

Epidemiological Insights into Mucormycosis: Demographics and Linkages with Previous COVID-19 Infection in Tertiary CareAtish Kumar B. Gujrathi¹, Sunayana G Kumthekar², Sushant S. Chavan³, Nishikant P. Gadpayale^{4*}¹Associate Professor, Department of Otorhinolaryngology and Head and Neck Surgery, Dr. Shamkarrao Chavan Government Medical College, Nanded Maharashtra, India² Assistant Professor, Department of Community Medicine, Government Medical College, Jalgaon, Maharashtra, India³Assistant Professor, Department of Community Medicine, Shri Bhausaheb Hire Government Medical College, Dhule, Maharashtra, India⁴Assistant Professor, Department of Otorhinolaryngology and Head and Neck Surgery, Government Medical College, Jalgaon Maharashtra, India

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Abstract:**Background:** Fungal rhino sinusitis presents a complex clinical entity, and its association with demographic factors, comorbidities, COVID-19 history, and treatment patterns remains underexplored. This study aims to elucidate these associations to enhance understanding and guide tailored management strategies.**Methodology:** A retrospective cohort study was conducted at a tertiary healthcare centre, analysing demographic variables, history of COVID-19, comorbidities, and treatment received among patients diagnosed with fungal rhino sinusitis. Statistical analyses, including descriptive statistics and regression models, were employed to discern associations.**Results:** Demographic analysis revealed a higher prevalence of fungal rhino sinusitis among individuals aged 41 to 60 years, with a marked predominance in males. Notably, a substantial association was found between fungal rhino sinusitis and a history of COVID-19 infection. Comorbidities, particularly diabetes mellitus, emerged as significant predisposing factors. Treatment patterns revealed widespread use of steroids and oxygen therapy, highlighting their therapeutic relevance.**Conclusion:** The study highlights significant associations between demographic factors, comorbidities, COVID-19 history, and treatment patterns in fungal rhino sinusitis. Tailored interventions for high-risk populations and cautious administration of therapies are warranted. Further research, including prospective studies, is essential to validate these findings and refine clinical approaches.**Keywords:** Fungal rhino sinusitis, demographics, comorbidities, COVID-19, treatment patterns, retrospective cohort study.

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Introduction

Mucormycosis, a rare but severe fungal infection, has emerged as a critical concern amidst the COVID-19 pandemic. The surge in mucormycosis cases, particularly among individuals recovering from or concurrently battling COVID-19, has raised alarms within healthcare systems globally. This alarming trend has prompted a need for comprehensive research to discern the determinants and factors contributing to the increased incidence of mucormycosis, especially among patients admitted to tertiary healthcare centres.

The association between COVID-19 and mucormycosis has been a subject of growing interest due to reported cases worldwide.

Mucormycosis, caused by various fungi belonging to the Mucorales order, manifests predominantly in immunocompromised individuals, and recent studies suggest a potential link between COVID-19 and immunosuppression, making patients more susceptible to opportunistic infections like mucormycosis.[1-7]

Understanding the interplay between COVID-19 infection, its treatment modalities, and subsequent vulnerability to mucormycosis is pivotal for devising effective preventive strategies. Moreover, exploring the demographic profiles of individuals affected by mucormycosis within tertiary healthcare settings is imperative. Factors such as

age, gender, comorbidities, and socio-economic status might influence susceptibility to this fungal infection and its severity among patient cohorts.[8,9]

This research aims to bridge the knowledge gap by examining the determinants of mucormycosis among patients admitted to tertiary healthcare centres. Through a comprehensive analysis encompassing demographic variables and the association with past COVID-19 infection, this study seeks to unravel crucial insights into the epidemiology and potential risk factors contributing to the increased incidence of mucormycosis.

Materials and Methods

This retrospective cohort study was conducted at a tertiary healthcare centre over a period of one year. The study aimed to evaluate the determinants of mucormycosis among patients admitted to the facility, with a particular focus on demographic variables and their association with past COVID-19 infection.

The study included 246 patients diagnosed with mucormycosis during the specified timeframe. Patients aged 18 years and above, admitted to the

tertiary healthcare centre with confirmed mucormycosis, formed the cohort for analysis. Data were retrieved from electronic health records (EHR) and case registries. Demographic information, including age, gender, residential details, and comorbidities, was collected. Additionally, clinical data regarding the occurrence of COVID-19 infection preceding or concurrent with mucormycosis, COVID-19 severity, treatment modalities, and duration from COVID-19 diagnosis to mucormycosis manifestation were documented.

