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RESEARCH ARTICLE

AN INSTITUTIONAL STUDY ON COVID-19 ASSOCIATED RHINO-ORBITAL-CEREBRAL MUCORMYCOSIS

Dr. Reshma S.[1], Dr. Arun Ingale[2], Dr. Vinayak Kuradagi[3] and Dr. Sharath Babu K.[4]

1. Final Year Resident, Department of ENT, Gadag Institute of Medical Sciences, Gadag, Karnataka, India.
2. Assistant Professor, Department of ENT, Gadag Institute of Medical Sciences, Gadag, Karnataka, India.
3. Senior Resident, Department of ENT, Gadag Institute of Medical Sciences, Gadag, Karnataka, India.
4. Professor & HOD, Department of ENT, Gadag Institute of Medical Sciences, Gadag, Karnataka, India.

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Abstract

Background: Prior to the COVID-19 pandemic, the prevalence of mucormycosis in India was approximately 0.14 cases per 1000 population. With the second wave of the COVID-19 pandemic, there has been a tremendous increase in the number of Rhino-Orbital mucormycosis cases with a high mortality of 30.7%.This paper discusses the institutional experience of 67 cases of rhino–orbital–cerebral mucormycosis related to COVID-19 infection.

Methods: In this case series, 67 proven cases of COVID-19 associated rhino-orbital-cerebral mucormycosis were analyzed retrospectively from April 2021 to March 2022. Clinical profile of all the patients were studied for signs and symptoms at presentation, possible risk factors and comorbidities. Microbiological and imaging studies was done in all patients and taken up for surgical management which included open or endoscopic debridement, maxillectomy, orbital decompression, orbital exenteration etc. Postoperatively patients were started on parenteral antifungal and discharged on oral antifungal after repeat imaging and endoscopy to rule out residual or recurrent disease.

Results: The mean age of presentation was 49.1 years. Diabetes and use of steroids during covid treatment was seen in 91% and 83.5% of cases respectively. Unilateral headache and nasal obstruction were the most common symptoms. Open debridement using Weber Ferguson incision and medial maxillectomy was the most common surgical approach followed in our institution with good recovery and less chances of need for revision surgery.

Conclusion: Timely diagnosis and intervention in the form of thorough surgical debridement and antifungal therapy are critical aspects in improving clinical outcomes in such patients.

Introduction:-

During the second wave of covid 19, India faced the major morbidities and mortalities in the form of post-COVID-19 sepsis and the abrupt spike of COVID-19 associated mucormycosis (CAM). Mucormycosis is an opportunistic angioinvasive disease caused by an opportunistic and ubiquitous fungus that belongs to the class Phygomycetes,

Corresponding Author:- Dr. Sharath Babu K.
Address:- Professor & HOD, Department of ENT, Gadag Institute of Medical Sciences, Gadag, Karnataka, India.

subclass Zygomycetes, order mucororales, family mucroraceae.[1] This uncommon but fatal fungal infection initially involves nasal cavity and paranasal sinuses (presenting with features similar to acute sinusitis) but has tendency for rapid spread to orbital and intracranial sites in an immunocompromised host[2-4] with consequent progressively worsening clinical outcome. The clinical hallmark of invasive mucormycosis is tissue necrosis resulting from angioinvasion and subsequent thrombosis. Invasive fungal infection or mucormycosis is almost always confined to the patients with altered host defenses such as in transplant recipients, diabetics, patients with malignancies, and patients on corticosteroid therapy (autoimmune disorders). Hyperglycemia or uncontrolled diabetes, particularly diabetic acidosis, is considered as the strongest and very well known risk factor for mucormycosis.

Prior to the COVID-19 pandemic, the prevalence of mucormycosis in India was approximately 0.14 cases per 1000 population, about 80 times the prevalence in developed countries.[5,6] With the second wave of the COVID-19 pandemic, there has been a tremendous increase in the number of Rhino-Orbital mucormycosis cases. Even though the organisms are present universally in nature; however, in the background of COVID-19 infection has a high mortality of 30.7%.[7] This paper discusses the institutional experience of 67 cases of rhino–orbital–cerebral mucormycosis related to COVID-19 infection.

