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RESEARCH ARTICLE

A SURVEY ON RHINO - ORBITAL - CEREBRAL MUCORMYCOSIS PATIENTS - A POST COVID OCCURRENCE IN TERTIARY HOSPITAL

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Abstract

With increasing case reports of Rhino – Orbital – Cerebral Mucormycosis, a secondary infection to Post COVID condition, the present study aimed to find the occurrence of Mucormycosis across various age groups, its presence among vaccinated population, relation between hyperglycemia and mucormycosis, site of involvement of nasal/ sinus mucormycosis and the Culture based genus classification of fungal Mucormycosis. A total number of 250 patients diagnosed with either Confirmed/ Suspected Mucormycosis, a Post COVID infection were included in the study. For all the patients, their demographic data, comorbities, vaccination details, imaging findings and follow up information were obtained and statistically analyzed for the study. The results show that: a) A major of 36.4% of mucormycosis patients were found between the age range of 51 – 60 years. B) Vaccinated population is less vulnerable to COVID and its secondary infection – Mucormycosis. C) Site of involvement of Nasal/ Sinus Mucormycosis is found as a Combined Maxillary+Ethmoid+orbit involvement in 80.8% followed by Ehtmoidal involvement and palatal involvement. D) Presence of diabetes mellitus was present among 93.2% of the participants and E) The genus classification shows the occurrence of Rhizopus Arrhizus was the cause for mucormycosis found in many of the culture based fungal infection among the Post COVID patients involved in the study. The study concludes that patients treated for COVID in the age group of 30 years to 70 years are more vulnerable to acquire Mucormycosis. Glycemic control among the COVID treatment patients will grossly prevent the occurrence of Mucormycosis infection.

Introduction:-

Coronavirus disease (COVID-19) has spread globally in a very rapid manner. Even after greater efforts the treatment of the disease is not definitive. However, prevention, Vaccination and symptomatic management are the best options. COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been associated with a bacterial and fungal infections as secondary infections. Both **Aspergillus** and **Candida** have been reported as the main fungal pathogens for co-infection in people with COVID-19. Recently, several cases

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of mucormycosis in people with COVID-19 have been increasingly reported world-wide, in particular from India. The primary reason that appears to be facilitating Mucorales spores to germinate in people with COVID-19 is an ideal environment of low oxygen (hypoxia), high glucose (diabetes, new-onset hyperglycemia, steroid-induced hyperglycemia), acidic medium (metabolic acidosis, diabetic ketoacidosis [DKA]), high iron levels (increased ferritins) and decreased phagocytic activity of white blood cells (WBC) due to immunosuppression like SARS-CoV-2 mediated, steroid-mediated or background comorbidities coupled with several other shared risk factors including prolonged hospitalization with or without mechanical ventilators. Mucormycosis is an angioinvasive disease caused by mold fungi of the genus **Rhizopus**, **Mucor**, **Rhizomucor, Cunninghamella, Arrhizus** and **Absidia** of Order-Mucorales, Class- Zygomycetes. The **Rhizopus Oryzae** is most common type and responsible for nearly 60% of mucormycosis cases in humans and also accounts for 90% of the Rhino-orbital-cerebral (ROCM) form. Mode of contamination occurs through the inhalation of fungal spores. Globally, the prevalence of mucormycosis varied from 0.005 to 1.7 per million population, while its prevalence is nearly 80 times higher (0.14 per 1000) in India compared to developed countries, in a recent estimate of year 2019–2020.

Aims & Objectives:-

The aims of the current study are to compare the Post COVID Mucormycosis patients with the following analysis:

1. Comparison of presence of Mucormycosis across various age groups and Gender
2. Occurrence of Mucormycosis among Vaccinated population
3. Relationship between Mucormycosis & Hyperglycemia
4. Involvement of site of occurrence of Nasal/ Sinus Mucormycosis
5. Culture based genus classification of fungal Mucormycosis

Materials and Methods:-

The current study was an observational prospective study which was undertaken at Madurai Medical College and Government Rajaji Hospital, Madurai, India, over a period of two months from May 2021 to June 2021. All patients presented with invasive mucormycosis of paranasal sinuses who directly came to Department of ENT as outpatient or following department referrals, and who were either COVID positive or recovered from coronavirus infection, were included for the study.

