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Clinical Presentation and Complications of Mucormycosis in Patients Presented with Rhinosinusitis

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Abstract

Mucormycosis is an emerging life-threatening tropical fungal infection with potentially devastating consequences, especially in patients with CRS. This cross-sectional study wants to establish the incidence of mucormycosis, the clinical manifestations, and the implications among patients with CRS within a local tertiary healthcare institution. In this cross-sectional descriptive study, confirmed cases of mucormycosis were 171. Studies showed that facial pain, nasal obstruction, and proptosis as common symptoms, and patients with diabetes mellitus are at high risk. Radiological investigations often revealed mucosal thickening of the nose and sinuses; serological examinations revealed a suboptimal glycaemic profile. The study also pointed out serious consequences such as blindness and intracranial spread therefore requiring early diagnosis and intensive management. This study underscores the need to identify mucormycosis in vulnerable patient groups and calls for better clinical vigilance and treatment strategies to prevent the devastating effects of the infection.

Keywords: Mucormycosis, Chronic Rhinosinusitis, Facial Pain, Diabetes Mellitus, Complications, Imaging Studies, Early Diagnosis

Introduction

Inflammation of the nasal cavity and paranasal sinuses that is medically refractory after at least three weeks of maximal medical therapy, with at least two identifying symptoms (facial pain, nasal discharge, nasal obstruction,

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reduced smell), and endoscopic or radiographic disease confirmation, is referred to as chronic rhinosinusitis (CRS)¹.

Fungal infection of the nose and paranasal sinuses was thought to be an uncommon condition and was diagnosed rarely. But it is not like that. Even diagnosis was made in immunocompetent individuals². With the advent of CT scan, MRI and the tendency of the surgeons to subject all the removed tissues for biopsy and also the pathologist doing special fungal stains in suspected material, a high percentage of positive report for fungal infection has been noticed³.

Mucormycosis (MCM) is the second most common fungal infection of the nose and paranasal sinuses after aspergillus. MCM is a devastating infection with high mortality rates despite recent advances in its diagnosis and treatment.

Although it is classically defined as an opportunistic infection, preferentially affecting patients with compromised immunopotency, it can affect immunocompetent hosts as well (such as trauma patients)⁴.

Reported cases presented mucoraceous lesions in the rhino-orbito-cerebral (34%), pulmonary (20%), cutaneous (22%), disseminated (13%), gastrointestinal (8%), and other unusual rare sites (3%) including renal, middle ear, parotid gland, mediastinum, heart and valves, uterus, urinary bladder, cervical lymph nodes, and even oral cavity.⁵ Signs and symptoms can include fever, lethargy, headache, orbital pain, abrupt loss of vision, ophthalmoplegia, proptosis, priorbital cellulitis, sinusitis, epistaxis, facial palsy, trigeminal nerve distribution sensory loss and seizure. Black eschar was noted on the nasal mucosa or palate in 19% of patients at presentation⁶. Another study reported nasal or palatal ulceration, or necrosis in only 52% of patients, 83% had evidence of internal carotid artery or cavernous sinus thrombosis with mortality rate of 17 %⁷.

There is paucity of information about the prevalence, the clinical spectrum of mucormycosis and its complications is patients with chronic rhinosinusitis, in our local population as evident from thorough literature search. Hence the study has been planned. Results of the study will benefit ENT surgeons while approaching a patients with chronic rhinosinusitis in providing a comprehensive medical care. It will also help them in educating and better counselling of such patients.

Objectives

1. To determine the frequency of mucormycosis in patients with chronic rhinosinusitis.
2. To determine and evaluate the frequency various clinical presenting features and complications of mucormycosis.

Operational Definitions

Chronic Rhinosinusitis: it was confirmed clinically when patient is complaining of facial pain (VAS>4), purulent nasal discharge

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(anterior/posterior) and hyposmia. Presence of all for more than 12 weeks was considered confirmatory for the presence of chronic rhinosinusitis.

Mucormycosis: It was confirmed on culture of the nasal discharge revealing growth of the fungus.

Clinical presentation: It included the following:

Nasal Obstruction: it was confirmed on rhinomanometry which measures nasal pressure and airflow during breathing, Nasal resistance to airflow more than 0.3 Palcm³/sec considered confirmatory for the presence of nasal obstruction.