Methods:-

A retrospective descriptive study was done on 67 proven cases of covid related mucormycosis diagnosed in the Department of ENT at Gadag Institute of Medical Sciences, Gadag, Karnataka during the time period from April 2021 to March 2022. All patients diagnosed with mucormycosis in our hospital either during covid infection or post covid were included in the study. Clinical profile of all the patients were studied for signs and symptoms at presentation, possible risk factors and comorbidities. Aseptically collected medial meatal nasal swab or representative tissue were sent for KOH (potassium hydroxide) staining, fungal culture, gram stain and bacteriological culture and reports noted.MRI with Gadolinium contrast was done in all patients to know the extent of the disease (nasal cavity, paranasal sinuses, orbit and intracranial structures). Ophthalmological and neurological consultation was done in case of any related symptoms or findings. Also, samples for relevant hematological and biochemical investigations including glycosylated hemoglobin (HbA1c) were sent.

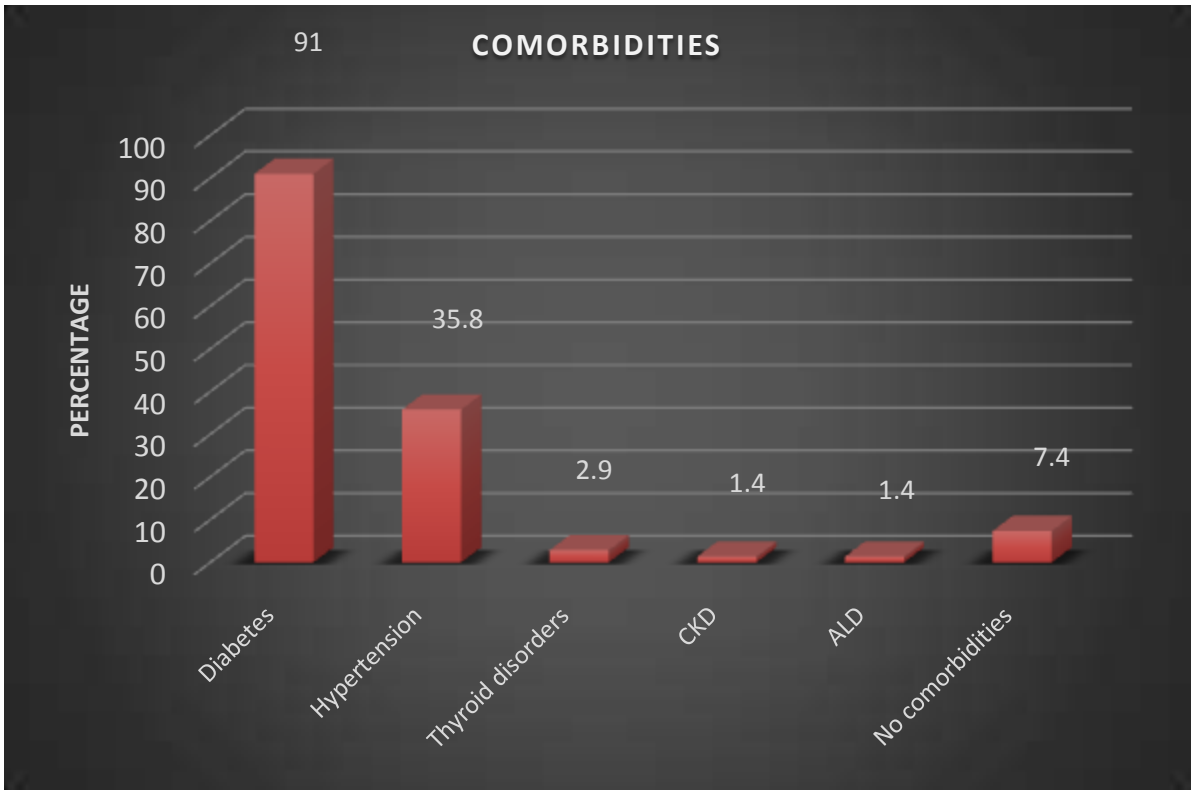
After basic investigations and work up, patients were taken up for surgical management and necrotic and debrided samples were sent for KOH mount, fungal culture and histopathological examination. Surgical procedures included open or endoscopic debridement, maxillectomy, orbital decompression with or without optic nerve decompression, sequestrectomy, orbital exenteration etc. Open surgical debridement using Weber Ferguson incision and medial maxillectomy was the most common surgical approach. Either partial (medial maxillectomy, inferior maxillectomy or subtotal maxillectomy) or total maxillectomy was done. Endoscopic or sublabial (Caldwell luc) approach was done in few cases. Orbital exenteration was performed with external eyelid sparing for those with optic nerve involvement.

