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RESEARCH ARTICLE

TO ASSESS THE ROLE OF RANDOM BLOOD SUGAR IN MONITORING OF PATIENTS DEVELOPING MUCORMYCOSIS

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Abstract

Introduction: Rhinoorbital Cerebral mucormycosis caused by fungi of family mucoracea is seen in covid era.Patients at risk for fatal illness is sharply rising because of increased incidence of diabetes. To identify its association and further stop the onset or progression of mucormycosis, we evaluated Random Blood Sugar (RBS) levels in patients who had developed the disease in this study.

Materials and Methods:A total of 63 patients who developed Mucormycosis between April 2021 to October 2021 and enrolled in the department of ENT, SAMC and PGI Indore. We evaluated role of Blood sugars in patients developing Mucormycosis and identified the improvement in recovery of Mucormycosis patients after sugar monitoring and early management.

Result: Total 63 patients were reviewed against the guidelines for sugar levels set by American Diabetes Association. There was mortality in 10 out of 63 patients (15.87%).All of these patients were from the group of DM with Uncontrolled sugars. There was uneventful transfer from our side to medical side for medical management in 53 out of 63 patients.

Conclusion: The study highlights correcting the practice of monitoring blood sugar and its management. Early diagnosis, Early monitoring and Early Management is the key to better prognosis.

Introduction:-

Mucormycosis is rare condition associated with potential impending mortality chances with invasive fungal illness that primarily affects diabetics and other immunocompromised people. Both the morbidity and fatality rates for this illness were high. Furthermore, the speed at which Mucormycosis spread is unpredictable, even a slight delay in diagnosis has fatal consequences. Recent reports of mucormycosis linked to COVID-19 have increased, particularly in situations of uncontrolled diabetes. Suppressed immunity caused by SARS-CoV-2 frequently worsens an inflammatory situation in patients with type I diabetes mellitus and hyperglycemia, increasing the risk of subsequent infections.[1] Immune system dysfunction is the primary risk factor for these invasive fungal diseases in other fungi diseases. Although there have been occurrences of zygomycosis in otherwise healthy patients[2], persons at risk typically have impaired defence mechanisms due to conditions like diabetes mellitus (DM), haematological illnesses including leukaemia or lymphoma, intravenous drug usage, or cytotoxic medication.[3,4,5]

Diabetes mellitus (DM) is a metabolic syndrome linked to insulin secretion or function. It is one of the biggest new health dangers of the twenty-first century. In 2025, there will likely be 380 million instances of DM.[6] In addition,

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DM has been linked to decreased T cell response, abnormal neutrophil function, and problems of humoral immunity. [7,8,9]. As a result, DM makes people with DM more vulnerable to getting sick from the majority of common microbial pathogens as well as from fungi that cause mucormycosis. These infections, in addition to the consequences, can result in DM complications such hypoglycemia and ketoacidosis. Globally, there are more people with diabetes mellitus. [10] The number of individuals at risk for this fatal illness is sharply rising because of the increased incidence of DM. In order to identify its association and further stop the onset or progression of Mucormycosis, we evaluated the biochemical parameter of Random Blood Sugar (RBS) Levels in patients who had developed the disease in this study.

So, the concerned study is reflective of the relation of biochemical parameter with clinical presentation and prognosis of the disease.

Materials and Methods:-

The aims and objectives of the study are -To evaluate the Role of Blood sugars in patients developing Mucormycosis and to identify the improvement in recovery of mucormycosis patients after sugar monitoring and early management.A total of 63 patients who developed Mucormycosis between April 2021 to October 2021 and enrolled in the department of ENT, SAMC and PGI Indore. A proper clinical history was taken and thorough examination done with nasal endoscopic evalauation and KOH mount sent. Ophthalmological evaluation and documentation of vision also done by ophthalmology department, and the sugar levels were assessed and based on that patients were classified as[13]: Non diabetic, Newlyonset DM, DM with Controlled sugars, DM with uncontrolled sugars. They were assessed according to American Diabetic Association Criteria of DM.**Non diabetic:** Fasting Plasma Glucose less than 100 mg/dl**. Newly Onset DM:** New-onset diabetes was defined as initiating antidiabetic medication according to annual medication inventories or by a single, in-study fasting plasma glucose >126 mg/dl.**DM with controlled Sugars:** Patients who have already been diagnosed with Diabetes Mellitus previously but whose sugar levels are less than 126 mg/dl.

