Correlates of depression, anxiety, self-esteem, and suicidal ideas in COVID-associated mucormycosis patients and the effects of treatment

Aim: The aim was to study the correlates of depression, anxiety, self-esteem, and suicidal ideas in patients of COVID-associated mucormycosis (CAM) and effects of treatment. Materials and Methods: A cross-sectional, analytical study was performed in a tertiary care center in Western Maharashtra. By purposive sampling, 34 patients of CAM were included in the study with their informed consent and after obtaining ethical clearance. A self-made questionnaire to include demographic and clinical details was filled. Hospital Anxiety and Depression Scale (HADS), Rosenberg Self-Esteem Scale (RSES), and Suicidal Ideation Attributes Scale (SIDAS) were applied after initial diagnosis. The HADS, RSES, and SIDAS were reapplied after their operative treatment. Results: A significant reduction in anxiety and depression scores postoperatively was seen. No significant difference was found in self-esteem or suicidal ideas postoperatively in the study population. However, patients who underwent orbital exenteration showed a significant reduction in level of self-esteem with anxiety and depression postoperatively. No specific correlation was found between the computed tomography score, family history, intensive care unit admission, or orbital exenteration with anxiety, depression, self-esteem, and suicidal ideas. Conclusion: Levels of anxiety and depression in patients of CAM reduced significantly after treatment, but self-esteem worsened in males more than females owing to disfigurement. There is a need of psychological counseling in patients of mucormycosis undergoing a debilitating surgery both pre- and postoperatively for a better outcome and recovery.

Keywords: Anxiety, depression, mucormycosis, orbital exenteration, self-esteem, suicidal ideas

Mucormycosis was a rare opportunistic fungal infection in the population occurring mainly in severely immunodeficient individuals till the second wave of COVID-19 pandemic hit India. Although uncommon, the infection always has had dreadful consequences among those infected by it. People at risk comprise those with immunocompromised states such as poorly controlled diabetes, patients on chemotherapy and immunosuppression, HIV infection, and renal failure. In COVID-infected individuals with uncontrolled diabetes, inadvertent use of steroids, raised serum ferritin levels, high oxygen requirement, and prolonged intensive care unit (ICU) stay have been hypothesized to predispose for Mucor infection. The appearance of symptoms of mucormycosis has been noted commonly between the 7th day of COVID-19 infection till 2–3 weeks after recovery. The clinical features range from nasal blockage or sinusitis most frequently followed by facial pain or headache,
pharyngitis, unilateral facial swelling or numbness, foul-smelling blackish nasal discharge, or rarely an intranasal mass. In more severe cases, loss of vision, restricted eye movements, proptosis, lethargy, or confusion may be seen suggesting orbital and cerebral involvement. In a survey conducted between January 2016 and September 2017, there were 465 cases of mucormycosis reported across the country. However, the Health Ministry reported 8848 cases of COVID-associated mucormycosis (CAM) across the entire country within a span of 3 months during the second wave of COVID-19 pandemic. As the infection progresses rapidly, the window period between appearance of signs and effective treatment is very narrow. Moreover, due to lack of awareness in the general public, the time taken by COVID-infected/recovered patients to report to the hospital is also delayed. In fulminant cases with complete loss of vision and severe orbital disease threatening cerebral involvement, a life-saving orbital exenteration is needed. Among those infected, there is increased apprehension toward the consequences of this infection upon them and their family members. Despite early diagnosis and aggressive combined surgical and medical therapy, the prognosis for recovery from mucormycosis is poor. Even in the survivors after having undergone orbital exenteration, the loss of an eye is not easy to deal with. The two main disadvantages of orbital exenteration are mutilation and loss of vision, as the morbidity associated with the procedure is practically nil. Yet, as many patients already present with irreversible blindness, survival should precede other considerations. Several studies have gauged the importance of psychological interventions in patients undergoing disfigurement surgeries. Timely management of mental health also reduces the time in rehabilitation and hastens recovery postoperatively. One study observed that 50% of the patients who underwent orbital exenteration felt strongly uncomfortable or dissatisfied with the cosmetic effect of the surgery, 60% suffered unwelcome comments, and 50% uncomfortable stare from close friends and relations. The scarcity of such data in patients of CAM in India warrants studies describing the psychological impact of this debilitating disease upon the survivors. The present work was undertaken in this context to study the correlates of depression, anxiety, self-esteem, and suicidal ideas in patients of CAM and effects of treatment.

