DISSERTATION ON

"ROLE OF SPECIAL MUCOR SCREENING OPD IN THE MANAGEMENT OF POST COVID MUCOR EPIDEMIC"

This Dissertation is submitted to

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REGISTRATION No: 221914011

BONAFIDE CERTIFICATE

This is to certify that this dissertation entailed ***"ROLE OF SPECIAL MUCOR SCREENING OPD IN THE MANAGEMENT OF POST COVID MUCOR EPIDEMIC "*** submitted by **Dr.GAAYATHRI T , appearing** for M.S. ENT., Branch IV Degree examination in May 2022 is a bonafide record of work done by her under my direct guidance and supervision in partial fulfillment of regulations of the Tamil Nadu Dr. M.G.R. Medical University, Chennai, Tamil Nadu, India.

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CERTIFICATE - I

This is to certify that, Dr. GAAYATHRI T., postgraduate (2019-2022) in the Upgraded Institute of Otorhinolaryngology, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai, has done this dissertation titled **"*ROLE OF SPECIAL MUCOR SCREENING OPD IN THE MANAGEMENT OF POST COVID MUCOR EPIDEMIC*"** under my direct guidance and supervision in partial fulfilment of the regulations laid down by the Tamil Nadu Dr. M.G.R Medical University, Chennai for M.S. Branch – IV Otorhinolaryngology Degree Examination.

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CERTIFICATE – II

This is to certify that this dissertation work titled **"*ROLE OF SPECIAL MUCOR SCREENING OPD IN THE MANAGEMENT OF POST COVID MUCOR EPIDEMIC*"** of the candidate Dr. GAAYATHRI T., with Registration Number 221914011 for the award of M.S. Degree in the Branch of OTORHINOLARYNGOLOGY. I personally verified the urkund.com website for the purpose of Plagiarism Check. I found that the uploaded thesis file contains from the Introduction to Conclusion pages and result shows 4 percentage of plagiarism in the dissertation.

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DECLARATION

I solemnly declare that the dissertation **"ROLE OF SPECIAL MUCOR SCREENING OPD IN THE MANAGEMENT OF POST COVID MUCOR EPIDEMIC***"* is done by me at the Madras Medical College and Government General Hospital, Chennai during 2019-2022 under the guidance and supervision of **Prof.** ***Dr. R.MUTHU KUMAR MS.,DLO.,DNB***

This dissertation is submitted to The Tamilnadu Dr. M.G.R. Medical University, towards partial fulfillment of regulation for the award of **M.S. DEGREE IN OTORHINOLARYNGOLOGY (BRANCH-IV)**

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ABBREVATIONS

IFS	:	Invasive Fungal Sinusitis
CAM	:	Covid Associated Mucormycosis
ROCM	:	Rhino Orbital Cereberal Mucormycosis
DKA	:	Diabetic Keto Acidosis
EOM	:	Extra Ocular Movements
PAS	:	Periodic Acid Schiff stain
RM	:	Retro Maxillary
PM	:	Pre Maxillary
ICE	:	Intra Cranial Extension
KOH	:	Potassium Hydroxide
DNE	:	Diagnostic Nasal Endoscopy
CT	:	Computerized tomography
MRI	:	Magnetic resonance imaging
HPE	:	Histopathological examination

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BACKGROUND

The 2019 novel coronavirus (2019-nCoV) or severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) first reported in Wuhan, Hubei province in China, quickly spread to other parts of the world forming a global pandemic. The disease pattern of COVID-19 can range from mild to life-threatening pneumonia with associated bacterial and fungal coinfections.

Rhinocerebral mucormycosis is an acute, fulminant, and often lethal opportunistic infection typically affecting diabetic or immunocompromised patients. It is caused by one of the members of the mucoraceae family including Absidia , Mucor , and Rhizopus. Clinically, presenting symptoms are nonspecific including headache, low-grade fever, facial swelling, and orbital or paranasal sinus syndrome. After infection of the nasal cavity and paranasal sinuses, the fungi cause a necrotizing vasculitis that extends rapidly into deep face, orbits, cranial cavity, and brain through skull base partitions and foramina.

It is important to distinguish the Invasive disease from the Non invasive because treatment and prognosis are different in each. Early diagnosis is vital in these infections because delay in initiation of treatment can be life threatening due to the propensity of the fungi to invade adjacent blood vessels and embolize to distant organs including brain. Mucor screening clinic with the availability of General Physician, ENT, Ophthalmology, Diabetology, Mycology and Microbiologist under one roof helps in early identification of Mucormycosis .[1]

INTRODUCTION

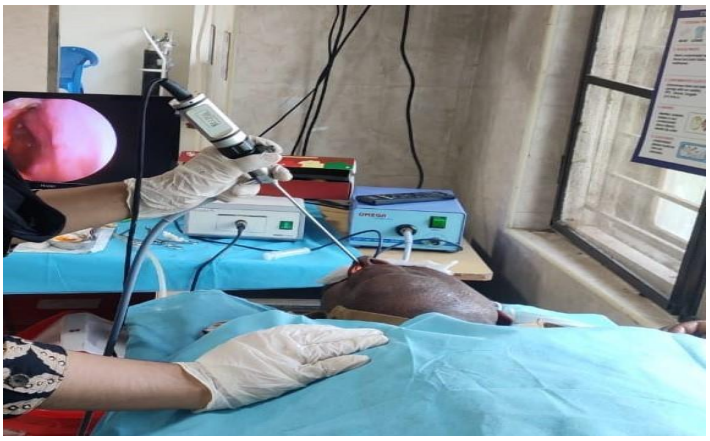
MUCORMYCOSIS SCREENING CLINIC :

Following the 2nd wave of COVID, the state was hit by an unprecedented wave of mucormycosis across the state. Mucormycosis is a devastating fungal infection which has its entry through the upper respiratory tract affecting the Nose, orbit and brain. Incidence of Mucormycosis globally varies from 0.005 to 1.7 per million population, in India it is estimated as 140 per million population ,which is 80 times higher than in developed countries. Detecting and Treating Mucormycosis at an early stage prevents the progression to advanced stages and hence avoids the morbidity and mortality connected with this dreadful disease. The diagnosis often involves multidisciplinary evaluation and the patient has to visit several departments. Hence this novel idea of bringing all the facilities under one roof was mooted out to avoid unnecessary hardships to patients.

The screening clinic was highly efficient in the early detection and prevention of further progression in this epidemic.

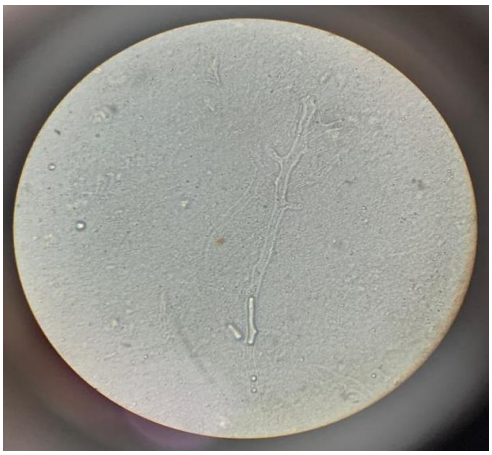
DIAGNOSTIC FACILITIES OFFERED IN THIS CLINIC:

1.**ENT examination** – Nasal Endoscopy for taking Nasal Smear and Biopsy for Histopathological Examination



2.**OPHTHALMOLOGICAL EXAMINATION** including visual acuity and retinal/fundus examination, evaluation of vision, fundus examination by indirect ophthalmoscopy & orbital evaluation.

3.**MYCOLOGICAL EXAMINATION**-KOH mount to detect invasive fungus(mucorales) ,results were known to the patients within 2 hours.



4.**DIABETOLOGY AND PHYSICIAN EXAMINATION**

5.**PATHOLOGY** – HPE to detect invasive fungus

6.**MICROBIOLOGICAL EXAMINATION**- Fungal Culture and Sensitivity

-People are made aware of the symptoms and made to visit to the screening clinic at the earliest.

MUCORMYCOSIS –SYMPTOMS:

NOSE

EARLY SYMPTOMS:

- Nasal block
- Nasal Discharge –Blackish or Brownish
- Headache
- Fever
- Lethargy
- Facial Pain (sinusitis)

LATE SYMPTOMS:

- Facial swelling
- Black eschar over face (Necrotic Eschar)

EYE

EARLY SYMTPOMS:

- Redness and congestion of Eye
- Eye pain
- Watering of eye
- Decreased Vision

LATE SYMTOMS:

- Double Vision
- Blindness(Partial or Complete)
- Protrusion of Eye Ball
- Drooping of Upper Eyelid (Ptosis)
- Loss of movements of the Eye Ball

ORAL CAVITY:

- Toothache
- Loosening of Teeth
- Falling of Teeth
- Loss of Tooth Sensation
- Black Eschar over Palate (Roof of Mouth)

CENTRAL NERVOUS SYSTEM:

- Altered consciousness
- Lethargy
- Paralysis
- Cranial neuropathies

FOLLOW UP CLINIC :

1.Follow up clinic is also a part special mucor screening OPD, where patients post-operative follow up of the patients are carried out in an integrated manner.

2. T.Posaconazole is issued for the discharged patients weekly

3. Readmission if necessary.

MUCORMYCOSIS –HISTORY

In 1791 first description about fungal sinusitis was made by Plaignand.

The upper airway mucormycosis was first explained by Paultauf in the year 1885 and also he coined the term mycosis mucorina. Now it is popularly called as mucormycosis

In 1943, Gregory et al described the first case of rhino-orbital cereberal mucormycosis in a diabetic patient.

The distinction between invasive and non invasive sinusitis ,based on clinical findings was first made by Hora in 1965.

In 1967,Sudan decribed cases of chronic granulomatous disease.

In 1980 ,Mc Gill et al,reported a fulminant form of invasive fungal sinusitis in a immunocompromised person with malignant course .

In 1980,Talbot et al classified Invasive Fungal Sinusitis into

1)Fulminant aspergillosis

2)Rhinocereberal Mucormycosis

3)Aspergilloma

In 1997, DeShazo et al, proposed classification and diagnostic criteria for invasive fungal sinusitis

Diagnostic Criteria was based on Histopathological Evidence of hyphal forms within the sinus mucosa, submucosa, blood vessels or bone.

NON INVASIVE FUNGAL SINUSITIS	INVASIVE FUNGAL SINUSITIS
Allergic fungal sinusitis	**Acute fulminant**
Sinus mycetoma or fungal ball	**Chronic invasive**
Saprophytic fungal infection	**Chronic granulomatous invasive**

The term 'MUCORMYCOSIS' was coined by American pathologist **R.D.BAKER.**

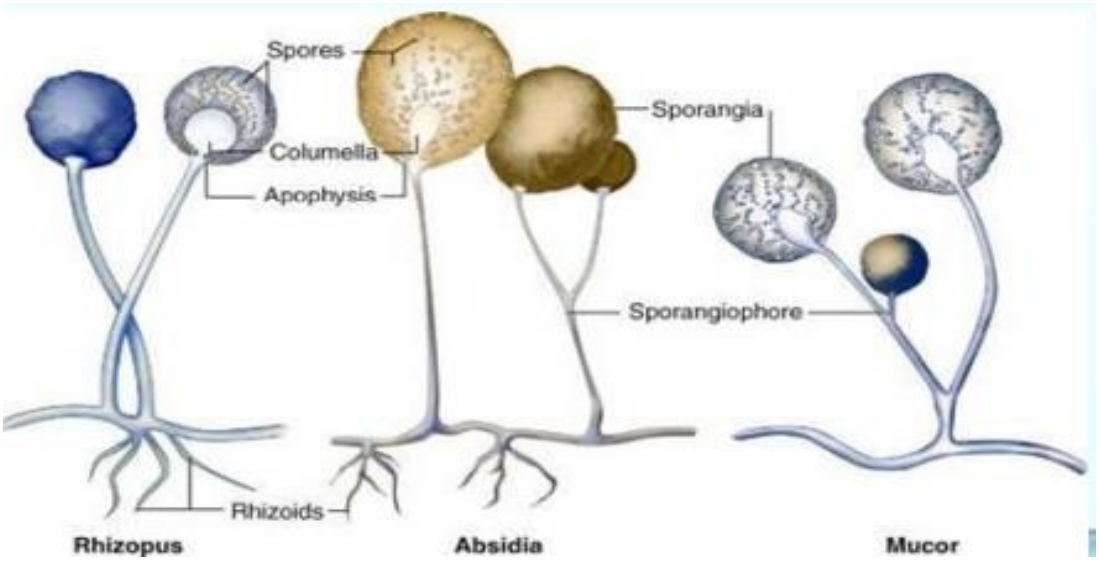
FUNGAL ANATOMY

Mucormycosis is a fatal fungal infection . It is a saprophytic fungi commonly found in soil and decaying organic matter.The order mucorales (Zygomycetes) characteristically produce large, ribbon like hyphae that are irregular in diameter and contain occasionally septa. Because the septa may not be apparent in some preparations, this group sometimes has been characterized as aspetate.

