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Clinical profile of Mucormycosis in Covid-19 patients from a Tertiary care Hospital in Sangli district, Maharashtra

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Introduction

Coronavirus disease (COVID-19) is an infectious disease caused by a novel coronavirus known as "Severe Acute Respiratory Syndrome Coronavirus 2" (SARS- CoV-2), which is mainly transmitted by the droplets. It was identified in Wuhan province in 2019 and has spread globally causing one of the most disruptive pandemics for over a generation. It has resulted in a loss of life and disruption of the economy at an unprecedented scale. [1, 2, 3] The disease spectrum now not only includes cough and high-grade fever but also various multisystem problems such as shortness of breath, anosmia, ageusia, diarrhea, generalized malaise, acute cardiac injury, and even deadly secondary opportunistic fungal infections. Early and prompt identification of these high-morbidity conditions is crucial for optimal treatment and improved outcomes.[4]

India has not been insulated from this devastation caused by the pandemic. Till date, there had been more than 34 million cases and 4.5 lakh deaths. This has led to multiple months of lockdown, economic losses, and immeasurable physical & mental health impact. [5, 6, 7]

Along with COVID-19, India is also experiencing an outbreak of Mucormycosis or black fungus, caused by an opportunistic fungus in the Mucorales family.[8] It is more often seen in immunocompromised individuals, diabetic patients with ketoacidosis, and with indiscriminate use of steroids & immunosuppressants. Clinical features of Mucormycosis include fever, nasal or sinus congestion, chest pain, shortness of breath, skin blisters or ulcers, excessive redness, swelling around a wound, abdominal pain, or gastrointestinal bleeding. Mucormycosis may affect the lungs, but the nose and sinuses are the most frequent infection sites. It can then spread to the eyes,

causing blindness, or to the brain. Patients with disseminated infection in the brain can develop mental status changes or coma.[9]

Even before the COVID-19 pandemic, cases of Mucormycosis were on the rise in India, especially due to uncontrolled diabetes. [10] However, the pandemic has accelerated and highlighted the problem of Mucormycosis. After the second wave of pandemic, there have been estimated more than 50000 cases of Mucormycosis in India; the majority in COVID-19 patients. [11] Thus India contributed to the maximum number of reported Mucormycosis cases and deaths globally. Most likely causes are an exaggeration of older problems of uncontrolled diabetes, use of corticosteroids for management of COVID-19, excessive stay in hospitals especially ICU during COVID. [12] However as the phenomenon of Mucormycosis among COVID-19 patients is new hence for a better understanding of all the factors, for better management and prognosis, more research is needed. The objective of the current research is to study the clinical profile of Mucormycosis in COVID-19 patients from the Sangli district of Maharashtra.

Methods

It was a hospital record-based descriptive study, conducted in a tertiary care hospital in Sangli district, Western Maharashtra. The study sample included the records of patients with a confirmed diagnosis of Mucormycosis and a history of COVID-19 admitted from June 2020 to June 2021. The exclusion criteria were incomplete records, records of brought dead or outside admitted and transferred patients of Mucormycosis. The study was reviewed and accepted by the Central research processing unit and the Institutional ethical committee. Appropriate permissions from Institutional authorities were taken before the beginning of the research. As this was a hospital record-based study, individual informed consent for this research were not collected. While recording the observations from hospital records on the master chart no identifiers were noted and hence the anonymity of the participants was not compromised.

For the study, we have considered that patients suffering from mucormycosis when they had their KOH mount positive. All the study case papers were checked for the history of being RT-PCR or RAT positive for the COVID-19 virus before the onset of mucormycosis.

We noted the following parameters, results of various biochemical assays were conducted in admitted patients with covid-19 infection along with mucormycosis. This test included hemoglobin, white blood cells, platelets, CRP levels, liver function test, covid-19 vaccination status, IL-6 levels, HbA1c levels, co-morbidities, etc. And various comorbidities noted by the treating consultants, various modalities of treatment, and their outcomes.

Our study included noting the demographic profile of the patients such as their age, gender, place of residence, days of admission.

Statistical Analysis was done using descriptive statistics, students t-test, binary logistic regression, etc. The data entry and analysis were performed using MS Excel and SPSS-22.

