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A CLINICAL STUDY OF INVASIVE FUNGAL RHINOSINUSITIS WITH RESPECT TO MANAGEMENT AND OUTCOME

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Abstract

Introduction: Invasive fungal rhinosinusitis (IFRS) is a rapidly progressive life-threatening condition. The invasive nature of the fungus causing invasive fungal rhinosinusitis (IFRS) is characterized by rapid disease extension into blood vessels, resulting in vasculitis with thrombosis, haemorrhage, tissue infarction, and central nervous system involvement. Fungal rhinosinusitis (FRS) can be divided depending on fungal invasion of the mucosal layer into two categories based on histopathological findings: invasive and non-invasive.

Materials and Methods: In the Retrospective arm, records of all patients already treated for invasive fungal sinusitis at our hospital will be traced from the medical records section and from the department records in which the details of these patients are entered, the observations will be used for obtaining data. No active intervention or invasive procedure will be performed for the study. Details of findings of post-operative diagnostic nasal endoscopies done as indicated post operatively will also be collected from the ENT Register. As it will be difficult to contact these patients, we request for waiver of informed consent. Patient's personal information will be confidential and his/her identity will not be revealed in any way. These patient's data will be checked only till discharge.

Results: This is retrospective study consisting of 30 patients of either sex in which we study various clinical presentations of invasive fungal sinusitis and outcomes of medical and surgical management of invasive fungal sinusitis. In our study of the 30 patients the youngest patient was 28 years old and the oldest was 72 years. The maximum number of patients i.e. 20 were between 51 to 60 years, 6 patients in the age group of 41-50 years. The mean age of patients was 53 years. In our study, diabetes mellitus was the most commonly found comorbidity being present in 23 patients (73%). Our study also showed 6 patients were in state of chronic renal failure with raised blood urea level and creatine level. 2 patients were leukaemia patients. 2 were immunocompromised patients secondary to HIV.

Conclusion: Invasive fungal rhinosinusitis is a life-threatening disease largely affecting immunocompromised patients and has a fatal outcome if not managed timely and intensively. An early diagnosis favours a better prognosis, disease clearance with less destructive and morbid debridement salvages vision of the patient and ultimately leads to a better quality of life and a shorter duration of hospital stay. The emphasis must be laid on the management being multidisciplinary and not just surgical alone as the patients present with multiple comorbities and complications due to the disease.

Key Words: Invasive fungal rhinosinusitis, prognosis, leukaemia, fungal sinusitis.

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INTRODUCTION

Invasive fungal rhinosinusitis (IFRS) is a rapidly progressive life-threatening condition. The invasive nature of the fungus causing invasive fungal rhinosinusitis (IFRS) is characterized by rapid disease extension into blood vessels, resulting in vasculitis with thrombosis, haemorrhage, tissue infarction, and central nervous system involvement. Fungal rhinosinusitis (FRS) can be divided depending on fungal invasion of the mucosal layer into two categories based on histopathological findings: invasive and non-invasive.[1] Hora in 1965 recognized two categories of fungal rhinosinusitis (FRS): non-invasive, behaving clinically like chronic bacterial sinusitis, and invasive, in which the infection results in a mass that behaves like a malignant neoplasm, eroding the bone and spreading into adjacent tissue. Jahrsdoerfer et al., 1979 further confirmed the invasive nature of the disease by histopathology. deShazo in 1997 proposed a new classification for invasive fungal rhinosinusitis (IFRS) based on clinical condition, immune status, histopathology, and fungal infection: acute (fulminant) invasive, granulomatous invasive and chronic invasive types.[2]

Nowadays, the most commonly accepted classification divides fungal rhinosinusitis (FRS) into invasive and non-invasive diseases based on histopathological evidence of tissue invasion by fungi. The non-invasive diseases include saprophytic fungal infestation, fungal ball and allergic fungal rhinosinusitis.[3] Invasive fungal rhinosinusitis (IFRS) include acute invasive (fulminant) fungal sinusitis, chronic invasive fungal sinusitis, and granulomatous invasive fungal sinusitis. Mucor, Rhizopus, Rhizomucor, Absidia and other Mucorales fungi that belong to the division Zygomycota, or Aspergillus species that belong to the division Ascomycota may be responsible for the disease.[4] These organisms are found saprophytically in decomposed substances, soil and fruits, and in the throats, faeces and as commensal in the nasal cavity of healthy individuals; but they may become pathogenic in susceptible individuals especially who are immunocompromised patients and with uncontrolled diabetes mellitus. High glucose levels in diabetic patients facilitate tissue invasion.[5]

This is a retrospective and prospective study in which we study various clinical presentations and outcomes of medical and surgical management of invasive fungal rhinosinusitis (IFRS) which will help formulate a treatment protocol for this rare but life-threatening condition.

AIMS AND OBJECTIVES

- To study various modes of presentation of invasive fungal rhinosinusitis.
- To study microbiological profile of cases of invasive fungal rhinosinusitis.
- To study various treatment modalities for management of invasive fungal rhinosinusitis.
- To study the role of prompt surgical debridement, medical management with antifungal agents and control of underlying predisposing condition with respect to its influence on the final outcome.
- To study patients with orbital and intracranial extension with respect to management and final outcome.
- To study the various factors that influence the final outcome in these patients.

MATERIALS AND METHODS

Study Design: Retrospective and prospective observational study.

Study Duration: 5 years (5 years retrospective from October 2014 to date of ECARP approval)

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Sample Size: No formal sample size calculation has been done. Based on our records of the last one year, the number of patients with acute invasive fungal rhinosinusitis was 06. Hence, we have kept the sample size as maximum of 30 patients over the period of 5 years.

Method Of Sample Collection

The cases will be collected by consecutive sampling method.

Inclusion Criteria

1. All cases diagnosed with invasive fungal rhinosinusitis on histopathology or microbiological examination.
2. Patients whose age is more than 18 years of age.

Exclusion Criteria

1. Patients who are not giving consent for prospective study.
2. Patients who are lost to follow up hence complete data could not be collected.

The study will be carried out in retrospective arm:

In the Retrospective arm, records of all patients already treated for invasive fungal sinusitis at our hospital will be traced from the medical records section and from the department records in which the details of these patients are entered, the observations will be used for obtaining data. No active intervention or invasive procedure will be performed for the study. Details of findings of post-operative diagnostic nasal endoscopies done as indicated post operatively will also be collected from the ENT Register. As it will be difficult to contact these patients, we request for waiver of informed consent. Patient's personal information will be confidential and his/her identity will not be revealed in any way. These patient's data will be checked only till discharge.

Assessment Parameter

No evidence of disease at 6 months follow up diagnostic nasal endoscopic examination or on radiological examination. Diagnostic nasal endoscopy at 3 weeks, 6 weeks, 3 months and 6months to look for crusting any mucosal changes. Radiological assessment in the form of Computed Tomography or Magnetic Resonance Imaging as indicated will be done in case of any suspicious finding on diagnostic nasal endoscopy as and when required.

Statistical Analysis

The data obtained from all the patients will be entered into a worksheet. The findings of the study will be analysed by appropriate statistical tests. As most of the data is descriptive in nature, like assessing the various etiological factors, radiological findings etc. Frequency distribution tables and percentages will be used. There will be analysis of comparison of the pre- & post-operative effects and surgical outcomes.