**MATERIALS AND METHODS**

This longitudinal, analytical study was conducted in the department of ophthalmology and department of psychiatry in a tertiary care hospital and research center located in Pimpri, Pune. Clearance for the ethical aspects of the study was obtained from the institutional ethics committee before starting the study. Written informed consent was obtained from every patient included in the study.

**Sample size calculation**

The sample size was calculated using the Fisher’s formula.

Description:

\[
 n = \frac{t^2 \times p(1-p)}{m^2}
\]

- **n** = Required sample size
- **t** = Confidence level at 95% (standard value of 1.96)
- **p** = Estimated prevalence of mucormycosis in India (0.14%)
- **m** = Margin of error at 5% (standard value of 0.05)

Calculation:

\[
 n = \frac{1.96^2 \times 0.0014(1-0.0014)}{0.05^2}
\]

Sample size was calculated to be approximately ~ 20.

**Sample**

A total of 80 patients were admitted for CAM during the study period. Out of these, 40 patients gave consent to participate in the study, with a subsequent loss to follow-up in 6 patients. Hence, by purposive sampling, 34 patients of CAM were finally included in the study.

**Inclusion criteria**

All patients diagnosed as CAM admitted in the tertiary care center with COVID-positive status in the past 6 weeks and who are cooperative to participate were included in the study.

**Exclusion criteria**

Those with history of psychiatric illness or on psychotropic medication and having had electroconvulsive therapy in the past 6 months and those having previously undergone a disfiguring surgery were excluded from the study.

**Study tools**

**Self-made questionnaire**

It included the demographic details such as age, sex, marital and education status, occupation and history of any comorbid medical or surgical illness or previous treatment history, substance history, detailed COVID-19 history, and treatment received followed by CAM history. It contains 36 questions along with demographic details and comorbid illnesses.

**Hospital Anxiety and Depression Scale**

The hospital Anxiety and Depression Scale (HADS) is a self-rating scale developed to assess the psychological
distress in hospital-admitted patients. It consists of 2 subscales Anxiety and Depression, with 14 questions regarding feelings of the patient in the past week.\textsuperscript{[8]}

**Rosenberg Self-Esteem Scale**

Rosenberg Self-Esteem Scale (RSES) is a 10-item self-report measure of self-esteem with an internal consistency of 0.77. A lower score indicates low self-esteem.\textsuperscript{[9]}

**Suicidal Ideation Attributes Scale**

Suicidal Ideation Attributes Scale consists of 5 items each targeting an attribute of suicidal thoughts: frequency, controllability, closeness to attempt, level of distress with the thoughts, and impact on daily functioning. Responses are measured on a 10-point scale such that a higher total score reflects more severe suicidal thoughts.\textsuperscript{[10]}

**Methods**

All the patients with confirmed diagnosis of CAM and admitted to the tertiary care center were approached for participating in the study. After explaining the aims and objectives of the study, written informed consent was obtained. The patients were under treatment of physician and ophthalmologist. The HADS, RSES, and SAS were applied within 2 days of diagnosis. They were under treatment of ophthalmologist and physician. In the 3\textsuperscript{rd}-4\textsuperscript{th} week of hospitalization, all the patients underwent surgery (functional endoscopic sinus surgery/retrobulbar amphotericin B injection/exenteration). On postoperative day 2, the HADS, RSES, and SAS were again applied to the patients.

**Psychological counseling**

All the patients included in the study were counseled individually and with their family members before operative treatment about the type of surgery, risk and outcomes, and need for rehabilitation with available prosthetic options. A regular psychological counseling follow-up was maintained pre- and postoperatively.

**Statistical analysis**

Data were processed using the Statistical Package of the Social Sciences (SPSS, IBM, Atlanta, Georgia, USA). Descriptive statistics were used to calculate the mean, percentage, and standard deviation of the sample. Wilcoxon’s test was applied to compare the findings at the time of admission and discharge. Spearman’s correlation coefficient was applied to find the correlates. For measurement continuous data, t-test was applied. For frequency data, Chi-square test was applied. A multiple regression analysis by stepwise method was run to determine the predictors of preoperative depression in CAM patients.