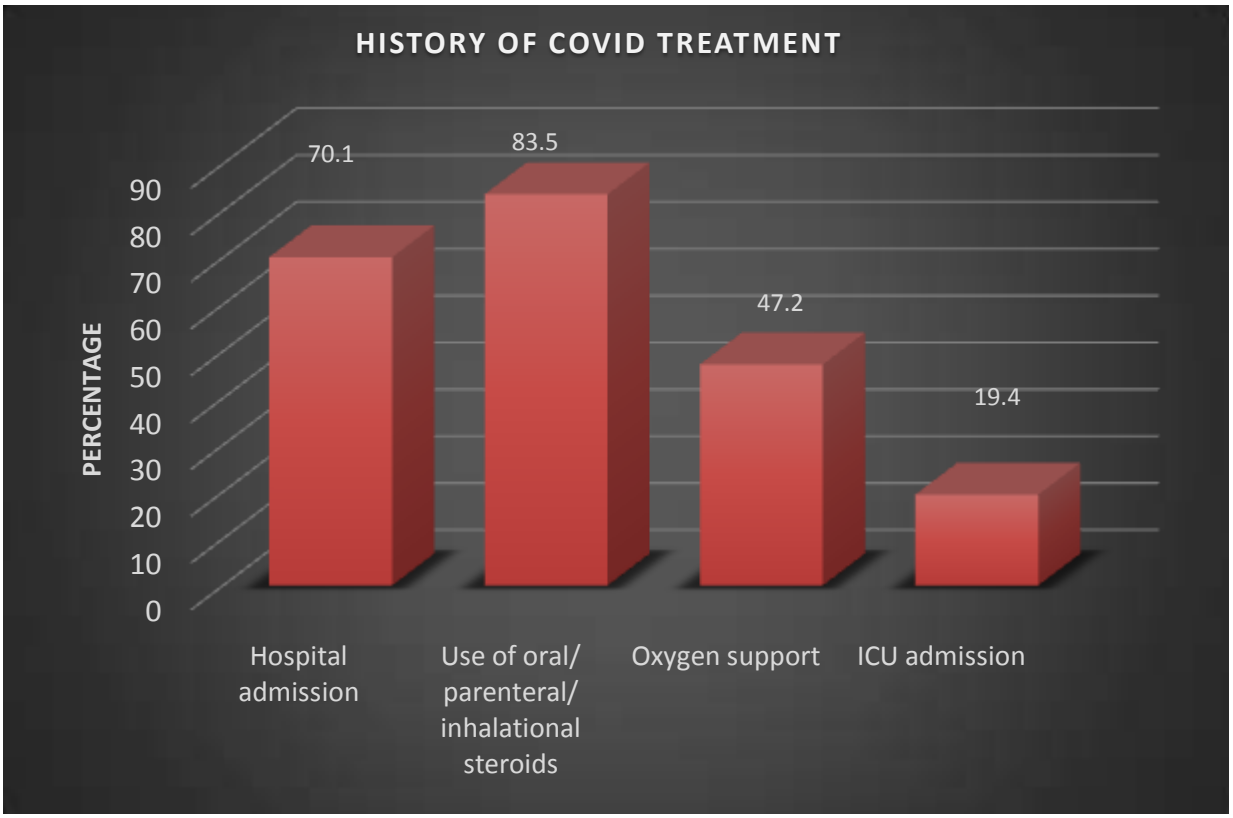
Postoperatively, proper wound care was given and all the patients were administered parenteral Liposomal Amphotericin B at a dose of 5 mg/kg/day. A minimum targeted cumulative dose of 1.5 to 2 gm Liposomal Amphotericin B was given to all patients except for 6 who died before completion of treatment. Few patients were given more doses of Liposomal Amphotericin B depending on the extend of disease. Close monitoring of renal functions and serum electrolytes was done during the entire course of Liposomal Amphotericin B. Dose titrations and flush therapy was given for those who developed acute renal injury. Appropriate correction of serum electrolytes was also done. In all patients of mucormycosis, repeat imaging and endoscopy was performed between post-operative days 3 and 7 to see the course of disease and to take measures for further debridement if needed. Those who showed evidence of residual or recurrent disease was taken up for revision surgery and Liposomal Amphotericin B was continued.