RESULTS

This is retrospective study consisting of 30 patients of either sex in which we study various clinical presentations of invasive fungal sinusitis and outcomes of medical and surgical management of invasive fungal sinusitis.

Table No 1: Sex Wise Distribution of Study Group

SEX	FREQUENCY	PERCENT
MALE	20	80
FEMALE	10	20
TOTAL	30	100

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Chart No 1: Sex Wise Distribution of Study Group

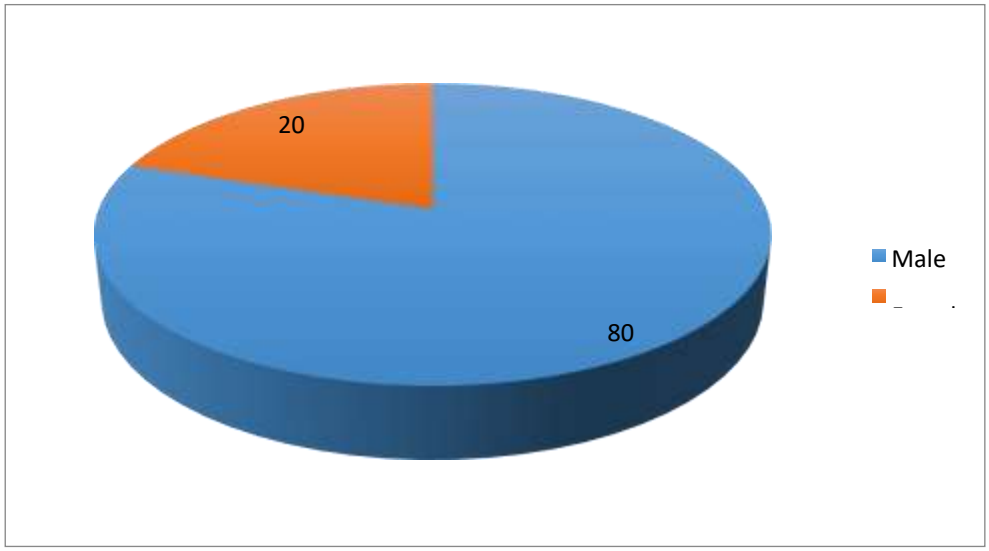

Table No 2: Distribution of Study Group as per Age

AGE	NO. OF PATIENTS
0-10	0
11-20	0
21-30	1
31-40	3
41-50	6
51-60	15
61-70	3
71-80	2

Chart No 2: Distribution of Study Group As per Age

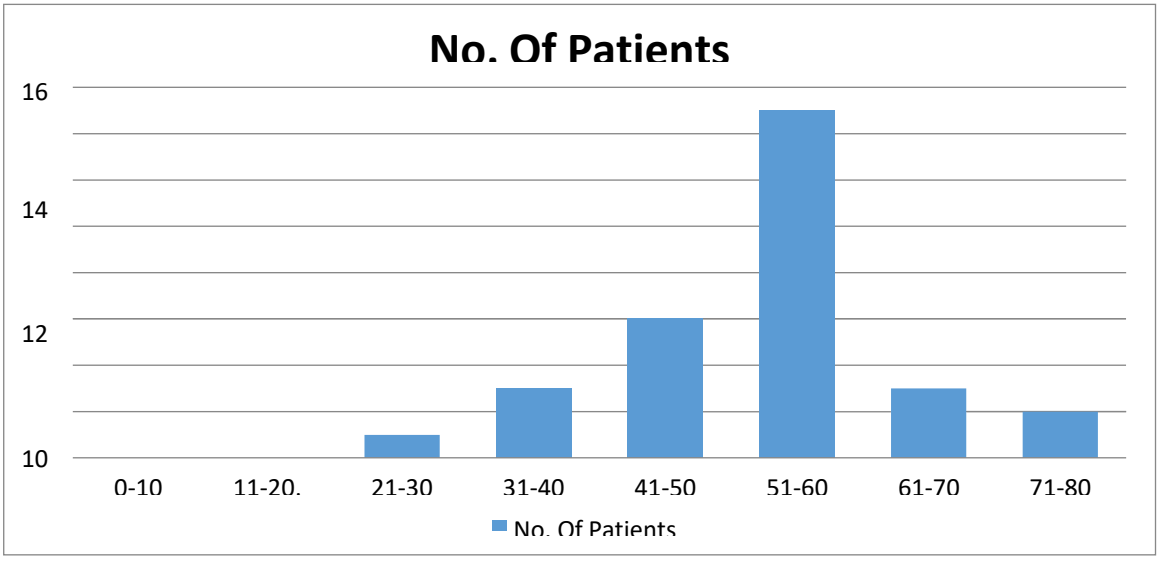

Table No 3: Distribution of Study Group as per co-morbidities

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CO MORBIDITY	FREQUENCY	PERCENTAGE
DIABETES	22	73
MEDICAL RENAL DISEASE	3	10
LEUKAEMIA	3	10
HIV	2	7

