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Research Article

EPIDEMIOLOGICAL STUDY OF MUCORMYCOSIS CASES ADMITTED AT CIVIL HOSPITAL, AHMEDABAD DURING COVID-19 PANDEMIC

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ABSTRACT

Background: An Epidemic of Mucormycosis along with second wave of covid-19 pandemic was seen in Gujarat and other states also which was very serious problem. So, aim of this study was to know the epidemiology of mucormycosis during covid-19 pandemic.
Methods: A Cross-sectional study was conducted at Civil Hospital, Ahmedabad which included total of 769 confirmed cases of mucormycosis admitted between 11th May to 21st June, 2021. Information like socio-demography, diagnosis, clinical features, Site of infection, Risk factors etc. were collected.
Results: It was observed that 2/3rd of Males and 1/3rd of Females were affected. The mean age was 53.2± 12.6years. 78.9 % of patients had history of Covid 19 disease in the past and among them 70.0% were treated with steroids, 45.3% required Oxygen therapy during Covid. Of total, 17.0 % were Partially vaccinated, 4.2% were fully vaccinated. Headache (58.5%) was observed as most common clinical manifestation of Mucormycosis and Para-nasal sinus (57.6%) was most commonly affected site. Diabetes (71.9 %) was found to be the most common comorbidity. There was no significant association found between diabetes and covid-19 status of patients. (p= 0.2794)
Conclusion: Cases of mucor were prominently seen in the patients who had h/o covid-19 infection with concurrent use of steroid and who were diabetic. So judicial use of steroid, regular monitoring of blood sugar level must be ensured among covid-19 disease management.

INTRODUCTION

Mucormycosis is an angioinvasive fungal infection caused by a group of molds called mucormycetes. Depending on the clinical presentation it is classified as rhinocerebral, pulmonary, cutaneous, gastrointestinal, disseminated or otherwhich includes uncommon rare forms, such as endocarditis, osteomyelitis, peritonitis, renal, etc.

At the end of 2019, a new type of coronavirus appeared in China - SARS-CoV-2. On 11 March 2020, the WHO declared SARS-CoV-2 as a pandemic which causes novel coronavirus disease 2019 (COVID-19) which, rapidly spreading around the world, has become a huge challenge for the health care system.(1) COVID-19 disease may vary in severity, from very mild/asymptomatic to life-threatening pneumonia accompanied by bacterial or fungal co-infections.(2,3) Opportunistic infections are especially common in patients with current history of COVID-19 disease and also in those having comorbidities like diabetes or COPD, treated with mechanical ventilation, took antibiotic therapy, monoclonal antibodies and the use of corticosteroids. Corticosteroids are commonly used to treat serious form of COVID-19 disease but unfortunately, corticosteroids are immunosuppressive and also increase blood sugar levels in both diabetic and non-diabetic patients. Both these effects are now believed to contribute to mucormycosis.(4) Indian Council of Medical Research (ICMR) recommends to pay special attention on signs of mucormycosis such as sinus pain, nasal obstruction on one side, one-sided headache, swelling or numbness, toothache, and loosening of the teeth, blurred or double vision.

Mucormycosis with COVID-19 infection can be very serious problem and there are very few studies done on epidemiology of mucormycosis during covid-19 pandemic. Henceforth, aim of this study is to know the epidemiology of mucormycosis during covid-19 pandemic.

MATERIALS AND METHODS

A Cross-sectional study was carried out at Civil Hospital, Ahmedabad from 1st June-2021 to 22-June 2021.

All the patients(n=769) who were admitted in Civil Hospital, Ahmedabad from 11th May-2021 to 21st June-2021 with biopsy proven, or whose CT/MRI findings were suggestive of Mucormycosis.
A Pre-designed, Pre tested questionnaire was used to collect data. Informed verbal consent was obtained from all study

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Participants. Ethical approval was obtained from our institutional ethical committee. Information like socio-demography, diagnosis, clinical features, Site of infection, Risk factors etc. were collected. Data was compiled and analyzed in Microsoft Excel-2019. Proportion and Chi square test were applied for statistical analysis. p-value ≤ 0.05 was considered as significant.

RESULTS

In Current study, we observed 2/3rd of Males and 1/3rd of Females was affected. Majority (43.69%) among the affected belonged to the age group of 45-59 years followed by 60-74 years (28.48%). The mean age was 53.2± 12.6years and the median age was 54 years (range,4-92 years).[Table 1]

Table 1 Age and Sex Distribution of Patients (N=769)

Variable	No. (%)
Age	
0-14	1 (0.1)
15-29	20 (2.6)
30-44	157 (20.4)
45-59	336 (43.7)
60-74	219 (28.5)
75+	36 (4.7)
Sex	
Male	515 (67.0)
Female	254 (33.0)

Majority of the patients were educated up to primary (31.2%) followed by secondary (24.7%). There were 20.5% of illiterate among total patients. One fourth of the patients were farmers by Occupation.