After completion of Liposomal Amphotericin B, oral Posaconazole was started, as 300 mg twice a day as a loading dose on first day followed by 300 mg once daily and the patients were discharged when they had no evidence of disease with clinical and general physical improvement. Regular follow up was done after 2 weeks, 1 month and 2 months.

Results:-

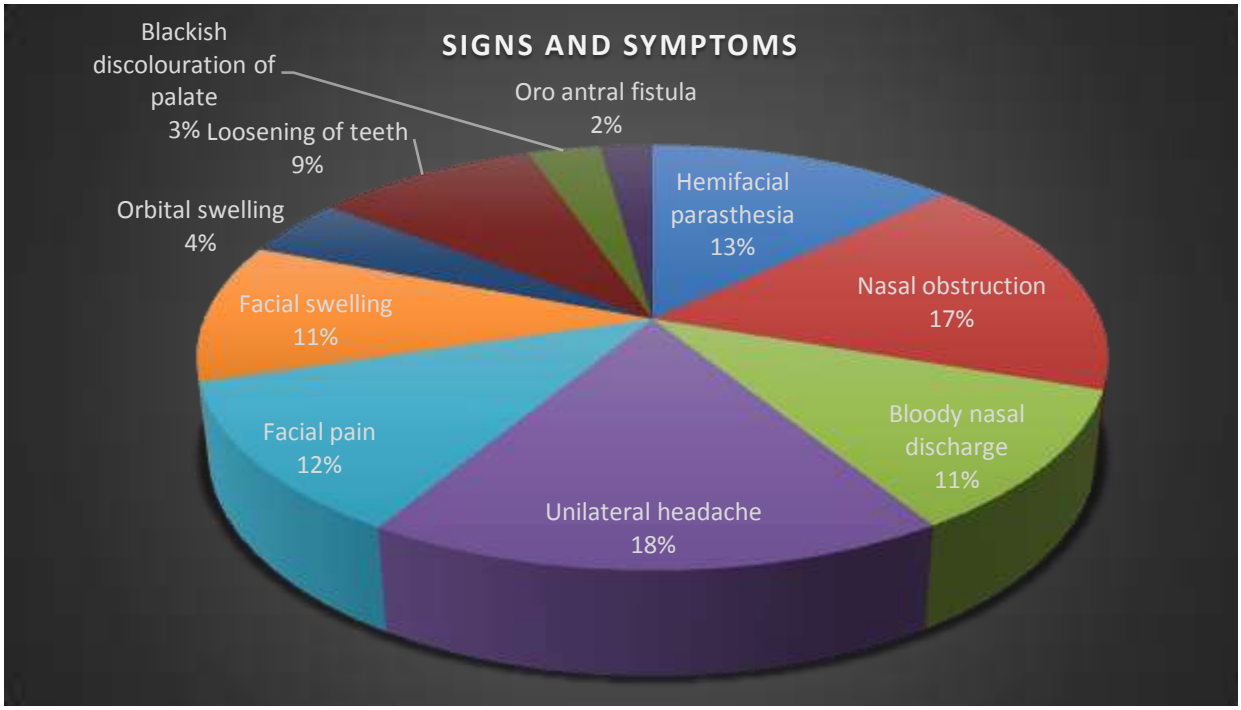
Out of 67 operated cases of mucormycosis included in the study, 52 were males and 15 females with a male: female ratio of 3.4:1. The mean age was 49.1 years with range of 23 to 84 years at presentation.All the patient had history of covid-19 infection.12 patients were diagnosed and operated during active covid-19 infection while the rest 55 patients were diagnosed during post covid-19 status after an initial recovery.