The patient's demographic data, comorbities, vaccination details, imaging findings and follow up information were obtained and analyzed for the study. A total of 250 Post COVID patients with Invasive Mucormycosis were included for the study with 170 Male and 80 Female in the age range of 10 years to 80 years.

Results & Discussion:-

The results of the present study analyzed the comparison of age, gender, vaccination, hyperglycemia, involvement of occurrence of Nasal/ Sinus and culture based classification of fungal mucormycosis among these 250 patients. The results of the present study are as follows:

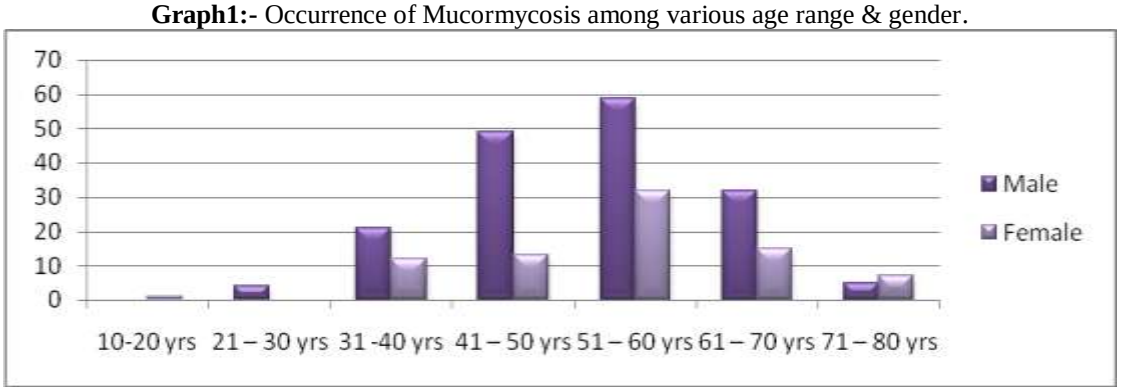
Age & Gender

The occurrence of Mucormycosis among 250 patients was scattered between 10 years to 80 years and the results are depicted in Table:1 and Graph:1.

Table 1:- Occurrence of Mucormycosis among various age range & gender.

AGE RANGE	10-20 yrs	21 – 30 yrs	31 -40 yrs	41 – 50 yrs	51 – 60 yrs	61 – 70 yrs	71 – 80 yrs	GENDER TOTAL
Male	0	4	21	49	59	32	5	**170**
Female	1	0	12	13	32	15	7	**80**
TOTAL	**1**	**4**	**33**	**62**	**91**	**47**	**12**	**250**

Graph1:- Occurrence of Mucormycosis among various age range & gender.



From Table:1 & Graph:1 it can be inferred that the occurrence of Mucormycosis found majorly between 31 years to 70 years and more among Males than Females. A peak with highest number of Mucormycosis patients were found in the age group of 51 years to 60 years with a total of 91 patients. Hence, around **36.4%** of Mucormycosis patients falls between the age range of 51 years to 60 years. The percentage of occurrence of Mucormycosis was found to be more in Males with **68%** and **32%** among Females.