Chart No 3: Distribution of Study Group as per co-morbidities

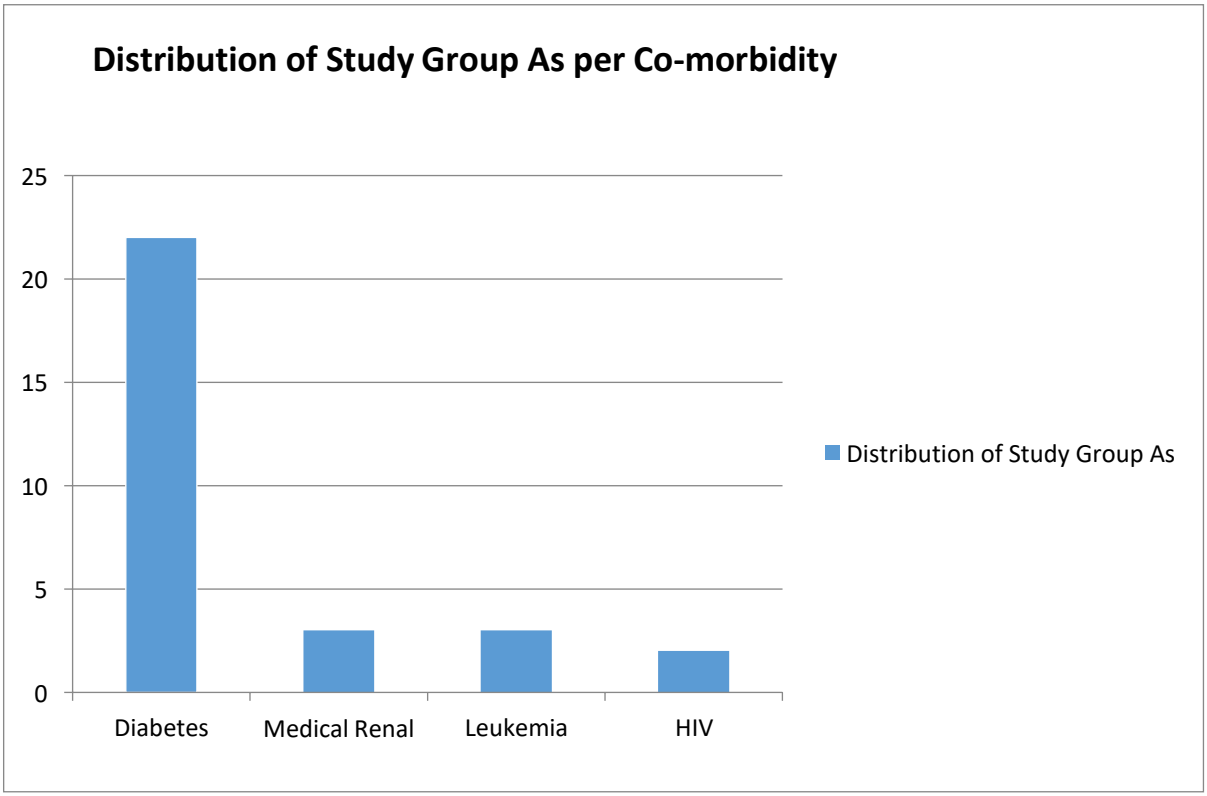

Table No 4: Distribution of Study Group As per Nasal Complaints

NASAL COMPLAINTS	FREQUENCY	PERCENTAGE
NASAL OBSTRUCTION	27	90
NASAL DISCHARGE	21	70
NASAL CRUSTING	24	80

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Chart No 4: Distribution of Study Group As per Nasal Complaints

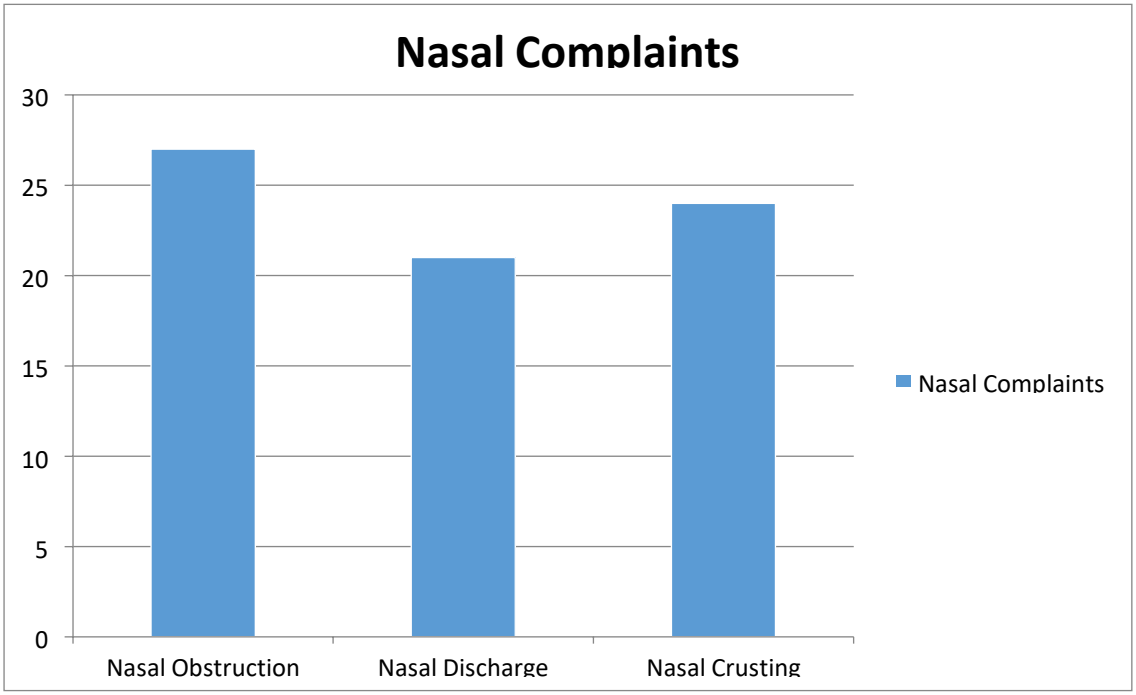

Table No 5: Distribution of Study Group as per Orbital Complaints

ORBITAL COMPLAINTS	FREQUENCY	PERCENTAGE
DIMINUTION OF VISION	15	50
PROPTOSIS	3	10
OPTHALMOPLEGIA	6	20
RETRO ORBITAL PAIN	2	7

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Chart No 5: Distribution of Study Group as per Orbital Complaints

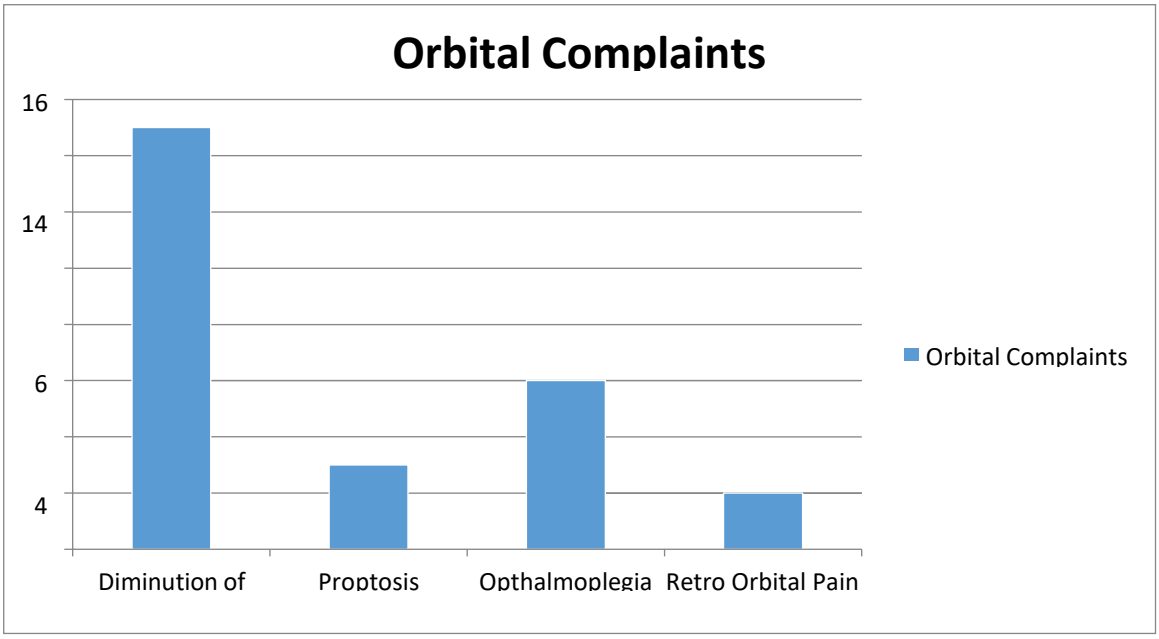

Table No 6: Distribution of Study Group as per Other Complaints

OTHER COMPLAINTS	FREQUENCY	PERCENTAGE
FEVER	21	70
FACIAL SWELLING	12	40
HEADACHE	15	50

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Chart No 6: Distribution of Study Group As per Other Complaints