Descriptive statistics were employed to characterize the study population. Factors associated with mucormycosis occurrence were assessed using regression analysis, accounting for potential confounders such as age, gender, comorbidities, and COVID-19-related variables. Subgroup analyses were conducted to explore variations in mucormycosis incidence across different age groups and genders. This study was conducted following the principles of the Declaration of Helsinki. Institutional review board approval was obtained prior to data collection. Patient confidentiality was strictly maintained, and all data were de-identified during analysis.

Results

Table 1: Demographic distribution of Subjects

Demographic Variables		
	No. of patients	Percentage (%)
Age Group		
0-10	0	0.0
11-20	0	0.0
21-30	3	1.2
31-40	35	14.2
41-50	68	27.6
51-60	70	28.5
61-70	47	19.1
71 & above	23	9.3
Gender		
Male	175	71.1
Female	71	28.9

The demographic distribution of patients diagnosed with mucormycosis at the tertiary healthcare centre revealed a notable pattern across age groups. The majority of cases were observed in individuals between the ages of 41 and 60 years, constituting approximately 71.1% of the total cohort.

Specifically, patients aged 41-50 years (27.6%) and 51-60 years (28.5%) represented the largest proportion within the study population. Notably, a smaller yet significant percentage of cases were identified in individuals aged 31-40 years (14.2%), 61-70 years (19.1%), and those aged 71 years and above (9.3%). Patients aged 0-30 years constituted a minimal percentage of the cohort, with no

reported cases among individuals aged 0-10 and 11-20 years.

Regarding gender distribution, the analysis revealed a marked predominance of male patients, accounting for 71.1% of the total cases, while female patients represented 28.9% of the cohort. This distribution of mucormycosis cases across age groups highlights a notable concentration within the middle-age brackets, particularly among individuals aged 41 to 60 years. Additionally, the higher representation of male patients in the cohort emphasizes a potential gender-related susceptibility to mucormycosis within this tertiary healthcare setting.

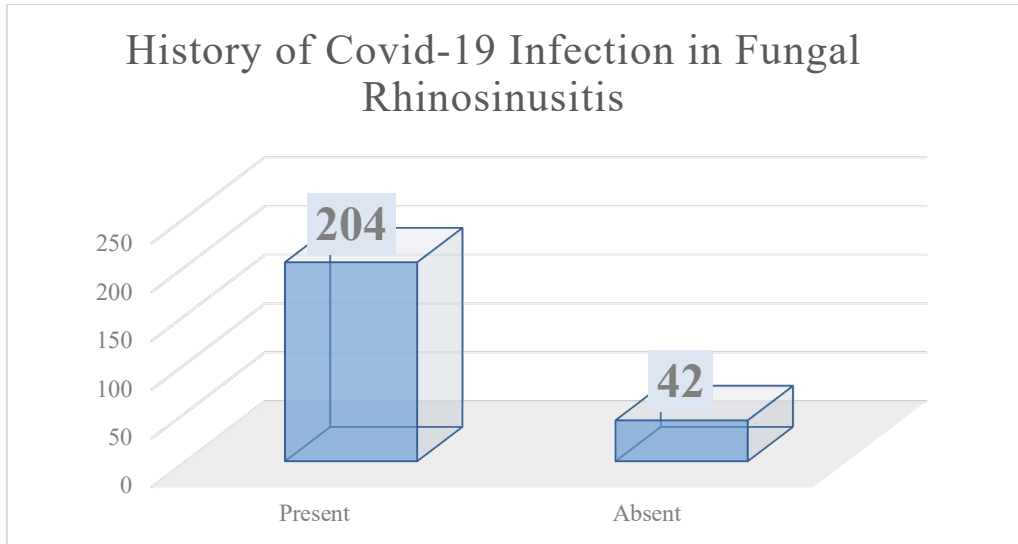


Figure 1: History of COVID-19 infection in relation to fungal rhino sinusitis cases

The association between a history of COVID-19 infection and the prevalence of fungal rhino sinusitis was examined within the patient cohort at the healthcare facility.

Among the patients diagnosed with fungal rhino sinusitis, a substantial majority, comprising 204 individuals (approximately 82.9% of the cohort), had a documented history of COVID-19 infection.

In contrast, 42 patients (17.1%) presented with fungal rhino sinusitis without a prior history of COVID-19 infection.