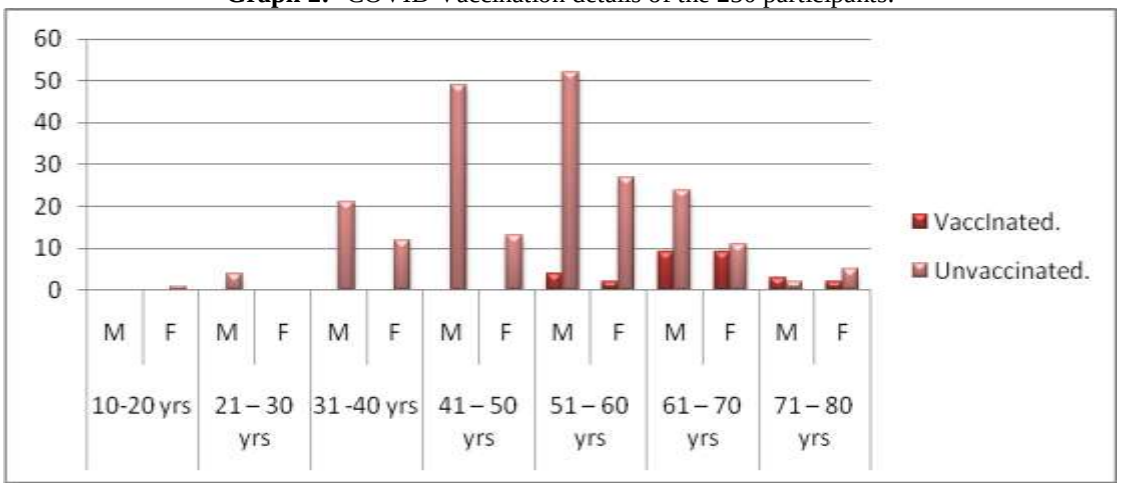
Details of COVID vaccination

COVID Vaccination details were collected from the participants and the results are shown in Table: 2 and Graph: 2.

Table 2:- COVID Vaccination details of the 250 participants.

AGE	10-20 yrs		21 – 30 yrs		31 -40 yrs		41 – 50 yrs		51 – 60 yrs		61 – 70 yrs		71 – 80 yrs		TOTAL
Gender	M	F	M	F	M	F	M	F	M	F	M	F	M	F	
VaccInated.	0	0	0	0	0	0	0	0	4	2	9	9	3	2	**29**
Unvaccinated.	0	1	4	0	21	12	49	13	52	27	24	11	2	5	**221**

Graph 2:- COVID Vaccination details of the 250 participants.



The results show that only 11.6 % of the Mucormycosis patients were vaccinated. All the 29 subjects of vaccinated population got their First Dose of Vaccine alone. And, a major of 88.4% of the participants were Unvaccinated. Hence, the results show that the occurrence of secondary infection to COVID (i.e. Mucormycosis) is found to be less among the vaccinated population when compared to that of the unvaccinated group which was supported by previous articles that occurrence of Symptomatic COVID found to be less among the vaccinated population.

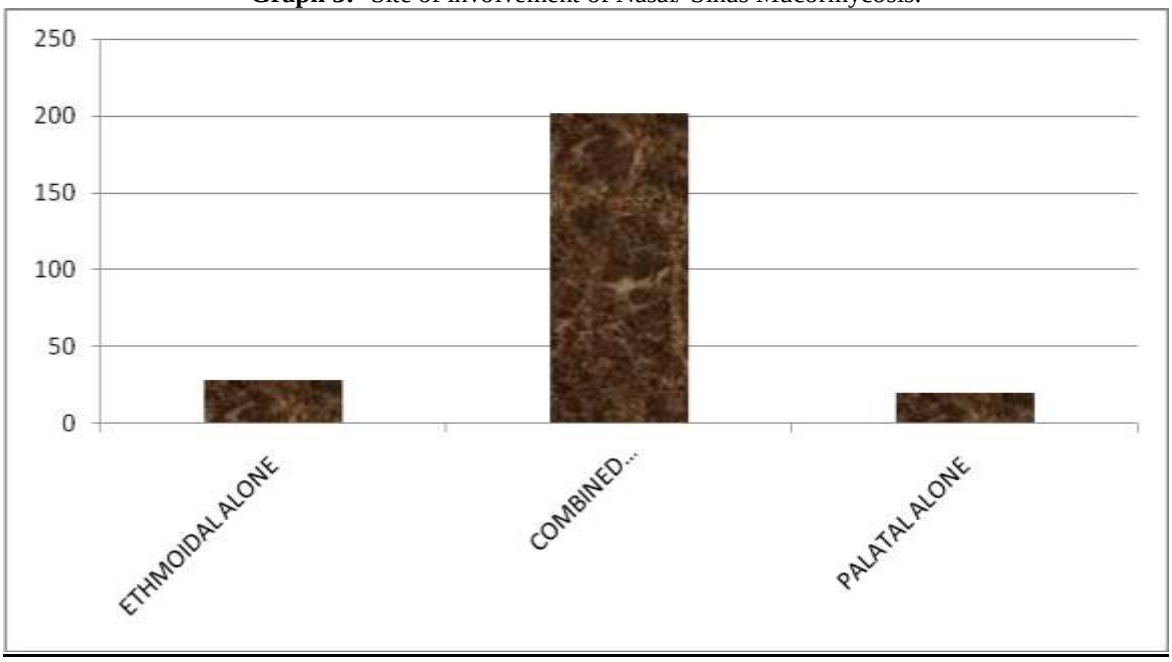
Involvement of Occurrence of Nasal/Sinus Mucormycosis