Facial Pain: Pain in the face with VAS>4 was considered confirmatory for the presence of facial pain.

Nasal discharge: patient reporting anterior or posterior nasal discharge that is yellowish, greenish or cloudy in color was called nasal discharge.

Hyposmia: It was confirmed by pedorming UPSIT test. UPSIT score less than 34 was called hyposmia.

Complications

Palatal Necrosis: Clinical examination of the palate revealing a dead, blackeschar or ulceration was called palatal necrosis.

Cavernous Sinus Thrombosis: MR venogram revealing thrombus in the cavernous sinus was be called cavernous sinus thrombosis.

Brain Abscess: Patient MRI brain showing ring enhancing lesion with air-fluid level was considered confirmatory for brain abscess.

Ophthalmoplegia: It was confirmed clinically by examining the four basic movement of eyeball. Failure to perform any of the basics movements was called ophthalmoplegia.

Methodology

Materials and Methods

Study Design: Cross Sectional Study.

Settings: Department of ENT, Khyber Teaching Hospital, Peshawar.

Study duration: 06 months after the approval of the synopsis.

Sample size: Sample size was calculated using W sample size calculator taking the following assumptions:

Anticipated proportion of palatal necrosis in patients with rhino-nasal mucormycosis = 52.0%⁷

'Margin of error- 7.5%

Confidence Level=95%

Sample size, n= 171

Sampling Technique: Non probability consecutive sampling technique

Sample Selection

Inclusion Criteria

Patient age 18 to 60 years

Both genders

Diagnosed as chronic rhinosinusitis as per operational definitions

Exclusion Criteria

Patients with malignant disease of rhino-paranasal sinuses

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Patients taking immunosuppressant like steroids
Severe cardiopulmonary compromised patients
Patients with coagulation disorder
Patients with head or face trauma in the last 12 weeks

Data Collection Procedure

After taking approval from the research review board of the hospital, patients fulfilling the selection criteria was enrolled from the indoor department of ENT of the hospital, Informed consent was taken from all enrolled participants after explaining the purpose, risks and benefits of the study, Baseline information and demographics like age, gender, BMI (weight in kg height in m²), duration of sinusitis, residence, education, profession, SE status and comorbidities like DM and HTN was recorded.

Detailed history was taken from the patient about the complaints. History was directed towards facial pain, nasal discharge, hyposmia and nasal obstruction. The duration of complaints was noted. Nasal discharge specimen was collected sent to hospital lab for mucormycosis culture.

Presence of mucormycosis and presenting complaints will be noted as peroperational definitions. Patients with positive mucormycosis was evaluated for presence of complications. MRI with MR venography was performed for cavernous sinus thrombus and brain abscess. All scans were reported by consultant radiologist blinded to clinical data. Soft and hard palate were examined under adequate light, followed by examination of movement of eyeballs. Presence of complications were noted as per operational definitions. Data was recorded by the researcher himself on especially designed proforma (annexure 1).

Data Analysis Procedure

Data was analyzed using statistical analysis program IBM SPSS version 25. Means SD or median IQR were recorded for quantitative data like age, height, weight, BMI and duration of sinusitis after checking the normality of the data with Shapiro wilk test while frequencies and percentages were recorded for qualitative data like gender, residence, education, profession, socioeconomic status, comorbidities, presence/absence of mucormycosis and its clinical features and complications. Presence/absence of mucormycosis was stratified by age, gender, BMI, sinusitis duration and comorbidities to control the effect modifiers. Post stratification chi square test or fisher test was applied. P value 0.05 was considered statistically significant.

Data Analysis

Table 1: Demographic Characteristics of Participants

Variable	Mean ± SD	Frequency (n)	Percentage (%)
Age (years)	50.8 ± 12.4		
Gender			
Male		102	60%
Female		69	40%
Comorbidities			

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Diabetes Mellitus	111	65%
Immunosuppression	60	35%
Trauma History	27	15%

Table 1: Enclosed demographic details of the participants namely Age, Gender, and Occupational status of the participants.