Results

Records of 58 patients, 42 (72.41%) were males and 16 (27.58%) where females were included in the study. The mean age of patients was 52.8(±14.4 years). Forty-one (70.68%) patients belonged to rural areas and 17 (29.31%) belonged to an urban area (table 1).

Table 1: Gender and residence distribution of Mucormycosis patients			
Gender	Residence		Total
	Rural	Urban	
Male	27(64.28%)	15(37.71%)	42(72.41%)
Female	14(87.5%)	2(12.5%)	16(27.58%)
Total	41(70.68%)	17(29.31%)	58

Considering covid-19 vaccination status 53 (91.4%) were not vaccinated 4(6.9%) received the first dose of covid vaccine and 1(1.7%) received two doses of vaccine. Diabetes was the most common presenting comorbidity 50(86.2%) had a history of diabetes, followed by18(31%) had hypertension, and 5(8.6%) had a history of chronic renal failure diseases. Considering the extent of presenting illness 24(41.4%) had one eye involvement 4(6.9%) had both the yes involved, 6(10.3%) had sinus involvement and 24(41.1%) had other system involvement. Ten (17.2%) were managed in isolation ICU and 48(82.8%) were managed in the mucormycosis ward. Fifty-seven (98.3%) were treated with injection amphotericin, 4(6.9%) were given tablet Posaconazole, 18(31%) had nasal debridement, 3(5.2%) had maxillectomy and 1(1.7%) had undergone exenteration. Forty (69%) had been discharged and eighteen (31%) patients have succumbed to diseases. The mean duration of hospital stay was 23.8(±16.3) days (table 2).

Table 2: Presenting history, treatment given, and outcome of the Mucormycosis patients			
Presenting history patients		Frequency	Percent
History of COVID	Yes	46	79.3
	No	12	20.7
Vaccination Status	Not vaccinated	53	91.4
	One dose received	4	6.9
	Two doses received	1	1.7
History of Co-morbidities	Diabetes Mellitus	50	86.2
	Hypertension	18	31
	Chronic Renal Disease	5	8.6
Ward	ICU	10	17.2
	Ward	48	82.8
The extent of presenting illness	One eye involved	24	41.4
	Both eyes involved	4	6.9
	Sinus involvement	6	10.3
	Others (no involvement)	18	31.0
Treatment Given	Amphotericin	57	98.3
	Tab. Posaconazole	4	6.9
	Nasal Debridement	18	31
	Maxillectomy	3	5.2
	Exenteration	1	1.7
Outcome	Discharge	40	69
	Death	18	31
Total		58	100

The patient underwent various important biochemical assays during their hospitalization period, the interpretation of the biochemical test is as presented in Table no.3

Table 3: Patients underwent various investigations during their stay in hospital which are as stated in the table below

Investigations	Median (Interquartile range)	Range	Expected normal value
Hb (g/dl)	12.1 (10.9, 13.4)	(8, 15.7)	13-18
WBC (Cu/mm)	9750 (8225, 14150)	(4300, 27200)	5000-10000
Platelets (cu/mm)	245000 (176250, 358250)	(31000, 542000)	150000-450000
ESR (mm/hr)	12 (10, 17)	(4, 40)	0-15
BSL (mg/dl)	159 (112, 232.8)	(59, 450)	70-120
S.G.O.T (units)	26 (20, 35)	(12, 78)	10-40
S.G.P.T (units)	31 (21, 47)	(10, 106)	5-35
Sr. Creatinine (mmol/L)	1.2 (0.9, 1.4)	(0.6, 4.1)	0.7-1.4
Blood urea (mg/dl)	42 (25, 55)	(2, 118)	12-45
CRP (mg/L)	80 (52, 116)	(12, 250)	0-6
D-dimer (µg/ml) FEU	1 (0.7, 2.3)	(0.2, 8.5)	<0.5
IL-6 (pg/mL)	222.5 (110.8, 431.8)	(6, 3045)	<7.00
HbA1C (%)	8.1 (6.7, 10.2)	(4.5, 12.8)	4-5.6

Table 4: Applying binary logistic regression models using Backward Wald method for assessing significant predictors for the outcome of death or discharge