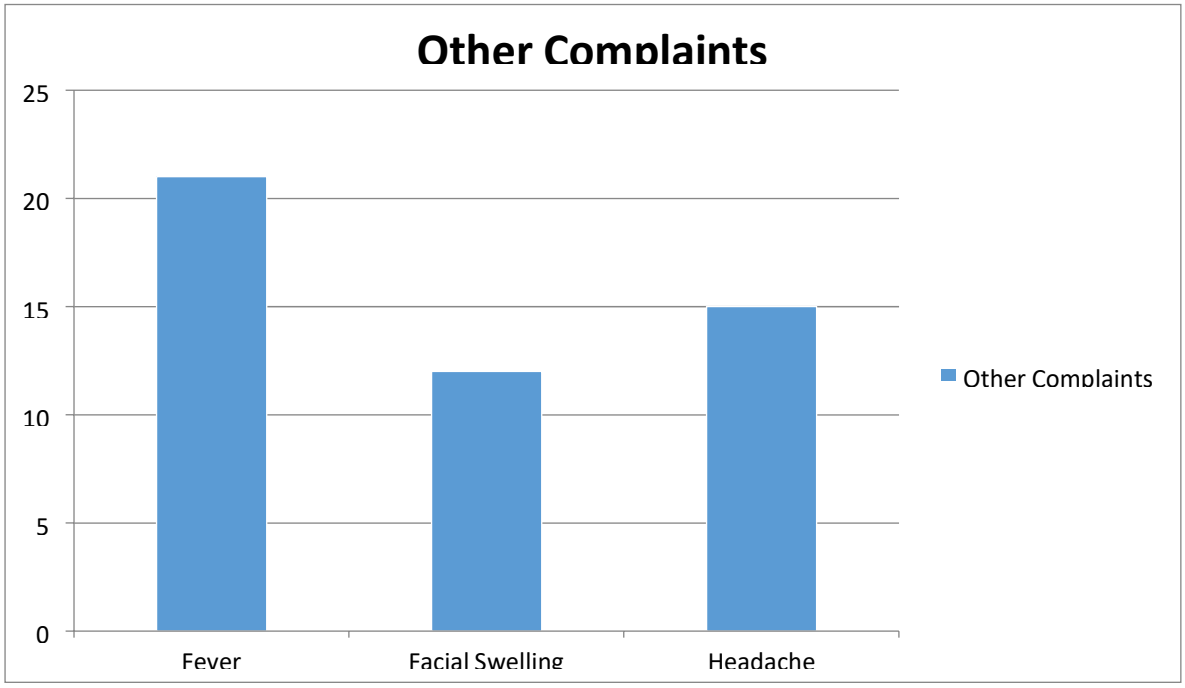

Table No 7: Distribution of Study Group as per Palatal Involvement

PALATAL INVOLVEMENT	FREQUENCY	PERCENTAGE
YES	6	20
NO	24	80

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Table No 8: Distribution of Study Group as per Fungal Species on Culture

FUNGAL SPECIES	FREQUENCY	PERCENTAGE
ASPERGILLUS	10	33
MUCOR	18	60
CANDIDA	0	0
FUSARIUM	2	7

Table No 9: Distribution of Study Group as per Intra-Orbital Extent

INTRA ORBITAL EXTENT	FREQUENCY	PERCENTAGE
NO INVOLVEMENT	15	50
LAMINA PAPYRACEA	9	30
ORBITAL PERIOSTEAL	3	10
ORBITAL APEX	6	20

Table No 10: Distribution of Study Group as per Intracranial Spread

INTRACRANIAL SPREAD	FREQUENCY	PERCENTAGE
YES	6	20
NO	24	80

Table No 11: Distribution of Study Group as per Cranial Site Involvement

CRANIAL SITES	FREQUENCY	PERCENTAGE
CAVERNOUS SINUS THROMBOSIS	2	33.3%
PARA SELLAR INVOLVEMENT	1	16.6
EXTRADURAL INVOLVEMENT	5	83.3
ANTERIOR CRANIAL FOSSA	0	0
BRAIN ABSCESS	1	16.6

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Table No 12: Distribution of Study Group as per CT Scan Findings

CT SCAN FINDINGS	FREQUENCY	PERCENTAGE
MAXILLARY	24	80
FRONTAL	7	23
SPHENOID	12	40
ETHMOID	24	80
MIDDLE TURBINATE	18	60
SEPTAL	9	30
PALATAL INVOLVEMENT	6	20
LAMINA	21	70
INTRACRANIAL	6	20

Table No 13: Analysis of Study group as per Outcome

FUNGAL SPECIES	NO. OF CASES	CURED	RECURRENCE		DEATH (TOTAL)	OVERALL CURED	CURE RATE
			CA SE S	DEATH			
MUCOR	18	13	3	2	2	13	72%
ASPERGILLUS	10	6	2	2	2	6	60%
FUSARIUM	2	2	0	0	0	0	100%

Figure 1: Clinical picture showing ophthalmoplegia and ptosis in a patient ofmucormycosis

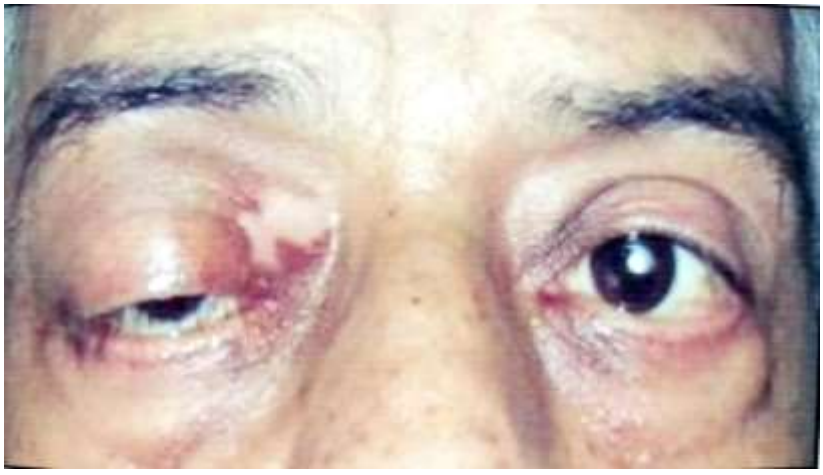

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Figure 2: Clinical picture showing orbital involvement with chemosis andophthalmoplegia in a patient of mucormycosis

Figure 3: Clinical picture showing palatal involvement in a patient ofmucormycosis

