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Association of COVID-19, Diabetes in Mucormycosis Patient- A Hospital-Based Study

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Abstract

Mucormycosis (previously called zygomycosis) is a serious but rare fungal infection caused by a group of moulds called mucormycetes. These moulds live throughout the environment. Mucormycosis mainly affects people who have health problems or take medicines that lower the body's ability to fight germs and sickness. This research aimed to study the association of COVID, diabetes and mucormycosis in a population reporting to Saveetha Dental College and Hospitals, Chennai in a period from June 2019 to June 2023. The data of patients reporting to Saveetha Dental College and Hospitals was reviewed and patients with mucormycosis were selected for the study. It included parameters like age, gender, Coronavirus Disease-19(COVID-19) history and systemic disease. Frequency test was used to detect the significance between age, gender, COVID-19 history and systemic condition. Chi-square tests were carried out using age, and gender as independent variables and COVID-19 history, and systemic condition as dependent variables. Statistical analysis was done by Pearson's chi-square test. P value < 0.05 was considered statistically significant. In this study, we observed that the most common age group diagnosed with mucormycosis was found to be 41-60 years of age (56%) and males were more commonly affected (88%). More than 50% of patients gave a history of COVID-19 and 50% were diabetic. The most common intraoral presentation was found to be palatal swelling (19%), and most of the patients had unilateral swelling. When associating swelling with different age groups, unilateral swelling was found to be more in young adults (56%) while bilateral swelling was profound in older people. The chi-square value was found to be significant (0.035). In this study, we observed that the most common age group diagnosed with mucormycosis was found to be 41-60 years of age and males were more commonly affected. The majority of them had a history of COVID-19 and were diabetic. The most common intraoral presentation was found to be palatal swelling, and most of the patients had unilateral swelling. Collectively, these findings suggest a familiar connection between mucormycosis, COVID-19 and diabetes.

Keywords: *COVID-19, Diabetes, Immune Compromised, Mucormycosis.*

Introduction

Mucormycosis (previously called zygomycosis) is a serious but rare fungal infection caused by a group of moulds called mucormycosis [1]. These moulds live throughout the environment. Mucormycosis mainly affects people who have health problems or take medicines that lower the body's ability to fight germs and sickness. It most commonly infects the nose, sinuses, eye and brain resulting in a runny nose, one-sided facial swelling and pain, headache, fever, blurred vision, swollen and bulging eyes, and tissue death [2].

Mucormycosis is a fungal infection caused by fungi in the order Mucorales. In most cases,

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it is due to an invasion of the genera *Rhizopus* and *Mucor*, common bread moulds. Most fatal infections are caused by *Rhizopus oryzae* [3].

It is spread by spores, most often through inhalation, contaminated food, or contamination of open wounds. These fungi are common in soils, decomposing organic matter (such as rotting fruit and vegetables), and animal manure. The fungal spores are in the environment, can be found on for instance mouldy bread and fruit and are breathed in frequently, but cause disease only in some people [4]. In addition to being breathed in to be deposited in the nose, sinuses and lungs, the spores can also enter the skin via blood or directly through a cut or open wound or grow in the intestine if eaten. Once deposited, the fungus grows branch-like filaments which invade blood vessels, causing clots to form and surrounding tissues to die [5].

Mucormycosis mainly affects people who have health problems or take medicines that lower the body's ability to fight germs and sickness [6]. Predisposing factors for mucormycosis include conditions where people are less able to fight infection, have a low neutrophil count or metabolic acidosis. Risk factors include poorly controlled diabetes mellitus (particularly Diabetic Ketoacidosis), organ transplant, iron overload, cancers such as lymphomas, kidney failure, long-term corticosteroid and immunosuppressive therapy, liver disease and severe malnutrition [7].

There is no haematological investigation that can confirm the diagnosis. Diagnosis requires identifying the mould in the affected tissue by biopsy and confirming it with a fungal culture. Because the causative fungi occur all around, culture alone is not decisive. Tests may also include culture and direct detection of the fungus in lung fluid, blood, serum, plasma and urine [8].

Mucormycosis is usually rare but is now ~80 times more common in India [9]. People of any age may be affected, including premature infants. The disease has been reported in natural disasters; the 2004 Indian Ocean tsunami and the 2011 Missouri tornado. During the COVID-19 pandemic 2020/21, an association between mucormycosis and COVID-19 has been reported. This association is thought to relate to reduced immune function during the illness and may also be related to glucocorticoid therapy for COVID-19. A rise in cases was particularly noted in India [10].