DM with uncontrolled sugars:
Patients who have already been diagnosed with Diabetes Mellitus previously but whose sugar levels are more than 126 mg/dl.

The Inclusion criteria was all patients presenting with confirmed mucormycosis. The Latest Random Blood Sugars were taken at the time of enrolment of patients in the study and in this who had developed Mucormycosis were admitted, started on IV antibiotics and sugar monitoring was done on regular basis. After stabilizing the patient, the patient was posted for endoscopic debridement surgery after obtaining fitness from medicine, ophthalmology, oral surgery and clearance from anaesthesia department. After surgery, patients were managed medically by intravenous Liposomal Amphotericin B and orally by Posaconazole tablet along with antibiotics and nasal douching.

Clinical Pathway-

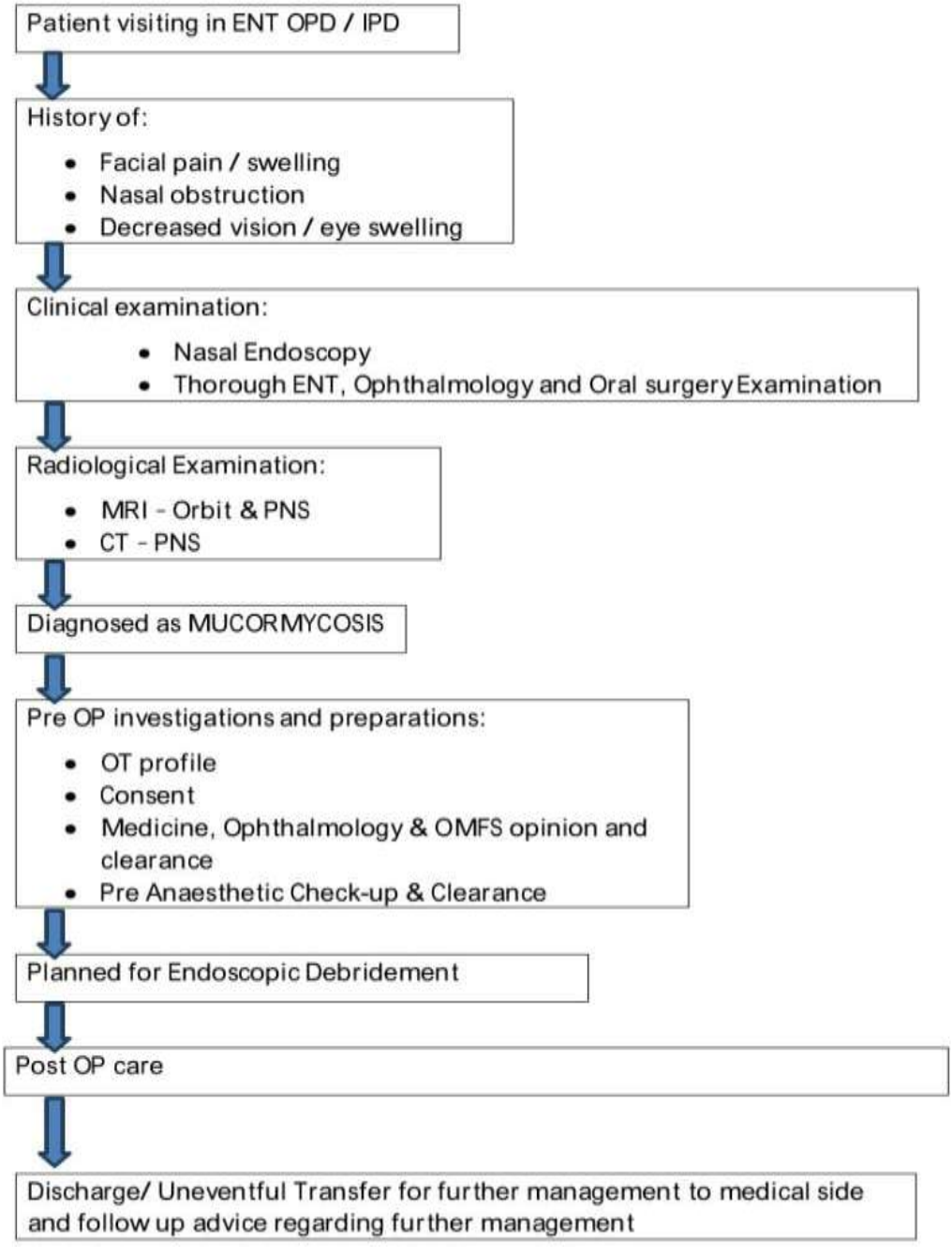


Figure 1:- Management protocol for Mucormycosis at ENT Deptt, SAMC and PGI, Indore.