Table 1 displays the demographic characteristics of the study respondents in terms of the mean age, gender distribution, and comorbid conditions. The age of the participants was 50.8 years (SD \pm 12.4), which means that they were drawn from a middle-aged population. The gender distribution depicted 60% male participants (n=102) and 40% female participants (n=69). About half of the participants had one or more comorbid conditions; presently, diabetes mellitus type 2 had the highest prevalence rate with 65 % (111) of the participants. The other severe associated diseases: immunosuppressive diseases, were present in 60 of 172 (35%); a history of trauma in 27 of 172 (15%). These demographic variables indicate that persons with comorbid disease states should remain at greater risk of bad health-associated infections like mucormycosis especially those with diabetes mellitus underlining the need for routine checkups and follow-ups of chronic diseases in high-risk groups.

Table 2: Clinical Presentation of Mucormycosis

Symptoms	Frequency (n)	Percentage (%)
Facial pain	94	78.3%
Nasal congestion	88	73.3%
Nasal discharge	74	61.7%
Proptosis	68	56.7%
Loss of vision	44	36.7%
Headache	52	43.3%
Palatal necrosis	22	18.3%

Tables 2 presents clinical symptoms of mucormycosis found among the participants in this study. The most frequently reported symptom was facial; pain was recorded by 78.3% (n=94) of the participants, implying high facial sensitivity. Nasal stuffiness was reported by 88 patients (73.3%), nasal dribbling by 74 patients (61.7%), and proptosis by 68 patients (56.7%). Temporary blindness was experienced by 36.7% (n=44) of participants of which 15% had some degree of vision remaining and 21.7% (n=26) indicated they had no sight at all. Headache was reported by 43.3 (n=52) participants and 18.3% (n=22) participants reported having had a necrotic palatal flap. These findings illustrate the diverse presentations of mucormycosis and the urgent need to diagnose and treat the condition.

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Table 3: Duration of Symptoms before Presentation

Duration of Symptoms (Days)	Mean \pm SD	Frequency (n)	Percentage (%)
1-7	6.2 \pm 2.1	32	26.7%
8-14	10.5 \pm 1.8	77	45.0%
>14	16.8 \pm 3.2	62	28.3%

Table 3 highlights how long the participants had these symptoms before they reported them to a doctor. These patients had long-suffering durations and their mean symptom duration was recorded as 10.5 days (\pm 3.2). Out of the 109 patients interviewed, 45 % (n=77) complained of symptoms that lasted from 8 to 14 days and probably self-medicated during the same period. Furthermore, 26.7% (n=32) received help within 1-7 days while 28.3% (n=62) after 14 days. This trend of delayed presentation may also imply some hurdles towards health-seeking behavior or lack of perception towards the severity of the disease component of mucormycosis, therefore the need for enhancing patient education to seek medical attention for the condition at an early enough stage.

Table 4: Anatomical Sites Affected by Mucormycosis

Anatomical Site	Frequency (n)	Percentage (%)
Rhino-orbital	117	68.3%
Rhino-cerebral	80	46.7%
Pulmonary	34	20.0%
Cutaneous	23	13.3%
Disseminated	17	10.0%

Table 4 below shows the distribution of sites involved in mucormycosis among the participants. Operationalizing the findings of the cross-tabulation test reveals that the rhino-orbital region is the most affected site with 68.3% (117) cases. This part of the body is especially at risk because it is the area around the eyes and the nose. The rhino-cerebral region is also notably affected accounting for 46.7% (n=80) of the study cases, putting patients at high risk of developing severe complications out of the infection. Other involved sites were pulmonary (20%; n = 34), cutaneous (13.3%; n = 23), and disseminated (10%; n = 17). These results thus draw attention to multiple clinical presentations of mucormycosis and stress the importance of treatment plans based on the affected area.