The specific identification of these organisms is confirmed by observing the characteristic sac like fruiting structures

(sporangia),which produce internally ,yellow or brown spores (sporangiospores). Each sporangium is formed at the tip of a supporting structure (sporangiophore) . During maturation , the sporangium becomes fractures and sporangiospores are released into the environment .Sporangiophores are usually connected to one another by occasionally septate hyphae called stolons, which attach at a point where root like structures (rhizoids) . May appear and anchor the organism to the agar surface .

Identification of the mucorales is partly based on the presence or absence of rhizoids and position of rhizoids in relation to the sporangiophores.



Primary mode of spread is through inhalation of fungal spores. Small spores of mucorales (3 – 11µm) reach up to distal alveolar spaces causing sinopulmonary mucormycosis. **Large spores (>10µm)** may lodge in the nasal turbinates causing sinusitis. To affect human, fungal spores generally overcome phagocytosis by macrophages and neutrophils and germinate into hyphae.[3]

MUCORALES ORDER

- Mucorales
- Rhizopus
- Mucor spp
- Actinomucor *elegans*
- Cokeromyces *recurvatus*
- Litcheimia *spp*
- Cunninghamella
- Rhizomucor pusilus
- Saksenaea *spp*
- Apophysomyces *spp*
- Syncephalastrum *racemosum*

COVID ASSOCIATED MUCORMYCOSIS (CAM)

- COVID-19 has tendency to worsen diabetes and also precipitate diabetes in previously normal individuals .
- The Covid 19 infection itself is associated with leucopenia and may lead to immune compromise caused by impaired or inappropriate immune responses.
- Immunosuppressive treatments are being widely used for treatment of Covid-19 infection .
- Despite the fungus being ubiquitous , The severity of Mucor infection is largely dependent on the patient's immunity and general health.
- Neutropenic disorder is the main risk factor for development of this disease.
- Coexistence of Covid – 19 infection with high blood sugar levels, and immunosuppressive treatments would expectedly increase incidence and severity of Mucormucosis.
- Severe form of COVID 19 infection can decrease the levels of lymphocytes and neutrophils markedly.
- Mucor infection may occur during Covid-19 infection or after a few days.

PATHOPHYSIOLOGY OF CAM:

HOST FACTORS :

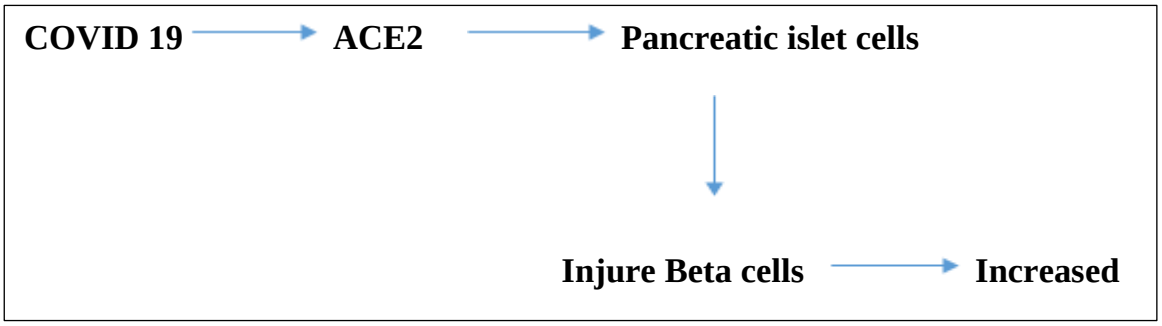
Innate immunity is primarily responsible for clearing the spores from mucosal surfaces in healthy individuals.The convential risk factors for Invasive Fungal infection include

Diabetes mellitus, neutropenia, hematological malignancies, solid organ transplantation, hematopoietic stem cell transplant, immunosuppressive therapies.

DIABETES and COVID 19:

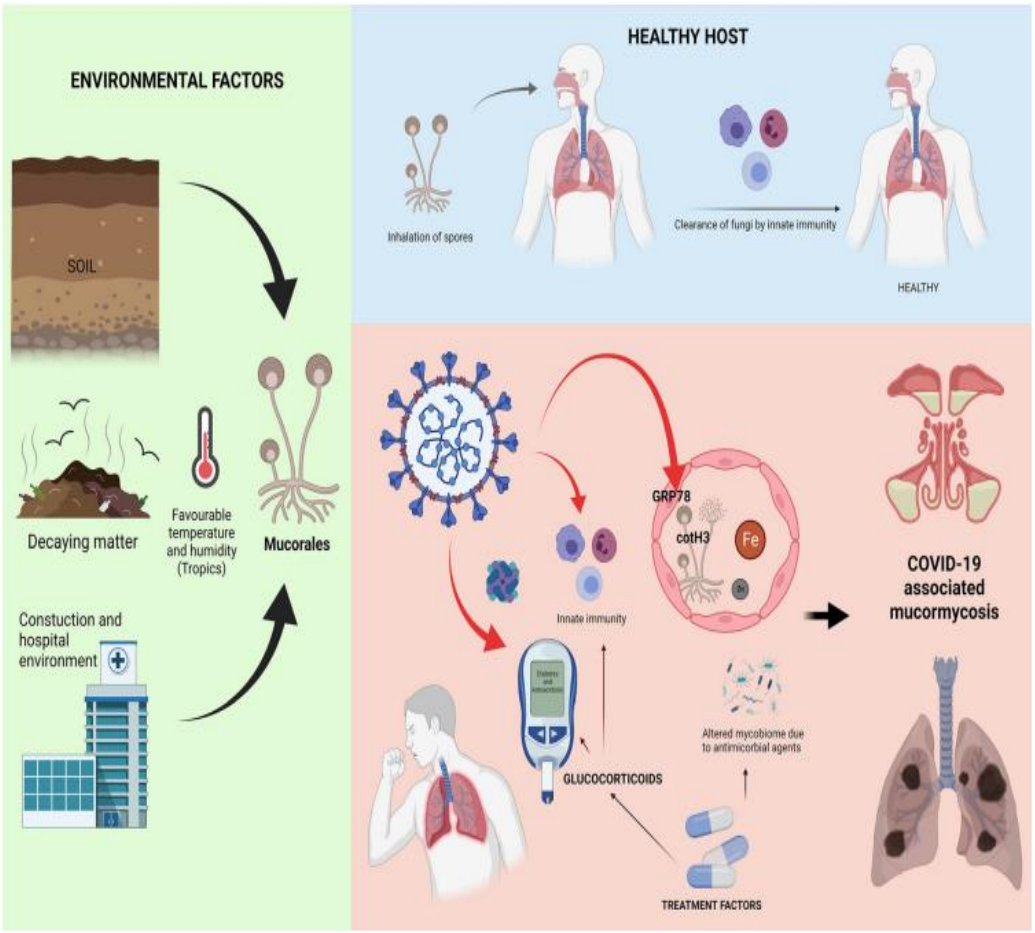
Diabetes mellitus being the most common underlying risk factor and is associated with increased mortality due to COVID 19.Diabetes impairs innate immnuntiy .

COVID 19 can lead to diabetes. COVID 19 virus acts on Angiotensin converting enzyme 2 (ACE 2),which is found in the lungs and pancreas , serves as an entry for COVID 19.



Patients with DKA are even more prone to mucormycosis. Hyperglycemia increases Glucose regulated 78kDa protein (GRP78) on endothelial cells .The essential receptor for vascular invasion by mucorales is through its spore core protein (CotH) . Mucorales interacts with GRP78 on nasal epithelial cells via CotH3 damage nasal epithelial cells leading to angioinvasion .

Expression of GRP78 and CotH3 is significantly enhanced by high glucose, iron and ketones.



OTHER FACTORS

Iron metabolism:

Hyperferritinemia, due to profound inflammation is a characteristic feature of COVID 19. Acquisition of iron from the host is essential for the growth of Mucorales. In patients with DKA , acidosis temporarily dislocates iron bound to transferrin . The ketoacid , - β hydroxybutyrate indirectly compromises the ability of transferrin to chelate iron.

GLUCOCORTICOIDS:

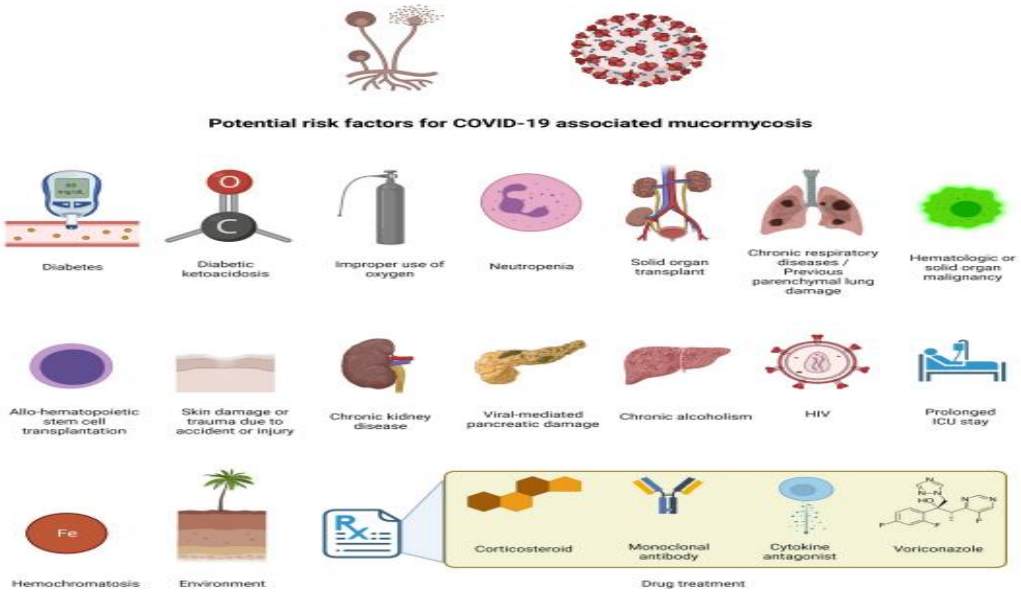
Prolonged use in COVID 19 patients seems to be risk factor .In a study mentioned that doses and duration of dexamethasone more than 6 mg upto 10 days were associated with increased risk . Further diabetes increases cortisol release .[2]

ENDOTHELIAL DYSFUNCTION:

Use of **Biological Agents** –particularly toclizumab inhibits interleukin IL-1 & IL-6 and may further increase the risk for infection.

Industrial Oxygen –impurities in industrial oxygen is under further study.[2]

Zinc supplements enhances Fungal growth particularly in acidosis . Fungal transporters work optimally at acidic pH.



Steam inhalation –Nasal mucosal epithelium shows decreased ciliary beat when exposed temperature beyond 45° C and results in cell death. Nasal microbial imbalance suppresss local immunity

TYPES OF MUCORMYCOSIS:

- Rhino Orbital Cereberal Mucormycosis **(MOST COMMON)**
- Pulmonary Mucormycosis
- Cutaneous Mucormycosis
- Gatrointestinal Mucormycosis
- Disseminated Mucormycosis

STAGES OF MUCORMYCOSIS:

STAGE I : INVOLVEMENT OF THE NASAL MUCOSA

IA: limited to the middle turbinate

IB: involvement of the inferior turbinate or ostium of the nasolacrimal duct

IC: involvement of the nasal septum

ID: bilateral nasal mucosa involvement

SYMPTOMS: nasal stuffiness, nasal discharge, foul smell , epistaxis

SIGNS:

Foul smelling sticky mucoid or black-tinged or granular or haemorrhagic nasal discharge ,nasal mucosal inflammation ,erythema, violaceous or blue discolouration, pale ulcer,anaesthesia,ischaemia , eschar

STAGE II: INVOLVEMENT OF PARANASAL SINUSES

IIA: one sinus

IIB: two ipsilateral sinuses

IIC: >two ipsilateral sinuses and /or palate /oral cavity

IID: bilateral paranasal sinus ,involvement of the zygoma or mandible

SYMPTOMS: STAGE I + facial pain, facial edema, dental pain, systemic symptoms (malaise ,fever)

SIGNS: STAGE I + unilateral or bilateral,localized or diffuse facial edema ,edema localized over the sinuses ,localized sinus tenderness

STAGE III:INVOLVEMENT OF THE ORBIT

IIIA: nasolacrimal duct,medial orbit ,vision unaffected

IIIB: diffuse orbital involvement (>1 quadrant or >2 structures),vision unaffected

IIIC: central retinal artery or ophthalmic artery occlusion or superior ophthalmic vein thrombosis ,involvement of the superior orbital fissure, inferior orbital fissure ,orbital apex, loss of vision

IIID: bilateral orbital involvement

SYMPTOMS: STAGE I AND II + ,pain ,proptosis, ptosis diplopia, loss of vision

SIGNS:

Conjuctival chemoses ,isolated ocular motility restriction ,ptosis ,proptosis, infra orbital nerve anaesthesia,CRAO,V1 and V2 nerve anaesthesia and features of III,IV and VI nerve palsy indicating orbital apex/superior orbital fissure involvement

STAGE IV: INVOLVEMENT OF THE CNS

IVA: focal or partial cavernous sinus involvement and/or involvement of the cribriform plate

