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Research Article

COVID-19 Associated Mucormycosis (CAM) - A Case Series from a Tertiary Care Hospital in India

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Abstract

Purpose: Coronavirus disease (COVID-19) remains a health concern with new emerging challenges as rise of opportunistic mucormycosis infections in COVID-19 patients has been found to increase morbidity and mortality. Even though rare, COVID-19 associated mucormycosis has been reported from across the world. We present a retrospective cases series of 132 patients diagnosed as COVID-19 associated mucormycosis in a tertiary care hospital in North India during May 9th to 30th 2021.

Materials and Methods: Our 1500 bed tertiary care hospital is one of the partners in the Mycotic Infections in COVID-19 (MUNCO) registry, Albert Einstein College of Medicine, Bronx, New York. Data were collected in the REDCap database. Profile of the patients has been presented according to demographic profile, comorbidities, laboratory parameters, ICU admission, oxygen support and treatment outcomes. Analysis of risk factors for mortality has been undertaken along with a prediction model for mortality.

Result: The proportion of males and females was 72.7% and 27.3% respectively. The mean age of the study subjects was 53.1 years. The major comorbidity was Diabetes (57.6%) followed by Hypertension (40.9%) and Coronary artery disease (11.4%). About 13% patients used long term corticosteroid. Further, 70.5% patients required an ICU admission and 47.0% patients required oxygen support whereas ventilator requirement was for 13.6% patients. Overall death rate of mucormycosis patients was 16.7%. The risk factors identified for death were raised levels of CRP >73, Ferritin >358, SGOT >39 and Creatinine >1.15 as well as oxygen requirement.

Conclusion: Clinicians must examine the possibility of concomitant fungal infection in COVID-19 patients especially who are geriatric or comorbid with Diabetes Mellitus. Those with raised levels of CRP, Ferritin, SGOT and Creatinine levels as well as those needing oxygen need to be vigilantly monitored to minimize the risk of mortality.

Keywords: Coronavirus disease; Mucormycosis; CAM; Fungal infections

Introduction

Mucormycosis has been reported in patients suffering from covid-19 which is described as COVID-19 Associated Mucormycosis (CAM) [1]. According to the World Health Organization (WHO), mucormycosis is a rare but serious angio-invasive infection caused by a group of fungi called mucormycetes [2]. CAM has been detected mainly in patients with pre-existing conditions, such as diabetes mellitus, diabetic ketoacidosis, hematological malignancies, transplantation, and prolonged neutropenia or on corticosteroids [3].

Across the globe, the highest number of mucormycosis cases has been observed in India with more than 4,000 cases with COVID-19 associated mucormycosis [4]. Herein, we describe a case series of 132 patients with mucormycosis associated with COVID-19 infection.

Materials and Methods

This was a retrospective study of all hospitalized cases of mucormycosis associated with COVID-19 infection admitted to a tertiary, 1500-bed hospital, NCR, India during the month of May 2021, immediately following the second peak of COVID (March-April 2021). The patients diagnosed with mucormycosis were identified with a positive KOH mount and associated clinical features suggestive of fungal infection. Our tertiary care hospital is one of the partners in the Mycotic Infections in COVID-19 (MUNCO) registry, Albert Einstein College of Medicine, Bronx, New York wherein data were collected in the REDCap database. Study was approved by the Institutional Ethics Committee (MICR No: 1315/2021 dated June 17, 2021) and registered with the Clinical Trial Registry of India (NCT04935463).

The statistical analysis included profiling of patients on different demographic, preexisting comorbidities, laboratory parameters, ICU procedure, oxygen support requirement and treatment outcomes. Quantitative parameters were expressed as mean and standard deviation and categorical as absolute number and percentage. Student t-test and One Way ANOVA was used for testing of difference in mean between groups. Chi square test was used for testing of associations. The diagnostic accuracy of risk factors in predicting unfavorable outcome were assessed by receiver operating characteristic (ROC)

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curve analysis and obtained the optimal cut-off value with the best combination of sensitivity and specificity. Univariate logistic regression analysis was used to explore the association between explanatory variables and unfavorable outcomes. The variables showing significant association on univariate logistic regression analysis were considered in step wise multivariate logistic regression analysis. Importantly, a predictive model for risk of death has been developed based on significant risk factors as revealed by step wise multivariate logistic regression. The predictive power of the model has also been assessed. P-value <0.05 was considered statistically significant. All analysis was done using SPSS software, version 24.0.