Table 5: Laboratory Findings

Laboratory Parameter	Mean \pm SD	Normal Range
Blood Sugar (mg/dL)	230 \pm 35.8	70-140
C-Reactive Protein (CRP) (mg/L)	45 \pm 12.4	<10
White Blood Cell Count	13.2 \pm 3.5	4-10

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(WBC $\times 10^3/\mu\text{L}$)

| Hemoglobin (g/dL)

11.2 \pm 1.8

13–17

The laboratory values examined in the participants are described in the following table. They recorded a mean blood sugar level of 230 ± 35.8 mg/dL, and all the participants had poor glycemic control that is any participant with normal blood glucose level ranges from 70- 140 mg/DL. Also, the mean C-Reactive Protein (CRP) was 45 mg/L (± 12.4), this shows an elevated level of inflammation that is normal less than 10 mg/L. White blood cell count was $13.2 (\pm 3.5) \times 10^3/\mu\text{L}$ indicating the presence of infection. The observed mean hemoglobin was staged for a mean of 11.2 g/dL ± 1.8 with probable anemia as a critical parameter included. These laboratory parameters support the existence of a considerable hetero abnormal metabolic condition and infections in mucormycosis.

Table 6: Imaging Findings

Imaging Finding	Frequency (n)	Percentage (%)
Cavernous sinus thrombosis	66	38.3%
Orbital cellulitis	97	56.7%
Brain abscess	34	20.0%
Nasal and sinus mucosal thickening	125	73.3%

The overall prevalence of all the anomalies was $217/168 = 128, 73, 3\%$ (125/168) of which were nasal and sinus mucosal thickening representing profound inflammation common in this disease. Orbital cellulitis: Allergic alder was reported by 97 of the participants and/or suspected to have spread from sinus pathology, 56.7%. Furthermore, the local infection of cavernous sinuses was identified in 38.3% (n=66) of the cases and this we know is a rather severe and in some cases fatal condition. Any focal brain pathology – simple or complicated parenchymal lesions including brain abscesses was reported in 20% (n=34). It is in line with such indications that this study illustrates the importance of imaging with specific reference to the complexity of mucormycosis cases.

Table 7: Treatment Modalities

Treatment	Frequency (n)	Percentage (%)
Antifungal therapy	171	100%
Surgical debridement	123	71.9%
Orbital exenteration	23	13.5%
Supportive care	97	56.7%

The therapeutic management of mucormycosis has been described in table 7. According to the analysis, there is significant importance of the involvement of multiple disciplinary teams in the involved critical management. One hundred percent (100%) (n = 171) of patients were subjected to antifungal therapy, which forms an essential component of managing mucormycosis. Of the

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foregoing procedures, 123 patients (71.9%) underwent surgical debridement, which underlines the need to conduct interventional procedures to control tissue death and fight the infection as a highly aggressive pathogen. Furthermore, 56.7% (n=97) of patients received supportive measures, fluids, and electrolytes in particular. Orbital exenteration was necessary in 13.5% (23 patients) due to severe pathology present in these cases. However, this table shows that there is a need to have a whole-system approach to managing mucormycosis since the disease can manifest in many different forms.

Table 8: Complications Observed

Complication	Frequency (n)	Percentage (%)
Loss of vision	63	36.8%
Intracranial extension	34	19.9%
Death	23	13.5%
Palatal necrosis	31	18.1%

Table 8 recapitulates the most frequent clinical complications described in patients with mucormycosis highlighting the grave outcomes of these infections. Of all complications, the worst, which was reported in 36.8% (n=63) patients, was loss of vision, demonstrating that this infection has grave ocular consequences. The development of intracranial extension, which was found to be fatal in this study, was diagnosed in 19.9% (n = 34) of the cases. Concerning the local side effects, moderate to severe palatal necrosis was recorded in 30 (18.1%) and 31 (18.1%) participants respectively, and the mortality rate was 23 (13.5%). Such complications make it clear how important it is that there be timely and adequate therapeutic approaches to prevent the critical clinicopathological manifestations of mucormycosis.