**RESULTS**

The mean age of male CAM patients was 45.6 years and females 52.2 years [Table 1]. Majority of the study population consisted of males (n = 24; 70.6%), while 29.4% (n = 10) were females. All 34 patients of the study population were married. About 61.7% of the participants were diabetics. The mean duration of diabetes was 1.8 years. The mean blood sugar level of patients was 240 mg/dl with a standard deviation of 87.29 and warranted insulin therapy in 60%. Thirty-two percent of the patients were known case of hypertension, and the duration of illness was around 3 years. History of alcohol consumption was present in 4 patients (11.7%), all of whom were male, whereas tobacco consumption was present in 6 patients (17.6%), out of which 66.6% were male. 76.4% of the patients were hospitalized for COVID, 69.2% of which were male and 30.8% were female. The average stay in the hospital for male patients was 9.79 days and 7.9 days for females. Total 5 patients (4 males and 1 female) were admitted in the ICU and 47% of the study population (11 males and 5 females) required oxygen therapy [Table 2]. None of the patients needed ventilator support during the course of their illness. Only about

| Table 1: Demographic characteristics and comorbidities in patients with COVID-associated mucormycosis |
| --- |
| Demographic | Males (n=24), n (%) | Females (n=10), n (%) |
| Age, mean (SD) | 45.66 (17.44) | 52.2 (10.53) |
| Marital status | 24 (100) | 10 (100) |
| Education in years, mean (SD) | 18.04 (3.55) | 8.3 (7.54) |
| Diabetes | 12 (50) | 9 (90) |
| DM in years, mean (SD) | 1.36 (3.10) | 3.14 (4.44) |
| HTN | 6 (25) | 5 (50) |
| Alcohol consumption | 2.29 (4.39) | 2.80 (4.53) |
| Tobacco consumption | 4 (16.6) | 2 (20) |

HTN – Hypertension; SD – Standard deviation; DM – Diabetes mellitus

| Table 2: Course of COVID infection in male and female patients of mucormycosis |
| --- |
| COVID | Males (n=24), n (%) | Females (n=10), n (%) |
| CT score, mean (SD) | 9.21 (7.05) | 5.66 (4.55) |
| Hospitalization | 18 (75) | 8 (80) |
| Days in hospital, mean (SD) | 9.79 (9.70) | 7.9 (6.47) |
| O2 | 11 (43) | 5 (50) |
| Steam | 7 (29.1) | 2 (20) |
| ICU | 4 (16.6) | 1 (10) |
| Steroids | 15 (62.5) | 5 (50) |
| Insulin | 12 (50) | 8 (80) |
| Family history of | 11 (45.83) | 5 (50) |

ICU – Intensive care unit; SD – Standard deviation; CT – Computed tomogram
15% \((n = 5)\) of the study population were aware of the risk of CAM. The mean onset of symptoms of mucormycosis was 10 days. The most common symptom of CAM was headache seen in 29.5% \((n = 10)\) of the patients, followed by nasal stuffiness and toothache (11.76%). About 80% \((n = 27)\) of the patients could procure injection amphotericin B with some difficulties. 32.35% \((n = 11)\) of the patients underwent orbital exenteration, 63% of which were male. Twenty-six (76.4%) patients from the study population reported to feel anxious or sad prior to surgery, which was also associated with depressive features and low self-esteem preoperatively [Table 3]. There was a significant reduction in anxiety and depression scores and suicidal ideas postoperatively in the entire group and patients undergoing orbital exenteration and male patients undergoing orbital exenteration. However, no significant difference was found in anxiety, depression, self-esteem, or suicidal ideation postoperatively in female patients undergoing orbital exenteration [Table 4]. Increasing age was associated with incidence of hypertension and orbital exenteration in patients of CAM. A negative correlation was found between education and occurrence of diabetes mellitus in the patients. Development of hypertension increased with age, but these patients were also more likely to have depressive symptoms preoperatively. The mean computed tomography (CT) score of patients showed a positive correlation with previous history of alcohol consumption and use of steroids during hospital stay [Table 5].