Results

A total of 132 patients diagnosed with COVID-19 associated mucormycosis admitted in our hospital between May 9th to May 30th 2021. Out of 132 patients, 40 (30.3%) were diagnosed with Sino-orbital mucormycosis (SOM), 75 (56.8%) with rhino-cerebral mucormycosis (RCM) and 17 (12.8%) had pulmonary (PM) involvement (Table 1).

Demographics

The proportion of male and female was 72.7% and 27.3% respectively. The mean age of the study subjects was 53.1 (±12.7) years. Though there were differences in the gender and age profile across three mucormycosis groups of patients, these differences were not statistically significant (p>0.05) (Table 1).

Preexisting comorbidities

Diabetes was the major comorbidity reported by 76 (57.6%) followed by Hypertension - 54 (40.9%). Coronary artery disease was reported by 15 (11.4%) patients. The use of long-term corticosteroid was by 17 (12.9%) patients. Importantly the proportion of diabetics was significantly higher among Sino-Orbital Mucormycosis (76.3%) followed by Rhino-Cerebral Mucormycosis (51.9%) and least among Pulmonary Involvement (41.2%) (p=0.016) (Table 1).

ICU procedure & oxygen support

Out of 132 patients, 93 (70.5%) patients required ICU admission and 62 (47.0%) patients required oxygen support during their

Table 1: Association of baseline characteristics with types of Mucormycosi and Survival status of the patients.

	Total (n=132)	Types of Mucormycosis				Survival Status		
		Pulmonary Involvement (n=17)	Rhino-cerebral (n=77)	Sino-orbital (n=38)	p-value	Death (n=22)	Alive (n=110)	p-value
Gender								
Male	96 (72.70%)	14 (82.40%)	54 (70.1%)	28 (73.7%)	0.585	14 (63.6%)	82 (74.5%)	0.294
Female	36 (27.30%)	3 (17.60%)	23 (29.9%)	10 (26.3%)		8 (36.4%)	28 (25.5%)	
Age (Years)								
< 31	4 (3%)	0 (0%)	4 (5.20%)	0 (0%)	0.246	0 (0%)	4 (3.60%)	0.010*
31 - 40	23 (17.40%)	2 (11.80%)	16 (20.8%)	5 (13.2%)		0 (0%)	23 (20.9%)	
41 - 50	27 (20.50%)	4 (23.50%)	17 (22.1%)	6 (15.8%)		5 (22.7%)	22 (20%)	
51 - 60	37 (28%)	7 (41.20%)	16 (20.8%)	14 (36.8%)		5 (22.7%)	32 (29.1%)	
61 - 70	34 (25.80%)	2 (11.80%)	22 (28.6%)	10 (26.3%)		8 (36.4%)	26 (23.6%)	
> 70	7 (5.30%)	2 (11.80%)	2 (2.60%)	3 (7.90%)		4 (18.2%)	3 (2.70%)	
Mean ± SD	53.1±12.7	55.2±1.7	51.1±13.3	56.2±11.7	0.099	60.8±11.2	51.5±12.4	0.001*
Comorbidities								
Diabetes	76 (57.60%)	7 (41.20%)	40 (51.9%)	29 (76.3%)	0.016*	15 (68.2%)	61 (55.5%)	0.270
Hypertension	54 (40.90%)	9 (52.90%)	31 (40.3%)	14 (36.8%)	0.524	12 (54.5%)	42 (38.2%)	0.154
Long term corticosteroid use	17 (12.90%)	3 (17.60%)	9 (11.7%)	5 (13.2%)	0.81	3 (13.6%)	14 (12.7%)	0.97
Coronary artery disease	15 (11.40%)	2 (11.80%)	8 (10.4%)	5 (13.2%)	0.96	5 (22.7%)	10 (9.10%)	0.066
Number of Comorbidities								
No Comorbidities	21 (15.90%)	4 (23.50%)	14 (18.2%)	3 (7.90%)	0.176	1 (4.50%)	20 (18.2%)	0.110
At least 1 Comorbidities	66 (50%)	5 (29.40%)	42 (54.5%)	19 (50%)		9 (40.9%)	57 (51.8%)	
At least 2 Comorbidities	39 (29.50%)	8 (47.10%)	17 (22.1%)	14 (36.8%)		10 (45.5%)	29 (26.4%)	
At least 3 Comorbidities	6 (4.50%)	0 (0%)	4 (5.20%)	2 (5.30%)		2 (9.10%)	4 (3.60%)	
ICU Procedure & Oxygen Support								
ICU Admission	93 (70.50%)	11 (64.70%)	57 (74%)	25 (65.8%)	0.566	20 (90.9%)	73 (66.4%)	0.021*
Oxygen Required	62 (47%)	10 (58.80%)	31 (40.3%)	21 (55.3%)	0.183	15 (68.2%)	47 (42.7%)	0.029*
Ventilator	18 (13.60%)	2 (11.80%)	9 (11.7%)	7 (18.4%)	0.595	5 (22.7%)	13 (11.8%)	0.173
HFNC	33 (25%)	6 (35.30%)	15 (19.5%)	12 (31.6%)	0.213	10 (45.5%)	23 (20.9%)	0.015*
ECMO	7 (5.30%)	2 (11.80%)	3 (3.90%)	2 (5.30%)	0.424	1 (4.50%)	6 (5.50%)	0.862
Nasal Prongs	7 (5.30%)	1 (5.90%)	3 (3.90%)	3 (7.90%)	0.663	1 (4.50%)	6 (5.50%)	0.862