Further analysis based on gender revealed that of the 204 individuals with a history of COVID-19 infection, 148 were male, accounting for approximately 72.5% of this subgroup, while 56 were female, constituting 27.5% of the total cases with a COVID-19 history. Similarly, among the 42

patients without a history of COVID-19 infection, 27 were male (64.3%) and 15 were female (35.7%).

This observation highlights a substantial prevalence of fungal rhino sinusitis among individuals who had previously encountered COVID-19. The significantly higher proportion of cases with a documented history of COVID-19 infection, compared to those without, underscores a potential association between prior COVID-19 infection and the development of fungal rhino sinusitis. The gender-based distribution within the subgroups further accentuates the higher incidence of fungal rhino sinusitis following COVID-19 among males compared to females. This disparity in gender distribution may suggest a differential susceptibility or varied immunological responses to fungal infections following a preceding COVID-19 infection.

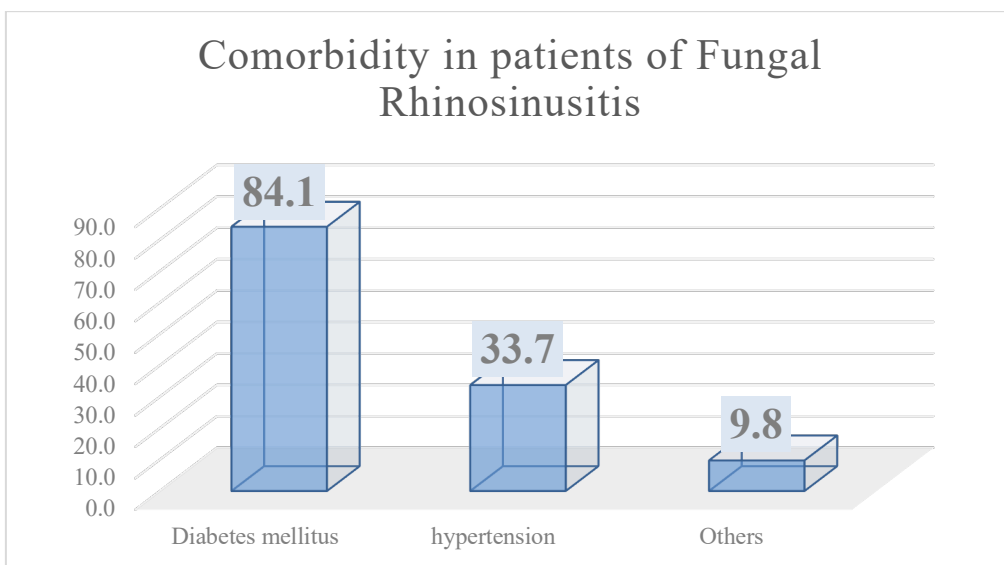


Figure 2: Comorbidities among patients diagnosed with fungal rhino sinusitis

Comorbidities were assessed among individuals diagnosed with fungal rhino sinusitis, revealing a notable prevalence within the patient cohort. Among the total cases, 217 individuals (constituting approximately 88.3% of the cohort) exhibited various comorbid conditions, while 29 patients (11.7%) presented without any documented comorbidity.

Further analysis delineated the specific comorbid conditions prevalent within this cohort. Diabetes mellitus emerged as the most prevalent comorbidity, identified in 207 patients, representing a significant 84.1% of the total cases.

Hypertension was the second most common comorbidity, observed in 83 patients, accounting

for approximately 33.7% of the cohort. Additionally, a smaller proportion of patients (9.8%) presented with other comorbidities, comprising 24 individuals within the study population.

The substantial prevalence of comorbidities, particularly diabetes mellitus and hypertension, among patients diagnosed with fungal rhino sinusitis underscores the potential impact of underlying health conditions on predisposing individuals to this fungal infection.

The notably high incidence of diabetes mellitus within this cohort highlights its prominence as a significant comorbidity associated with fungal rhino sinusitis.

Table 2: The treatments received by subjects during Covid 19 Infection

Treatment Received by Subjects		
	No. of patients	%
Steroid used		
Present	194	78.9
Absent	52	21.1
O2 therapy used		
Present	140	56.9
Absent	106	43.1
Steroid+O2		
Present	137	55.7
Absent	49	19.9

The treatments administered to subjects diagnosed with fungal rhino sinusitis were analysed to ascertain the prevailing therapeutic approaches within the patient cohort. The majority of patients, totaling 194 individuals (approximately 78.9% of the cohort), received steroid therapy as part of their treatment regimen. In contrast, 52 patients (21.1%) did not receive steroid treatment. Regarding oxygen (O₂) therapy, 140 patients (56.9%) underwent O₂ therapy as part of their treatment, while 106 patients (43.1%) did not require such intervention.