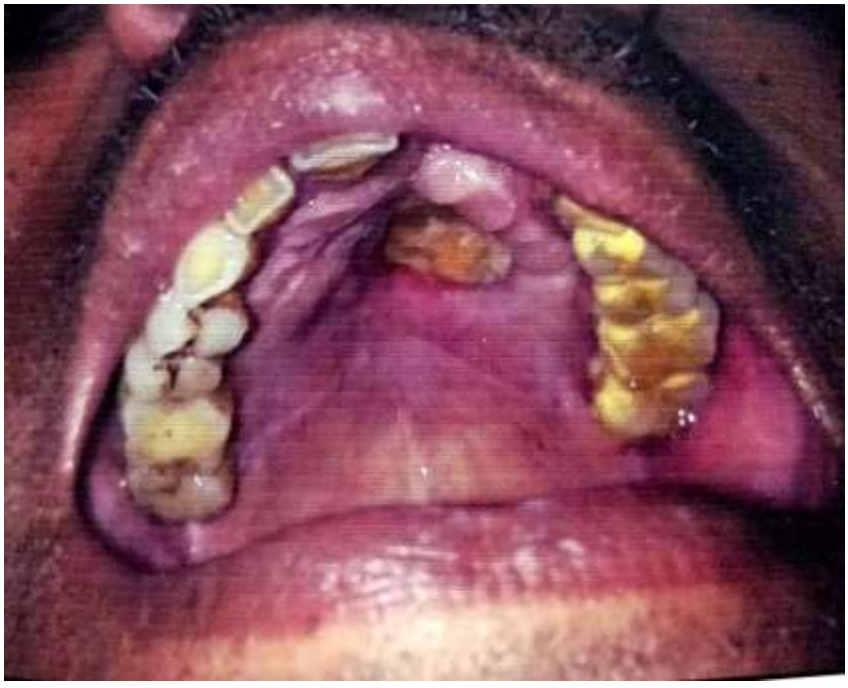

Figure 4: Clinical picture showing facial swelling in a patient of mucormycosis

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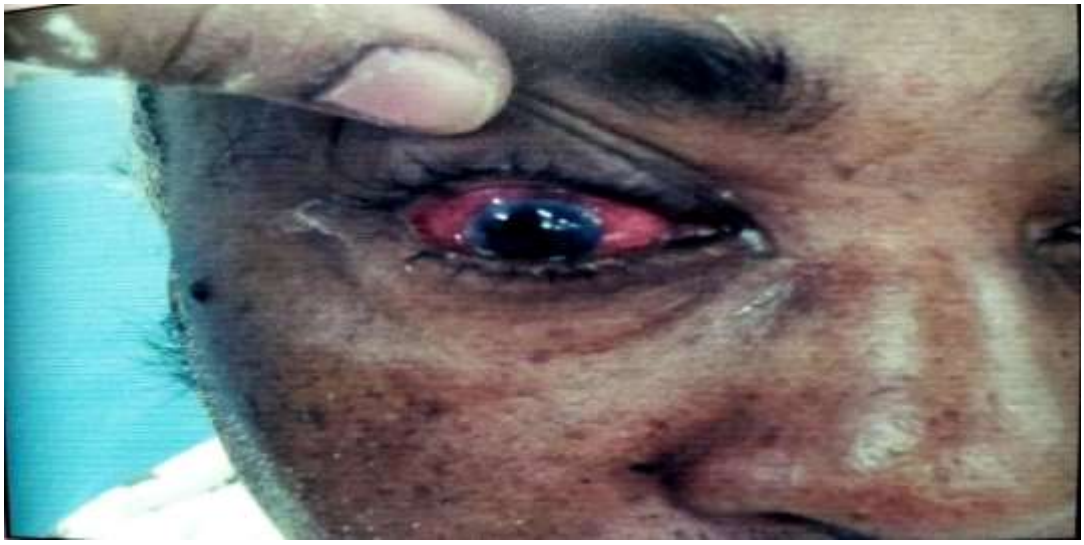

Figure 5: Clinical picture showing orbital involvement with chemosis andophthalmoplegia

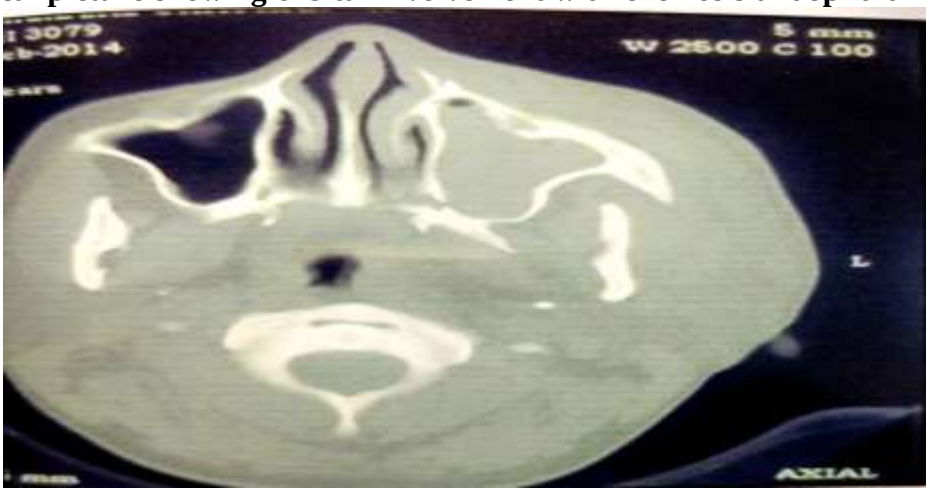

Figure 6: Computed tomography showing maxilla involvement in a patient ofmucormycosis

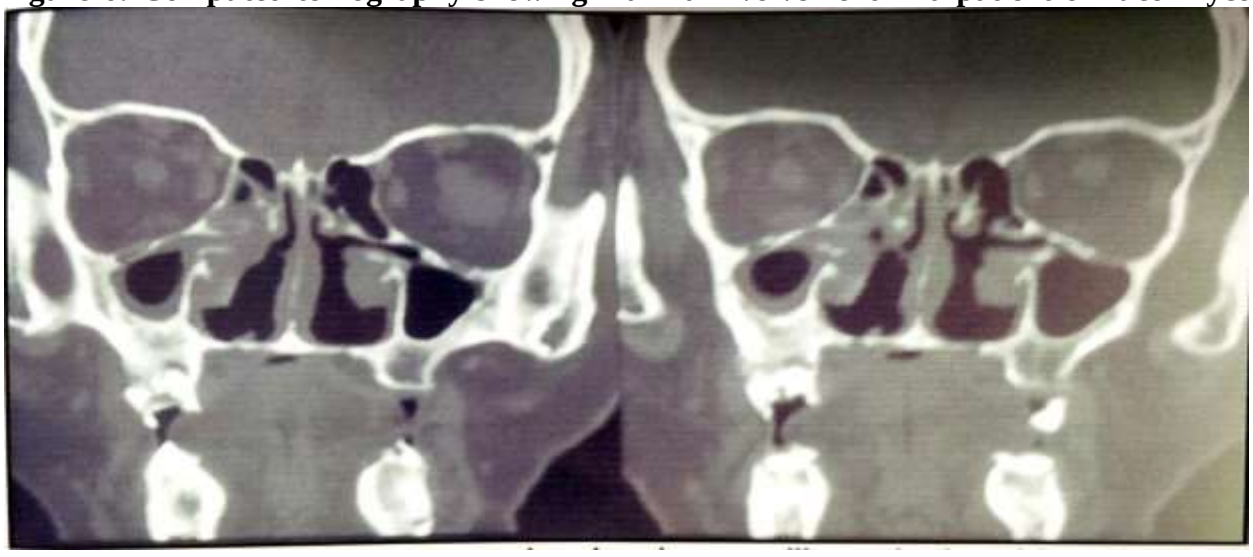

Figure 7: Computed tomography showing maxilla and Ethmoid involvement in a patient of mucormycosis