Laboratory parameters								
Hospital stay (days)	10 (6 - 15)	11 (4 - 15)	10 (7 - 15)	9 (6 - 15)	0.926	13 (9 - 17)	10 (6 - 15)	0.098
Hb (g/dl)	10.4±2.1	11±2.1	10.7±2.1	9.6±1.8	0.022*	9.8±2	10.5±2.1	0.129
TLC (10^3/ul)	10.7±5.5	8.6±4.1	11.3±6.1	10.4±4.3	0.168	12.8±7.8	10.2±4.8	0.043*
CRP (mg/L)	71.8±69.2	76.6±5.2	71.5±74.4	70.1±67.1	0.95	131.4±70.1	60.2±63.1	0.001*
Ferritin (ng/ml)	389.1±473.1	371.8±261.8	365.6±352.1	444.4±709.8	0.697		315.3±270.7	0.001*
Bilirubin (mg/dl)	0.7±0.5	0.7±0.4	0.6±0.3	0.7±0.8	0.53	1±1	0.6±0.3	0.001*
Albumin (gm/dl)	4.5±20.3	2.9±0.6	5.8±26.6	2.7±0.7	0.75	13.2±49.8	2.8±0.7	0.028*
SGOT (U/L)	46.3±380.4	61.3±57.3	47.1±4.4	37.9±16.4	0.18	57±40.3.	44.1±37.8	0.153
SGPT (U/L)	45.6±325	61.4±54.3	44.4±25.6	41±31.1	0.87	46.2±27.2	45.5±33.5	0.923
Creatinine (mg/dl)	1.1±0.8	1.08±0.61	1.13±0.8	1.13±0.89	0.973	1.6±1.1	1±0.7	0.002*
Na (mmol/l)	151.4±121.8	136.8±10.4	148.6±113.7	163.3±160.2	0.726	139.7±7.3	153.7±133.4	0.626
K (mmol/l)	4.2±4.1	3.4±0.9	4.6±5.3	3.6±0.7	0.34	3.7±0.7	4.3±4.5	0.550
RBS (blood glucose) (mg/dl)	155.3±58.4	155.7±57.3	148.1±49.8	169.8±72.5	0.172	171±86.9	152.2±50.9	0.167
Outcome								
Death	22 (16.70%)	1 (5.9%)	13 (16.9%)	8 (21.1%)	0.377	-	-	-

Table 2: Area under the Curve (AUC) with optimal cut-off values of the risk factors for the prediction of Death.

