6)	23 (20.5)	55 (22.7)
50-59	26 (20.0)	42 (37.5)	68 (28.1)
≥60	24 (18.5)	4 (3.6)	28 (11.6)
Total	130 (53.7)	112 (46.3)	242

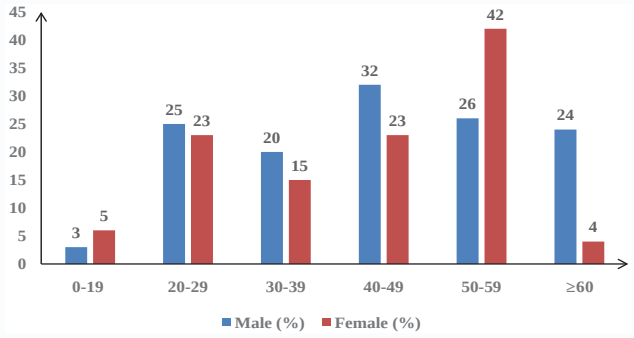

Figure 1: Age and gender distribution of study participants (N=242).

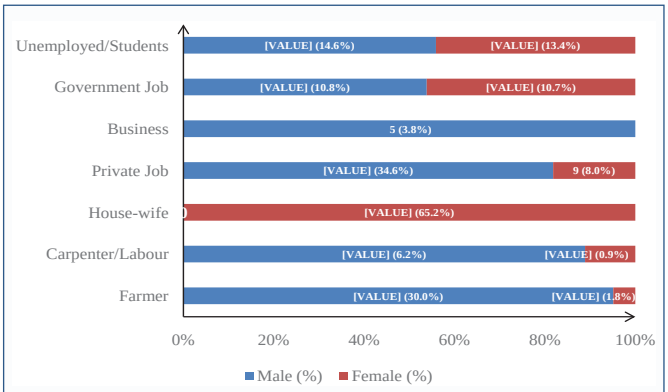

Figure 2: Gender and occupation distribution of the study participants(N=242).

below. A statistically significant association was found between being educated, working status and having awareness about mucor-mycosis (p value < 0.05). Table 2 Presenting symptoms and signs of COVID-19 infection were fever (87.6%), malaise (5.8%), weakness (72.3%), vertigo (5.0)%, cough/cold (76.4%), shivering (22.3%), chills (23.1%), loss of taste (61.2 %), rashes (25.6%). Around 5.8% of the patients were asymptomatic and around 84.7% showed multiple signs and symptoms (Figure 4).

Pre-COVID health status showed that 71.9% patients were healthy, 14.0% were unhealthy, and 11.6% were having average health status before COVID-19 infection. However, there was no statistically significant correlation between health status before and after COVID-19 infection (p value 0.962). Table 3 Diabetic mellitus was present in 16.9% of the participants by patient self-report, and 24.7% of the participants reported themselves as hypertensives.

Proportion of Mucormycosis: A total of 46 patients (19.4%) gave history of mucormycosis. Although the diagnosis could not be confirmed from a self-reported questionnaire, the determinants and socio-demographic factors associated with the disease were studied.

Table 2: Socio-demographic parameters of the participants based on awareness about mucormycosis (N=242).

	Heard of mucormycosis (black fungus)			
Education	**Yes (%)**	**No (%)**	**Total**	**p value**
10th Class and below	58 (33.5)	43 (62.3)	101 (41.7)	0.0007*
Undergraduate	29 (16.8)	5 (7.2)	34 (14.0)	
Graduate	63 (36.4)	18 (26.1)	81 (33.5)	
Post-Graduate	23 (13.3)	3 (4.3)	26 (10.7)	
Gender				
Male	99 (76.2)**	31 (23.8)**	130 (53.7)	0.086
Female	74 (66.1)	38 (33.9)	112 (46.3)	
Age (mean ± SD)	41.87 (±13.62)	44.65 (±12.21)		0.963
Occupation				
Working/Studying	97 (56.1)	20 (28.9)	117 (48.3)	0.0001*
Not Working	76 (43.9)	49 (71.0)	125 (51.7)	
Total	173 (71.2)**	69 (28.8)**	242	

*statistically significant p value **row percentages.

Table 3: Pre-COVID and Post-COVID health status among the study participants.