Hence the research aims to study the association of COVID-19, diabetes and mucormycosis in a population reporting to a private dental hospital in Chennai.

Materials and Method

Study Design and Study Setting

The present study was conducted in a university setting (Saveetha Dental College and Hospital, Chennai, India). Thus, the data available is of patients from the same geographic location and have similar ethnicity. The retrospective study was carried out with the help of digital case records of 16 patients who reported to the hospital. Ethical clearance to conduct this study was obtained from the Scientific Review Board of the hospital. The ethical approval number for the present study is SDC/SIHEC/2023/DIASDATA/0620-0325

Sampling

Data from 16 patients (14 males and 2 females) were reviewed and then extracted. All patients with Mucormycosis in the given duration of period were evaluated. Only relevant data was included to minimize sampling bias. A simple random sampling method was carried out. Cross-verification of data for error was done by the presence of additional reviewers and by photographic evaluation. Incomplete data collection was excluded from the study.

Data Collection

A single calibrated examiner evaluated the digital case records of patients who reported to Saveetha Dental College from June 2019 to

June 2023. For the present study, inclusion criteria were data from patients with Mucormycosis. Data obtained were age, gender, COVID history and history of systemic conditions. All obtained data were tabulated into Microsoft Excel documents.

Statistical Analysis

The collected data was tabulated and analysed with the Statistical Package for Social Sciences for Windows, version 20.0 (SPSS Inc., Vancouver style) and results were obtained. Categorical variables were expressed in frequency and percentage. Chi chi-square test was used to test the association between categorical variables. Chi-square tests were carried out using age, and gender as independent variables and COVID history, systemic conditions, intraoral presentation, swelling, and radiological findings as dependent variables. The statistical analysis was done by the Pearson chi-square test. P value < 0.05 was considered statistically significant.

Results

A descriptive study done on the study population shows the distribution of age groups in Figure 1. Patients within the 20-40 years age group were 25%, 41-60 years age group were 56.25%, and 61-80 years age group were 18.75%. The distribution of males and females is shown in Figure 2. Patients with Mucormycosis were predominantly higher in 87.50% in males when compared to 12.50% in females. The distribution of patients with a COVID history is seen in Figure 3. Approximately 56.25% of the patients diagnosed with Mucormycosis gave a history of COVID.

The distribution of patients based on systemic conditions is seen in Figure 4. Most of the patients (50%) were diabetic, were suffering from coronary heart disease (12.50%), hypertensive (6.25%), while some gave no history of any systemic condition (31.25%).

The association of age and systemic conditions is shown in Figure 5. The most common systemic condition in older age groups was found to be diabetes. Systemic conditions were associated with gender and males were found to have more systemic conditions, diabetic was more common 43.75% when compared to females (Figure 6).

The association of age and COVID history of the patients is shown in Figure 7. The most common age group to have given a positive COVID history was 41-60 years 31.25%.

On Associating COVID history with gender, males 50% were predominantly higher when compared to females (Figure 8).

When associating swelling with different age groups, unilateral swelling was found to be more in young adults 56% while bilateral swelling was profound in older people 13%. The chi-square value was found to be significant (0.035). (Figure 9)

Various intraoral findings were presented in patients such as ulcers 6.25%, periodontitis12.5%, abscess 12.5%, palatal swelling 18.75%, and exposed bone 6.25%; when these findings were associated with age, the most common intraoral presentation among all age groups was palatal swelling. (Figure 10)

Radiological investigations revealed the extent of involvement of mucormycosis; maxillary sinus 25%,37.5%, and 18.75% among 20-40 years,41-60 years, and 61-80 years respectively were found to be the most involved among all age groups (Figure 11).