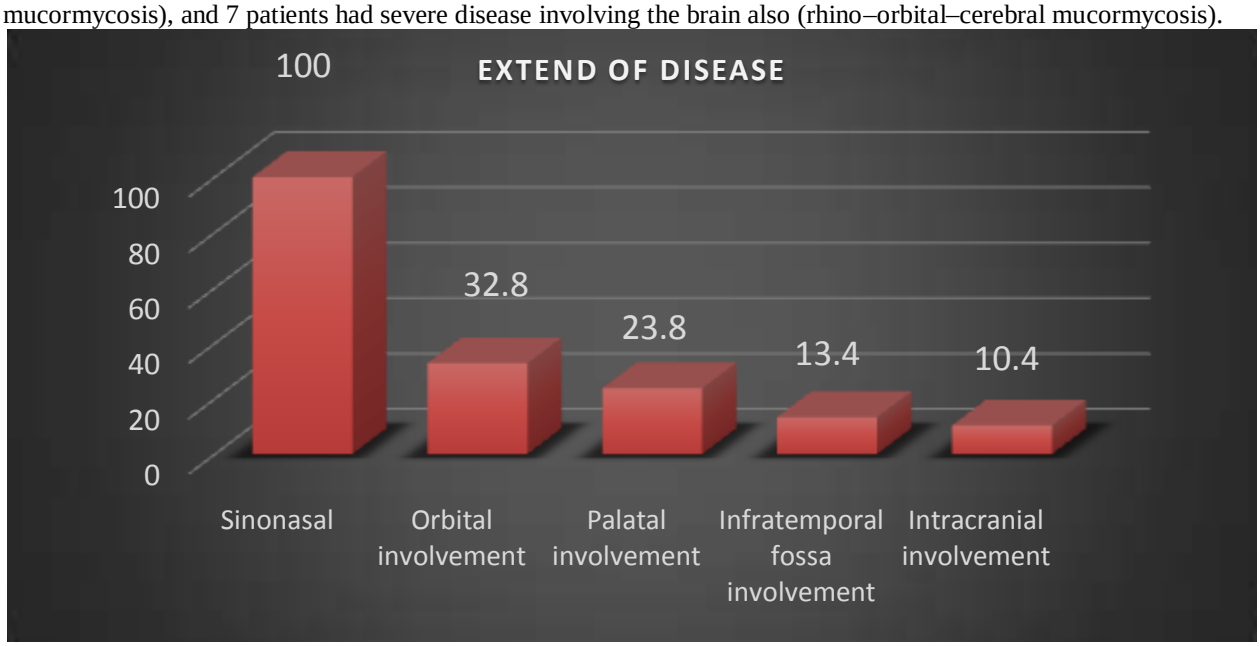
The most common comorbidity found among the patients was Diabetes which was seen in 61 cases (91%). Few had history of hypertension (35.8%) while 5 patients (7.4%) had no history of any comorbidities. Also 56 out of 67 cases