Health status	Pre-COVID (%)	Post-COVID (%)	(rho ρ)	p value
Unhealthy	34 (14.0)	27 (11.2)	Pearson Correlation Coefficient =0.003	0.962
Average	28 (11.6)	92 (38.0)		
Healthy	174 (71.9)	85 (35.1)		
Very Healthy	6 (2.5)	38 (15.7)		
Total	242	242		

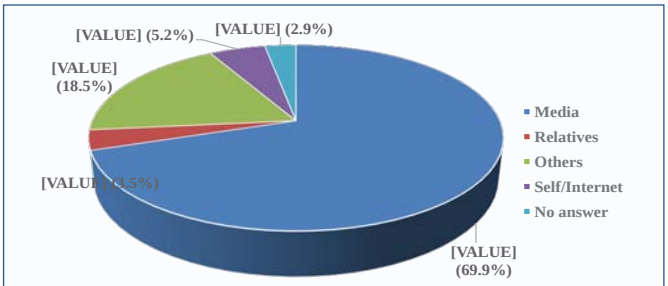

Figure 3: Pie chart showing mode of awareness about mucormycosis among the aware participants (N=242).

A statistically significant association was found between reported history of mucor-mycosis and duration of steroid use (p value=0.003), being educatedand aware about the disease (p value=0.000) and older age (p value=0.000) (Table 4).

Discussion

The World Health Organization declared the COVID-19 a pandemic on March 22, 2020, around three months after the first case of the disease was identified [21,22]. Since then, the disease continues to spread in an unprecedented manner across the world causing loss of millions of lives. As of May 24th, 2022, there have been 523 million confirmed cases of COVID-19 and nearly 6.3 million people have lost their lives due to the diseases [1]. In India, around 43 million have been infected with the virus and more than 525 thousand persons have died [1].

While the countries continue to grapple with the rising number of COVID-19 cases, there is growing evidence on lingering COVID-19 symptoms extending up to a few months from the initial diagnosis

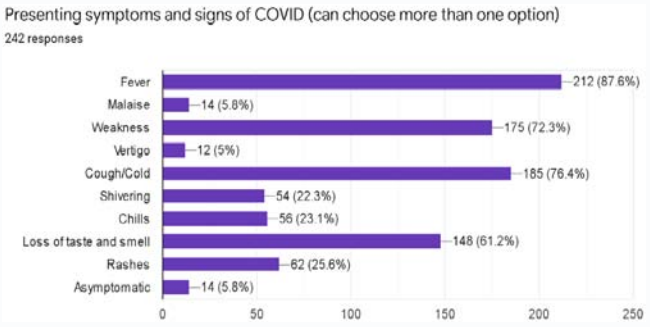

Figure 4: Presenting signs and symptoms of COVID-19 infection among study participants (N=242).

Table 4: Association between socio-demographic factors, pre-existing health impairments and steroid therapy with history of mucor-mycosis in the study participants (N=242).

Determinants	History of mucor-mycosis			
Gender	**Yes (%)**	**No (%)**	**Total**	**p value**
Male	22 (47.8)	108 (55.1)	130 (53.7)	0.379
Female	24 (52.2)	88 (44.9)	112 (46.3)	
Age (mean ± SD)	44.59 (±13.19)	35.47 (±13.37)		0.000*
Duration of steroid use (days)	20.96 (± 8.82)	14.51 (± 13.95)		0.003*
Education				
10th class and below	6 (13.0)	95 (48.5)	101 (41.7)	0.000*
Undergraduate	9 (19.5)	25 (12.8)	34 (14.0)	
Graduate	18 (39.1)	63 (32.1)	81 (33.5)	
Post Graduate	13 (28.3)	13 (6.6)	26 (10.7)	
PreCOVID-19 Health				
Unhealthy	4 (8.7)	30 (15.3)	34 (14.0)	0.018
Average	5 (10.9)	23 (11.7)	28 (11.6)	
Healthy	33 (71.7)	141 (71.9)	174 (71.9)	
Very Healthy	4 (8.7)	2 (1.0)	6 (2.5)	
H/o Diabetes Mellitus				
Yes	5 (10.9)	36 (18.4)	41 (16.9)	0.227
No	41 (89.1)	160 (81.6)	201 (83.1)	
H/o Hypertension				
Yes	10 (21.7)	50 (25.5)	60 (24.8)	0.610
No	36 (78.3)	146 (74.5)	182 (75.2)	
Total	46 (19.0)	196 (80.9)	242	