IVB: diffuse cavernous sinus involvement and/or cavernous sinus thrombosis

IVC: involvement beyond the cavernous sinus, involvement of the skull base, internal carotid artery occlusion, brain infarction

IVD: multifocal or diffuse CNS disease

SYMPTOMS:STAGE I to III + bilateral proptosis, paralysis, altered consciousness, focal seizures

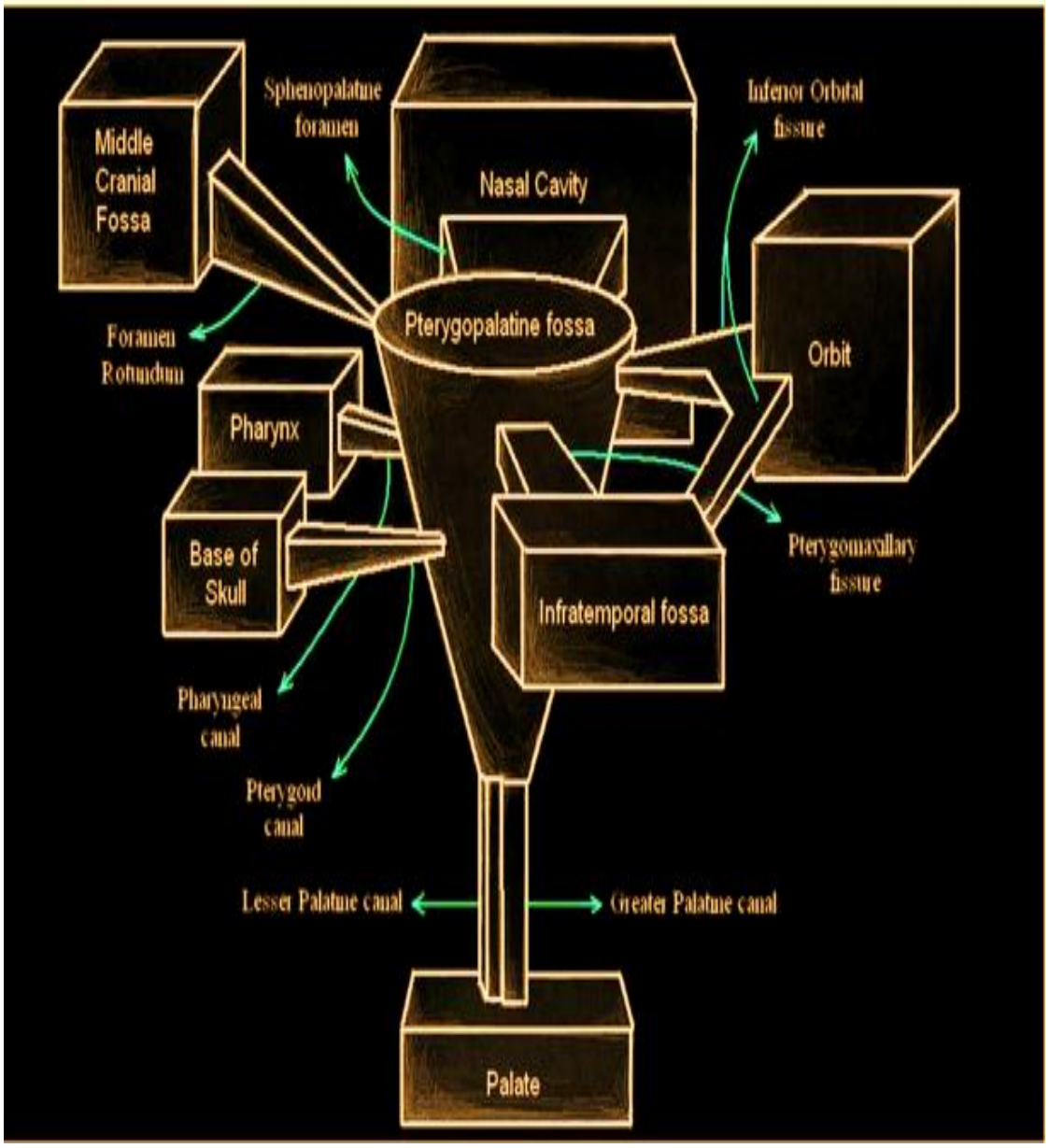
SIGNS:

STAGE I –III with cavernous sinus involvement hemiparesis, altered conscious ness and focal seizures indicate brain invasion and infarction. [4]

RED FLAG SIGNS AND SYMPTOMS OF ROCM:

- Epistaxis
- Nasal discharge –mucoid, purulent,blood tinged or black
- Nasal mucosal erythema, purple or blue discolouration, eschar
- Eyelid –periocular ,facial discolouration
- Worsening headache
- Proptosis
- Sudden loss of vision
- Facial paresthesia ,anaesthesia
- Sudden ptosis
- Ocular motility restriction , diplopia
- Facial palsy
- Fever , altered sensorium , paralysis ,focal seizures[11]

MUCORMYCOSIS – ROUTES OF SPREAD



Mucormycosis is the most invasive rapidly progressive fungal infection ,hence early detection and treatment are the key elements for survival .The fungus initially inoculates the nasal mucosa , spreading to the paranasal sinuses. The pterygopalatine fossa is the main reservoir for mucor and acts as a conduit for the spread of infection. Since, angio

invasion occurs early than bony invasion in most of the cases posterior wall of pterygoplatine fossa is intact. From the nasal mucosa, mucor spreads to petrygoplatine fossa via sphenopalatine foramen and through the pterygomaxillary fissure into the infratemporal fossa. Orbital invasion can even occur without the involvement of paranasal sinuses and this occurs due to extension from pterygoplatine fossa to orbit and retrobulbar space through inferior orbital fissure results in edema of eyelids and chemosis. Invasion of optic nerve and/or central thrombosis of central retinal artery results in vision loss.

Ocular paralysis is due to invasion of extraocular and retrobulbar muscle. Orbital apex involvement leads to subsequent involvement of cavernous sinus. Involvement of inferior orbital nerve results in paraesthesia in the infra orbital region. Paralysis and paresthesia of the face is due to submucosal infiltration of facial muscles by mucor. As the disease progress obliteration of vessels occurs leading to thrombosis of skin over the face. Intracranial extension occurs through foramen rotundum into middle cranial fossa and through cribriform plate into the frontal lobe . Palatal invasion occurs through greater palatine canal with the involvement of descending platine and nasoplatine vessels .So, Pterygopalatine fossa is the **CENTRAL HUB OF MUCORMYCOSIS**.

CLINICAL EXAMINATION:

- **ANTERIOR RHINOSCOPY:**
- **ORAL CAVITY**
- **OCULAR EXAMINATION** :

-Vision

-Pupillary reflex

- Extra Ocular movements (EOM)

INVESTIGATIONS:

DIAGNOSTIC NASAL ENDOSCOPY:

Commonest finding encountered is

-Pale middle turbinate

-ESCHAR/slough involving Middle turbinate ,septum

-Secretions in Middle turbinate

RADIOLOGICAL EVALUATION:

- Computed tomography of Paranasal sinuses (axial & coronal) with contrast
- Magentic Resonance Imaging with Gadolinium contrast

Computed tomography of the paranasal sinuses shows isodense to muscle/brain. Opacification of sinuses is noted with characteristic Premaxillary and Retromaxillary fat stranding which is more evident of Invasive fungal sinusitis .On Post contrast Computed Tomography , contrast enhancement and involvement of extra sinus structures including

orbit, pterygopalatine fossa, masticator space, cavernous sinus were noted. Bony erosions are better made out in CT. Orbital cellulitis was seen as stranding in the retrobulbar fat, without overt abscess formation

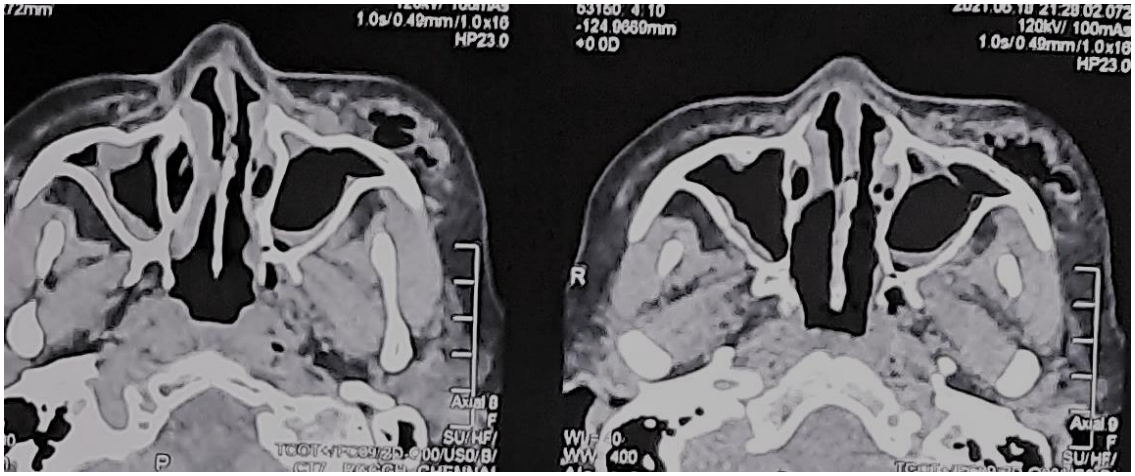


Fig: showing pre and retro maxillary fat stranding

Magnetic Resonance Imaging with Gadolinium contrast is considered as **GOLD STANDARD**. Extent of infection and enhancement of lesion were better delineated with Fat suppressed Post Gadolinium images . Black turbinate sign described by **Safder et al** is an early feature of mucormycosis. Involvement of Cavernous sinus , carotid , intracranial enhancement and abscess is made out.

Retroantral, facial and orbital fat stranding indicates perinerual spread /perivascular invasion without destroying the bone .T2 hypointense in MRI is due to ***presence of iron and manganese in fungal elements*** . Mucor is a disease of angio invasion hence skull base osteomyelitis and bone involvement usually seen in late stage of disease.

FUNGAL IDENTIFICATION :

SPECIMEN COLLECTION,TRANSPORT AND PROCESSING

Blood cultures are not appropriate for diagnosis of mucormycosis. Specimens from deep lesions or tissues and sterile sites should be collected rapidly and aseptically. Sufficient quantity is essential to improve the identification and recovery of the fungal isolate.

Samples collected for the diagnosis of rhino Orbital cereberal forms of infection should include

- Nasal Discharge Or Scrapings,
- Sinus aspirate
- Tissue specimen from a vascularized tissue. Mucorales are extremely sensitive to environmental changes

General considerations:

- Specimens should be collected aseptically in sterile containers and transported to the laboratory within 2 hours.
- Avoid sending swabs if pus or sterile body fluid can be aspirated or when tissue can be obtained. Swabs may give false negative reports.
- However, swabs need to be appropriately collected from certain body sites such as nasopharynx, throat etc., from

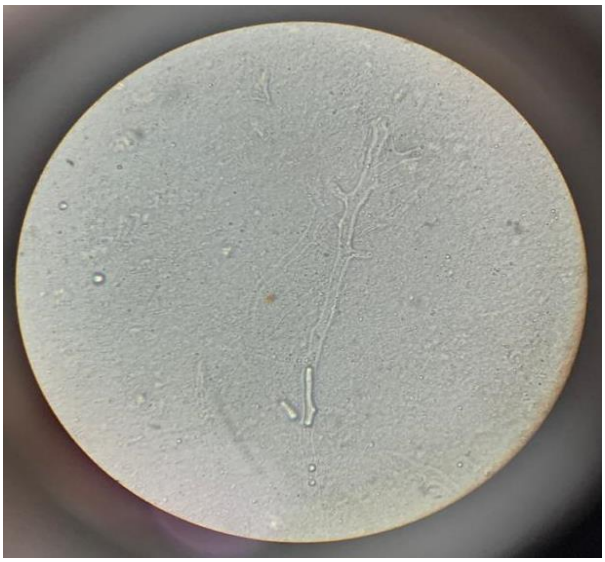
where no other specimen can be obtained. In such situation swabs should be moistened with sterile normal saline and then swabbed over the site of collection. Collect two or more swabs ensuring that material is present on swabs. Never use dry swabs to collect specimen.

- Tissues should be sent in sterile normal saline and never in formalin for Culture sensitivity.
- Simultaneously tissue in formalin should be sent for Histopathology.

TYPE OF SUSPECTED MM	SPECIMEN COLLECTION	UNACCEPTABLE SPECIMEN
RHINORBITAL MUCORMYCOSIS	Scraping or exudate from nares, hard palatal lesions, sinus material, biopsy from extracted tooth socket area. Endoscopic collection of debrided tissue/biopsy	Nasal dry swabs
CUTANEOUS	Aspirations collected with sterile needle and syringe from undrained abscess. Pus expressed from abscess opened with scalpel; transported to laboratory either in sterile container/syringe and needle Tissue should be collected from both center and edge of the lesion.	Swab or materials from open wound dry swabs

STAINS:

Mucormycosis is diagnosed rapidly by examining tissue specimens or exudate from infected lesions in a potassium hydroxide preparation or calcofluor white can be used .If the sample is too thick, a false negative result may occur because of insufficient dissociation of tissues. It is therefore recommended that the negative slide be maintained overnight and reviewed again the next day. Branching, broad -diameter predominantly non septate hyphae are observed .10% KOH is routinely used to fix the specimen ,if the sample is too thick upto 40% KOH can be used . Non-septate or pauci-septate, irregular, ribbon-like hyphae; Wide-angle of non-dichotomous branching (≥45-90 degree) and greater hyphal diameter as compared to other filamentous fungi. These are 6-25 μm in width.