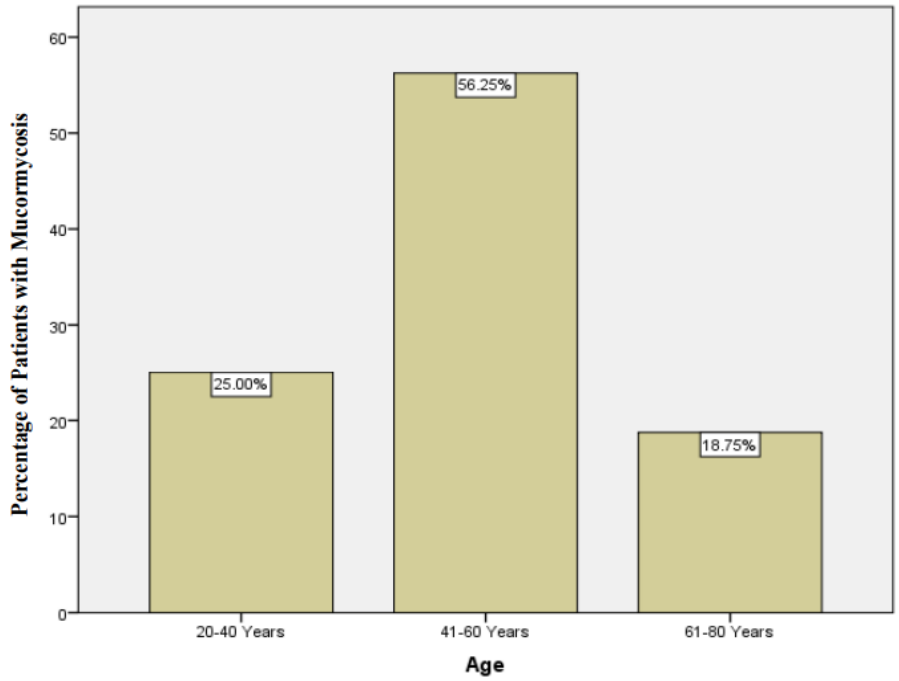

Figure 1. Bar Graph Represents the Distribution of Patients with Mucormycosis Based on Age

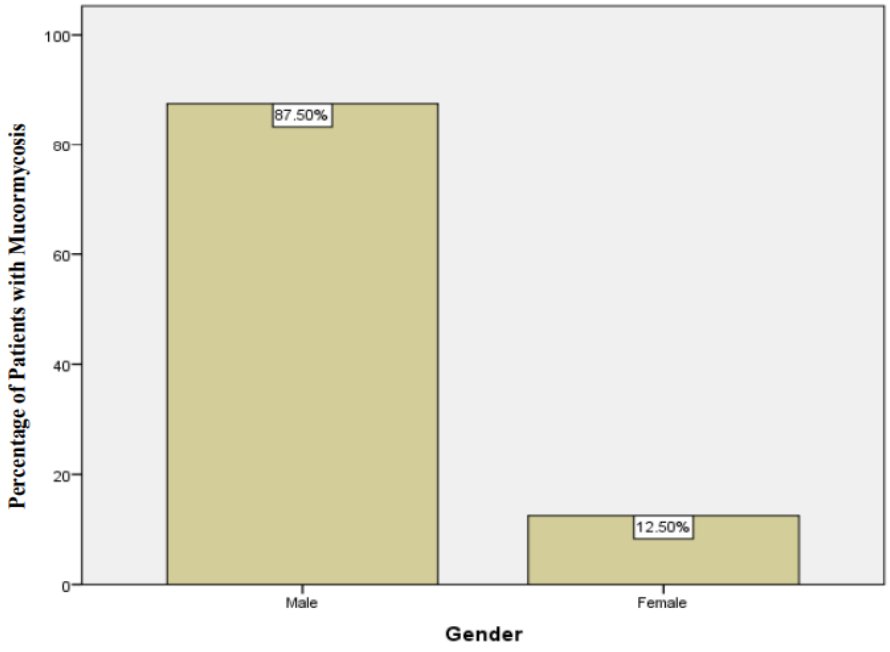

Figure 2. Bar Graph Represents the Distribution of Patients with Mucormycosis Based on Gender.