Test Result Variable(s)	AUC (95% CI)	Optimal Cut-off Point	Sensitivity (Sn)	Specificity (Sp)	Positive Predicative Value (PPV)	P-value
Age (Years)	0.683 (0.565 - 0.801)	57	59.10%	63.60%	24.50%	
CRP (mg/L)	0.784 (0.667 - 0.901)	73	81.00%	75.00%	38.60%	
Ferritin (ng/ml)	0.674 (0.528 - 0.821)	358	59.10%	76.40%	33.30%	
SGOT (U/L)	0.646 (0.527 - 0.765)	39	68.20%	55.50%	23.40%	
Creatinine (mg/dl)	0.677 (0.539 - 0.815)	1.15	68.20%	70.00%	31.30%	

*p-value <0.05, statistically significant.

hospital stay whereas ventilator was required for 18 (13.6%) patients. 33 (25.0%) and 7 (5.3%) patients required High flow Nasal Cannula (FHNC) and Extracorporeal Membrane Oxygenation (ECMO) procedures respectively. Nasal prongs required among 7 (5.3%) patients. The differences for these parameters among three types of mucormycosis patients were not statistically significant (Table 1).

Haemoglobin level was significantly lower among Sino-Orbital Mucormycosis (9.6±1.8) followed by Rhino-Cerebral Mucormycosis (10.7±2.1) and Pulmonary Involvement (11±2.1) (p=0.022). No statistically significant differences were observed in all other laboratory parameters among three types of mucormycosis patients (Table 1).

Outcome at discharge

Median length of hospital stay (days) was 10 (IQR: 6–15) days which was not statistically different among the three types of mucormycosis (p=0.926). The overall death rate of mucormycosis patients was 16.7% (n=22). Further, death rates among Sino-orbital mucormycosis, rhino-cerebral mucormycosis and pulmonary involvement were 1/17 (5.9%), 13/77 (16.9%) & 8/38 (21.1%) respectively. However the difference was not statistically significant (p=0.377) (Table 1).

Risk factors and prediction of death

The significant risk factors associated with death are higher age, requirement of ICU admission and need for oxygen support during the hospital stay as well as HFNC procedure (p<0.05) (Table 1).

Based on the laboratory parameters, the risk factors identified for Death were raised levels of TLC, CRP, Ferritin, Bilirubin, Albumin (serum) and Creatinine (p<0.05) (Table 1).

Area under the curve (AUC) and optimal cut-off points of laboratory parameters

ROC curve analysis revealed that the predicting ability of risk factors for Death among mucormycosis patients were Age (AUC=0.683; p-value=0.008), CRP (AUC=0.784; p- value=0.0001), Ferritin (AUC=0.674; p-value=0.012), SGOT (AUC=0.646; p-value=0.034) and Creatinine (AUC=0.677; p-value=0.011). ROC analysis further revealed that the optimal cut-off value of age was 57 years, CRP >73, Ferritin >358, SGOT >39 and Creatinine >1.15 (Table 2).

Univariate logistic regression for prediction of risk

On univariate logistic regression analysis, ICU Admission, Oxygen Required, HFNC, TLC, CRP >73, Ferritin >358, Bilirubin >0.621, SGOT >39 and Creatinine >1.15 were observed as independent predictor of Death. The CRP >73 (OR=12.75, p=0.0001) had a higher power for predicting Death followed by Bilirubin (OR=5.35, p=0.016), ICU Admission (OR=5.07, p=0.035), Creatinine >1.15 (OR=5.00, p=0.001), Ferritin >358 (OR=4.67, p=0.002), HFNC (OR=3.15, p=0.019), Oxygen Required (OR=2.87, p=0.034), SGOT >39 (OR=2.67, p=0.048) and TLC (OR=1.08, p=0.049) (Table 3).