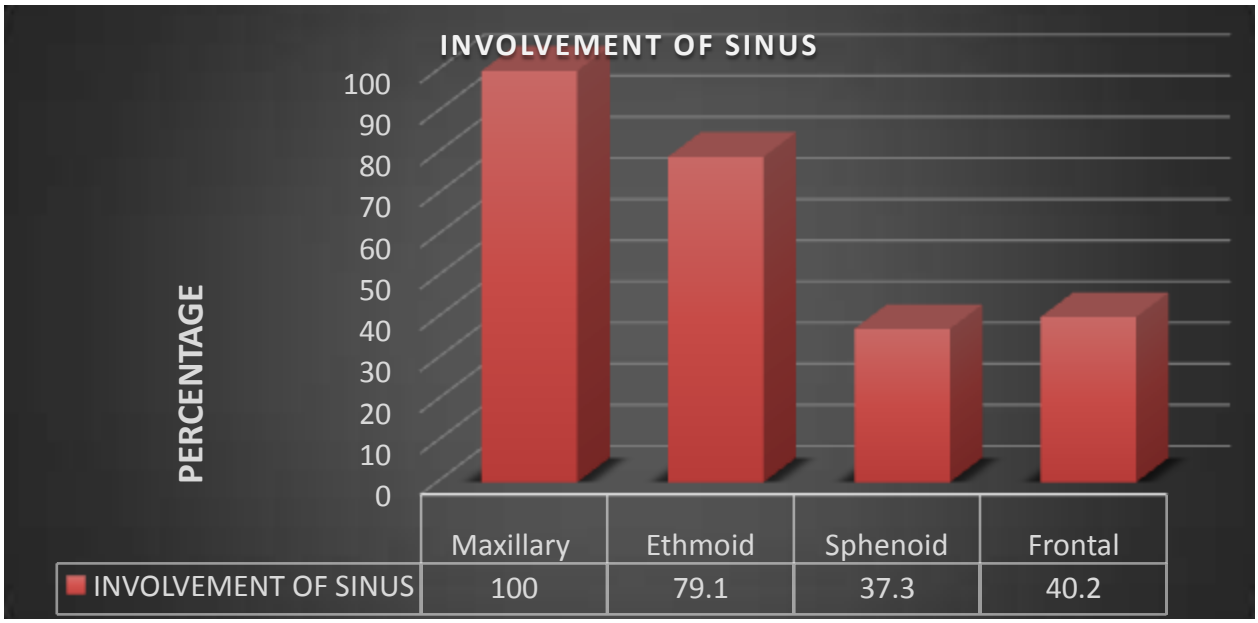
(83.5%) had history of use of oral/ parenteral/ inhalational steroids during covid treatment. 47 patients (70.1%) were admitted in hospital during covid-19 infection but only 13 (19.4%) had history of ICU admission. 32 patients (47.2%) had history of need for oxygen support during covid-19 infection.



The most common symptoms found among our patients were unilateral headache (94%) and nasal obstruction (92.5%) followed by hemifacial parasthesia, facial pain and bloody nasal discharge. Loosening of teeth was noticed in 50.7% of cases. 8 cases (11.9%) had oro antral fistula on examination while 11 cases (16.4%) had blackish discolouration of palate. Orbital swelling was present in 16 cases (23.8%).

According to radiological reports, out of these 67 patients of mucormycosis, 45 patients had disease restricted to nose and paranasal sinuses (PNS) (rhino-mucormycosis), 15 showed orbital involvement as well (rhino–orbital mucormycosis), and 7 patients had severe disease involving the brain also (rhino–orbital–cerebral mucormycosis).