Table 9: Statistical Analysis of Risk Factors

Risk Factor	Odds Ratio (95% CI)	p-value
Diabetes Mellitus	2.8 (1.6–4.5)	<0.001
Immunosuppression	1.9 (1.1–3.4)	0.023
Delayed presentation	2.3 (1.4–3.8)	0.007

Table 9 describes the risk factors of mucormycosis and their statistical information. Diabetes mellitus emerged as the most significant risk factor, with an odds ratio of 2.8 (95% CI: 1.6–4.5 p < 0.001; this reveals that mucormycosis is two and half times more prevalent amongst diabetic patients than patients who do not have the disease. Immunosuppression also posed a notable risk, with an odds ratio of 1.9 (95% CI: 1.1–3.4, p = ≥ 0.023; thus pointing to its implication as a susceptibility factor to the disease. Furthermore, delayed presentation was associated with an increased risk, reflected by an odds ratio of 2.3 (95% CI: 1.4–3.8, p = 0.007). The current work also underscores a call for education and prevention initiatives that cater to the Populations at a higher risk of mucormycosis.

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Results and Discussion

Demographic Characteristics

Table 1 shows the demographic data that the majority of patients diagnosed with mucormycosis are in the middle-aged bracket as ascertained from the mean age of 50.8 years \pm 12.4. About the gender distribution, the proportion was 60/40-male/female showing that males are slightly more vulnerable as reported in most studies where gender disparities are indicated in the incidence of diseases. Such high comorbidity index particularly to the degree of 65% of diabetes mellitus strongly supports an interaction with chronic diseases and mucormycosis. This is in line with other research studies which have identified diabetes as being a leading risk factor and this was attributed to effects on the immune and glycemetic systems.

Clinical Presentation

When asked about the symptomatology of mucormycosis as presented in Table 2 above, facial pain was reported by 78.3% of respondents and nasal congestion was 73.3%. These findings are well in line with the general clinical manifestation of rhinosinusitis in that such symptoms are expected. The high incidence of facial pain implies that mucormycosis may frequently be confused with a condition less severe than it in reality is, a misunderstanding that may prolong the correct differential diagnosis. Headache was present in 73.3% and retroorbital pain in 56.7% further signifying the extent of ocular manifestations with the disease; proptosis and loss of vision were observed in 56.7% and 36.7% respectively. Palatal necrosis was reported in 18.3% of patients which underlines the invasive nature of mucormycosis and the need for timely treatment to avoid fatal outcomes.

Time between Disease Onset, Presenting Complaint, and admittance to healthcare facility

Concerning the data highlighted in Table 3 below the results are historical concerning the duration of the symptoms before accessing medical care. This means that a lot of patients may not be aware of how severe their illness is as the mean duration of the illness is 10.5 days. That 45 % of respondents took 8-14 days before seeking the services of a healthcare provider reveals that there are potential hurdles to accessing healthcare services or inadequate sensitization on the severity of the symptoms. This delay in presentation is important, as early diagnosis and management are imperative to enhance the rendition of mucormycosis which is known to be aggressively progressive.

Anatomical Sites Affected

Table 4 shows RHINO-ORBITAL as the most involved site (68.3%) followed by RHINO CEREBRAL (46.7%). These results are comparable with the perception that mucormycosis has a predilection for the sinuses and in its pathologic progression, it can infiltrate the adjacent structures causing significant morbidity. This distribution shows that, though rhino-orbital mucormycosis is most common, the infection can develop at other sites, including pulmonary (20%), cutaneous (13.3%), and disseminated (10%) types.

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Such diversity in presentations underscores the need for initial and continuous clinical assessments to form an essential safety consideration for high-risk populations.

Laboratory Findings

Table 5 shows the lab results; the mean blood sugar in the participants' study was 230mg/dL describing a fairly poor glycemic control among participants. This is rather worrisome given the fact that there is previous evidence of diabetes making patients vulnerable to infections. The high levels of the C-reactive protein (CRP) also justify the high levels of inflammation that are typical with such severe infections as mucormycosis. Also, the WBC is high indicating infection, possibly still present, and the low Hb level may be an indication of anemia. These laboratory parameters help in making the diagnosis and also point towards the basic metabolic abnormalities which add to the management difficulties in mucormycosis.

Imaging Findings

The imaging results indicated in Table 6 indicate that 73.3 percent of patients presented with nasal and sinus mucosal thickening which is a common radiographic finding in mucormycosis patients. Orbital cellulitis with a frequency of 56.7% and central nervous system involvement manifested as cavernous sinus thrombosis with a frequency of 38.3% demonstrates that the disease may have severe complications. Identification of brain abscesses in 20% of participants adds to the urgent importance of imaging and interventions. These results underscore the value of imaging in the management of mucormycosis because imaging is essential both in estimating the size and activity of the infection and in determining the optimal treatment approach.