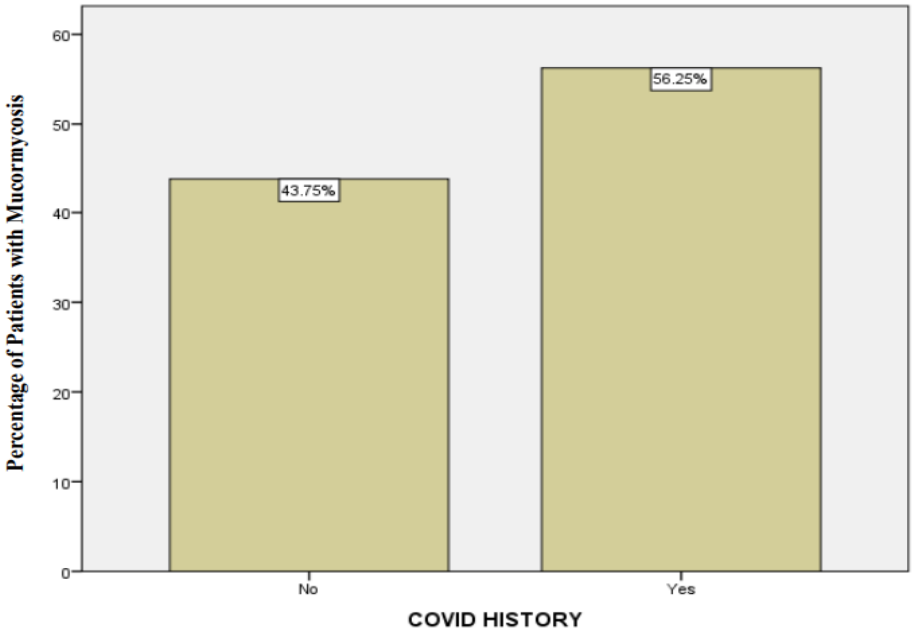

Figure 3. The Bar Graph Represents the Distribution of Patients with Mucormycosis Based on the COVID History of the Patients.

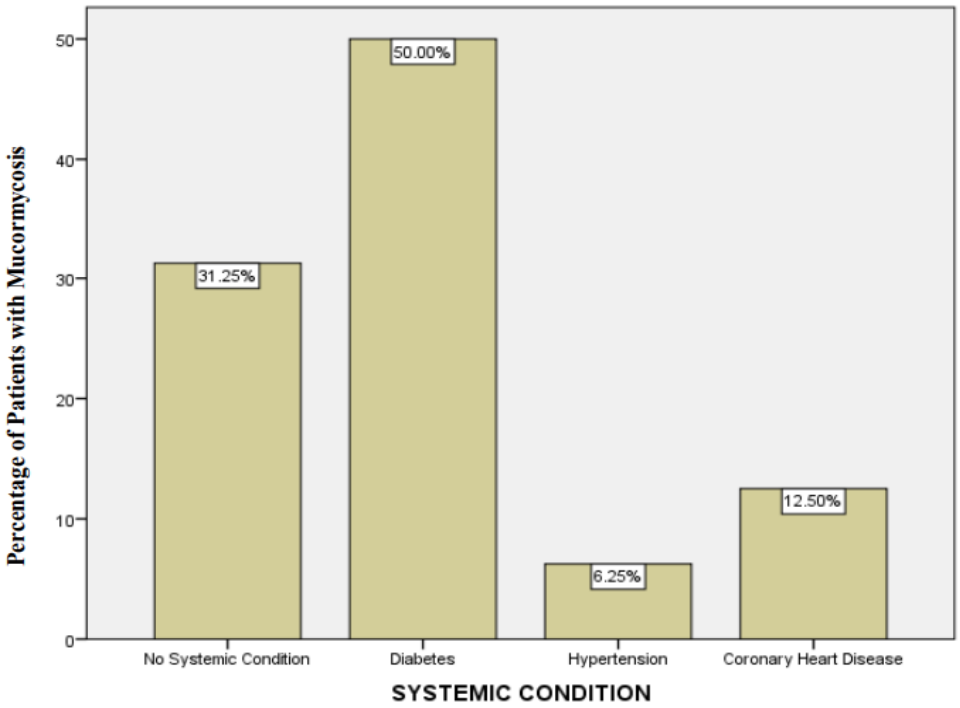

Figure 4. Bar Graph Represents the Distribution of Patients with Mucormycosis Based on the Systemic Conditions of the Patients.