Multivariate logistic regression for prediction of risk

A Step Wise Forward Multivariate Logistic Regression was

Table 3: Univariate Logistic Regression analysis for prediction of Death.

	Beta Coefficient	Std. Error	Odds Ratio (OR)	95% CI for OR		P-value
				Lower	Upper	
Age > 57 Years	0.93	0.48	2.53	0.99	6.44	0.052
Female	0.5	0.49	1.65	0.63	4.36	0.309
ICU Admission	1.62	0.77	5.07	1.12	22.86	0.035*
Oxygen Required	1.06	0.5	2.87	1.09	7.6	0.034*
Ventilator	0.79	0.59	2.19	0.69	6.95	0.182
HFNC	1.15	0.49	3.15	1.21	8.21	0.019*
ECMO	0.19	1.11	1.21	0.14	10.59	0.862
Nasal Prongs	0.19	1.11	1.21	0.14	10.59	0.862
Hospital stay (Days)	0.02	0.02	1.02	0.97	1.06	0.41
Hb (g/dl)	-0.18	0.12	0.83	0.66	1.06	0.131
TLC (10^3/ul)	0.08	0.04	1.08	1	1.17	0.049*
CRP (mg/L)	2.55	0.6	12.75	3.95	41.21	0.0001*
Ferritin (ng/ml)	1.54	0.49	4.67	1.79	12.15	0.002*
Bilirubin (mg/dl)	1.68	0.7	5.35	1.37	20.91	0.016*
Albumin (gm/dl)	0.02	0.03	1.02	0.96	1.09	0.436
SGOT (U/L)	0.98	0.5	2.67	1.01	7.06	0.048*
SGPT (U/L)	0	0.01	1	0.99	1.01	0.922
Creatinine (mg/dl)	1.61	0.5	5	1.87	13.4	0.001*
Na (mmol/l)	0	0	1	0.99	1.01	0.654
K (mmol/l)	-0.07	0.14	0.93	0.7	1.23	0.609
RBS (blood glucose) (mg/dl)	0	0	1	1	1.01	0.178
Long term corticosteroid use	0.08	0.68	1.08	0.28	4.14	0.908
Coronary artery disease	1.08	0.61	2.94	0.89	9.67	0.076
Diabetes	0.54	0.5	1.72	0.65	4.55	0.274
Hypertension	0.66	0.47	1.94	0.77	4.89	0.159
No Comorbidities	1	-	-	-	-	-
At least 1 Comorbidities	1.15	1.09	3.16	0.38	26.52	0.29
At least 2 Comorbidities	1.93	1.09	6.9	0.82	58.21	0.076
At least 3 Comorbidities	2.3	1.34	10	0.72	138.68	0.086

*p-value <0.05, statistically significant.

attempted. The variables entered in the model at different steps along with the risk of death in the presence of risk factors are presented in Table 4.

The above analysis indicates that the risk of death with CRP (mg/L) >73 alone as 38.7%; CRP (mg/L) >73 and Ferritin (ng/ml) >358 as 59.4%; CRP (mg/L) >73, Ferritin (ng/ml) >358 and Oxygen Required as 75.0%; CRP (mg/L) >73, Ferritin (ng/ml) >358, Oxygen Required and SGOT (U/L) >39 as 86.2% & CRP >73 and Ferritin (ng/ml) >358, Oxygen Required, SGOT (U/L) >39 and Creatinine (mg/dl) >1.15 as 92.3% (Table 4).