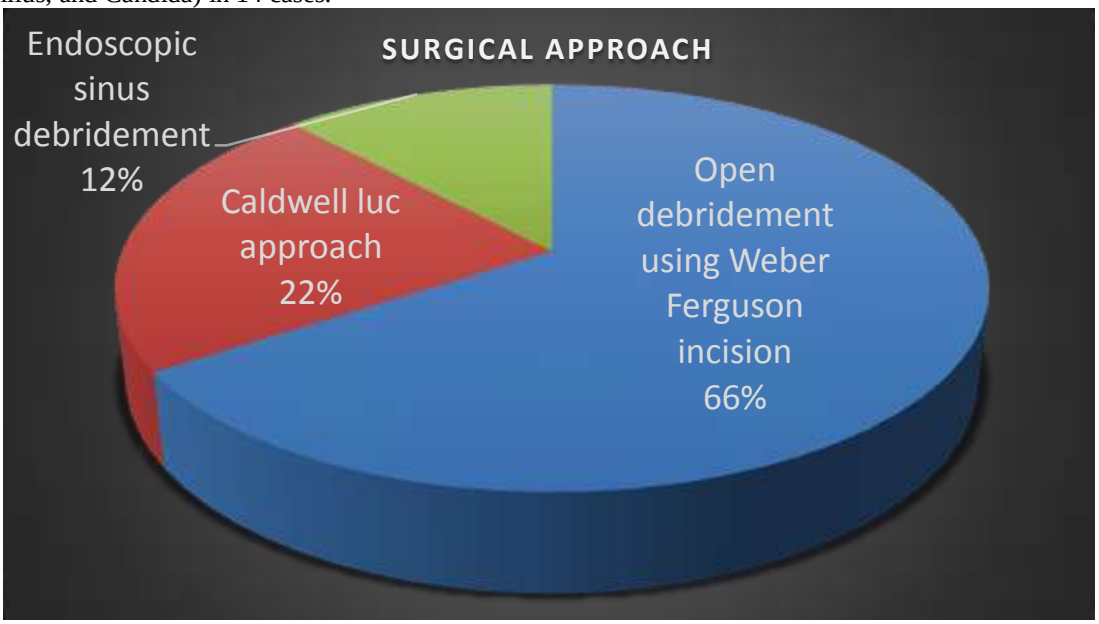




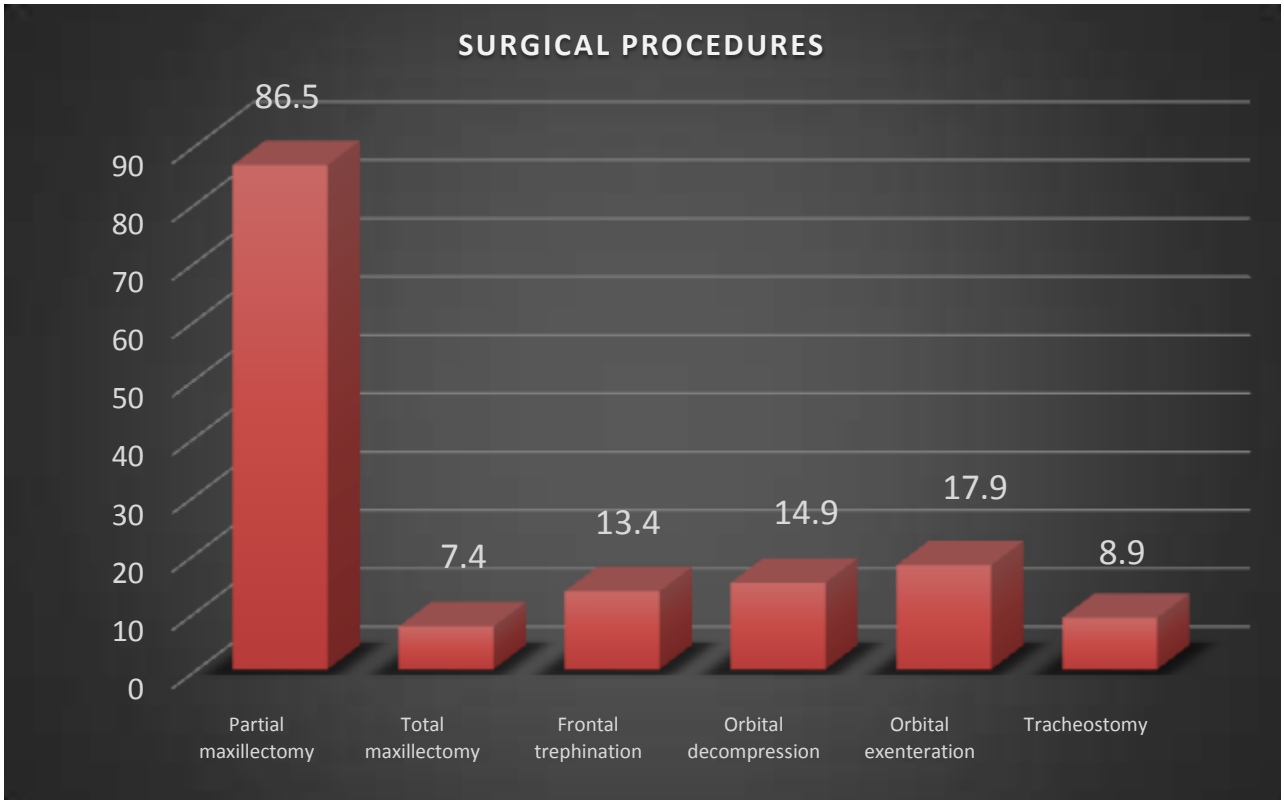
Maxillary sinus involvement was seen in all cases followed by ethmoid sinus in 53 cases. Frontal and sphenoid sinus involvement was seen in only 27 and 25 cases respectively. 7 cases of rhino-orbital mucormycosis and 5 cases of rhino-orbital-cerebral mucormycosis had no perception of light with dilated non-reactive pupils (total ophthalmoplegia), whereas rest had just diminished vision of variable grade.