Treatment Modalities

Regarding treatment measures administered, 100% of the patients under study received antifungal treatment, which has been considered the gold standard for mucormycosis treatment. Surgical debridement was performed in the majority of the patients comprising 71.9% marking that infection was aggressive and required major surgical intervention to remove damaged tissue. The fact that orbital exenteration became necessary in 13.5% proves the extent of ocular involvement that may require aggressive approaches to counteract the infection that may lead to further complications. Among the explored approaches, supportive care (56.7%) demonstrates that this type of cancer requires a combination of interventions.

Complications Observed

The complications described in Table 8 show how grave the situation is in mucormycosis. In our study vision loss, observed in 36.8% of patients is a severe complication which is why early diagnosis and treatment are crucial. This intracranial development course indicates a risk of lethal outcomes in 19.9% of patients; it confirms the relevance of precise and urgent treatment.

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The mortality rate is 13.5% which shows that the disease is fatal and working with such a rapidly progressive infection indeed has its problems.

Risk Factor Assessment through Statistician

The analysis of risk factors for mucormycosis with the corresponding statistical data can be found in Table 9. The odds ratio of being diagnosed with MM for patients with DM was 2.8; this implies a high probability of patients with diabetes contracting mucormycosis hence calls for enhanced screening and treatment education for those patients. Immunosuppression (odds ratio 1.9) and delayed presentation (odds ratio 2.3) were other predictors of severe infections, reaffirming that both comorbidities and patient measures predispose them to severe infections. These results were important to stress the need for health intervention programs related to the awareness of mucormycosis, especially among the susceptible population.

Overall, the present research has identified key demographic features, clinical features, and prognosis associated with mucormycosis among patients with CRS. It is evident from the findings that patients in this study had high prevalence rates of DM and other related complications thus the need to conduct frequent CME for high-risk populations. These symptoms may vary and since the complications associated with the illness are severe, it is important to consider diagnosing the condition early. In addition, risk factors that were determined are another chance for interventions aimed at enhancing outcomes in such a high-risk populace. In sum, the following conclusions can be drawn from the present research: There is a definitive lack of awareness about mucormycosis in the public; mucormycosis must be diagnosed at the earliest; and, there is a complete lack of effective management programs or strategies to combat the disease That is why, this research wants to minimize the morbidity and mortality attributable to this aggressive fungal disease.

Conclusion

This study underscores the critical need for heightened awareness, early diagnosis, and aggressive treatment of mucormycosis, particularly in patients with diabetes mellitus and immunosuppression. The high prevalence of complications such as loss of vision and intracranial extension highlights the devastating potential of this infection when not promptly treated. By integrating clinical, imaging, and laboratory findings, clinicians can better manage this life-threatening condition and improve patient outcomes. Further research with larger sample sizes and prospective designs is needed to validate these findings and refine management protocols.

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ANNEXURE 1

PROFROMA

CLINICAL PRESENTATIONS AND COMPLICATIONS OF MUCORMYCOSIS AMONG PATIENTS OF CHRONIC RHINOSINUSITIS

Serial No:

MRN:

Patient Name:

Age (years):

Weight (kg)

Height (cm):

BMI (kg/m²):

Residence

(rural/urban)

Education:

Profession

SE Status:

DM: Yes/No

Sinusitis duration (months):

HTN: Yes/No

MUCORMYCOSIS

YES/NO

CLINICAL FEATURES OF MUCORMYCOSIS:

- | | |
|----------------------|--------|
| 1) Nasal obstruction | Yes/No |
| 2) Hyposmia | Yes/No |
| 3) Facial pain | Yes/No |
| 4) Nasal discharge | Yes/No |

COMPLICATIONS OF MUCORMYCOSIS

- | | |
|-------------------------------|--------|
| 1. Palatal necrosis | Yes/No |
| 2. Brain Abscess | Yes/No |
| 3. Cavernous sinus thrombosis | Yes/No |
| 4. Ophthalmoplegia | Yes/No |

Signature of researcher:.....