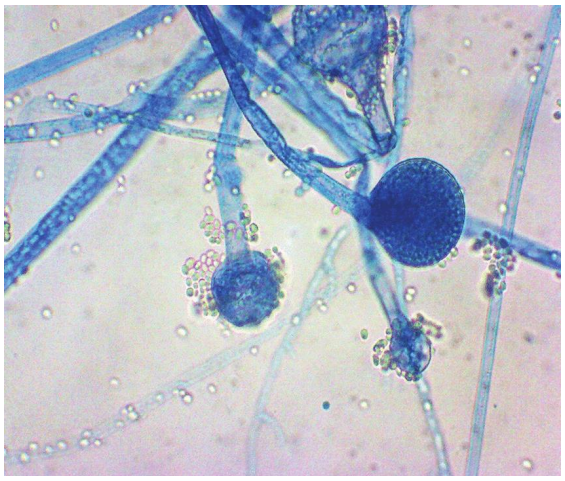
OTHER STAINS:

- Hematoxylin-Eosin
- Periodic acid-Schiff
- Grocott-Gomori's methenamine-silver stain
- Calcofluor white stain
- Lactophenol cotton blue

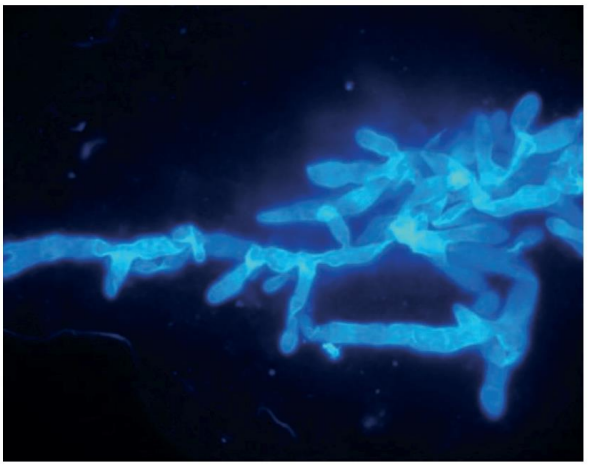
Direct microscopy has about 90% sensitivity. Obtaining the swab from clinically active lesions under endoscopy guidance may help improve the diagnostic yield.[4]

METHOD	TIME REQUIRED
POTASSIUM HYDROXIDE	5 min
PERIODIC ACID SCHIFF STAIN	20 min
SALINE WET MOUNT	1 min
CALCOFLUOR WHITE STAIN	1min
LACTOPHENOL COTTON BLUE	1 min

LACTOPHENOL COTTON BLUE

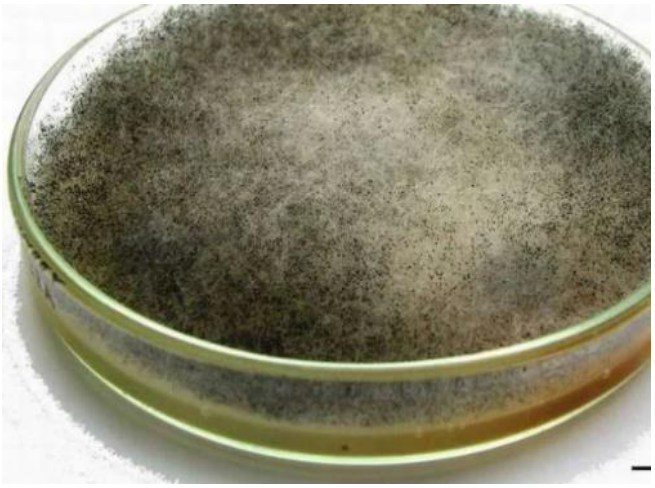


CALCOFLUOR WHITE STAIN



FUNGAL CULTURE:

- Potato dextrose or preferably Sabouraud dextrose agar with gentamicin
- 2% malt and cherry decoction (acidic) agars
- Brain heart infusion agar
- chloramphenicol and polymyxin-B, incubated at 30-37°C helps in genus and species identification and antifungal susceptibility testing.



Growth and development of the mycelium in the mucorales occurs within 24 to 48 hours. Subcultures should be incubated at 27 C to 30 C. Colonies characteristically produce a fluffy, white to gray or brown hyphal growth that resembles cotton candy and that diffusely covers the surface of the agar within 24 to 96 hours .The hyphae can grow very fast and may lift the lid of the agar plate , also known as **LID LIFTER**. The entire culture dish or tube rapidly fills with loose, grayish hyphae dotted with brown or black sporangia.The different genera and species of mucorales cannot be differentiated using colonial morphologic features.

Brain heart infusion agar, potato dextrose agar or preferably Sabouraud dextrose agar with gentamicin or chloramphenicol and polymyxin -B, but without cycloheximide, incubated at 30-37°C helps in genus and species identification and antifungal susceptibility testing.[26]

HISTOPATHOGICAL EXAMINATION:

Histopathologic evaluation of tissue biopsies is required to confirm the diagnosis of invasive fungal rhinosinusitis.

Fungal disease is determined to be invasive ,

1) Hyphal forms within the submucosa with or without vascular Invasion with accompanying thrombosis (ANGIOTROPISM OF FUNGI)

2) Luminal involvement may result in complete obstruction and thrombosis that may result in tissue necrosis (GRITTY type necrosis)

3) Tissue necrosis with minimal host inflammatory cell infiltration is the most obvious finding

4) Rarely , foreign body type multinucleated giant cells may be identified within which fungi may be identified.

Special stains such as Gomori Methenamine Silver Stain are useful if the organisms are not immediately visible on Haematoxylin and Eosin stain.

Necrosis not only affects the underlying tissue but also the fungal organisms, which can be deprived of oxygen and nutrients .When the fungal organisms die ,they become fragmented and more difficult to identify.

Antifungal therapy can also lead to distortion of the morphology of the hyphae.

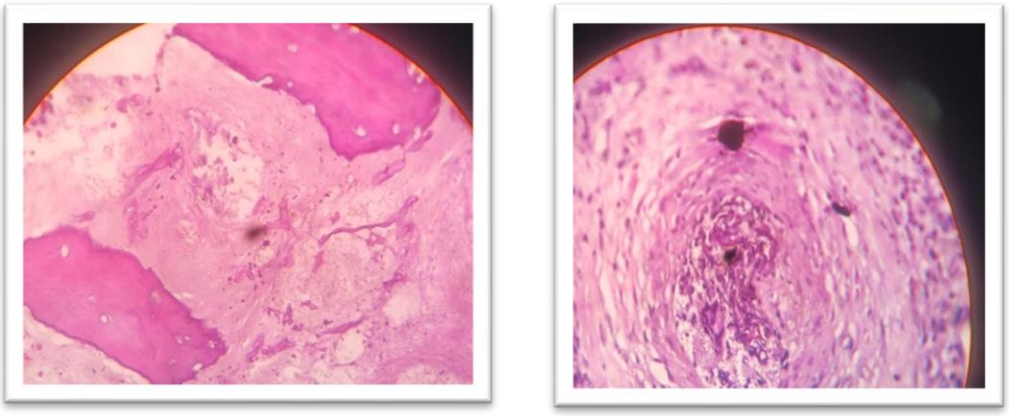


Fig : showing broad aspetate hyphae in vascular lumen and adipose tissue

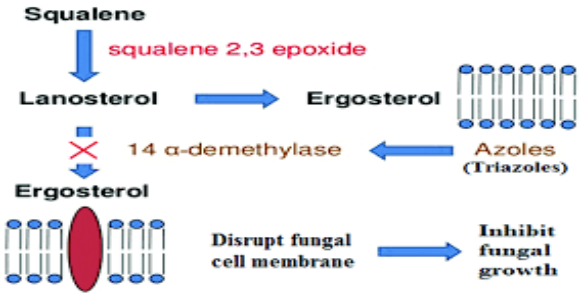
Ideally, tissue should be sent for frozen and permanent sections. Frozen section evaluation

- allows for a timely diagnosis
- Confirmation that all necrotic tissue that could be harbouring fungal elements has been removed

whereas permanent section with Gomori-methenamine silver stain confirms the diagnosis and provides important morphologic information that may be helpful in determining the fungal species[27]

PHARMACOLOGY OF POSACONAZOLE:

Posaconazole is a synthetic triazole broad spectrum antifungal with 4 fold greater activity against invasive fungus . It is used as a prophylaxis for invasive fungal sinusitis . As a modified release formulations it is given as a loading dose of 300 mg twice daily on day one , followed by 300mg once daily .Treatment is continued untill tissue response .Posaconazole is absorbed from gastrointestinal tract and has a large volume of distribution.



Peak plasma concentration occurs about 3 to 5 hours after an oral dose .Steady state plasma posaconazole concentration occur after 7 to 10 days of multiple dosage. The drug has a long half life of 35 hours. It has a large volume of distribution,indicating extensive distribution and penetration into tissues. Posaconazole is a substrate for intestinal P-glycoprotein ,an adenosine triphosphate dependent plasma membrane transporter responsible for drug efflux from cells . Multiple peaks in Posaconazole blood concentration have been observed, suggesting the effluxed drug is reabsorbed into systemic circulation. Plasma protein binding is 98%. Gastric acid improves posaconazole absorption so drugs that reduce gastric acid secretion decrease posaconazole absorption by 32 – 50%. The main eliminate of posaconazole is via faeces 71 to 77%, some amount via urine. Common adverse effects include nausea, vomiting, diarrhea, abdominal pain and headache.

AIMS AND OBJECTIVES

- To study the incidence of Rhinoorbital cereberal Mucor mycosis in Post covid patients attending multidisciplinary mucor screening clinic at RGGGH.

- To analyse the effectiveness of MUCOR SCREENING CLINIC in diagnosing rhino orbital Mucor mycosis in post covid patients.

- Early detection of stage 1 and 2 disease halting their progression .

- To make certain of how the screening test and available treatment influence the natural history of disease.

MATERIALS AND METHODOLOGY

STUDY PLACE:

Rajiv Gandhi Government General Hospital, Chennai – 600003.

COLLABORATING DEPARTMENT:

Upgraded Institute of Otorhinolaryngology

STUDY DESIGN:

Hospital based cross sectional study

STUDY PERIOD:

JUNE 2021 TO NOVEMBER 2021

ETHICAL CLEARANCE:

Obtained from the Institutional ethical committee

INCLUSION CRITERIA:

Post covid patients attending Mucor Screening Clinic at RGGGH,

Chennai -600003

Those who are willing to give informed consent.

EXCLUSION CRITERIA:

Patients with preexisting rhino-orbital mucormycosis

Those who are not willing to give consent

METHOD:

To collect a detailed clinical history , microbiological and radiological investigations in post covid patients with rhino-orbital mucormycosis

Study Tool:

By using semi structured questionnaire,

- Diagnostic Nasal Endoscopy
- Mycology (fungal KOH)
- Microbiological (fungal KOH & culture sensitivity)
- Radiological (CT PNS) investigations

Data Collection:

Data will be collected from post covid patients with rhinoorbital mucormycosis using semi structured questionnaire, microbiological and radiological investigations.

BENEFIT TO THE COMMUNITY:

a. Identification of incidence, clinical profile of Rhinoorbital mucormycosis in post covid patients attending Mucor Screening Clinic will provide useful knowledge .
b. Early identification, early treatment and early intervention in progressive disease and reduction of morbidity and mortality.
c. All multidisciplinary approaches under one roof avoiding unnecessary burden to the patient.
d. I chose this study to know the effectiveness of the novel intervention Mucor Screening Clinic in identifying the rhino-orbital mucormycosis especially in post covid patients in Tamilnadu.

REVIEW OF LITERATURE

In the year 2021**,Manjusha nambiar et al** in her study stated that "As the battle against the deadly covid-19 pandemic is still continuing worldwide, several complications are being reported in patients who have recovered post-covid. One such lethal complication being reported in patients in India in recent times, who have tested positive for Covid-19 and are gradually recovering, is a fungal disease called mucormycosis. With several hundereds of cases being reported all over the country, it is triggered an additional wave of panic among the general public. Post-Covid-19 patients who are more vulnerable to Mucormycosis are those with a history of poorly controlled diabetes mellitus and also those who are immuno-compromised and have been treated with steroids and other drugs for Covid-19. The aim of this short review is to briefly cover the epidemiology of mucormycosis, its possible pathophysiology in post covid scenario, the clinical presentation and its diagnosis and management.

