



RELATION BETWEEN THE OUTBREAK OF MUCORMYCOSIS AND COVID-19 VACCINE : AN AETIOLOGICAL AUDIT

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ABSTRACT In the era of covid-19 pandemic, severity of symptoms was mostly managed with corticosteroids, the disease itself was found to be hyperglycemic in nature and when combined with the use of infected ventilators, masks and oxygen ducting systems, all led to a decreased immunity. Due to which the opportunistic fungal infections had taken a rise. Mucormycosis was one such opportunistic fungal infection which saw an upsurge post the 2nd wave of covid19 pandemic. Our institute happened to treat a significant number of post covid mucormycosis patients and here is an observational study based on that data which deals with various etiological factors leading to the cause of mucormycosis during the outbreak, mainly focusing on the effect of covid 19 vaccine and incidence of mucormycosis.

KEYWORDS : COVID-19 vaccine, corticosteroids, infected ventilators mucormycosis, etiological factors

INTRODUCTION

In early December 2019, the novel coronavirus now named as SARS-CoV-2 caused series of acute respiratory disease outbreak which started in the capital city of Wuhan, China. The disease caused by this responsible virus was termed as coronavirus disease- 19 (COVID-19). Originally a zoonotic transmission was considered for this outbreak but later it was observed that human to human transmission played a major role in subsequent rapid spread of the disease. The global pandemic of covid-19 disease was declared by the world health organization (WHO). It is now widely recognized that symptoms of COVID-19 were insignificant or ranging from minimal to severe hypoxia with acute respiratory distress syndrome (ARDS). This has caused sudden increase in hospitalization for pneumonia with multi organ disease[1].

According to various literatures, Covid-19 caused by serious acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been associated with a wide range of opportunistic bacterial and fungal infection. Increase in opportunistic infection in Covid-19 can be because of low oxygen (hypoxia), high glucose (disease, new onset hyperglycemia, steroid induced hyperglycemia, acidic medium (metabolic acidosis, diabetes ketoacidosis), high iron levels (increased ferritins) and increased phagocytic activity of white blood cells (WBCs) due to immune-suppression (SARS- CoV-2 mediated, steroid mediated or associated comorbidities) with several other risk factors.[2]

After global pandemic of COVID-19 there are increasing cases of rhino-orbital mucormycosis in COVID-19 infected patients specially in India. Globally, the prevalence of mucormycosis varied from 0.005 to 1.7 per million population, while its prevalence is nearly 80 times higher in India compared to developed countries[3]. Initially occurrence of mucormycosis also known as black fungus disease was believed to be rare but due to COVID pandemic disease etiology has been evolved in recent times.

As said earlier mucormycosis is an extremely rare in healthy individual and it particularly targets immune-compromised high risk patients. These causative pathogens grow in suitable conditions which are more prevalent in covid-19. Here we aim to study systematic review of various etiological factors of mucormycosis and a special attention towards the role of covid 19 vaccine on its incidence.

MATERIALS AND METHOD

AIM: To identify and treat patients of mucormycosis, to take detailed COVID history, to enquire about the vaccination status and to analyze various etiological factors pertaining to causation of fungal disease along with correlating the vaccination status with mucormycosis.

Type Of Study: Retrospective observational study

131 patients were enrolled in this study with inclusion criteria of Invasive fungal sinusitis proven over KOH mount.

A detailed history was taken for all these 131 patients as a part of our routine management protocol. The history taking contained questions pertaining to the onset of DM and presence of any other comorbidities, onset of COVID, use of steroids during COVID treatment, use of remdesivir, need for ICU admission or O2 support, if patients requiring intubation or NIV and their vaccination status. The history was then analysed, studied and compared to yield the following results.

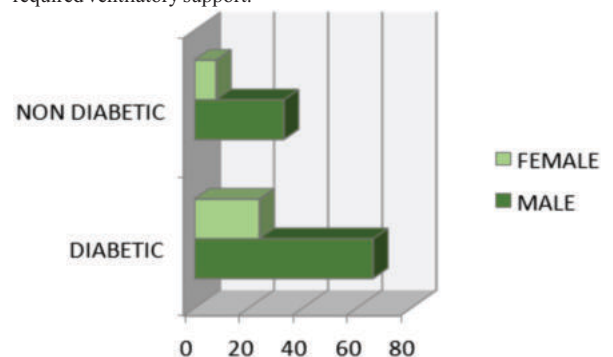
RESULTS

A total of 131 patients were enrolled out of which 99 were male and 32 were female.