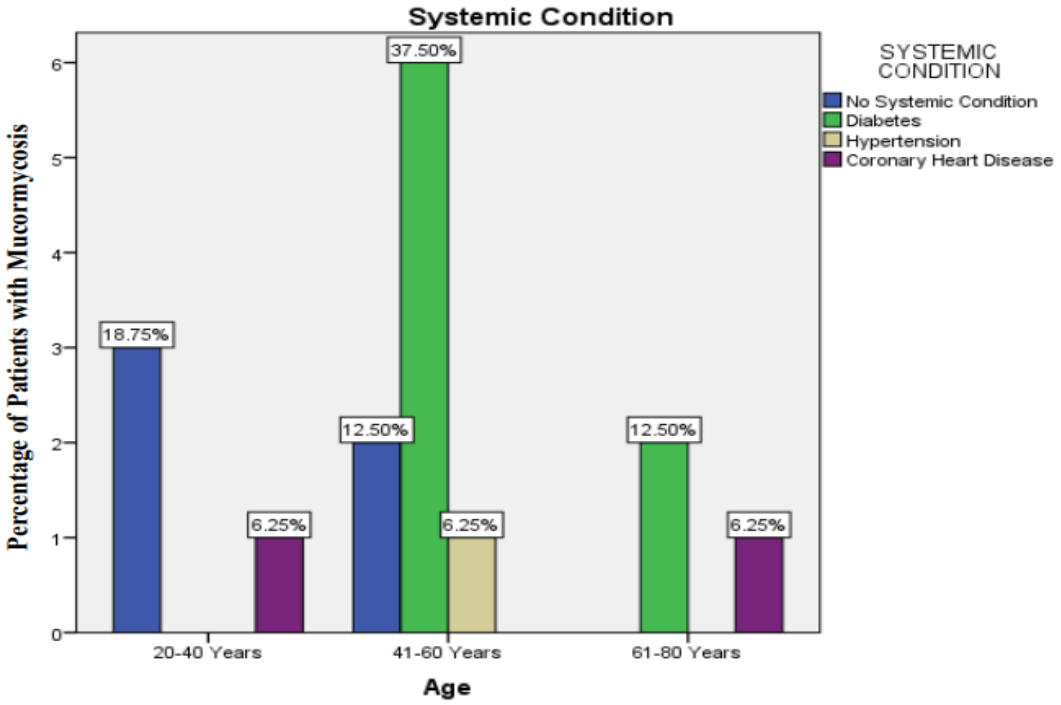

Figure 5. Bar Graph Represents the Association of Age with Systemic Conditions in Patients with Mucormycosis.

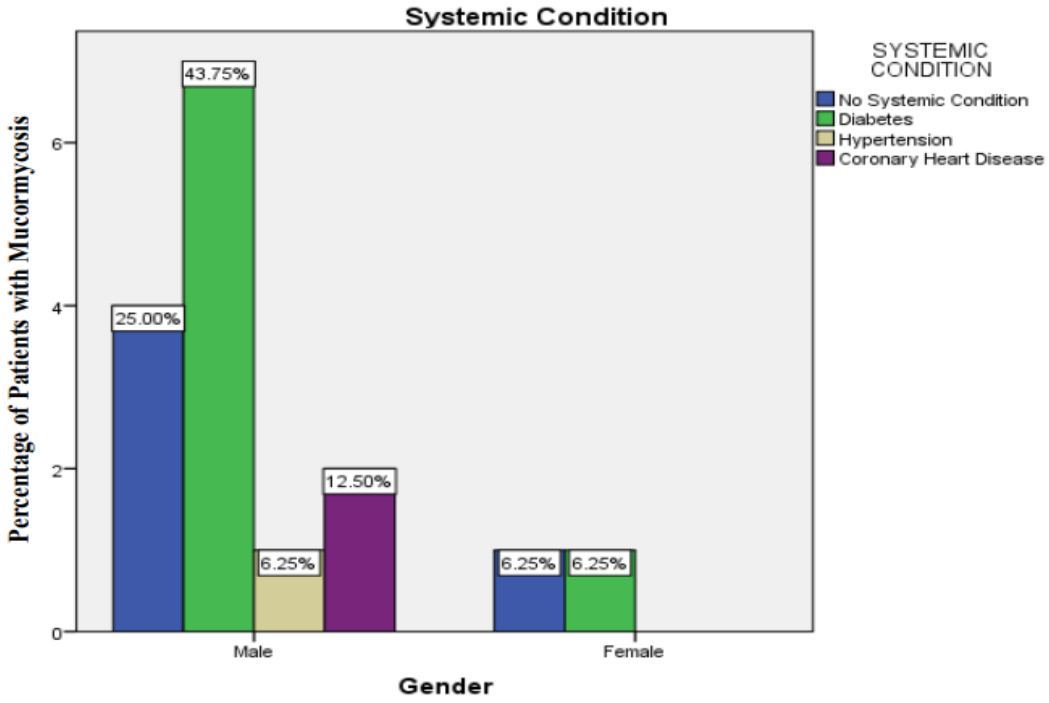

Figure 6. The bar graph Represents the Association of Gender with Systemic Conditions in Patients with Mucormycosis.