She concluded that the spreading awareness in the public and vigilance among the clinicians remains more important in successfully managing mucormycosis, and for reducing mortality. Many a hospitals in India have opened the outpatient department (OPD) for mucormycosis, to screen all patients with covid-19 and recovering from covid-19. They are screened from 10 days to 6 weeks, when they are more vulnerable to the

fungal infection. As recommended by ICMR, patients are advised to report to nearby urban primary health centre or designated OPDs in hospitals if patients have symptoms. Multidisciplinary team approach including specialists from medical and dental fraternity is needed for the early diagnosis and management of mucormycosis".[5]

In the year 2021 **Valliappan Muthu , Shivaprakash M, Rudramurthy , Arunaloke Chakrabarti , Ritesh Agarwal** explained how environmental factors leads to covid 19 associated mucormycosis .The fungi mainly rests in decaying vegetable matter, and its spores can become airborne.Despite being ubiquitous its is commonly encountered as an opportunistic infection in immnunocompromised host.They have encountered mucormycosis after exposure to contaminated air . The burden of mucormycosis (nonCOVID-19 and COVID-19-associated) is exceptionally high . More research is needed to identify the pathophysiologic basis of CAM, including the role of SARS-CoV-2 on host innate immunity and the interaction with the different species of Mucorales. The role of hospital outbreaks of COVID-19 as a contributor to the increase in cases and the relation of certain species in causing CAM .[2]

Awadhesh Kumar Singh et al .,14 May 2021in their study stated that ,out of 101 patients with mucormycosis 82 had a prior history covid 19 infection ,resulting COVID 19 associated mucormycois(CAM) is on increasing trend .Diabetes and steroid abuse was found to be the underlying cause .diabetes mellitus was found in 80% of their cases and steroid abuse in 78.9% of their cases . The primary reason that appears to be facilitating Mucorales spores to germinate in people with COVID-19 is an ideal environment of low oxygen (hypoxia), high glucose ,acidic medium (metabolic acidosis, diabetic ketoacidosis [DKA]), high iron levels and decreased phagocytic activity of white blood cells (WsBC) due to immunosuppression (SARS-CoV-2 mediated, steroid-induced,background comorbidities) coupled with several other shared risk factors including prolonged hospitalization with or without mechanical ventilators.[6]

Fungal infection study forum mentioned that covid19 associated mucormycosis is associated with high morbidity and mortality ,if a post covid patient presents intially with– nasal blockade or congestion, nasal discharge (bloody or brown/ black), local pain o Facial pain or numbness or swelling o Headache, orbital pain o Toothache, loosening of maxillary teeth, jaw involvement o Blurred or double vision with pain; paresthesia, fever, skin lesion, thrombosis & necrosis (eschar) a high suspicion should rise. Team approach is required with infectious disease specialist,

microbiologist, histopathologist, intensivist, neurologist, ENT specialist, ophthalmologist, dentist, surgeons, radiologists etc.

Muhammad Shakir, Muhammad Hassaan Arif Maan, Shahan Waheed in their study conducted on 12 July 2021, reported a 67year old male ,known case of type 2 diabetes mellitus with history covid 19 infection 2weeks back developed right cheek eschar and ophthalmoplegia .Intially the patient had right cheek swelling with defective vision within 6 days it progressed to eschar and loss of vision. Computed Tomography findings revealed pansinusitis with erosion of pterygoid plates , soft tissue orbital thickening in intraconal and extraconal compartements ,MRI revealed lesion seems extending to right temporal lobe.Patient was then taken for emergency surgical debridement and broad spectrum antibiotic and Intravenous amphotericin was given.They concluded that prompt recognition and management is necessary in cases of rhino orbital mucormycosis, as a delay of only 6 days can double mortality from 35 to 66 %. Hence, early detection and appropriate interventions in collaboration with multidisciplinary teams significantly can reduce morbidity and mortality.[8]

Manoj Kumar et al in their study conducted on August 8,2021 reported that mucormycosis made severe chaos in india during second wave of covid -19 by its devastating surge with upto 50% mortality rate .They found out that apart from diabetes mellitus being an underlying cause of mucormycosis in covid 19 patients ,they added on to high dose of steroid therapy,long term oxygen ventilator support also added to rise in mucor epidemic.Also steam inhalation which distress the nasal tract's beneficial microbe ,disproportionate use of zinc resulted in increased surge.So, understanding these mechanism will pave the way to control mucormycosis epidemic in COVID 19 pandemic.

Anna Skiada,Ioannis Pavleas and Maria Drogari Apiranthitou in the year 2010 described that direct microscopic examination by using KOH wet mounts is in expensive ,and gives rapidly a presumptive diagnosis and it is strongly recommended with histopathology,by European Confedreration of Medical Mycology,but these methods are not able to identify a fungus to the genus or species level.However, culture is essential for identification of fungus at genus and species level .A positive culture from a sterile site confirms the diagnosis ,while a positive culture from a non sterile site yields false positive results.They concluded that sensitivity of culture islow as it can be falsely negative ,becausegrinding or homogenization of tissue specimen can destroy delicate hyphae of mucor

.So, proper sampling and handling of specimens before examination are a prerequisite for an optimal yield .[10]

Aranjani JM, Manuel A, Abdul Razack HI, Mathew in their study conducted on November 18,2021 observed that rhino orbital cereberal form is the most common form observed and three fourth of them had diabetes mellitus .they said that prevention strategies primarily involve managing comorbid conditions in high risk groups.In their study they quoted that prior to COVID 19 the mortality in mucormycosis was 50% and with the surge of covid associated mucormycosis it has increased to 85 %. Since COVID associated Mucromycosis is not transmitted between humans , no tracking like COVID 19 is required, but the actual incidence helps to plan appropriate health resource utilization and prevention strategies . Such measures can avoid further surge of mucormycosis . They also mentioned ICMR regulation multidisciplinary team comprising otorhinolaryngologist,ophthalmologist,microbiologist,pathologist,dentist,internal medicine expert,diabetalogist to manage patients with COVID associated mucormycosis[11]

In the year 2005 **Brad Spellberg, John Edwards, Jrand Ashraf Ibrahim**,mentioned that Rhinocerebral mucormycosis continues to be the most common form of the disease, accounting for between one-half of all cases of mucormycosis . About 70% of rhinocerebral cases are found in

diabetic patients in ketoacidosis . Rhinocerebral mucormycosis has also occurred in patients who received a solid organ transplant or those with prolonged neutropenia . These cases have been associated with steroid use for graft-versus-host disease. The initial symptoms of rhinocerebral mucormycosis are consistent with sinusitis or ocular complications or facial pain and facial numbness, followed by the onset of blurry vision, and soft tissue swelling . Fever is variable and white blood cell counts are typically elevated. If untreated, infection usually spreads from the ethmoid sinus to the orbit, resulting in vision loss and loss of extraocular muscle function. Marked chemosis is seen. On Infected tissue progresses through an erythematous phase, before onset of a violaceous appearance, and finally the development of a black, necrotic eschar indicating thrombosis of the vessel wall and tissue invasion . Infection can sometimes extend from the sinuses into the mouth and produce necrotic ulcerations of the hard palate .Cranial nerve findings represent extensive infection and signalling a grave prognosis. Progressive vision loss and ultimately blindness may result either from involvement of the optic nerve or from arteriolar invasion resulting in infarction or from cavernous sinus thrombosis. Cranial nerves five and seven most commonly affected.[12]

OBSERVATION

AGE DISTRIBUTION:

In our study of 230 patients, the age distribution was as follows:

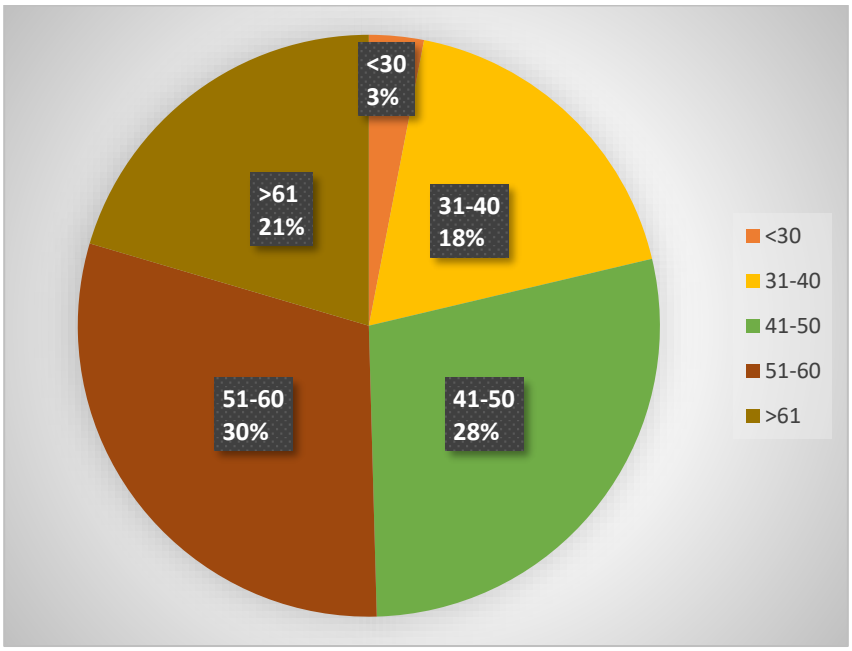


Fig: Pie chart showing the age wise distribution of patients in our study

- 7 patients were less than 30 years of age
- 69 patients were between 51 and 60 years of age
- 47 cases were more than 61 years of age

Table: Showing age distribution in our study

Age group	Frequency	Percent
<30	7	3.0
31-40	42	18.3
41-50	65	28.3
51-60	69	30.0
>61	47	20.4
Total	230	100.0

In our study, most patients were between 51 to 60 years of age (30%), followed by 41 to 50 years (28.3%), and 20.4% of cases were above 61 years of age. Only 3% of cases in our study were less than 30 years of age group.

GENDER DISTRIBUTION:

In our study males were more than females

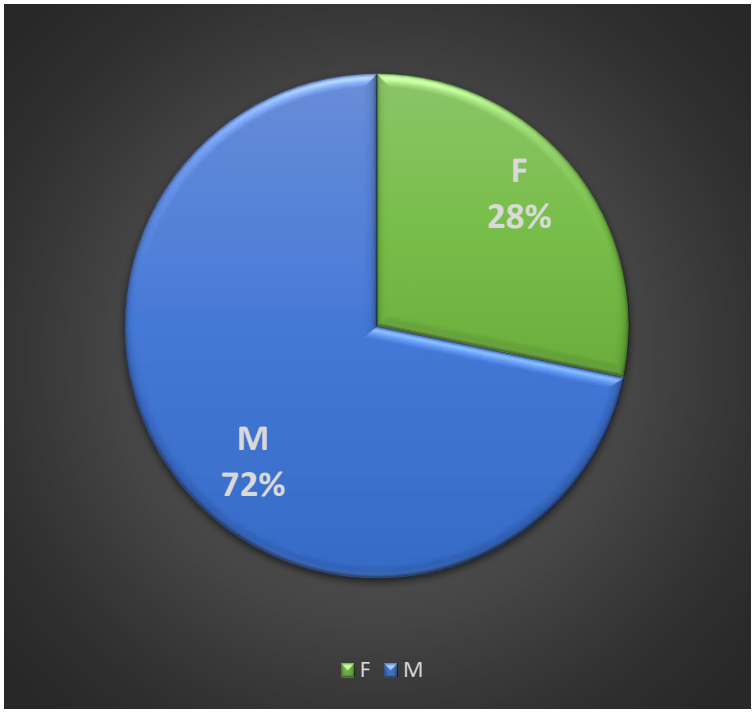


Fig: Pie chart showing the gender wise distribution of cases in our study

- 165 were male (72%)
- 65 were female (28%)

Table: Showing sex wise distribution of patients in our study

Gender	Frequency	Percent
F	65	28.3
M	165	71.7
Total	230	100.0

DURATION OF SYMPTOMS:

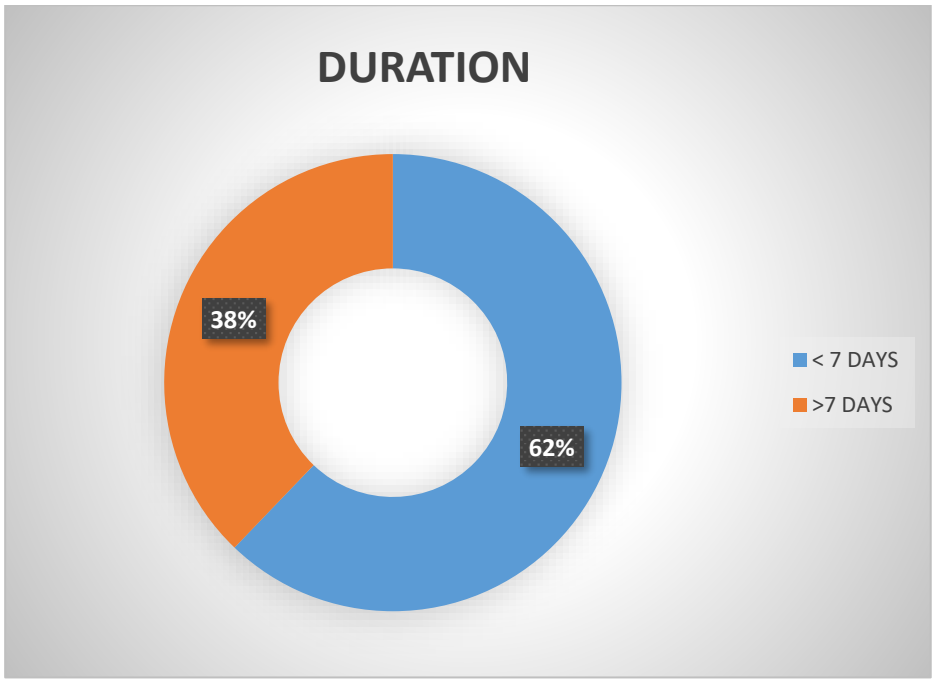


Fig: Pie chart showing distribution of cases by duration of symptom

Duration	Frequency	Percent
>7	87	37.8
<7	143	62.2
Total	230	100.0

In our study 87 patients (38%) presented at more than 7days of symptoms and 143 (62%) presented with less than 7 days of symptoms