*Statistically significant p value.

among the survivors. Mucor-mycosis had been recognized as a post COVID-19 disease in many studies. The number of cases identified during the pandemic is much higher than those reported in the literature in different settings in the pre-pandemic era [23]. Non-ocular manifestations of mucor-mycosis, like renal mucor-mycosis was reported by many authors, even before the pandemic [24]. After the onset of the pandemic, mucor-mycosis of the paranasal sinuses with intra-orbital extension was reported by many studies [25-27].

Uncontrolled diabetes and history of steroid use during coronavirus treatment have been recognized as risk factors for mucor-mycosis by previous studies [25,28,29] and the current study found a significant association with the duration of steroid use.

The current online study had a response rate of 56.8% and participation ratesrange from 50-80% in online surveys around the globe. The pandemic presented unique opportunities to conduct online studiesaround the globe. The study found that knowledge and awareness about mucor-mycosis is good in post COVID-19 recovered patients in Indian population. Alongside, numerous predictors like education, age, duration of steroid treatment for COVID-19 were found significantly associated with mucormycosis.

The older age groups were found to be less knowledgeable about mucormycosis compared to the younger age group, although the difference was not statistically significant. This study found that mucormycosis knowledge and awareness was less in female than male, and working people have more knowledge and awareness than non-working people. A previous study had revealed that the males had more knowledge about COVID-19 than their females counterparts in Bangladesh [30]. The same study also demonstrated Knowledge was significantly correlated with age ($p<0.005$), an education level ($p<0.001$), attitude ($p<0.001$), and urban location ($p<0.001$) [30].

A significant relationship was found between the history of mucormycosis and pre COVID-19 health.

Two previous studies amongthirty-one and fifteen patients of mucor-mycosis reported a mean age of 56.3 years and median of 52 years (range 14-71) respectively, which is higher than the mean age of 44.6 years reported in the current study [28,31]. A younger age profile can be explained by the fact that non-probability sampling and online data collection led to selection of a greater number of younger participants.

Older age was associated with mucor-mycosis in the current study, in conformity with previous studies [29].

The strength of the current study is that awareness and history of mucormycosis was assessed in individuals hospitalized as well as not admitted to hospital giving a better representation of the population. The limitations of the study are that sample size is small and it is not representative of the general population, since only purposive and conveniently sampled individuals were covered and data was collected using either smartphones or WhatsApp™. Those not having access to smartphones could not be included in the study. The reverse causality between predictors and mucormycosis could not be established, as the study was not longitudinal.

A larger study with more sample size, especially community-based studies will give a more representative picture of the mucormycosis problem among post COVID-19 recovered patients. Fungal infection and mucormycosis are not new phenomena but the emergence of mucormycosis associated with COVID-19 is a big concern. This study documented that the there was good knowledge and awareness about mucormycosis in post COVID-19 recovered patients. The knowledge and awareness about mucormycosis varies with age, gender, socio-economic status, literacy and occupation. Efforts to increase awareness about black fungus (mucormycosis) should be directed towards females, older ager groups and persons not employed or out of the active workforce. The duration of steroid therapy should be closely monitored and all precautions for the prevention of mucor-mycosis should be taken in hospitalized patients.

With millions of individuals recovering, the consequence of COVID-19 is likely to become an additional burden on the health care delivery system. Understanding mucor-mycosis and its associated

risk factors is crucial to reorient the eye infrastructure to make it more responsive to the growing needs for this disease. Hence, the current study can be used to guide the development of appropriate infrastructure and manpower thereby designing management strategies and patients care plan in hospital and rehabilitation facilities.

A major recommendation from the study is an integrated care model involving all relevant healthcare disciplines while managing mucor-mycosis in the outpatient setting at every healthcare facility, rather than organ-specific approaches.Continuous follow-up will be important to assess the further prolonged mucormycosis related health problems. A community-based rehabilitation program, including psychological support should be a part of post COVID-19 care.

Another important recommendation from the study will be to make policies and planning of developing awareness in the general public about this dreadful blinding orbital disease.

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