A multiple regression was run to predict preoperative depression from age, sex, education, diabetes, hypertension, alcohol, tobacco, CT score, steroids, exenteration, preoperative anxiety, postoperative anxiety, postoperative depression, self-esteem, and suicidal thought using the stepwise method. The value of \(\text{R}^2\) (the multiple correlation coefficient), a measure of the quality of the prediction of the dependent variable (preoperative depression), is 0.917, which indicates a good level of prediction. The \(\text{R}^2\) (the coefficient of determination) value is 0.812, implying that our independent variables explain 84.1% of the variability of our dependent variable, preoperative depression [Table 6]. In Table 7, the \(F\)-ratio tests whether the overall regression model is a good fit for the data. The table shows that the independent variables statistically significantly predict the dependent variable, \(F(5, 28) = 29.564, P < 0.0005\), clearly indicating that the regression model is a good fit of the data. In

Table 3: Mucormycosis details of study population (onset of symptoms post COVID, history of exenteration, and feeling preoperatively)

| Mucormycosis                  | Males, \(n\) (%) | Females, \(n\) (%) |
|-------------------------------|------------------|--------------------|
| Onset of symptoms, mean (SD)  | 13.1 (19.04)     | 6 (6.54)           |
| Exenteration                  | 7 (29.16)        | 4 (40)             |
| Anxious/sad preoperative      | 6 (25)           | 2 (20)             |

SD – Standard deviation

Table 4: Significant reduction in anxiety, depression suicidal ideation scores postoperatively in all COVID-associated mucormycosis patients as well as patients undergoing orbital exenteration

|                     | Mean (SD) | Wilcoxon | \(P\)   |
|---------------------|-----------|----------|---------|
|                     | Preoperative | Postoperative |       |
| All CAM patients    |            |           |         |
| Anxiety             | 11.35 (3.48)| 5.26 (3.87)| -5.023  | <0.0001 |
| Depression          | 9.61 (4.97)| 4.37 (3.71)| -4.869  | <0.0001 |
| Self-esteem         | 35.11 (4.74)| 35.53 (4.45)| -0.459  | 0.647   |
| Suicide             | 3.58 (5.88)| 1.0 (3.15)| -3.190  | <0.001  |
| Exenteration total sample |          |           |         |
| Anxiety             | 10.00 (2.93)| 3.64 (2.73)| -2.807  | 0.005   |
| Depression          | 10.73 (5.76)| 3.82 (4.29)| -2.805  | 0.005   |
| Self-esteem         | 36.55 (3.56)| 33.45 (4.87)| -1.898  | 0.058   |
| Suicide             | 7.18 (7.44)| 2.55 (5.22)| -2.379  | 0.017   |
| Exenteration (male) |            |           |         |
| Anxiety             | 10.00 (2.71)| 3.85 (3.34)| -2.207  | 0.027   |
| Depression          | 10.14 (5.08)| 4.00 (4.69)| -2.207  | 0.027   |
| Self-esteem         | 35.86 (4.14)| 33.57 (5.97)| -1.153  | 0.249   |
| Suicide             | 8.43 (8.08)| 3.71 (6.37)| -2.032  | 0.042   |
| Exenteration (female)|           |           |         |
| Anxiety             | 10.00 (3.74)| 3.25 (3.50)| -1.826  | 0.068   |
| Depression          | 11.75 (7.54)| 3.50 (4.12)| -1.826  | 0.068   |
| Self-esteem         | 37.25 (2.22)| 33.25 (2.75)| -1.890  | 0.059   |
| Suicide             | 5.00 (6.63)| 0.50 (4.00)| -1.342  | 0.180   |

CAM – COVID-associated mucormycosis; SD – Standard deviation
### Table 5: Correlation of demographic, clinical features and psychological disturbances with treatment in patients with COVID-associated mucormycosis