CO-MORBIDITIES:

1. DIABETES MELLITUS:

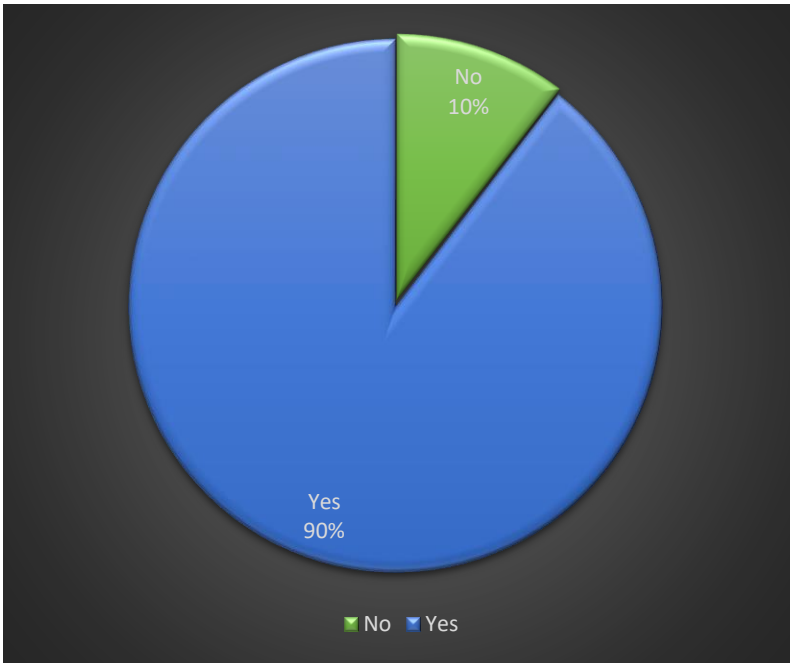


Fig: Pie chart showing frequency of patients with diabetes mellitus

DM	Frequency	Percent
No	24	10.4
Yes	206	89.6
Total	230	100.0

In our study 206 (90%) patients had diabetes mellitus as comorbidity and only 10% (24 cases) of cases were without diabetes mellitus

2. COVID-19 STATUS:

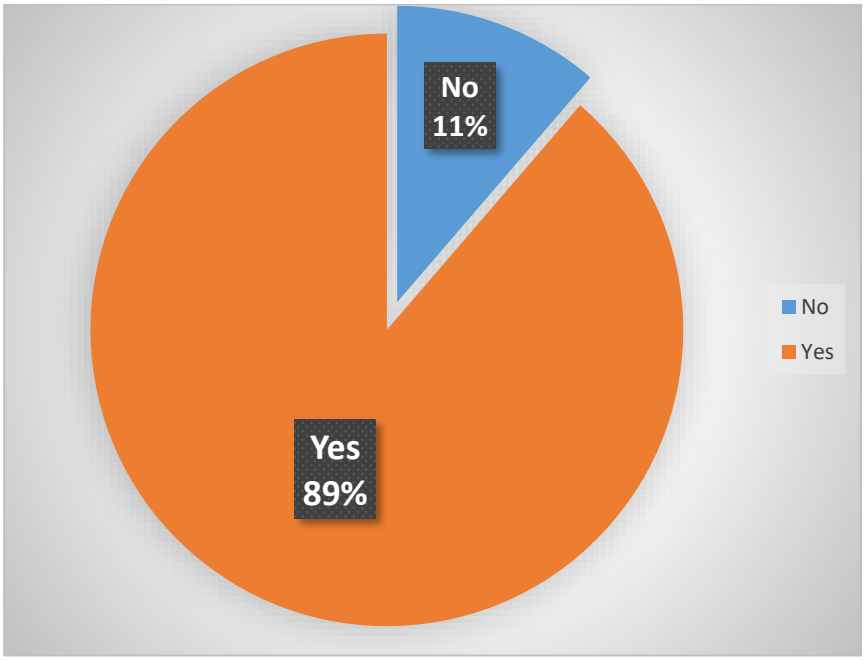
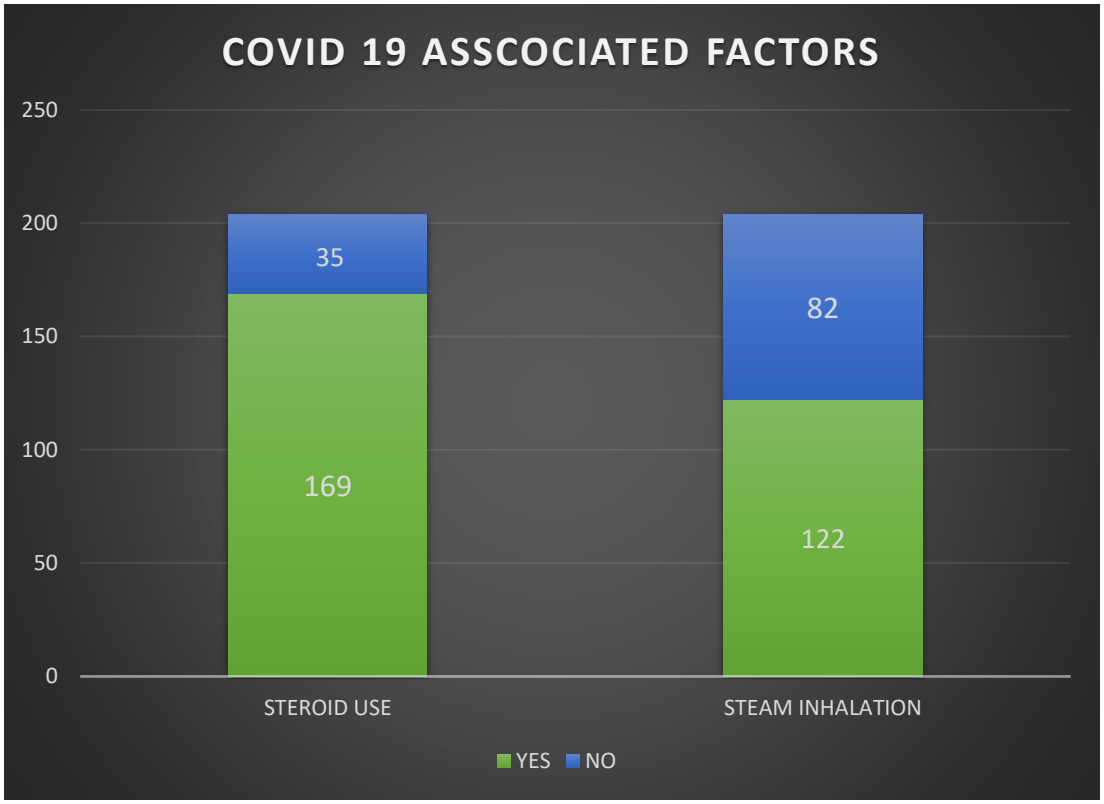


Fig: Pie chart and table showing covid status of patients in our study

Post-COVID	Frequency	Percent
No	26	11.3
Yes	204	88.7
Total	230	100.0

In our study of 230 cases, about 204 patients were post covid-19 infection (89%) and 11% (26 patients) were non covid cases.

COVID -19 WITH ASSOCIATED FACTORS :



In our study ,CAM was found in 204 patients, out of which

Steroid use present in 169 patients - 83%

Steam inhalation in 122 patients - 60%

CLINICAL DIAGNOSTIC NASAL ENDOSCOPIC FINDINGS:

1. ESCHAR IN NASAL CAVITY:

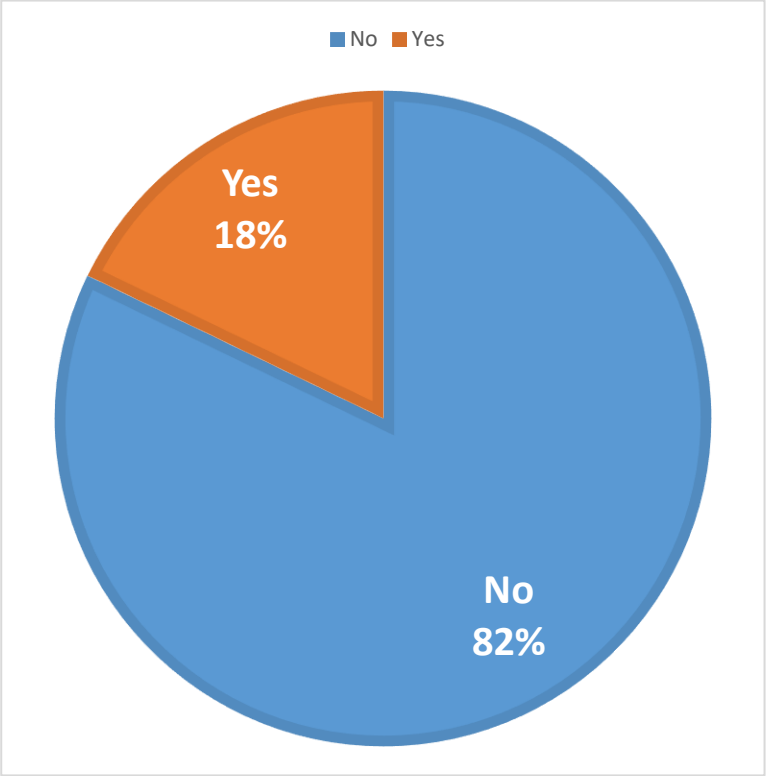


Fig: Pie chart showing patients with eschar in nasal cavity.

Table: Showing frequency of patients with eschar in nasal cavity

ESCHAR	Frequency	Percent
No	189	82.2
Yes	41	17.8
Total	230	100.0

In our study of 230 cases, around 41 cases had eschar in the nasal cavity in diagnostic nasal endoscopy while 82% of cases (189 patients) had no eschar.

2. SECRETION IN NASAL CAVITY:

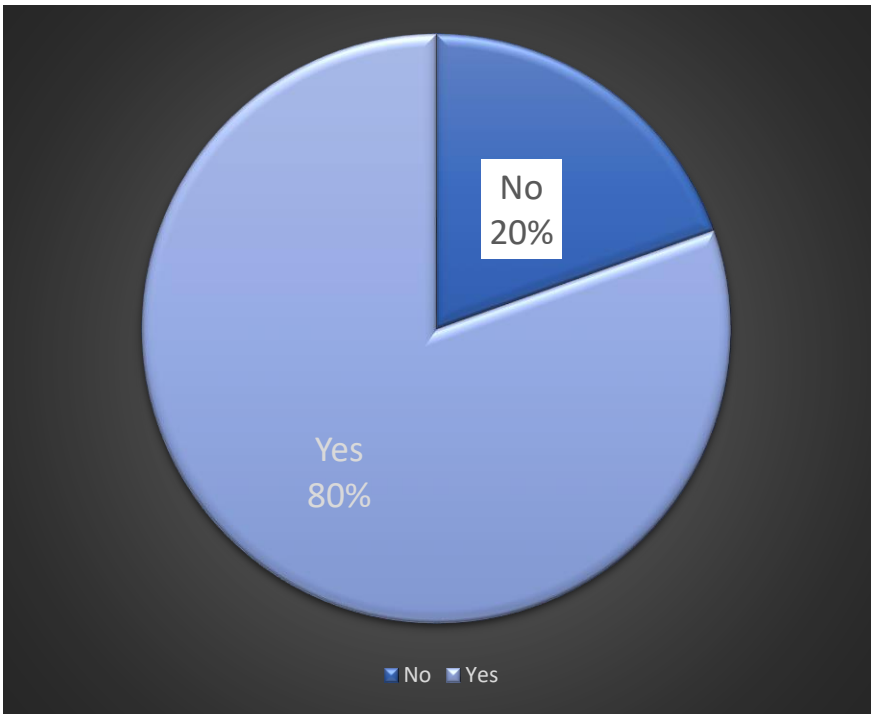


Fig: Pie chart showing distribution of cases by secretion in DNE

Table: Showing secretion in DNE

Secretion	Frequency	Percent
No	45	19.6
Yes	185	80.4
Total	230	100.0

In our study 185 out of 230 cases had secretion in nasal cavity in DNE and 20% (45 patients) cases had no secretions in DNE.