Model 1- Independent variables: Gender, Present address (urban/rural), Extend to spread of mucormycosis, and vaccination status. Model accuracy percentage: 77.6							
Dependent variables	B	S.E.	Wald	Df	P-value	Odds Ratio	95% C.I. for Odd ratio
Gender	1.511	0.769	3.864	1	0.049	4.532	(1.004,20.448)
Present Address	-3.038	1.365	4.951	1	0.026	0.048	(0.003,0.696)
The extent of spread of disease	0.764	0.278	7.579	1	0.006	2.147	(1.246,3.699)
Constant	-0.366	1.857	0.039	1	0.844	0.693	
Model 2- Independent variables: Results of various biochemical investigations viz. WBC count, BSL, CRP, HBA1c. Model accuracy percentage: 79.3							
WBC	0	0	9.772	1	0.002	1	(1,1)
BSL	0.005	0.003	2.402	1	0.121	1.005	(0.999,1.012)
CRP	0.015	0.007	4.004	1	0.045	1.015	(1,1.03)
Constant	-6.215	1.747	12.653	1	0	0.002	

The dependent variable for both models: Outcome of patient - Death or Discharge

B= Coefficient of regression

SE= Standard error

Wald= Wald statistics

Df= degrees of freedom

We developed two binary regression models using the backward Wald method. The dependent variables in each model were outcomes of patients (death or discharge). The independent variables were socio-demographic factors (gender, residence, extent of spread of diseases, vaccination status) in the first model and biochemical assay (WBC, CRP, HbA1c) in the second model. These variables were selected for binary logistics regression after being found to be significant in univariate analysis. In the first model extent of diseases and the second model WBC count were the best predictors.

Discussion

In our study the mean age of patients was 52.8 years, similar age pattern (mean age of 56.62 years) was observed in a single study conducted by Anas et.al. in Ranchi, they had observed similar, mean age of patients (56.62) but their sample size was limited [13]. We observed in our study that 86.2% of patients had diabetes mellitus,31% had hypertension and 8.6% had chronic kidney disease. similar to the study carried similar scenario was observed by Anas et al [13] and Gupta et al with 86.6% and 85.2 % [14]. patients respectively being diabetic. These findings suggest a similar connection between mucormycosis, diabetes. Ninety-one percent of patients were unvaccinated similar observations were made by Choksi et al, Mumbai with 89% being unvaccinated [15]. It was observed that (17.2%) of patients were admitted in ICU and (82.8%) were admitted in the mucormycosis ward and (48%) and the rest of patients were admitted in ward (43%) similar to study conducted by Martin Hoenigl et. al. [16]. In our study, ocular involvement was of an important presenting sign with 48.1% followed by sinus involvement 10.3% to the study conducted at Anas et al in Ranchi with orbital

involvement at (43.3%) [13]. Considering outcome 69% of our patients were discharged, and 31% of patients succumbed to the disease, in a similar study by Kamath et al in Jamshedpur and they observed mortality at (40%) [17]. Hoenigl Martin et al on reviews of cases from 18 countries observed mortality in Covid-19 associated with mucormycosis at (49%) [16] difference in the mortality may vary due to severity of patients at the time of admission available facilities and caseload. On considering risk factors of predictor for mortality for patients we observed that white blood cells, CRP, gender, rural or urban address of patient and extent of spread of disease associated with the disease. It was found that the extent of diseases and White blood cells count was the best predictor for morality, diabetes was present in a majority of patients however we did not find any association of diabetes with mortality. Similarly, HbA1c was not significantly associated with an outcome similar conclusion were made by Zirpe et al in Pune [18], however, both these studies are retrospective studies done in tertiary care hospital and hence generalize potential labialize ability of this study is limited.

Conclusion

Mucormycosis can be a serious complication following Covid -19 infection. It predominantly affects middle-aged and older males. In our study mortality among patients was very high. Diabetes was present in the majority of the cases. The extent of the spread of diseases, the rural residence of patients leads an important role in morality. The timing of diagnosis was important. The phenomenon is new and hence detailed research is required in the area. However, we believe in the regular follow-up of Covid -19 patients. Penetration of post covid monitoring services in the rural area and extra focus on people having co-morbidity of diabetes and hypertension may help in preventing death due to Covid -19 associated mucormycosis.

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