| Correlation | Age | Sex | Education | Diabetes | HTN | Alcohol | CT score | Steroids | Anxpre | Anxpost | Deppre | Deppost | SEpre | SEpost | Spre | Spost | Xentern |
|-------------|-----|-----|-----------|----------|-----|---------|----------|----------|--------|---------|--------|--------|-------|--------|------|-------|---------|
| **Contd...** |     |     |           |          |     |         |          |          |        |         |        |        |       |        |      |       |         |
|      | Age  | Sex  | Education | Diabetes | HTN  | Alcohol | CT score | Steroids | Anxpre | Anxpost | Deppre | Deppost | SEpre | SEpost | Spre | Spost | Xentern |
|------|------|------|-----------|----------|------|---------|----------|----------|--------|---------|--------|---------|--------|--------|------|-------|---------|
| CC   | 0.264| -0.139| -0.226    | -0.208   | 0.347*| 0.065   | -0.147   | 0.113    | 0.607**| 0.316** | 1.000  | 0.757** | -0.489**| -0.45**| 0.354*| 0.279 | 0.093 |
| Significant | 0.132| 0.435| 0.198     | 0.239    | 0.044 | 0.714   | 0.407    | 0.525    | 0.000  | 0.000   | 0.000  | 0.000   | 0.000  | 0.000  | 0.007 | 0.040 | 0.109 | 0.600 |
| Deppost | -0.010| -0.063| -0.124    | -0.272   | 0.097 | -0.169  | -0.310   | 0.068    | 0.596**| 0.816** | 0.757**| 1.000   | -0.464**| -0.274 | -0.046| 0.168 | -0.136|
| Significant | 0.954| 0.723| 0.484     | 0.119    | 0.585 | 0.339   | 0.074    | 0.704    | 0.000  | 0.000   | 0.000  | 0.000   | 0.006  | 0.117  | 0.798 | 0.342 | 0.444 |
| SEpre | -0.037| 0.080| 0.042     | 0.171    | -0.049| 0.122   | 0.069    | -0.163   | -0.618**| -0.611**| -0.489**| -0.46** | 1.000  | 0.518**| -0.060| 0.097 | 0.204 |
| Significant | 0.835| 0.654| 0.812     | 0.333    | 0.785 | 0.491   | 0.700    | 0.357    | 0.000  | 0.000   | 0.000  | 0.000   | 0.002  | 0.736  | 0.686 | 0.248 |
| SEpost | -0.142| 0.386*| 0.298     | 0.057    | -0.330| -0.127  | 0.062    | 0.102    | -0.560**| -0.409* | -0.452**| -0.274  | 0.518**| 1.000  | -0.166| -0.099| -0.350*|
| Significant | 0.413| 0.024| 0.087     | 0.749    | 0.056 | 0.474   | 0.728    | 0.568    | 0.001  | 0.016   | 0.007  | 0.117   | 0.002  | 0.347  | 0.780 | 0.043 |
| Spre  | 0.328| 0.117| -0.098    | -0.122   | 0.172 | 0.133   | 0.229    | 0.105    | -0.002 | -0.206  | 0.354* | -0.046  | -0.660  | -0.166 | 1.000 | 0.627**| 0.414* |
| Significant | 0.058| 0.511| 0.951     | 0.492    | 0.339 | 0.453   | 0.192    | 0.556    | 0.989  | 0.242   | 0.040  | 0.798   | 0.736  | 0.347  | 0.000 | 0.015 |
| Spost | 0.014| 0.134| 0.006     | 0.024    | 0.019 | 0.091   | -0.015   | -0.105   | -0.026 | 0.070   | 0.279  | 0.168   | 0.097  | -0.050  | 0.627**| 1.00  | 0.207 |
| Significant | 0.935| 0.451| 0.975     | 0.895    | 0.914 | 0.609   | 0.935    | 0.553    | 0.883  | 0.692   | 0.109  | 0.342   | 0.586  | 0.780  | 0.000 | 0.239 |
| Xentern | 0.340*| -0.106| -0.288    | -0.015   | 0.194 | 0.138   | -0.171   | -0.316   | -0.261 | -0.277  | 0.093  | -0.136  | 0.204  | -0.350*| 0.414*| 0.207 | 1.000 |
| Significant | 0.049| 0.553| 0.999     | 0.931    | 0.272 | 0.437   | 0.335    | 0.069    | 0.136  | 0.113   | 0.600  | 0.444   | 0.248  | 0.043  | 0.015 | 0.239 |