3. PALLOR OF NASAL MUCOSA:

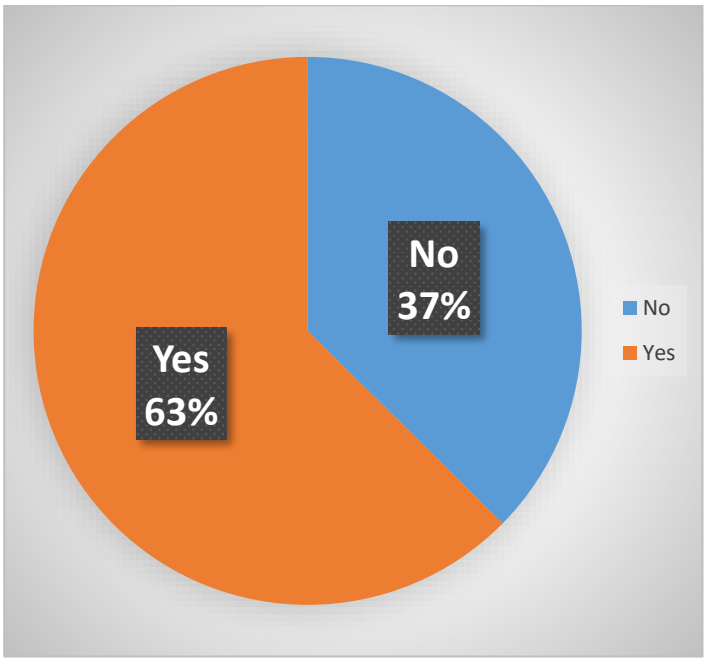


Fig: Showing pie chart and table showing pallor of mucosa in DNE

Pallor	Frequency	Percent
No	86	37.4
Yes	144	62.6
Total	230	100.0

In our study 63% of cases (144 patients) had pale nasal mucosa in DNE.

STAGE OF DISEASE:

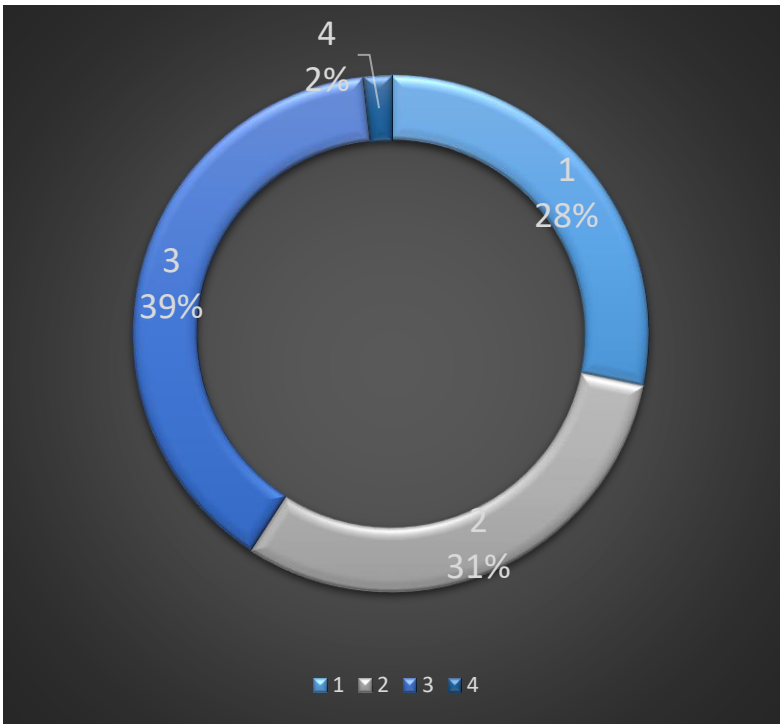


Fig: Pie chart showing stage of disease patient presented in our study

- 90 of cases presented in stage 3[87 Patients in 3a , 3 in 3b-d]
- 71 cases in stage 2
- 65 cases in stage 1
- Only 4 cases in stage 4

Stage	Frequency	Percent
1	65	28.3
2	71	30.9
3a	87	38
3b-d	3	1
4	4	1.7
Total	230	100.0

Table: Depicting the patients presented in different stage of disease

Around 31% of patients presented in stage 2

stage 3a 38% & stage 3b-d - 1% and only 2% of cases in stage 4.

FUNGAL KOH MOUNT:

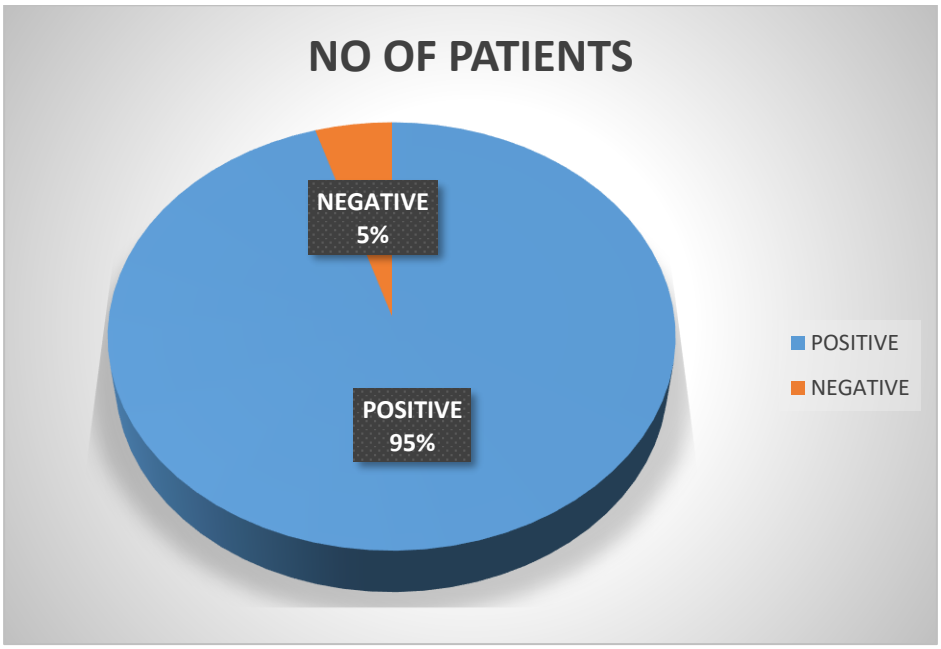


Fig: Pie chart and table showing fungal KOH mount result in our study

Fungal KOH	Frequency	Percent
NEGATIVE	11	4.8
POSITIVE	219	95.2
Total	230	100.0

In our study fungal KOH mount was positive in 219 patients (95%) and 11 cases (5%) had negative fungal KOH mount. It was done with eschar, secretion and scrapes from pale mucosa.

1. FUNGAL KOH IN ESCHAR:

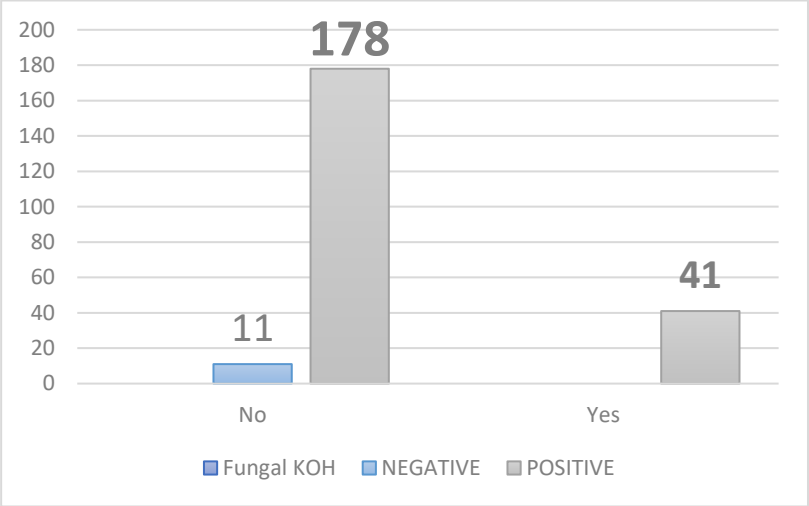


Fig: Clustered column chart showing fungal KOH results in eschar in our study

In our study, fungal KOH was positive in all the patients with eschar

Table: Depicts cases with eschar and fungal KOH mount results

			Fungal KOH		Total	P value
			NEGATIVE	POSITIVE		
ESCHAR	No	Count	11	178	189	0.113
		% within ESCHAR	5.8%	94.2%	100.0%	
	Yes	Count	0	41	41	
		% within ESCHAR	0.0%	100.0%	100.0%	
Total		Count	11	219	230	
		% within ESCHAR	4.8%	95.2%	100.0%	

About 41 patients had eschar in DNE, all of them had fungal KOH mount positive in our study.

Out of 189 patients with no eschar, 178 had fungal KOH mount positive and 11 cases had negative fungal KOH.

Thus patients with eschar in nasal cavity showed 100% positive fungal KOH mount with a p-value of 0.113 in our study.

FUNGAL KOH IN SECRETION:

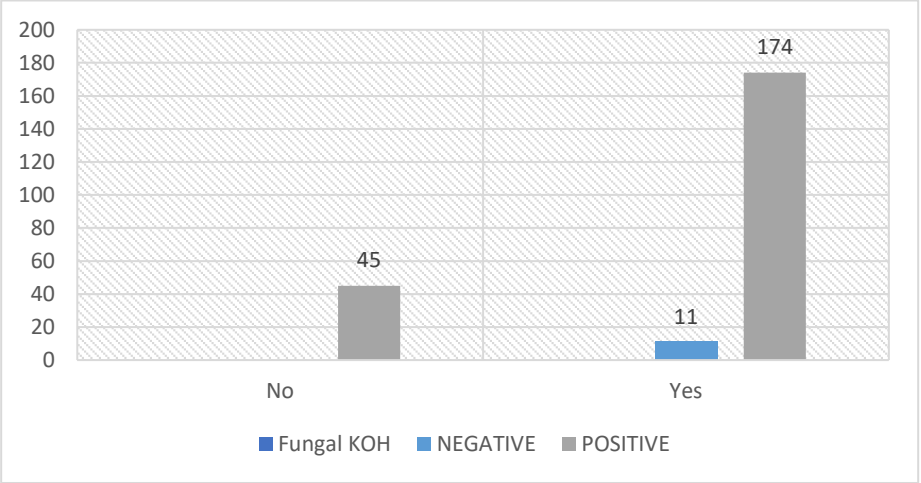


Fig: Cluster column chart showing fungal KOH results in secretions from nasal cavity.

Table: Depicts fungal KOH results in cases with secretion in nasal cavity

			Fungal KOH		Total	P value
			NEGATIVE	POSITIVE		
Secretion	No	Count	0	45	45	0.094
		% within Secretion	0.0%	100.0%	100.0%	
	Yes	Count	11	174	185	
		% within Secretion	5.9%	94.1%	100.0%	
Total		Count	11	219	230	
		% within Secretion	4.8%	95.2%	100.0%	

In our study out of 185 patients with secretion in nasal cavity, 174 cases had positive fungal KOH mount and 11 cases had fungal KOH mount negative.

Thus 94% patients with secretion in nasal cavity showed fungal KOH positivity with a p-value of 0.094 and 6% of patients with secretion in nasal cavity had negative fungal KOH mount in our study.

2. FUNGAL KOH FROM PALE MUCOSA:

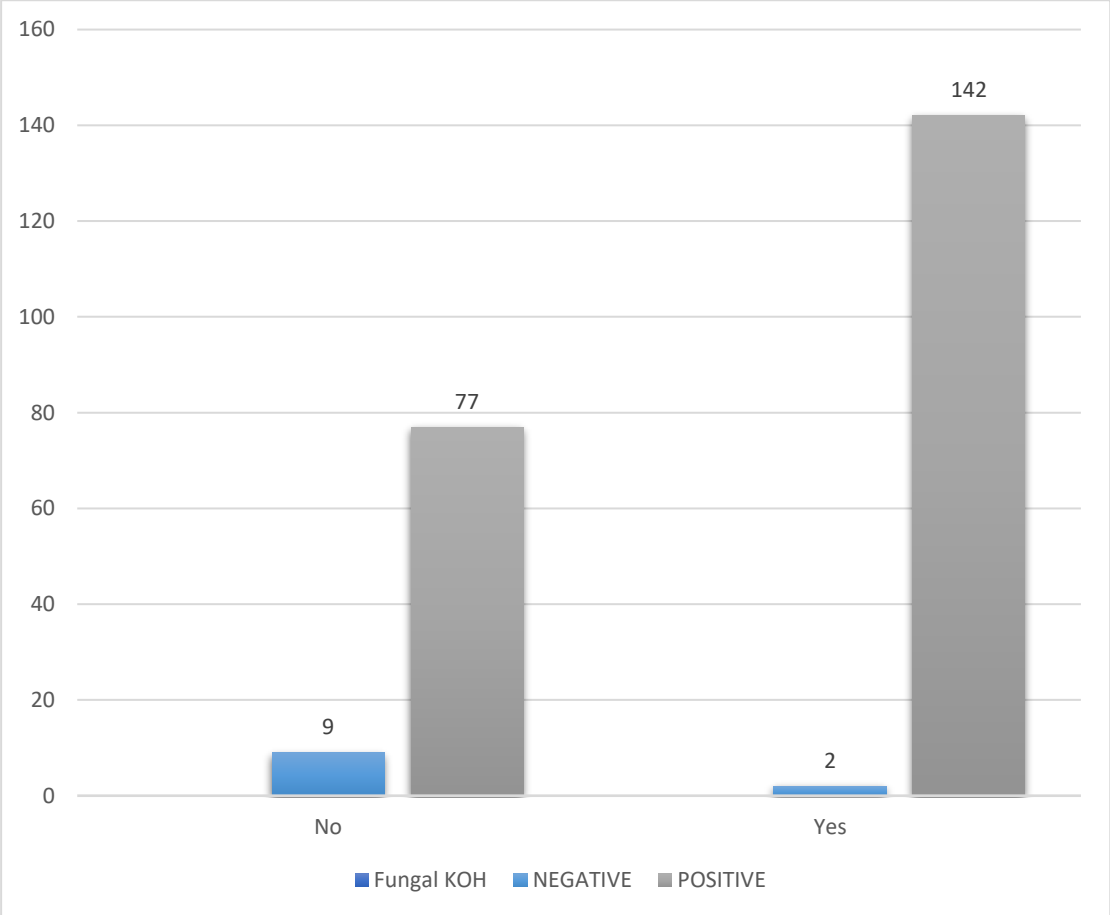


Fig: Cluster column chart showing fungal KOH mount results of scrapes from pale mucosa.