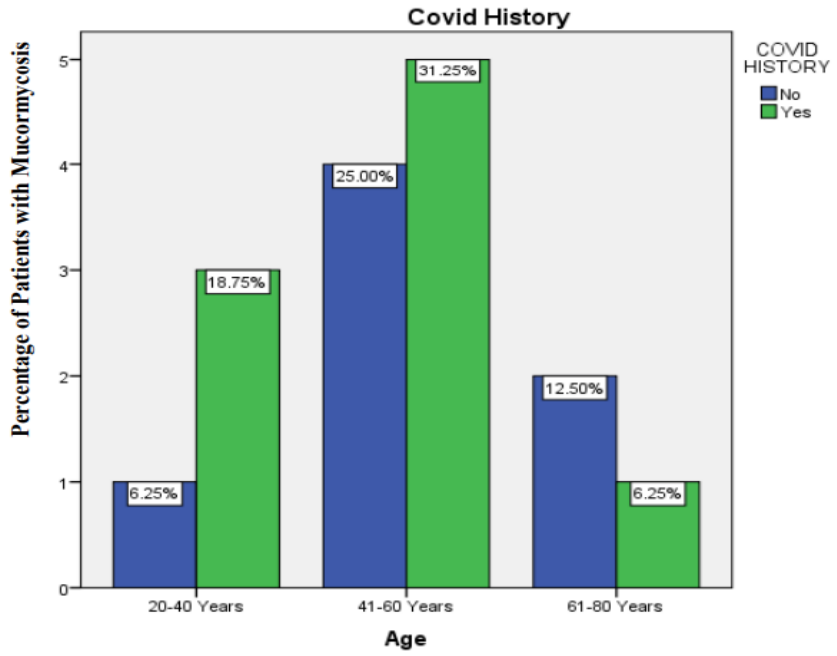

Figure 7. Bar Graph Represents the Association of Age with COVID History in Patients with Mucormycosis.

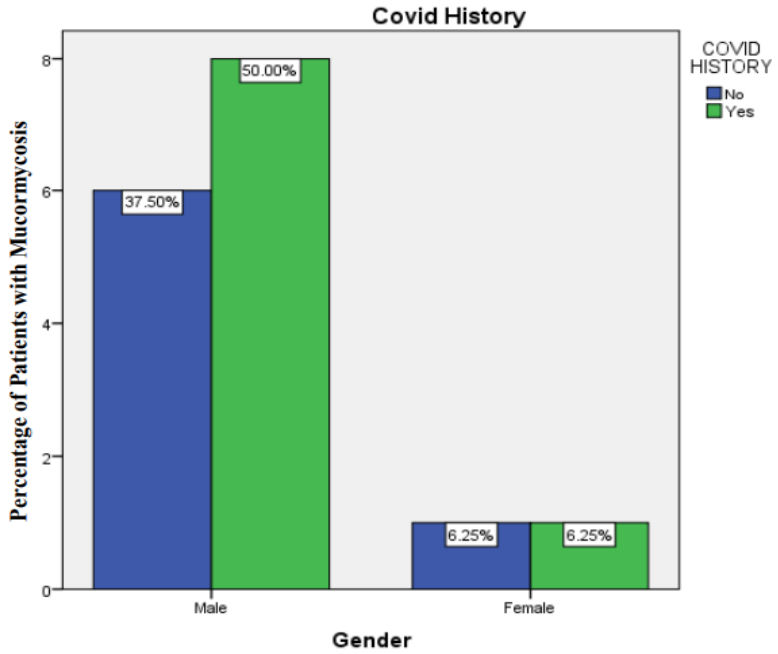

Figure 8. Bar Graph Represents the Association of Gender with COVID History in Patients with Mucormycosis.