The following Table: 3 & Graph: 3 shows the site of involvement of Nasal/ Sinus Mucormycosis

Table 3:- Site of involvement of Nasal/ Sinus Mucormycosis.

S.No	ETHMOIDAL ALONE	COMBINED MAXILLARY+ETHMOIDAL+ORBITAL	PALATAL ALONE
1.	28	202	20

Graph 3:- Site of involvement of Nasal/ Sinus Mucormycosis.



From Table 3 & Graph 3 it can be clearly inferred that among the 250 Mucormycosis patients, the site of involvement of Combined Maxillary, Ethmoidal & Orbital regions are found in 202 patients which is around 80.8%, followed by Ethmoid involvement alone in 28 patients (11.2%) and palatal involvement alone in 20 patients (8%)

Tabl3a:- Laterality of involvement of Nasal/ Sinus Mucormycosis.

	MALE	FEMALE
RIGHT	146	59
LEFT	30	15

Graph 3a:- Laterality of Occurrence of Nasal/ Sinus Mucormycosis.

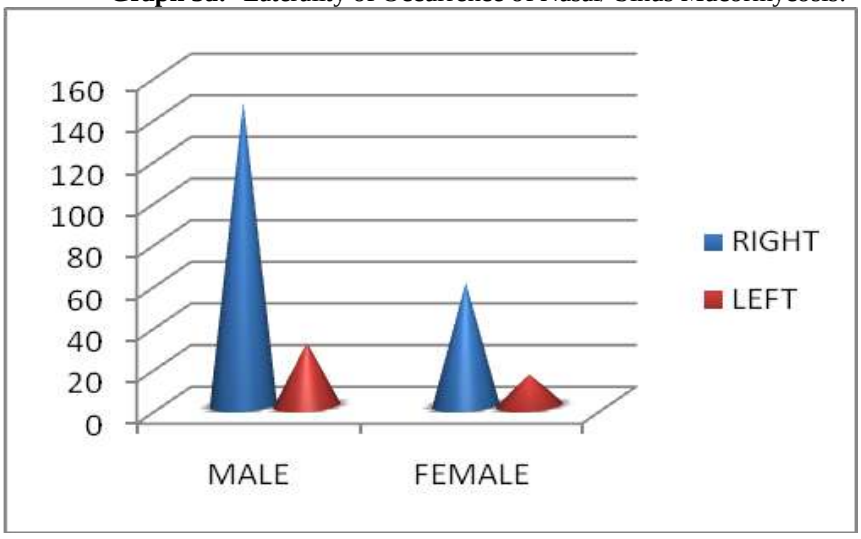


Table: 3a & Graph: 3a shows the Site of occurrence of Nasal/ Sinus Mucormycosis which clearly depicts that Right invasive fungal sinusitis is more compared to the Left side. The reason for occurrence could due to presence of Deviated Nasal Septum towards Right side and the accumulation of fungal infection towards the Deviated side. Few previous studies, Alireza Mohebbi et al (2012) also supported the increased prevalence of Deviated Nasal Septum towards Right side.