Results:-

During the study period between **April 2021 to October 2021**, 63 patients of Mucormycosis were taken in our study out of which 13 (21%) were females while 50 (79%) were males.

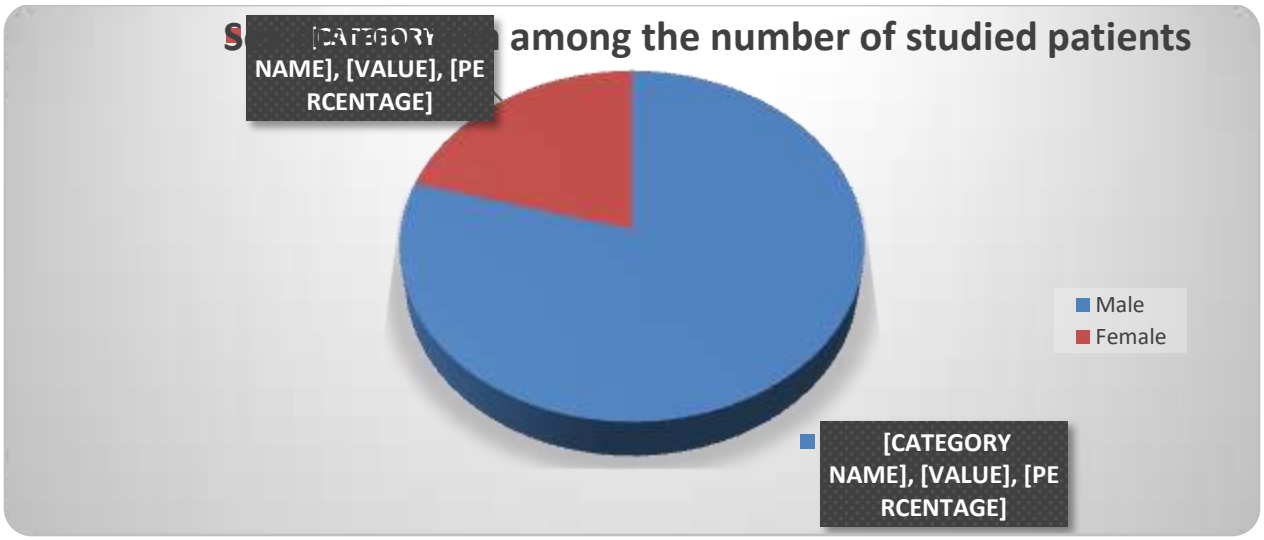


Fig 2:-Sex distribution among the number of studied patients.

According to the age group classification, none of the patients were from the age group of 0-20 or more than 80. Majority of the patients 34 out of 63 (54%) were from the age group of 41-60 years while 19 out of 63 (30%) were from the age group 21-40 years and 10 out of 63 (16%) were from the group corresponding to 61-80 years.