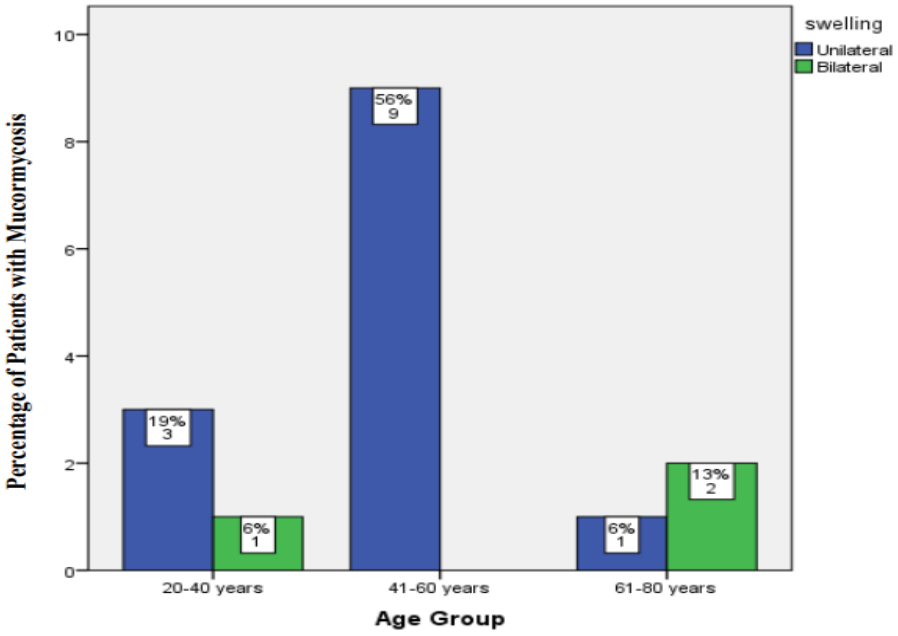

Figure 9. Bar Graph Represents the Association of Age with the Type of Swelling in Patients with Mucormycosis.

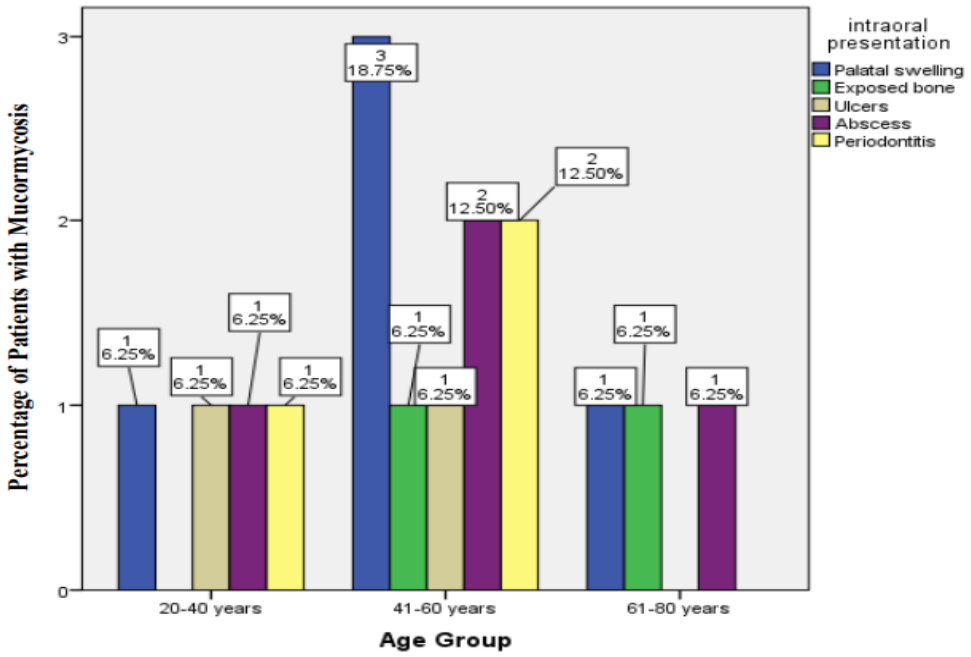

Figure 10. Bar Graph Represents the Association of Age with Different Intra Oral Presentations in Patients with Mucormycosis

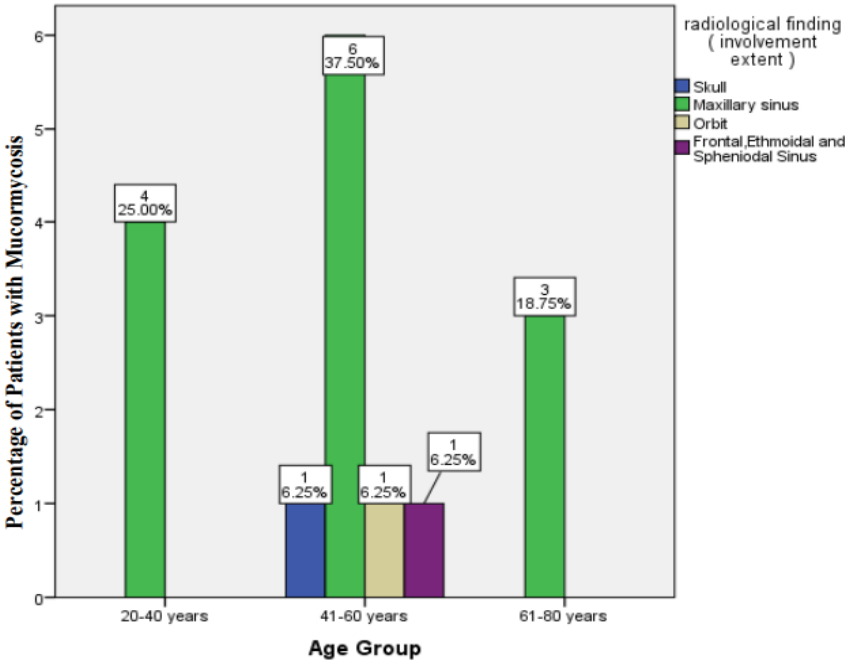

Figure 11. Bar Graph Represents the Association of Age with Radiological Findings (Involvement Extent) in Patients with Mucormycosis.