Model development

Odds are the ratio of two probabilities where the numerator is the probability p of an event and the denominator is the complementary probability of that event not occurring. That is:

$$\text{Odds of the Event} = \left(\frac{p}{1-p}\right) \qquad \text{(Eq.1)}$$

The logistic regression model, with usual notations is given by:

$$\text{Logit}(p) = ln\left(\frac{p}{1-p}\right) = \beta 0+\beta 1\ X1+\beta 2\ X2+\beta 3\ X3+\ldots+\beta nXn \qquad \text{(Eq.2)}$$

Probability of occurrence (p) is given by:

$$p = \frac{e^{\beta 0+\beta 1\ X1+\beta 2\ X2+\beta 3\ X3+\ldots+\beta nXn}}{1+e^{\beta 0+\beta 1\ X1+\beta 2\ X2+\beta 3\ X3+\ldots+\beta nXn}} \qquad \text{(Eq. 3)}$$

The predictors that entered into the final prediction model are CRP >73 (OR=15.78, p=0.0001), Oxygen Required (OR=5.50, p=0.012), Ferritin >358 (OR=4.43, p=0.025), SGOT >39 (OR=4.10, p=0.039) and Creatinine >1.15 (OR=3.72, p=0.048). Thus, that higher CRP, Ferritin, SGOT, Creatinine and the need of oxygen requirement increased the risk of death independently of the effect of possible confounders (Table 4).

From the equation (2), the logit of the model is given by:

Logit (Death) = -6.19 + (2.76*CRP>73) + (1.70*Oxygen Required)

Table 4: Multivariate Logistic Regression (Step Wise Forward LR Method) analysis for prediction of Death.

		Beta Coefficient	Std. Error	Odds Ratio (95% C.I. for OR)	p - value	Risk of Death (%)
Step 1	CRP (mg/L) > 73	2.55	0.6	12.75 (3.95 - 41.21)	0.0001*	38.70%
	Constant	-3.01				
Step 2	CRP (mg/L) > 73	2.47	0.62	11.82 (3.52 - 39.70)	0.0001*	59.40%
	Ferritin (ng/ml) > 358	1.52	0.56	4.56 (1.52 - 13.67)	0.007	
	Constant	-3.61				
Step 3	Oxygen Required	1.49	0.62	4.44(1.32 - 14.95)	0.016	75.00%
	CRP (mg/L) > 73	2.64	0.65	13.99 (3.92 - 49.98)	0.0001*	
	Ferritin (ng/ml) > 358	1.52	0.59	4.59 (1.45 - 14.56)	0.01	
	Constant	-4.55				
Step 4	Oxygen Required	1.52	0.63	4.56 (1.32 - 15.75)	0.017	86.20%
	CRP (mg/L) > 73	2.67	0.67	14.50 (3.89 - 54.02)	0.0001*	
	Ferritin (ng/ml) > 358	1.76	0.63	5.81 (1.68 - 20.04)	0.005	
	SGOT (U/L) > 39	1.31	0.64	3.71 (1.05 - 13.09)	0.042	
	Constant	-5.43				
Step 5	Oxygen Required	1.7	0.68	5.50 (1.46 - 20.71)	0.012	92.30%
	CRP (mg/L) > 73	2.76	0.72	15.78 (3.86 - 64.54)	0.0001*	
	Ferritin (ng/ml) > 358	1.49	0.67	4.43 (1.20 - 16.31)	0.025	
	SGOT (U/L) > 39	1.41	0.68	4.10 (1.07 - 15.67)	0.039	
	Creatinine (mg/dl) > 1.15	1.31	0.66	3.72 (1.01 - 13.61)	0.048	
	Constant	-6.19				

*p-value <0.05, statistically significant.

+ (1.49*Ferritin >358) + (1.41*SGOT >39) + (1.31*Creatinine >1.15)

Thus, the Probability of Death is given by:

$$p = \frac{e^{-6.19+(2.76*\text{CRP}>73)+(1.70*\text{Oxygen Required})+(1.49*\text{Ferritin}>358)+(1.41*\text{SGOT}>39)+(1.31*\text{Creatinine}>1.15)}}{1+e^{-6.19+(2.76*\text{CRP}>73)+(1.70*\text{Oxygen Required})+(1.49*\text{Ferritin}>358)+(1.41*\text{SGOT}>39)+(1.31*\text{Creatinine}>1.15)}} \quad \text{(Eq.4)}$$

The prediction model is robust with prediction power of 90.7%. The false positive (a case in that the patient would likely to die when, in fact it did not) and false negative (a case in that patients would not die, when in fact it did) rates are 9.1% and 9.3% respectively (Table 5).