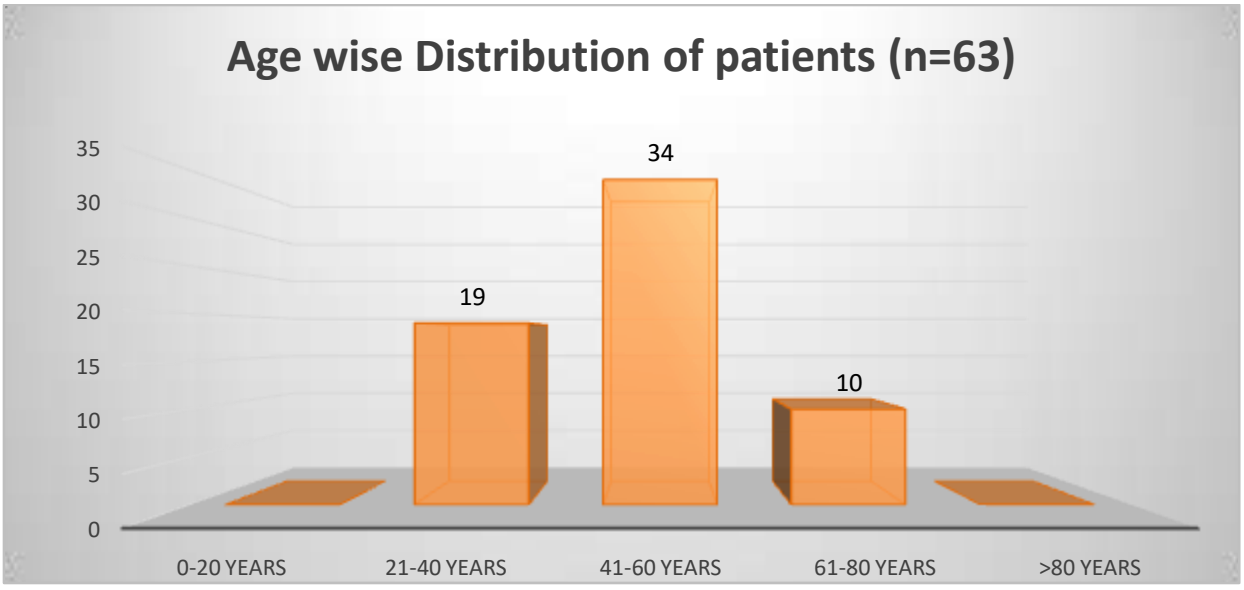


Fig 3:-Age wise Distribution of patients (n=63).

These 63 patients were reviewed against the guidelines for the sugar levels set by American Diabetes Association. There was mortality in **10 out of 63 patients (15.87%).** All of these patients were from the group of DM with Uncontrolled sugars. There was uneventful transfer from our side to medical side for medical management in 53 out of 63 patients.

Table I:-. Table Depicting Biochemical (Random Blood Sugar) Profile of patients (n= 63).

Diabetic status of patient	Number of patients	Percentage of patients	Recovery rate	Mortality
DM with uncontrolled sugar	45	71.4	Poor/ delayed	10
Newly onset DM	14	22.2	Good	0
DM with controlled sugar	2	3.17	Good	0
Non-diabetic	2	3.17	Good	0

Fig 5:-Number of patients : According to their biochemical profile in pie chart.

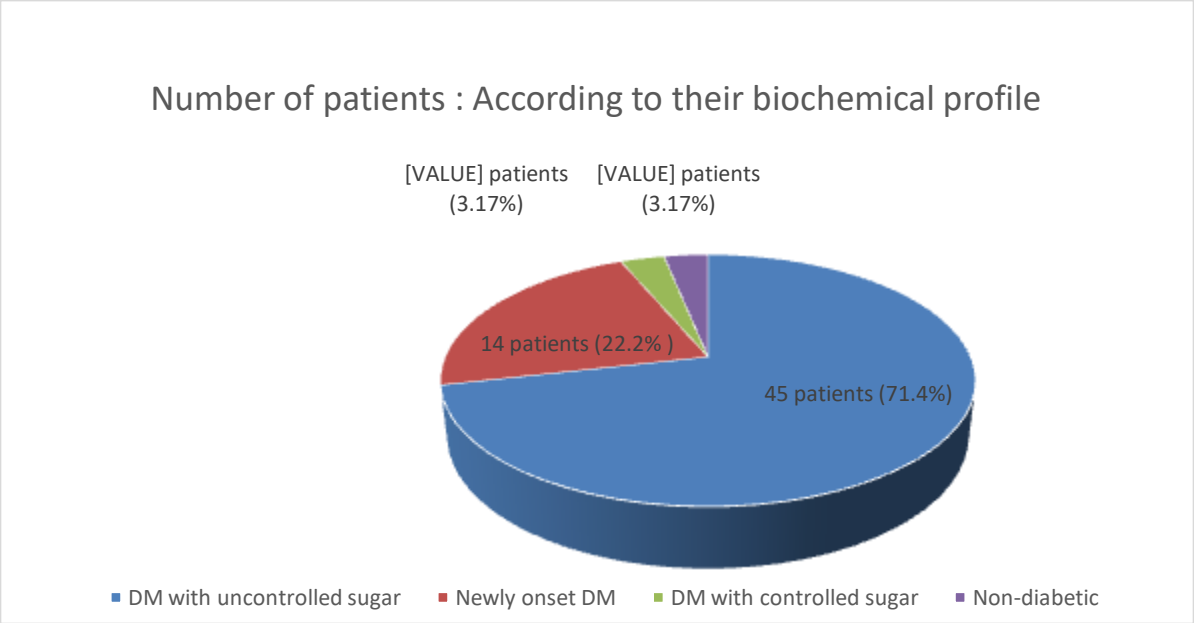
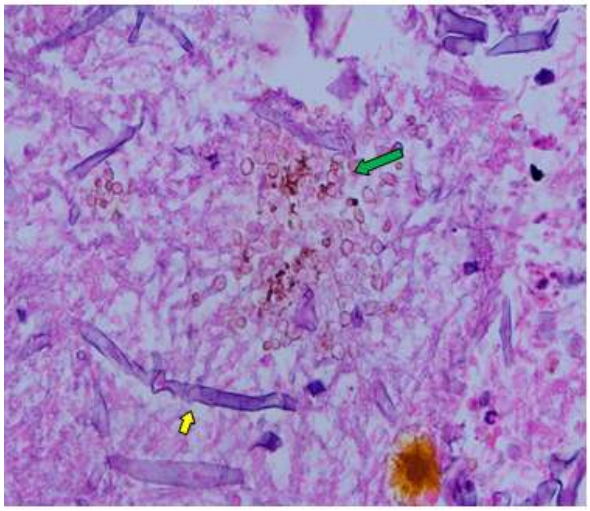