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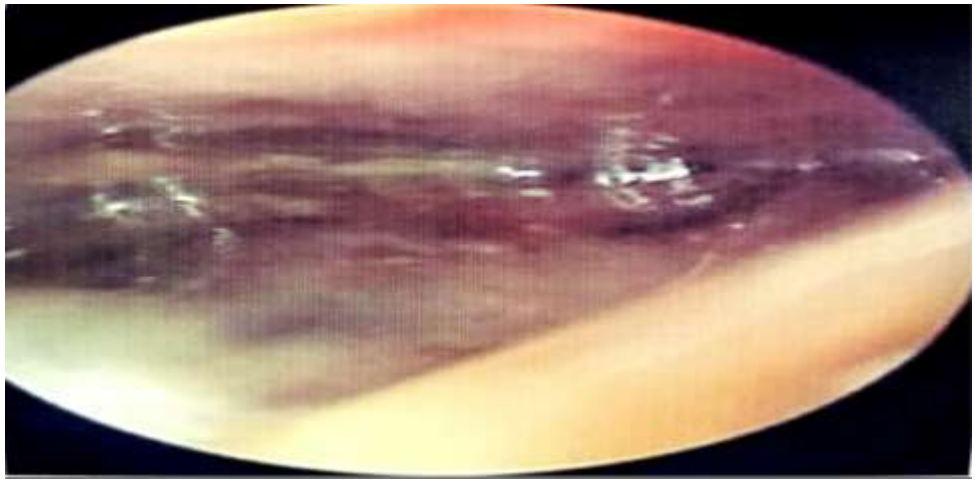

Figure 8: Intraoperative endoscopic picture showing mucosal pallor and mucopus in a patient of mucormycosis

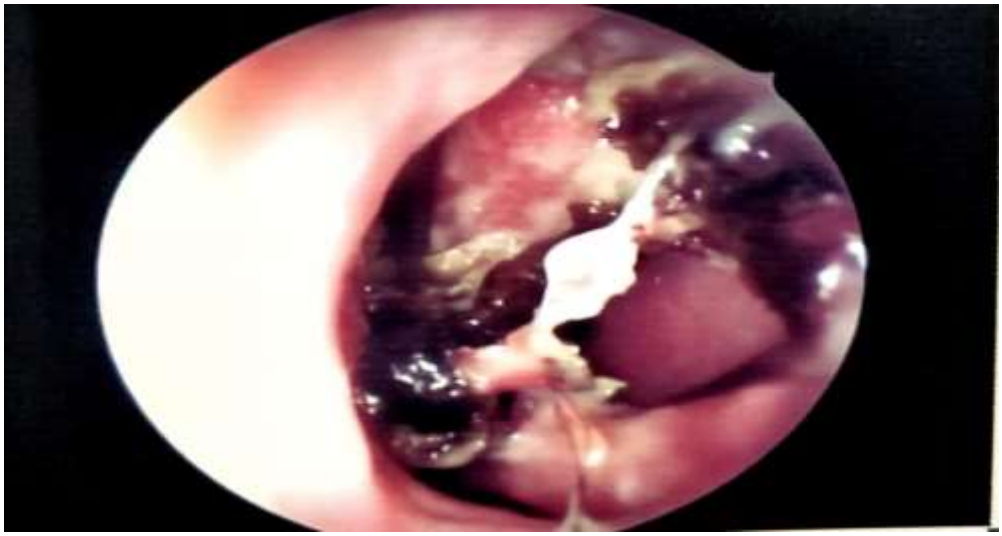

Figure 9: Intraoperative endoscopic picture showing black necrotic crusts in a patient of mucormycosis

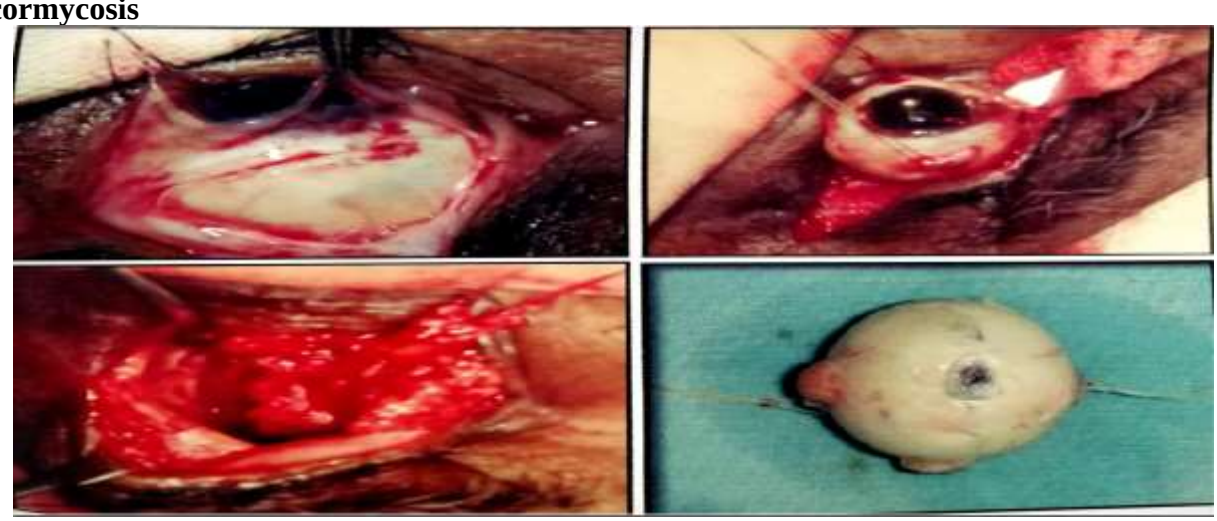

Figure 10: Intraoperative picture showing steps of orbital exenteration andexenterated specimen

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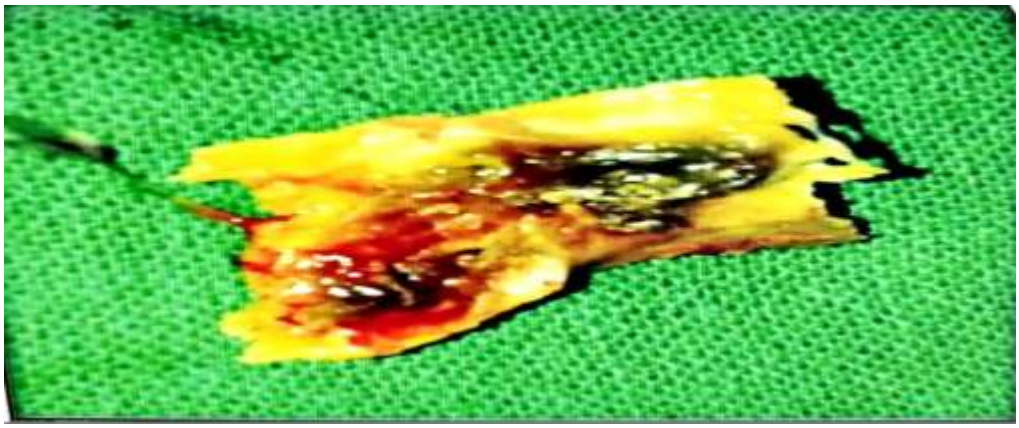

Figure 11: Clinical picture showing bony sequestrum removed from a patient of mucormycosis