TOTAL SAMPLE SIZE	MALE	FEMALE
131	99	32

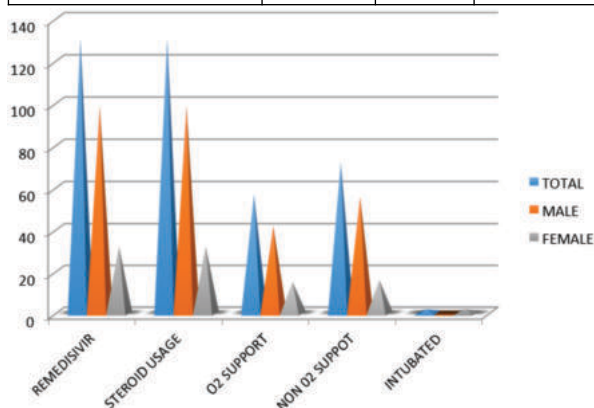
Amongst the 131 patients 90 were diabetic and 41 were non diabetic. Out of the 90 diabetic patients 66 were male and 24 were females, and amongst the non diabetic 33 were male and 8 were female.

When enquired about covid infection and management we documented that all our 131 patients received steroids in various doses and remdesivir as part of covid treatment. 57 patients required o2 support, out of which 42 were male and 15 were females. On the other hand 72 patients did not require o2 support. It is worth while to note that the 21 patients amongst the 57 o2 requiring patients were also on NiV support for few days out of which 14 were males and 7 were females. 2 female patients amongst the 131 were intubated and required ventilatory support.

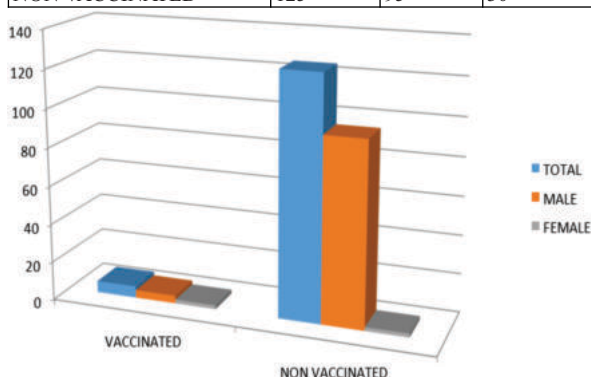


DIABETIC TOTAL	MALE	FEMALE
90	66	24
NON- DIABETIC TOTAL	MALE	FEMALE
41	33	8

PARAMETER	TOTAL	MALE	FEMALE
REMEDESIVIR	131	99	32
STERIOD	131	99	32
OXYGEN	57	42	15
NON- OXYGEN	72	56	16
NIV	21	14	7
INTUBATED	2	0	2



VACCINATION STATUS	TOTAL	MALE	FEMALE
VACCINATED	6	4	2
NON VACCINATED	125	95	30



We enquired about the vaccination status of all our patients and found out 125 patients were not vaccinated which included 95 males and 30 females.

Only 6 people were vaccinated amongst which 4 were males and 2 were females.

Amongst these 4 males only 2 of them received 2 doses, while the remaining two received only 1 dose of covid vaccine.

DISCUSSION

Mucormycosis is an opportunistic fungal infection caused by the fungus of order mucormycetes. Its incidence is seen in people with immune-compromised states like diabetes mellitus, solid organ transplantation, leukemias, patients with prolonged steroid therapies and recently added COVID19 infection. COVID 19 infection was the global pandemic caused by a single stranded RNA virus called SARS COV 2. The disease was life threatening and involved multiple organs causing damage at cellular level. One of its systemic side effects was hyperglycemia. The hyperglycemia in COVID19 was not only due to unprecedented use of steroid which was thought to be the mainstay treatment of the disease but also COVID19 infection itself emerged as a hyperglycemic state. It was observed that insulinopenia was one of the most distinguished feature of the disease. Upon further investigation it was found that SARS COV 2 virus had an affinity towards beta cells of pancreatic islets due to the expression of ACE2 receptor and related entry factors like TMPRSS2,

NRP1, TRFC on the beta cells, which led to the virus getting attached to the beta cells, ultimately leading to its destruction, this lead to

insulinopenia and in turn the hyperglycemic state. The cytokine storm adds on to the stress which causes insulin resistance and that when combined with the insulinopenia further adds to the hyperglycemia. This was further proved by a recent study from India which showed that glycaemic parameters in COVID associated newly diagnosed diabetes was much worse when compared to known diabetics[4]. It can only be imagined what would be the blood sugar levels when unprecedented use of steroids was done as a mainstay treatment of this hyperglycemia inducing disease.