HTN – Hypertension; CT – Computed Tomogram; CC – Correlation Coefficient; Anxpre – Anxiety Preoperative; Anxpost – Anxiety Postoperative; Deppre – Depression Preoperative; Deppost – Depression Postoperative; SEpre – Self-esteem Preoperative; SEpost – Self-esteem Postoperative; Spre – Suicidal ideation Preoperative; Spost – Suicidal ideation Postoperative; Xentern – Exenteration; *P<0.05; **P<0.01
summary, we may state that a multiple regression was run to predict preoperative depression from postoperative depression, preoperative suicidal thoughts, preoperative and postoperative anxiety, and presence of hypertension. All the variables statistically significantly predicted preoperative depression, $F (5, 28) = 29.564, P < 0.0005$, $R^2 = 0.812$. All five variables added statistically significantly to the prediction, $P < 0.05$ [Table 8].

### DISCUSSION

The emerging complications of COVID 19 such as mucormycosis had an unprecedented surge and high mortality. Though various studies were conducted to evaluate the risk factors and outcome of interventions, none focused on the psychological impact. In a multicenter epidemiological study conducted in 2020, a total of 187 patients of CAM were included with a mean age of 53.4 years and 3:1 male-to-female ratio. Consistent to other studies, the patients included by us, ranged from 40 to 70 years with a mean age of 45–52 years and a male preponderance. In a systematic review of CAM reported in India post COVID pandemic, preexisting history of diabetes and corticosteroid use was recorded in up to 80% of the patients.

There was a significant overlap of alcohol consumption with severity of COVID-19 illness (high CT scores) and poor outcomes as mentioned in another study conducted by the COVID-19 Host Genetics Initiative. The most common presenting complaint of patients of mucormycosis was nasal discharge, which was in contrast to our findings where patients presented more often with headache followed by nasal stuffiness and toothache.

The use of liposomal amphotericin B for treatment of more than 80% of the patients as compared to posaconazole used in CAM patients admitted in other centers throughout India could be because of the widespread availability and procurement facilities available in the area.

Patients undergoing disfiguring surgery are more worried about survival than appearance preoperatively. Anxiety levels were understandably high in these patients, which is consistent with our findings. A positive correlation was noted with preoperative depressive features in hypertensives. The fear associated with fatality of the disease was rising, patients felt relieved when provided with the available surgical options, even if it meant “loss of an eye.” This could be observed by a significant reduction in levels of anxiety and depression postoperatively. Interestingly, no correlation was found in patients who had family members affected by COVID with levels of anxiety and suicidal ideas. No such impact of ICU admission or higher CT scores was also seen on the psychological state of patients. However, the disfigurement and visual handicap in patients undergoing orbital exenteration led to a poorer self-esteem, even though they were less anxious, depressed, and had less suicidal ideation than earlier. A case report highlighting the importance of rehabilitation in postoperative cases of exenteration, mentioned that the self-esteem and confidence levels of the patients returned to normal after the use of orbital prostheses. However,
not all patients had the means to spend thousands of rupees on the ocular prosthesis. Psychological counseling and preparedness of the patients done preoperatively for the expected disfigurement with focus on recovery postoperatively, aided in the reduction of anxiety and depression levels in these patients. While the self-esteem was significantly lower after orbital exenteration, regular counseling could help in the rehabilitation, improved mental well-being, and better quality of life. It can be inferred from the above findings that the psychological impact of this rare but deadly infection is immense. An inadvertent and unexpected pandemic such as SARS-CoV-2 followed by serious complications and mortality shook the world in its entirety in a period of few months. While the entire medical system got together to fight the upsurge in COVID and CAM cases, there was a lack of focus on the psychological well-being of patients. Due to its rarity and associated panic, patients of mucormycosis are overwhelmed in anticipation to its complications and disfigurement. A long-term follow-up and team efforts by surgical as well as mental-health professionals are required to improve the quality of life in survivors of CAM.

Limitations
Due to the fear and stigma associated with the disease, not all patients were willing to participate in the study and so the sample size was modest.

CONCLUSION
Levels of anxiety and depression in patients of CAM reduced significantly after treatment, but self-esteem worsened in males more than females owing to disfigurement. A positive correlation of preoperative depressive features was found with hypertension. The utility and efficacy of psychological counseling in patients of CAM undergoing debilitating surgery needs detailed evaluation.

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Conflicts of interest
There are no conflicts of interest.

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