Table 5: Predictive power of the model.

Observed	Predicted	
	Outcome Classification	
	Death	Alive
Death	10	11
Alive	1	107
False Positives (FP) and False Negative (FN)	FP = 1/11 = 9.1%	FN = 11/118 = 9.3%
Overall Right Predication (ORP)	ORP = (10 + 107)/(21+108) = 117/129 = 90.7%	

Discussion

Although, few case reports and case series have been published, the association between COVID-19 and mucormycosis yet needs to be established. Hardeva Ram Nehara et al. [5] published a case series of five patients with rhinocerebral mucormycosis. Similarly, Amanda Werthman et al. [6] presented a case of rhino-orbital-cerebral mucormycosis. In our study, case series of one hundred and thirty two patients with mucormycosis associated with COVID-19 infection and showed that 71.9% had lymphocytopenia during hospital admission which confirmed lymphocytopenia as a risk factor for invasive fungal infection. A study conducted by Nikolay N. Klimko et al. [7] reported that 86% had lymphocytopenia and was consistent with our result. Our case series reported a large number of patients with a history of diabetes mellitus and corticosteroids used to treat COVID-19 infection. It was observed that proportion of diabetics were higher in Sino-orbital mucormycosis. Similarly, a study by Dora E Corzo-Leon et al. [8] showed diabetes as a major risk factor for mucormycosis. Another study conducted by Prashant Sirohiya et al. [9] reported similar comorbidities when compared with our study. A case series by Yudhyavir Singh et al. [10] analyzed the same laboratory parameters as our study and the results were found to be broadly similar.

A large number of rhino-cerebral mucormycosis patients were diagnosed in our case series which is considered as one of the most common type of mucormycosis.

Covid-19 associated mucormycosis is associated with high mortality which is due to severity of COVID-19. In our case series, the overall mortality rate is 16.7%. A case series by Garg et al. [11] reported 87.5% of mortality in patients with severe COVID-19. Another case series by Sharma et al. [12] reported no deaths, which was quite surprising. Our study observed that higher age, requirement of ICU admission and need for oxygen support during the hospital stay were significant risk factors associated with death. Based on laboratory parameters the risk factors identified for Death were raised levels of TLC, CRP, Ferritin, Bilirubin, Albumin (serum) and Creatinine. Globally, case fatality rate of mucormycosis is found to be

46% [13]. Diagnosis of mucormycosis is difficult. Early diagnosis and treatment is indispensable because a delay of even 6 days is associated with a doubling of 30-day mortality from 35% to 66%. In spite of early diagnosis and treatment, the recovery from mucormycosis is poor9. Mucormycosis is mainly spread through inhaled fungal spores [2]. Therefore, wearing of face masks to prevent COVID-19 should also be encouraged to prevent the spread of mucormycosis.

Conclusion

In our case series of 132 COVID-19 associated mucormycosis patients, Diabetes was the major comorbidity reported followed by Hypertension. Importantly proportion of diabetics was significantly higher among Sino-Orbital Mucormycosis followed by Rhino-Cerebral Mucormycosis and least among Pulmonary Involvement. In addition to this, long-term steroid use was more vulnerable to COVID-19 associated Mucormycosis. As to the risk factors for mortality, the significant ones were the raised levels of CRP >73, Ferritin >358, SGOT >39 and Creatinine >1.15 as well as oxygen requirement. These risk factors contribute to over 90% of mortality. Clinicians should therefore monitor these risk factors in the management of COVID-19 associated mucormycosis patients. Early diagnosis and on-time treatment is pivotal in the management of mucormycosis.

Limitations

We acknowledge few limitations, as this case series has covered patients' data from a single tertiary care center where most of the patients are referrals. So Individual medication history i.e. duration of steroid therapy etc. of each patient could not be extensively traced.

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