Discussion

Mucormycosis is a serious but rare fungal infection caused by a group of moulds called mucormycetes. Although mucormycosis is extremely rare in healthy individuals, several immunocompromised conditions predispose it. This includes uncontrolled Diabetes Mellitus (DM) with or without Diabetic Ketoacidosis (DKA), haematological and other malignancies, organ transplantation, prolonged neutropenia, immunosuppressive and corticosteroid therapy [11].

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 the year 2019–2020. In other words, India has the highest cases of mucormycosis in the world [12]. Notwithstanding, India already has the second-largest population with diabetes mellitus (DM) and was the diabetes capital of the world, until recently. Importantly, DM has been the most common risk factor linked with mucormycosis in India [13].

DM remains the leading risk factor associated with mucormycosis globally, with an overall mortality of 46% [14]. In a 2019 nationwide multi-centre study of 388 confirmed or suspected cases of mucormycosis in India before COVID-19, Prakash et al. found that 18% had DKA and 57% of patients had uncontrolled DM [15]. Also in a recent systematic review conducted until April 9, 2021, by John et al. that reported the findings of 41 confirmed mucormycosis cases in people with COVID-19, DM was reported in 93% of cases [16]. These findings are consistent with our findings with a case series of 17 mucormycosis cases, where 50% of cases had DM and 56% of cases had a history of COVID-19. Collectively, these findings suggest a familiar connection between mucormycosis and diabetes.

In our study, the majority of the cases diagnosed with mucormycosis were middle-aged adults, similar findings were seen in a

study done by *Kiran B et al 2015* where the mean age of patients diagnosed with mucormycosis was 40.43 [17].

In a study conducted by *Roden et al. 2005* of 929 patients diagnosed with mucormycosis, the disease was more common in males (65%) as compared to females (35%) [18]. Similar findings were found in our study where males (87.5%) were more commonly affected than females (12.5%).

In recent times mucormycosis and COVID-19 have been linked to each other and there appear to be several triggers that may precipitate mucormycosis in people with COVID-19 [19]. The presence of DM with or without DKA increases the risk of contracting mucormycosis and DM is often associated with increased severity of COVID-19 [20]. COVID-19 often causes a reduction in CD4+ and CD8+ T-cell levels and thus predisposes to secondary or opportunistic fungal infection. Uncontrolled hyperglycemia and precipitation of DKA are often observed due to corticosteroid intake. Low pH due to acidosis is a fertile media for mucor spores to germinate. Moreover, steroid use reduces the phagocytic activity of WBC [21].

In our study, the most common intraoral presentation in patients with mucormycosis was palatal swelling followed by periodontitis, ulcers and abscesses. These findings were reported by Bharat et al 2011, in a case report where a patient reported swelling and ulcerative growth on the right side of the palate [22]. Similar findings were reported in a case by Galitis ON et al 2015, where he observed a dark-brown necrotic ulcer with a white irregular border on the hard palate [23].

The limitation of the study is the smaller sample size. Further studies need to be done to diagnose fungal infections promptly, a high index of suspicion in certain clinical settings cannot be overemphasized. Mucormycosis, an insidious killer, should be an important differential diagnosis in progressive soft tissue infections and deep organ infections. In India, more cases can likely occur in the future due to the increasing immunocompromised population, and it is the need of the hour that all medical fraternities of the health community should have firsthand knowledge of this organism to make a timely diagnosis and save patients' lives.

Conclusion

In this study, we observed that the most common age group diagnosed with mucormycosis was found to be 41-60 years of age (56%) and males were more commonly affected (87.5%). More than 50% of patients gave a history of COVID-19 and 50% were diabetic. The most common intraoral presentation was found to be palatal swelling, and most of the patients had unilateral swelling. Collectively, these findings suggest a familiar connection between mucormycosis, COVID-19 and diabetes.

Conflict of Interest

Authors hereby affirm that there are no conflicts of interest.

Acknowledgement

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