Among 7 patients of cerebral involvement (rhino–orbital–cerebral mucormycosis), 4 showed cavernous sinus involvement, 5 developed cerebral abscess, and 1 patient showed isolated intracranial fungal lesion (likely hematogenous spread). 5 of them landed in ICU during the management, and the general condition of 4 patients deteriorated subsequently during ICU care and did not survive. Rest of the 3 patients recovered well with surgical debridement, amphotericin therapy and antiepileptic drugs.

Out of 67 cases, 39 cases showed aseptate fungal hyphae in KOH mount. Broad based irregular aseptate fungal hyphae with right angled branching resembling mucormycosis was isolated in fungal culture of 45 cases. Mucor fungal hyphae with tissue invasion in histopathology were seen in 53 cases and mixed fungal involvement (Mucor, Aspergillus, and Candida) in 14 cases.



The most common surgical approach was open debridement using Weber Ferguson incision and medial maxillectomy. According to the extent of disease, subtotal or total maxillectomy with alveolopalatectomy was done in few patients. Endoscopic sinus debridement was done only in 8 patients.



Out of 22 cases with orbital involvement, the decision of orbital exenteration was taken in 12 cases with no visual potential. The rest 10 cases underwent orbital decompression. All orbital exenterated patients had extensive necrotic orbital tissue which showed evidence of fungal elements. In 6 cases, tracheostomy was done during surgery either due to restricted mouth opening or due to extensive surgery. Out of 6 tracheostomy cases, 2 had died postoperatively and remaining 4 were decannulated successfully during post operative period.

Out of 67 cases, 13 were taken up for revision surgery due to evidence of recurrent or residual disease on repeat imaging. 3 out of 8 endoscopic debridement (37.5%), 4 out of 15 Caldwell luc approach (26.6%) and 6 out of 44 open debridement (13.6%) cases underwent revision surgery which suggested better results with open debridement.

Condition of 6 patients, 4 with rhino-orbital-cerebral mucormycosis and 2 with extensive rhino-orbital mucormycosis, deteriorated over the next few days after debridement surgery due to acute respiratory distress syndrome. 2 out of6 had underwent tracheostomy and the remaining 4 got intubated and were started on mechanical ventilation with ionotropic support. All 6 patients who were on ventilator support did not survive. Cause of death suspected to be thromboembolic event and eventually cardiac arrest was suspected in all of them.

Remaining 61 patients showed good recovery with completion of Liposomal Amphotericin B and was discharged on Tab Posoconazole. Regular follow up did not show any evidence of recurrence. Obturators of appropriate size was given to patients who sustained defects due to maxillectomy and prosthetic eye was provided to patients who underwent orbital exenteration. All of them showed improvement in general condition and was able to lead their day today life.

Discussion:-

In our study we observed strong association of hyperglycemia and steroid intake with development of mucormycosis in both active and recovered COVID-19 cases which warrants judicious use of corticosteroids and strict glycemic

control. MRI with Gadolinium contrast is the ideal radiological modality to know the extension of the disease especially orbital and intracranial. Open surgical approach gave advantage of better exposure and clearance of the disease and thereby reducing the need for repeated surgeries. Orbital exenteration is recommended for patients with optic nerve or globe involvement. Revision surgeries has to be done in patients showing residual or recurrent disease

Conclusion:-

The clinicians should now be cautious of possibility of development of invasive fungal infection during the management of COVID-19 patients with risk factors. The strong association of hyperglycemia and steroid intake with development of mucormycosis in both active and recovered COVID-19 cases warrants judicious use of corticosteroids and strict glycemic control. Considering the good clinical outcome achieved in our study, the significance of high degree of clinical suspicion, earliest recognition and treatment of mucormycosis with aggressive surgical debridement in combination with anti-fungal medication is of paramount importance. Timely diagnosis and intervention in the form of thorough surgical debridement and antifungal therapy are critical aspects in improving clinical outcomes in such patients. However, longer follow-up is required to ascertain the outcomes in these patients.

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