In our study Headache (58.5%) was observed as most common clinical manifestation of Mucormycosis followed by Facial Pain (48.0%), Eye swelling (44.3%) and least common was Facial swelling (0.6%).[Figure 1]

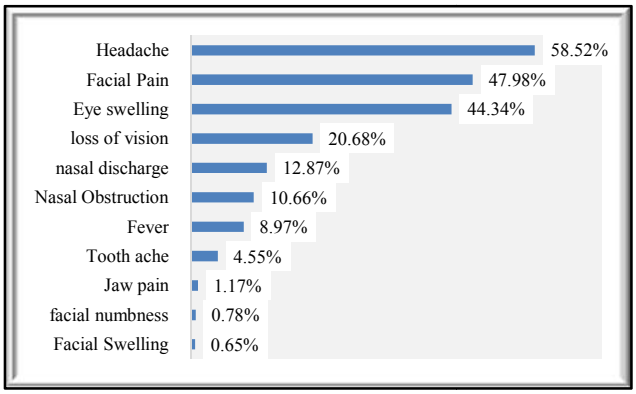

Figure 1 Distribution of Clinical features of mucormycosis patients (n=769)

Most common site involved in study group was Para-nasal sinus (57.6%) followed by orbit (52.4%), oral cavity (20.5%). Lung & Cerebral involvement were observed only among 2.2%and3.0%respectively. Diabetes was found to be the most common comorbidity with 49.0%having only diabetes, 22.9% were having both Diabetes and Hypertension and 6.4% having only Hypertension. Among infected patients 17.0% were Partially vaccinated and 4.2% were Fully vaccinated. [Table 2]

Table 2 Area involved, comorbidity and Vaccination status of patients (N=769)

Variable	No. (%)
Site of mucor	
Para nasal sinus	443 (57.6)
Eye	403 (52.4)
Oral	158 (20.5)
Skin & subcutaneous tissue	86 (11.2)
Cerebral	23 (3.0)
Lung	17 (2.2)
Co-morbidity	
Diabetes	377 (49.0)
Diabetes + Hypertension	176 (22.9)
Hypertension	49 (6.4)
No	167 (21.7)
Vaccination Status	
Not vaccinated	606 (78.8)
Partially vaccinated	131 (17.0)
Fully vaccinated	32 (4.2)

Nearly 78.9 % of patients had history of Covid 19 disease in the past and among them 70.0% were treated with steroids. There was no significant association found between gender and Risk factors. [Table 3]

Table 3 Risk factor identification according to gender

Variables		**Male (n=515) n (%)**	**Female (n=254) n (%)**	**p-value**
Covid Status	Covid Positive Status	402 (78.1)	205 (80.7)	0.3966*
	Covid Negative Status	113 (21.9)	49 (19.3)	
		Male (n=402) n (%)	Female (n=205) n (%)	p-value
Steroid use during Covid	Yes	277 (68.9)	148 (72.2)	0.4028*
	No	125 (31.1)	57 (27.8)	
Remdesivir use during Covid	Yes	200 (49.7)	106 (51.7)	0.6485*
	No	202 (50.2)	99(48.3)	
Hospitalization required during Covid	Yes	221 (55.0)	115 (56.1)	0.7924*
	No	181 (45.0)	90 (43.9)	
Any type of Oxygen therapy needed during Covid	Yes	180 (44.78)	95 (46.34)	0.7140*
	No	222 (55.22)	110 (53.66)	

* p-value > 0.05 was considered as statistically insignificant

In our study 162 Patients did not give any history of covid in the past. However, 68.5% of them were diabetic. There was no significant association in the diabetes status of covid 19 positive and negative patients. [Table 4]

Table 4 Association between covid status and Diabetes

	Diabetic status			p value
Covid status	Yes (n=553)	No (n=216)	Total	
Positive	442 (72.8 %)	165 (27.2 %)	607	0.2794*
Negative	111 (68.5 %)	51 (31.5 %)	162	

* p-value > 0.05 was considered as statistically insignificant

DISCUSSION

Mucormycosis, a serious but rare aggressive fungal opportunistic infection caused by a group of molds called mucormycetes in immune-compromised, debilitated patients. During ongoing COVID-19 pandemic, cases of mucormycosis increased rapidly in such a way that union ministry of health gave notice to Gujarat state in month of May to declare mucormycosis as an epidemic henceforth Gujarat state declared mucormycosis or black fungus as an epidemic under provision of Epidemic Diseases Act,1857 on 20th May 2021.(5)Covid-19 infection, pre-existing comorbidities like Diabetes and immunosuppression which results due to steroid use for Covid-19 treatment are major risk factors making patients susceptible to secondary infections like

mucormycosis. There are multiple other factors which might be responsible for mucormycosis outbreak like overuse of Zinc/multivitamin tablets, excessive steam inhalation and environmental factors favouring growth of fungal spores. Henceforth, it is important to know the clinical presentations, complications, risk factors and outcomes to take appropriate steps regarding prevention and treatment.