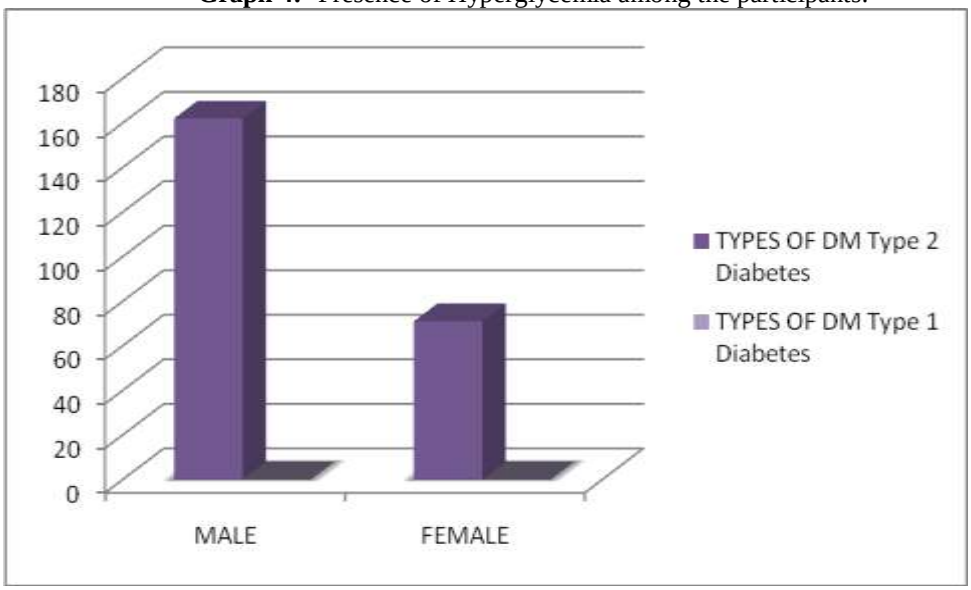
Hyperglycemia at presentation

The following results shown in Table: 4 and Graph: 4 depicts the relationship between Diabetes Mellitus and presence of Mucormycosis among Post COVID patients. Previous studies have shown that presence of DM is a major predisposing factor associated with mucormycosis in India, Patel et al (2021). Also a study by Awadesh kumar singh et al (2021), shows that occurrence of DM significantly increases the odds of contacting Rhino orbital Cerebral Mucormycosis by 7.5 folds. John et al (2021), reported the findings of 41 confirmed mucormycosis cases in people with COVID-19, DM was reported in 93% of cases, while 88% of them were receiving corticosteroids.

Table 4:- Presence of Hyperglycemia among the participants.

	TYPES OF DM	
	Type 2 Diabetes	**Type 1 Diabetes**
MALE	162	0
FEMALE	71	0

Graph 4:- Presence of Hyperglycemia among the participants.



From Table:4 and Graph: 4 it can be clearly inferred that a total of 233 subjects out of 250 subjects had Diabetes Mellitus either long standing controlled/ uncontrolled diabetes mellitus or during the time of presentation, which holds to 93.2% of the total participants had a predisposing factor of Diabetes mellitus. The results of the current study were also supported by the previous studies of Patel et al(2021) and John et al (2021). Also, all the 233 subjects with hyperglycemia had Type 2 Diabetes mellitus.

Culture based genus classification of fungal Mucormycosis

Among the 250 participants, 27 patients were confirmed with Mucormycosis and remaining 223 patients were suspected for Mucormycosis. The culture based genus classification of fungal mucormycosis shows that mold fungi of the genus Rhizopus Arrhizus found to be the major cause of Mucormycosis, which was found among 20 patients, followed by Mucorales – Mucor class among 7 patients. Though previous studies shows that **Rhizopus Oryzae** is most common type and responsible for nearly 60% of mucormycosis cases in humans and also accounts for 90% of the Rhino-orbital-cerebral (ROCM) form, the current study results shows that Rhizopus Arrhizus is found to be the most common type for the cause of Mucormycosis among Post COVID patients.

Type of Fungal Mucormycosis	Numbers
Mucorales - Mucor	7
Rhizopus Arrhizus	20

Conclusion:-

As per the results of the study, patients treated for COVID in the age group of 30 to 70 years are more vulnerable to acquire Mucormycosis. The underlying factor in most of the patients are uncontrolled glucose levels in their blood . Meticulous monitoring and Glycemic control among the COVID treatment patients will grossly prevent the occurrence of Mucormycosis infection. Diabetic control of the COVID patients will help them in preventing the dreadful fungal infection and long term follow up of the patients after COVID infection.

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