Figure 6:- H & E stain section (40X) showing necrotic tissue with broad aseptate fungal hyphae (yellow arrow) and spores (green arrow).



Discussion:-

Mucormycosis is a rare opportunistic infection, and COVID-19 patients are at risk of developing mucormycosis because of pre-compromised immune systems. A growing body of evidence supports that comorbidities (diabetes, transplantation, malignancies) and medications (steroids) make the patients more vulnerable to comorbidity associated with mucormycosis.[11-13]

Around 50% of cases were reported from India. A possible reason for this could be the deadly COVID-19 delta variant wave infecting around half a million people every day in recent months and a high prevalence of diabetes mellitus in patients [14]. Diabetes mellitus is a predisposing factor for the development of mucormycosis [15,16]. The potential mechanism is aggravation of the inflammatory state due to hyperglycemia and activation of antiviral immunity .[17]

In our study, the number of male mucormycosis patients was four times the number of female patients. These findings are aligned with a previously published study by Roden et al. that found mucormycosis in 65% of male patients and in our study it came 79%.[18]

Age wise distribution included 53.96% in age group of 41-60 years whereas in age group 61- 80 years 15.87% out of total of 63 patients. However, the Age wise incidence was not seen in progression partly due to the fact these rhino orbital cerebral mucormycosis cases were associated with covid 19 which was seen maximum in the age group of 41- 60 years

Mucormycosis may involve nose, sinuses, orbit, central nervous system (CNS), lung (pulmonary), gastrointestinal tract (GIT), skin, jaw bones but ROCM (rhino orbito cerebral) whichis the commonest variety clinically worldwide.[19]

Infection mostly develops in individuals with immunologically compromising conditions which are frequently the result of diabetes mellitus, cancer, chemotherapy or administration of immunosuppressive medications following organ transplantation.[20–23]

Mucormycosis being an angioinvasive disease by mold fungi of the genus Rhizopus, Mucor, Rhizomucor, Cunninghamella and Absidia of Order- Mucorales, Class- Zygomycetes.[24] The Rhizopus Oryzae is commonest type and responsible for nearly 60% of mucormycosis cases in humans and also accounts for 90% of the Rhinoorbital-cerebral (ROCM) form .[25]Mode of contamination occurs through the inhalation of fungal spores.

Patients without an underlying abnormality or apparent predisposition have also been affected . The incidence of disease has not been demonstrated to vary based on age or gender. The predisposition of patients with diabetes to acquire the disease may be particularly related to hyperglycemia and the presence of ketoacidosis is presumed to induce a neutrophil defect, resulting in reduced phagocytosis and chemotaxis.