Additionally, a subgroup analysis revealed that a substantial proportion of patients, constituting 137 individuals (55.7% of the cohort), received a combined treatment of both steroids and oxygen therapy. Conversely, 49 patients (19.9%) did not receive either steroids or oxygen therapy. The prevalence of steroid administration as a therapeutic intervention for fungal rhino sinusitis suggests its significant role in clinical management. The high utilization of steroids among patients underscores their perceived efficacy or established benefits in mitigating inflammation and controlling the progression of the fungal infection.

Similarly, the application of oxygen therapy, although not as prevalent as steroid use, indicates its relevance in managing the condition, particularly for individuals requiring respiratory

support due to the severity of the fungal rhino sinusitis or associated respiratory compromise. The concurrent use of both steroids and oxygen therapy in a substantial portion of the cohort highlights the clinical approach of combining these treatments to address the multifaceted aspects of fungal rhino sinusitis, emphasizing the complexity and severity of the cases requiring such comprehensive therapeutic measures.

Discussion

The distribution of fungal rhino sinusitis across age groups revealed a substantial prevalence among individuals aged 41 to 60 years, aligning with previous studies emphasizing a higher incidence within this age bracket.[10] Furthermore, the predominance of male patients in our cohort echoes the trend observed in fungal infections, suggesting a potential gender predisposition to such infections.[11,12] The striking association between fungal rhino sinusitis and a history of COVID-19 infection is evident in our findings, with a significant majority of cases having a prior COVID-19 history. This echoes emerging reports suggesting an increased risk of fungal infections, including mucormycosis, following COVID-19.[13] Such associations warrant heightened vigilance among clinicians managing post-COVID-19 complications. Comorbidities, notably diabetes mellitus, emerged as prominent factors associated

with fungal rhino sinusitis. The high prevalence of diabetes among affected individuals corroborates existing literature highlighting diabetes as a major predisposing factor for fungal infections, given its impact on immune function and tissue susceptibility.[14]

Our study revealed prevalent use of steroids and oxygen therapy in managing fungal rhino sinusitis cases. Steroid therapy is often employed to mitigate inflammation, yet its overuse may pose challenges due to potential immunosuppressive effects, potentially exacerbating fungal infections.[15] Oxygen therapy, while crucial in severe cases, necessitates careful administration to prevent further complications.[16] Understanding the demographic trends, association with COVID-19, impact of comorbidities, and treatment patterns in fungal rhino sinusitis is pivotal for tailored patient management. Targeted interventions for high-risk populations, such as those with diabetes or a history of COVID-19, and judicious use of immunosuppressive therapies are warranted.[17]

Conclusion

This study sheds light on the multifaceted aspects of fungal rhino sinusitis, revealing significant associations and patterns within the studied population. The demographic analysis underscored a higher prevalence of fungal rhino sinusitis among individuals aged 41 to 60 years, particularly in males. Moreover, the striking association with a history of COVID-19 infection emphasizes the potential link between COVID-19 and subsequent fungal rhino sinusitis, necessitating heightened vigilance in post-COVID-19 care.

Comorbidities, notably diabetes mellitus, emerged as critical factors significantly associated with fungal rhino sinusitis. The high prevalence of diabetes among affected individuals highlights the importance of managing underlying health conditions to prevent fungal infections.

Treatment patterns revealed widespread use of steroids and oxygen therapy in managing fungal rhino sinusitis cases. While these treatments play pivotal roles, their judicious use is crucial to prevent potential complications and adverse outcomes. Understanding these findings holds implications for clinical practice. Tailored interventions for high-risk populations, comprehensive management of comorbidities, and cautious administration of immunosuppressive therapies are crucial in optimizing patient outcomes.

The study underscores the need for further research, including prospective multicentre studies, to validate these findings and delve deeper into immune responses, treatment efficacy, and long-term outcomes in fungal rhino sinusitis. In

conclusion, the findings from this study provide valuable insights into the demographic, clinical, and therapeutic aspects of fungal rhino sinusitis. Utilizing this knowledge can aid healthcare practitioners in refining treatment protocols and optimizing patient care for better outcomes in fungal rhino sinusitis management.

Limitations

This study's retrospective nature and single-centre design might limit generalizability. Additionally, certain confounders and unmeasured variables could influence outcomes, warranting cautious interpretation of the findings.