Increase in the blood sugar levels alters the immune response of the body. There is failure of action of neutrophils and phagocytes, thus allowing opportunistic fungal infections to rampantly set in and spread.

Mucormycosis being one of such opportunistic infection was an outcome of this. To go into the minute details along with the COVID 19, the use of infected masks and ventilators, infected oxygen ducting system and use of industrial oxygen were all thought to be important etiological factors.

In our data of 131 patients only 59 patients required oxygen or made use of ventilators, while a majority of 72 patients did not make use of oxygen during COVID treatment. Thus proving that though industrial oxygen, infected mask and ventilators could be associated with fungus, it was not an obligatory etiological factor of it. However we cannot deny the use of steroids as one of the important etiological factors as all our patients were given steroid during COVID 19 treatment.

The treatment of COVID19 was possible due to an amalgamation of various drugs which included steroids, remdesivir, antipyretics, multivitamins etc. But a major relief was brought in after the introduction of vaccine. There were majorly 2 types of vaccines, one which was developed in a traditional method of vaccine formulation containing adjuvant inactive viral particle, which cannot infect a human but still can induce response required to produce antibodies to fight the COVID19 infection. Second vaccine used the chimpanzee adenovirus (CHADOX1) as a carrier for the COVID 19 spike protein into the human cell. These are incapable of infecting humans, but can teach the immune system to prepare a mechanism against such viruses.[5]

World statistics shows 64.2% were fully vaccinated. In India 68.2% population were fully vaccinated[6]. Maharashtra is a large state in terms of geography and the second highest populated state. 65% of its population was vaccinated[7]. However in our study which was conducted in Maharashtra it was noted, amongst the 131 patients of mucormycosis only 6 were vaccinated with 1 or 2 doses and 125 patients were non vaccinated which amounts to 95.4%. This is significant and points towards the fact that probably vaccination could reduce the severity of COVID 19 infection or infection per se and reduces the risk of its after effects like mucormycosis.

A question could always be raised about those 6 patients who were vaccinated and still developed mucormycosis, and the answer lies in carefully analyzing the data that amongst this 6 individuals 3 were given only 1 dose and remaining 3 were given 2 doses, while all these 6 patients were known case of diabetes mellitus, 2 of them also had kidney disorders.

It is worthwhile to note that the 3 patients who received 2 doses of the vaccine were given the second dose around 1 week prior to onset of mucormycosis. According to a study conducted in India it takes around 2 to 3 weeks for the COVID vaccine to act. Thus these patients who were given the second dose, 1 week prior would still be considered as not completely vaccinated, while the others had comorbidities which worsened their situation, despite of them taking COVID vaccine. Though the immunity against the mucormycosis infection wasn't up to the mark in the half vaccinated patients, but still it was noted that the vaccinated individuals had a less aggressive disease, lesser anatomical involvement, lesser surgical intervention requirement compared to others and a faster recovery rate which points towards the fact that even one dose of vaccine could reduce the severity of the mucormycosis infection.

CONCLUSION

Mucormycosis is an opportunistic fungal infection which is seen in

immunocompromised states. Hyperglycemia causes failure of neutrophils and phagocytes to act and thus lead to immunodeficiency. COVID 19 is a hyperglycemia inducing disease and vaccine prevents the severity of the COVID 19 infection. Thus reducing the hyperglycemia, preventing the immunodeficiency and augmenting the opportunistic fungal infections like mucormycosis. In our study we showed that most of our patients of mucormycosis were non - vaccinated and the ones which were vaccinated had other comorbidities which worsened their condition, thus establishing the fact that COVID vaccine could prevent the occurrence of mucormycosis and covid vaccination status should be considered and asked while dealing with post covid mucormycosis patients. This study also points towards the necessity of taking covid vaccine and preventing ourselves from covid and it's related diseases.

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