In this study Mean age of the affected patients was found to be 53.2 ± 12.6 years which was similar to study done by Swati A Ravani *et al*(6) and Mrittikasen *et al*(7) it was found 56.3 years and 60.5 ± 12 years respectively.

Headache was most common symptoms among affected patients. Daudia A *et al*(8) found that having pathology of Paranasal Sinus with the primary symptom being headache. If the fungal infection begins in the nose or sinus and extends to brain, symptoms and signs may include one-sided eye pain or headache, and may be accompanied by pain in the face, numbness, fever, loss of smell, a blocked nose or runny nose.(9)Fever, cough and shortness of breath are symptoms of some fungal diseases which are similar to those of COVID-19.(10) Both these infections can be confirmed by laboratory testing, and also sometimes there can be COVID-19 and fungal infection at the same time.

In Gujarat, from April 1 to June 30, there were total of 5,15,825 covid-19 cases and 6806 cases of mucormycosis. (11,12) Out of 6806 cases, 5682 cases had reported covid-19 infection; leading to the fact that 11 out of every 1000 covid-19 patients were infected with mucormycosis. Around 1.1% of covid-19 patients got mucor in Gujarat as compared to other states like Rajasthan, Telangana, Madhya Pradesh, Andhra Pradesh and Maharashtra. In the current study nearly 79% of them had history of Covid 19 in the past, whereas Swati A Ravani *et al*(6) reported 61% of covid positivity. Major risk factor was found to be covid positivity with concurrent use of steroid and Diabetes (70 %) considering Gujarat as Diabetic capital of India. However, Swati A Ravani *et al*(6) reported 96% of Diabetes among mucormycosis. This difference could be due to less sample size included in later study. Nearly 30% of the patients without Diabetes also had mucor which suggest other risk factor might be responsible among covid positive patients. Nearly 70% of the both covid positive and covid negative patients were Diabetes as compared to Ismaiel WF *et al*(13) found that 44.4% and 28.9% covid-19 positive and covid negative patients were diabetics. Though two third patients in the study were male butas such there was no general association between Risk factor and gender.

Patients with severe infections admitted in an intensive care unit (ICU), are particularly at more risk for contracting bacterial and fungal infections. Aspergillosis or invasive candidiasis are the most common fungal infections seen in patients having Covid-19.(14,15)Treatment of severe COVID-19, including high-dose corticosteroids and tocilizumab, increases the risk of patients having COVID-19 to get coinfection with mucormycosis. It has also been reported that patients with severe COVID-19 infection lack classical mucormycosis risk factors like diabetes, conditions or medications that weaken the immune system, and cancer.(4,16) Early diagnosis and treatment are essential to improve outcomes for patients with COVID-19–associated mucormycosis. Patients lacking classical risk factors for this disease having severe covid infection also have possibility of getting mucormycosis. In studies of Kursun *et al*.(17), Mohammadi *et al*.(18), the most common underlying disorders affecting the immune system were diabetes mellitus and to a lesser extent hematological malignancies and chronic renal insufficiency. This may be due to the fungal affinity for acidotic environments with high glucose concentrations.(19) Macrophages/neutrophil dysfunction or hyperglycaemia caused by use of steroids increases the risk of mucormycosis, though its confirmed relationship is yet to be established. (20,21)

In our study Most common site involved was Paranasal sinus which was similar to study done by Swati A Ravani *et al*(6), and Roden MM *et al*.(21)There was also 24% of pulmonary involvement in study of Roden MM *et al*(21)while in this study it was found to be only 2%.

Since this is a descriptive cross-sectional study so we could not evaluate the independent risk factors for mucormycosis perse.

CONCLUSION

Duringsecond wave of covid-19 pandemic in India, along with rising cases of covid-19, rise in cases of opportunistic infection such as mucormycosis especially in tertiary hospital. Cases of mucor were prominently seen in the patients who had h/o covid-19 infection with concurrent use of steroid and with diabetic. Since Gujarat is considered as a Diabetic hub of India thereby making it more vulnerable to mucormycosis cases than any other state in India. So that judicial use of steroid, regular monitoring of blood sugar level must be ensured among covid-19 disease management. To avoid delay in diagnosis and treatment of fungal co-infection, awareness about the symptoms is essential to prevent complications and death related to it.

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