References

1. A multicentre observational study on the epidemiology, risk factors, management and outcomes of mucormycosis in India - PubMed [Internet]. [cited 2023 Dec 22]; Available from: <https://pubmed.ncbi.nlm.nih.gov/31811914/>
2. Rawandale N, Jain J, Saple P, Chavan S. Effectiveness of Inj. Remdesivir in treatment of Covid 19 infection at a tertiary care hospital International Journal of Health and Clinical Research. 2023;
3. Epidemiology and Diagnosis of Mucormycosis: An Update - PMC [Internet]. [cited 2023 Dec 22]; Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7711598/>
4. Sen M, Honavar SG, Bansal R, Sengupta S, Rao R, Kim U, et al. Epidemiology, clinical profile, management, and outcome of COVID-19-associated rhino-orbital-cerebral mucormycosis in 2826 patients in India – Collaborative OPAI-IJO Study on Mucormycosis in COVID-19 (COSMIC), Report 1. Indian Journal of Ophthalmology 2021; 69(7):1670.
5. Mucormycosis in COVID-19: A systematic review of cases reported worldwide and in India - PubMed [Internet]. [cited 2023 Dec 22]; Available from: <https://pubmed.ncbi.nlm.nih.gov/34192610/>
6. (PDF) An epidemiological study to determine demographic factors influencing COVID-19 IgG antibody production among the adult population of urban area in Malegaon, Maharashtra - A cross sectional study [Internet]. [cited 2023 Dec 22]; Available from: https://www.researchgate.net/publication/364101394_An_epidemiological_study_to_determine_demographic_factors_influencing_COVID19_IgG_antibody_production_among_the_adult_population_of_urban_area_in_Malegaon_Maharashtra_-_A_cross_sectional_study?tp=eyJjb250ZXh0Ijp7ImZpcnN0UGFnZSI6InByb2ZpbGUiLCJwYXllIjoicHJvZmlsZS9fQ

7. Maini A, Tomar G, Khanna D, Kini Y, Mehta H, Bhagyasree V. Sino-orbital mucormycosis in a COVID-19 patient: A case report. *Int J Surg Case Rep* 2021; 82:105957.
8. Rising incidence of mucormycosis in patients with COVID-19: another challenge for India amidst the second wave? - *The Lancet Respiratory Medicine* [Internet]. [cited 2023 Dec 22]; Available from: [https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(21\)00265-4/fulltext](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00265-4/fulltext)
9. Chavan S, Suryawanshi M, Pagar V, Patil S, Kinge A. COVID-19 breakthrough infection among vaccinated individuals: A cross-sectional study. *Asian Journal of Medical Sciences* 2022; 13:8–13.
10. Fungal disease in the immunocompromised host - PubMed [Internet]. [cited 2023 Dec 22]; Available from: <https://pubmed.ncbi.nlm.nih.gov/9098638/>
11. Sex and Gender Impact Immune Responses to Vaccines among the Elderly - PMC [Internet]. [cited 2023 Dec 22]; Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4630198/>
12. Patil S, Chavan S, Kinge A, Pagar V. A study to determine adverse event following immunization using COVISHIELD vaccine for prevention of COVID-19 infection in a field practice area of urban health center. *Asian Journal of Medical Sciences* 2022; 13:1–6.
13. Sen M, Honavar SG, Bansal R, Sengupta S, Rao R, Kim U, et al. Epidemiology, clinical profile, management, and outcome of COVID-19-associated rhino-orbital-cerebral mucormycosis in 2826 patients in India - Collaborative OPAI-IJO Study on Mucormycosis in COVID-19 (COSMIC), Report 1. *Indian J Ophthalmol* 2021; 69(7):1670–92.
14. The endothelial cell receptor GRP78 is required for mucormycosis pathogenesis in diabetic mice - PMC [Internet]. [cited 2023 Dec 22]; Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2877958/>
15. Burden of fungal infections in Qatar - PubMed [Internet]. [cited 2023 Dec 22]; Available from: <https://pubmed.ncbi.nlm.nih.gov/26449507/>
16. Chronic Sinusitis - StatPearls - NCBI Bookshelf [Internet]. [cited 2023 Dec 22]; Available from: <https://www.ncbi.nlm.nih.gov/books/NBK441934/>
17. Mucormycosis in India: unique features - PubMed [Internet]. [cited 2023 Dec 22]; Available from: <https://pubmed.ncbi.nlm.nih.gov/25187095/>