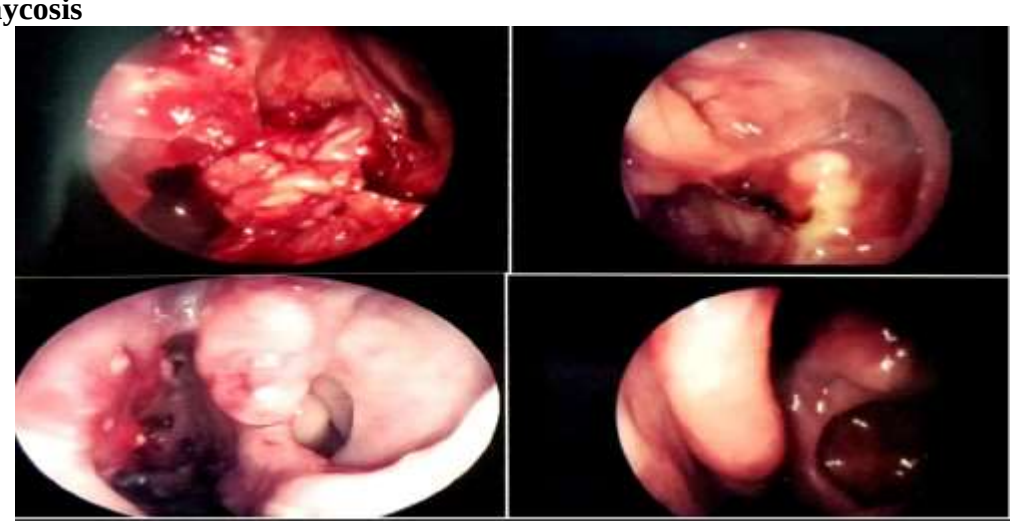

Figure 12: Intraoperative endoscopic picture showing crusting and unhealthy granulation tissue and sequestrum formation (top) and healing cavities after endoscopic debridement (below)

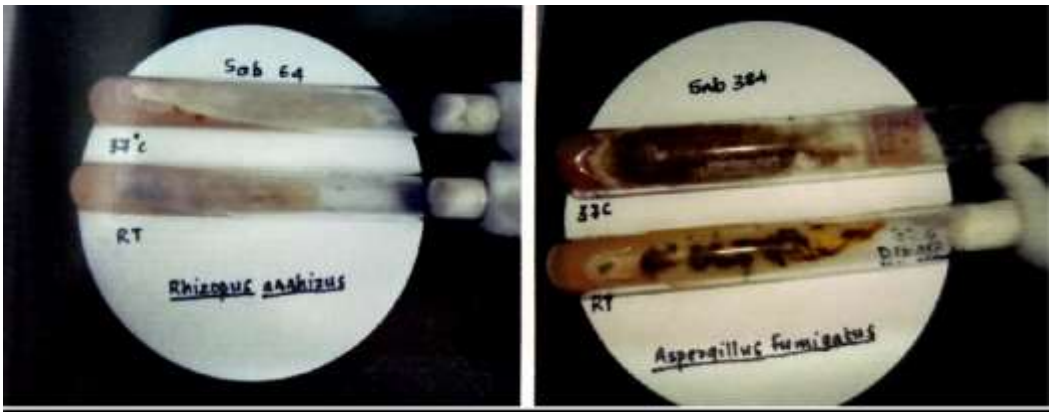

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Figure 13: Culture tube showing growth of Rhizopus and growth of aspergillusfumigatous

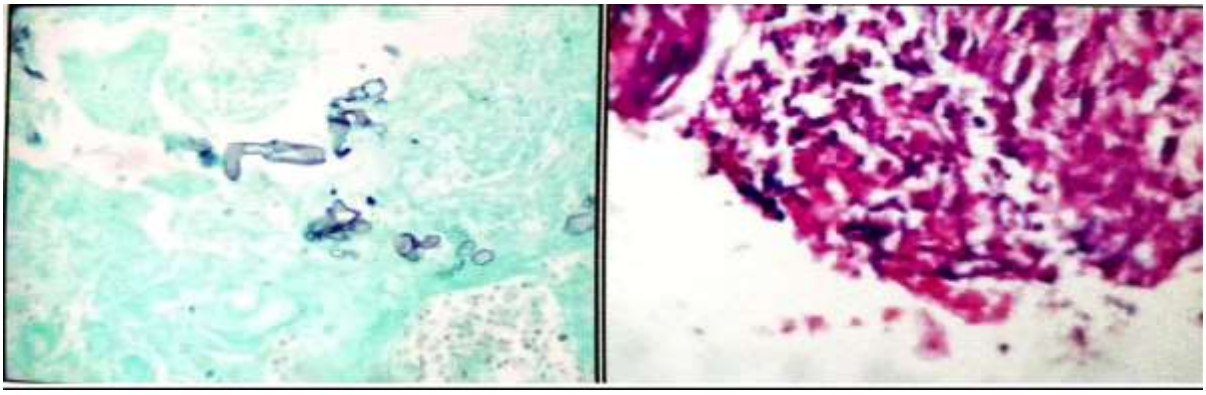

Figure14: Aseptate hyphae of Mucor on Gomori Methenamine Silver stain and septate hyphae of aspergillus on H and E staining

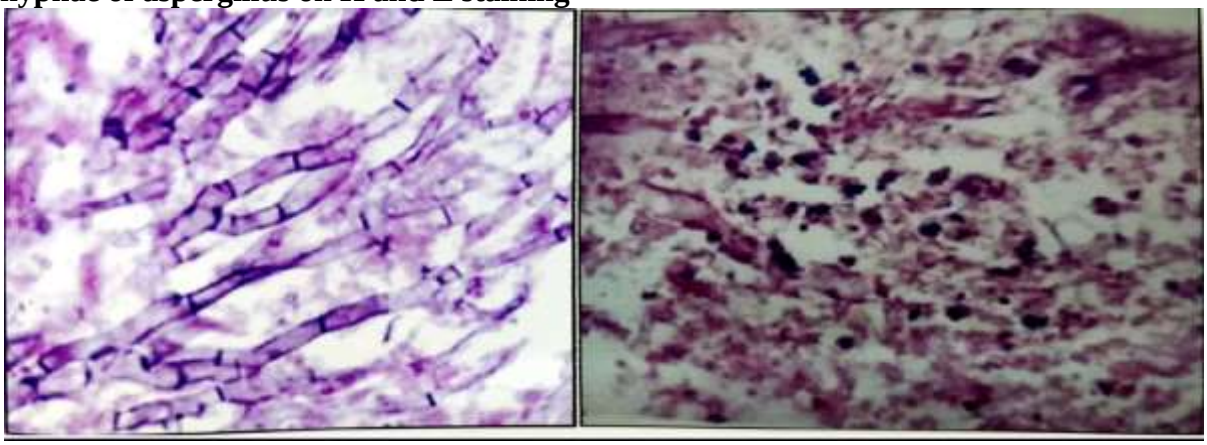

Figure 15: H and E stain showing Aspergillus with septate hyphae and Rhizopus with broad ribbon like non-septate hyphae