During the study period between April 2021 to October 2021, 63 patients of Mucormycosis were taken in our study and were reviewed against the guidelines for the sugar levels set by American Diabetes Association.

Increased synthesis of Advanced glycalation end products (AGEs) and pro-inflammatory cytokines, oxidative stress, are all resulted by hyperglycaemia and insulin resistance, in addition to increasing the development of adhesion molecules that mediate tissue inflammation.[26,27]

This inflammatory process results in underlying mechanism that causes a higher chances for infections and worse outcomes in diabetic people. [26]

Figure 7 (a) **Figure 7 (b)** **Figure 7 (c)**

Figure 7:- (a) Clinical Rhino Orbital Facial status – Normal : **Controlled DM**
(b) Clinical Rhino Orbital Facial status – Severe involvement : **Uncontrolled DM**
(c) Clinical Rhino Orbital Facial status – Limited involement : **Newly onset DM**

The most prevalent predisposing factor for rhinocerebral mucormycosis is diabetes mellitus. All of the patients in another study were diabetic [28], which was comparable to the findings of Nezafati et al. and Kolekar et al., [29,30] who showed that 90 percent and 80 percent of patients, respectively, had underlying diabetes .In our study however 63 patients were reviewed against the guidelines for the sugar levels set by American Diabetes Association. **All the cases were diabetic**. There was mortality in **10 out of 63 patients (15.87%).** All of these patients were from the group of DM with Uncontrolled sugars. There was uneventful transfer from our side to medical side for medical management in 53 out of 63 patients.

Mucormycosis is clinically confirmed by aggressive clinical features of disease in the compromised host and confirmed by histopathological examination of transnasal or cerebral biopsy.[31] Demonstration of broad non septate hyphae that branch at right angles are hallmark for diagnosis. Management therapy involves rapid control of underlying disease process, systemic antifungal and aggressive surgical debridement of necrotic tissue that is associated with improved outcomes.[32] Systemic therapy of amphotericin B, improved survival rates of patients with mucormycosis.[33] The usual starting dose is 5 mg/kg of liposomal amphotericin and clinicians can increase the dose as high as 10 mg/kg daily in an attempt to control spread of infection.[32] Also, lipid formulation of amphotericin B, posoconazole can be used for oral step down therapy. Intravenous posaconazole can be used as salvage therapy for patients who do not respond to or tolerate amphotericin B.[34] In addition to playing a role in diagnosis early and if required repeated surgery has been necessary to treat extensive disease. As fungus thrives in devitalized and necrotic tissue and ischaemic tissue is difficult for chemotherapeutic agents to penetrate, debridement has been recommended. Drainage and debridement of paranasal sinuses, exenteration of necrotic orbital contents, palatectomy and craniotomy have all been associated with cure.[32] The overall mortality form rhino-orbital-cerebral mucormycosis ranges form 25–60 % with the best prognosis in patients with infection confined to sinuses.The prognosis is poor for patients with brain, cavernous sinus or carotid involvement, although some patients with these complications have been cured of infection.[33, 35, 36]

Rhino-orbital and rhino-orbital-cerebral were the most common forms of mucormycosis observed in this study. In both forms of infection, the fungus invades the nasal mucosa and orbital wall and leads to the occurrence of symptoms such as facial pain, vision loss, proptosis, apoptosis, and ophthalmoplegia.[37,38] Patients with both surgical and medical management survived better than those with medical management alone.

Regular collaboration with Medicine and TB Chest department was done for taking nasal swabs and sugar management in high risk or clinically suspected patients of Covid-19 and Mucormycosis.

Early radiological assessments were made a protocol for patients who were highly suspicious like those in which nasal swab came positive for fungal hyphae or whose sugars were very high. So, a CT – PNS was done on early basis for these patients.

Biochemical monitoring of Random blood sugar helped prognosticate and prevent disease progression which is crucial in the management of the condition.

Conclusion:-

The study highlights correcting the practice of monitoring blood sugar and its management. It was found that our practice of monitoring blood sugars was in line with that of American Diabetes Association. Preventing of Mucormycosis in patients needs awareness and same was communicated to health care providers and so judicious steroid usage is recommended in all patients and especially Covid-19 patients. Creating Awareness regarding the above points in patients as well, so as to encourage them to present to health facilities at the earliest. Early diagnosis, Early monitoring and Early Management is the key to better prognosis .

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