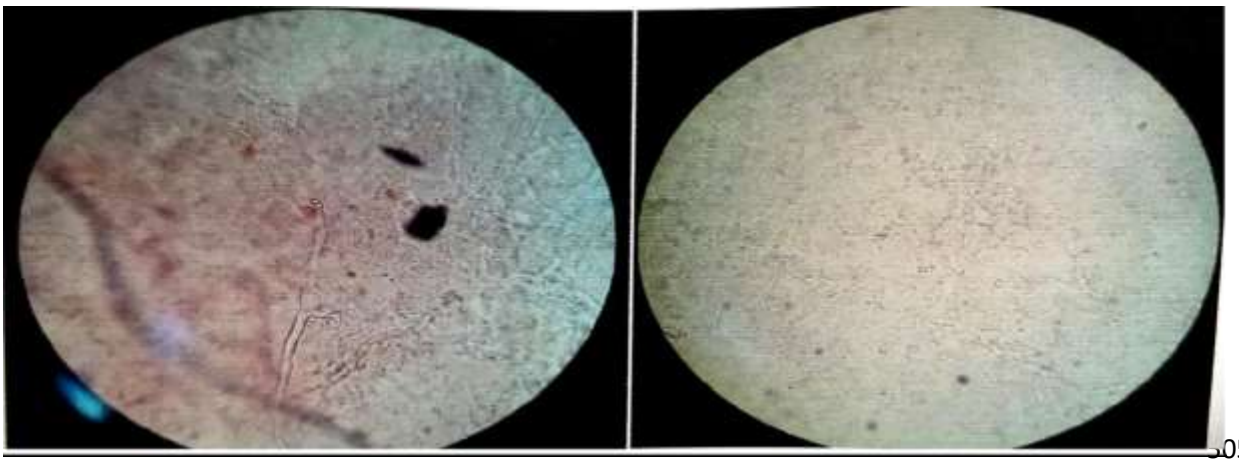

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Figure 16: Microscopic examination showing aspergillus (L) and Mucor species with acetates hyph

DISCUSSION

This is a retrospective study of 30 patients, in which we studied various clinical presentations, microbiological profile, treatment modalities of invasive fungal rhinosinusitis and outcomes of medical and surgical management of invasive fungal rhinosinusitis.

In our study of the 30 patients the youngest patient was 28 years old and the oldest was 72 years. The maximum number of patients i.e. 20 were between 51 to 60 years, 6 patients in the age group of 41-50 years. The mean age of patients was 53 years.

COMORBIDITIES

In our study, diabetes mellitus was the most commonly found comorbidity being present in 23 patients (73%). Our study also showed 6 patients were in state of chronic renal failure with raised blood urea level and creatine level. 2 patients were leukaemia patients. 2 were immunocompromised patients secondary to HIV.[6]

CLINICAL PRESENTATION

In our study, nasal obstruction was the most common presenting symptom noted in 27 patients (90%). 21 patients (70%) out of 30 patients had nasal discharge. 21(70%) patients out of 30 patients had fever, 15 patients had headache (50%) and 12 patients had facial swelling (40%).

Blitzer et al have also identified nasal obstruction (90%) and nasal discharge (85%) as the most common symptoms in their study. In our study, the most common orbital complaints were diminution of vision (DOV) in 50% of patients and ophthalmoplegia in 20% of patients. Other complaints were proptosis in 10% of patients and retro orbital pain present in 7% of patients.[7]

MICROBIOLOGICAL PROFILE

In our study, out of total 30 patients 17 were KOH positive, hence the positivity rate being. In all cases, the KOH report is tallied with the final culture report. The identification of species was done by culture on Sabourauds glucose agar. Out of 30 patients, 18 patients had Rhizopus on fungal culture and 10 patients had aspergillus and 2 patients had fusarium. No patient had negative culture report.[8]

HISTOPATHOLOGY

In our study, H and E (haematoxylin and eosin) was used for demonstration of fungal elements in tissue sections. Elmorsy et al in their study of 22 patients reported 13 patients (59.09%) with aspergillus and 9 patients (40.9%) with rhizopus.

RADIOLOGIC INVESTIGATIONS

CT PNS with 1mm orbital cuts done in patients to know exact extent of disease with special attention to orbital and intracranial involvement. In our study, most common finding was

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mucosal thickening which was seen in all patients and bony erosion seen in 70% of patients. The most commonly involved maxillary and ethmoidal sinus (80%) followed by sphenoid (40%) and frontal sinus (23%). Septal perforation was found in 9 patients (30%) and palatal involvement in 6 patients (20%).[9]

MEDICAL MANAGEMENT

In our study, amphotericin B deoxycholate was used in 24 patients with invasive fungal rhinosinusitis with an initial test dose of 1 mg in 50-100 ml of 5% dextrose and given slowly intravenous over 20 minutes. Then dose is stepped up to 0.25 to 1 mg/kg/day. 5 patients developed nephrotoxicity, in these patients we adjusted the dosage with nephrologist. 9 patients developed hypokalaemia for which dose was adjusted and potassium supplementation was given according to nephrologist, also, close follow up was done. In other 6 patients, injection liposomal amphotericin B was used. Out of 6 patients, 3 patients were chronic renal disease.[10]

SURGICAL MANAGEMENT

In our study, all 30 patients with invasive fungal rhinosinusitis were treated by early endoscopic assessment and debridement were done till bleeding margins are obtained. Almost all patients required repeated debridements. For all 30 patients, anaesthesia evaluation was done. High risk consent was explained to patients and relatives.

ENDOSCOPIC FINDING

In our study, the most common finding was black necrotic crust in the nose found in patients followed by pale nasal mucosa, mucopus.

Most commonly involved was maxillary sinus, ethmoid, sphenoid sinus and frontal sinus. Septal perforation was found in 8 pts (26%) and palatal involvement in 6 patients (20%). Elmorsy et al have reported black crusting and mucosal necrosis in all 22 patients (100%) and mucopus in middle meatus in 11 patients (50%).

MULTIDISCIPLINARY APPROACH is necessary in the management of invasive fungal rhinosinusitis. In our hospital, apart from routine DNEs and debridements, routine evaluation from various departments was also sought as per the individual requirement of the patient. Endocrinologist evaluation was done in all diabetic patients for glycaemic control. The ophthalmologic evaluation was done in patients with orbital involvement and to assess need for orbital exenteration. Neurosurgery evaluation was done for patients with clinical or radiological signs of intracranial involvement and for management of intracranial complications.

FOLLOW UP AND OUTCOME ANALYSIS

In our study, we had done regular follow up of patients for 6 months. Diagnostic nasal endoscopy at 3 weeks,6 weeks,3 months and 6 months with strict control of diabetes and other predisposing factors. In our study, on follow up 5 (16.7%) patients had recurrence, 4(13.3%) patients expired.

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Of 18 patients of mucormycosis, 13 patients (72%) remained disease free at 6 months. 2 patients died, 1 due to renal failure and 1 due to cardiac arrest. 3 patients had recurrence of disease and all 3 patients underwent repeat surgery. Out of 10 patients of aspergillosis, 6 remained disease free at 6 months (60%). 3 patients had recurrence and all patients underwent revision surgery. 2 out of these patients succumbed. In a series by Delgaudio et al, a success rate of 83% was found in patients with Sinonasal invasive fungal disease.

CONCLUSION

Invasivefungal rhinosinusitis is a life-threatening disease largely affecting immunocompromised patients and has a fatal outcome if not managed timely and intensively. An early diagnosis favours a better prognosis, disease clearance with less destructive and morbid debridement salvages vision of the patient and ultimately leads to a better quality of life and a shorter duration of hospital stay. The emphasis must be laid on the management being multidisciplinary and not just surgical alone as the patients present with multiple comorbities and complications due to the disease. It is imperative to have a good co-ordination evaluation among departments so that they can all work as a team for giving the patients the best possible outcome. Although the disease in itself can be fatal, a well-coordinated and productive team that approaches the disease aggressively is indeed life saving for the patient.

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