Table: Depicts cases with pale mucosa and their fungal KOH results

			Fungal KOH		Total	P value
			NEGATIVE	POSITIVE		
Pallor	No	Count	9	77	86	0.002
		% within Pallor	10.5%	89.5%	100.0%	
	Yes	Count	2	142	144	
		% within Pallor	1.4%	98.6%	100.0%	
Total		Count	11	219	230	
		% within Pallor	4.8%	95.2%	100.0%	

In our study 144 cases had pale mucosa in DNE, out of them 142 cases showed positive fungal KOH mount and only 2 cases had negative result.

In remaining 86 cases with no pale mucosa, 77 patients showed positive fungal KOH mount and 9 cases had no negative fungal KOH mount.

Thus 99% patients with pale mucosa in DNE showed fungal KOH mount positivity with a p-value of 0.002 in our study.

COMPARISION OF FUNGAL KOH & BIOPSY RESULTS :

All 41 Patients with Eschar showed positive biopsy results .

SECRETIONS		Fungal KOH		Total	POST OP HPE
		Positive	Negative		
Biopsy	Positive	107	0	107	POSITIVE
	Negative	67	11	78	
Total		174	11	185	

Among 185 patients with Secretions on DNE 174 patients tested positive for Fungal KOH , Among them 107 patients were biopsy Positive. 11 Patients who were KOH Negative were biopsy Negative and those patients were admitted based on the radiological findings .

PALLOR		Fungal KOH		Total	POST OP HPE
		Positive	Negative		
Biopsy	Positive	78	0	78	POSITIVE
	Negative	64	2	66	
Total		142	2	144	

Among 144 patients with Secretions on DNE 142 patients tested positive for Fungal KOH , Among them78 patients were biopsy Positive. 2 Patients who were KOH Negative were biopsy Negative and those patients were admitted based on the radiological findings.

COMPARISION OF FUNGAL KOH & BIOPSY IN DIFFERENT STAGES OF MUCORMYCOSIS :

STAGE I:

		BIOPSY		
		POSITIVE	NEGATIVE	P value
FUNGAL KOH	POSITIVE	32	23	<0.0001
	NEGATIVE	1	9	

In my study , out of 65 patients in STAGE I

Mycology showed positive results for 55 patients and HPE for 32 patients, with a P value of <0.0001 which is clinically significant and a sensitivity of 96.97% and an accuracy of 63.08 %

STAGE II:

		BIOPSY		
		POSITIVE	NEGATIVE	P value
FUNGAL	POSITIVE	52	19	
	NEGATIVE	0	0	

71 Patients in STAGE II, HPE showed positive results for 52 patients, Mycology positive for all patients with an accuracy of 73.24 %

STAGE III:

		BIOPSY		
		POSITIVE	NEGATIVE	P value
FUNGAL	**POSITIVE**	57	33	<0.0001
	NEGATIVE	0	1	

In my study, out of 90 patients in STAGE I

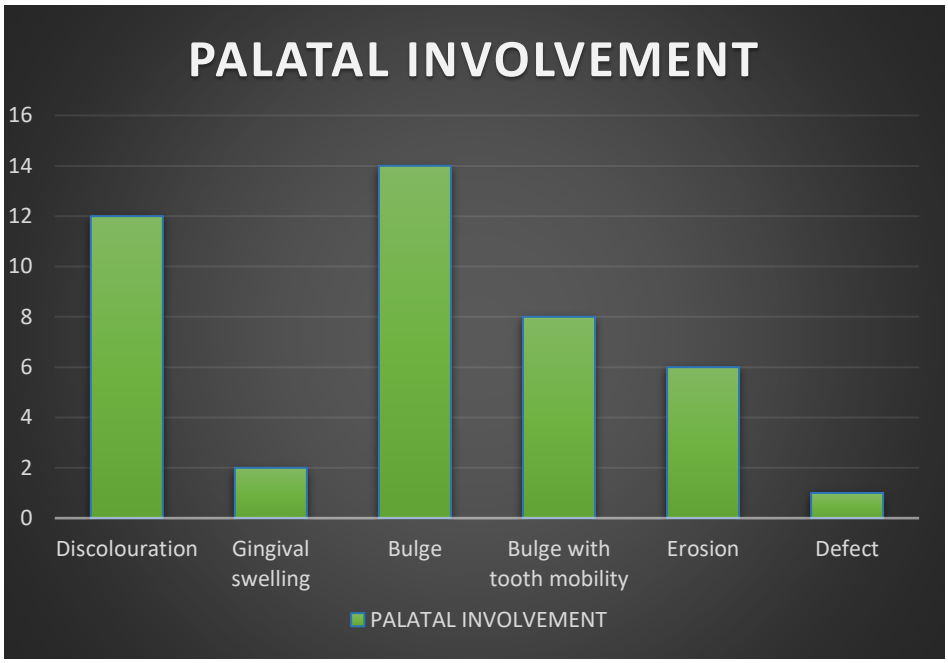
Mycology showed positive results for 89 patients and HPE for 57 patients, with a P value of <0.0001 which is clinically significant and a sensitivity of 100% and an accuracy of 63.33 %

STAGE IV:

		BIOPSY		
		POSITIVE	NEGATIVE	P value
FUNGAL	**POSITIVE**	4	0	
	NEGATIVE	0	0	

STAGE IV Patients showed positive results both for biopsy and histopathologically.

PALATAL INVOLVEMENT:



Discolouration -12 patients

Gingival swelling -2 patients

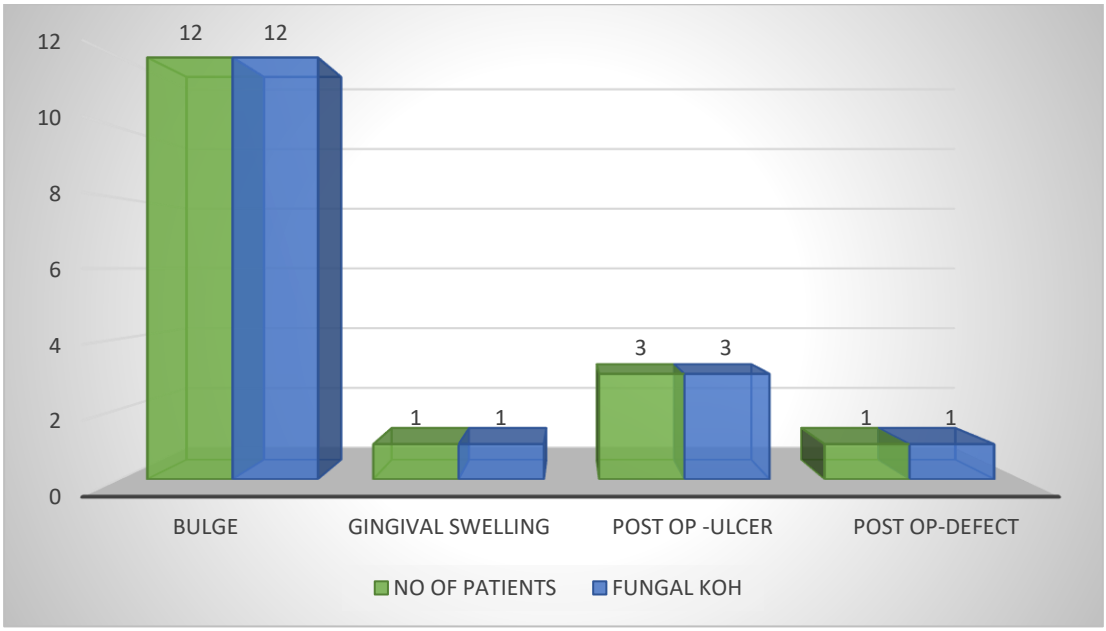
Bulge-14 patients

Bulge with tooth mobility -14 patients

Erosion-6 patients

Defect-1 patients

ISOLATED PALATAL INVOLVEMENT:



Isolated palatal involvement is seen in 17 cases

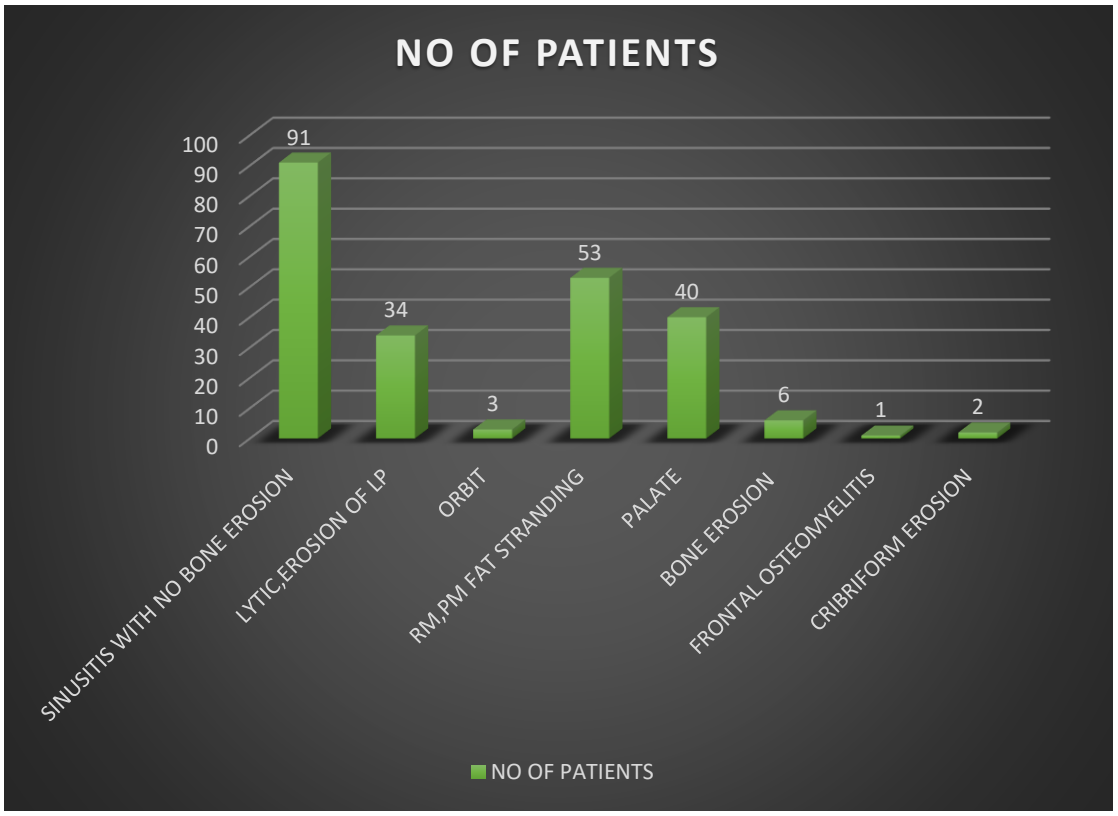
12 cases presented with loosening of tooth ,palatal bulge

1 case with gingival swelling .

For all the cases Fungal KOH and biopsy taken from the nasal mucosa showed positive results .

4 patients were Post operative patients presented after 2 months of intial debridement with isolated palatal involvement.(3 patients with palatal ulcer and one patient with palatal defect) .Biopsy & fungal KOH taken from the palatal lesion showed positive results .

RADIOLOGICAL EVALUATION:



76 people showed sinusitis characteristics of IFS without bony erosion, 1 patient presented with frontal osteomyelitis , 2 patients (Revision cases)

with Cereberal spinal fluid leak .

34 patients showed erosion in lamina papyracea

53 with retromaxillary ,premaxillary involvement

40 with palatal involvement

6 with bony erosion of maxillary walls ,sphenoid

RADIOLOGICAL CORRELATION OF EARLY SYMPTOMS :

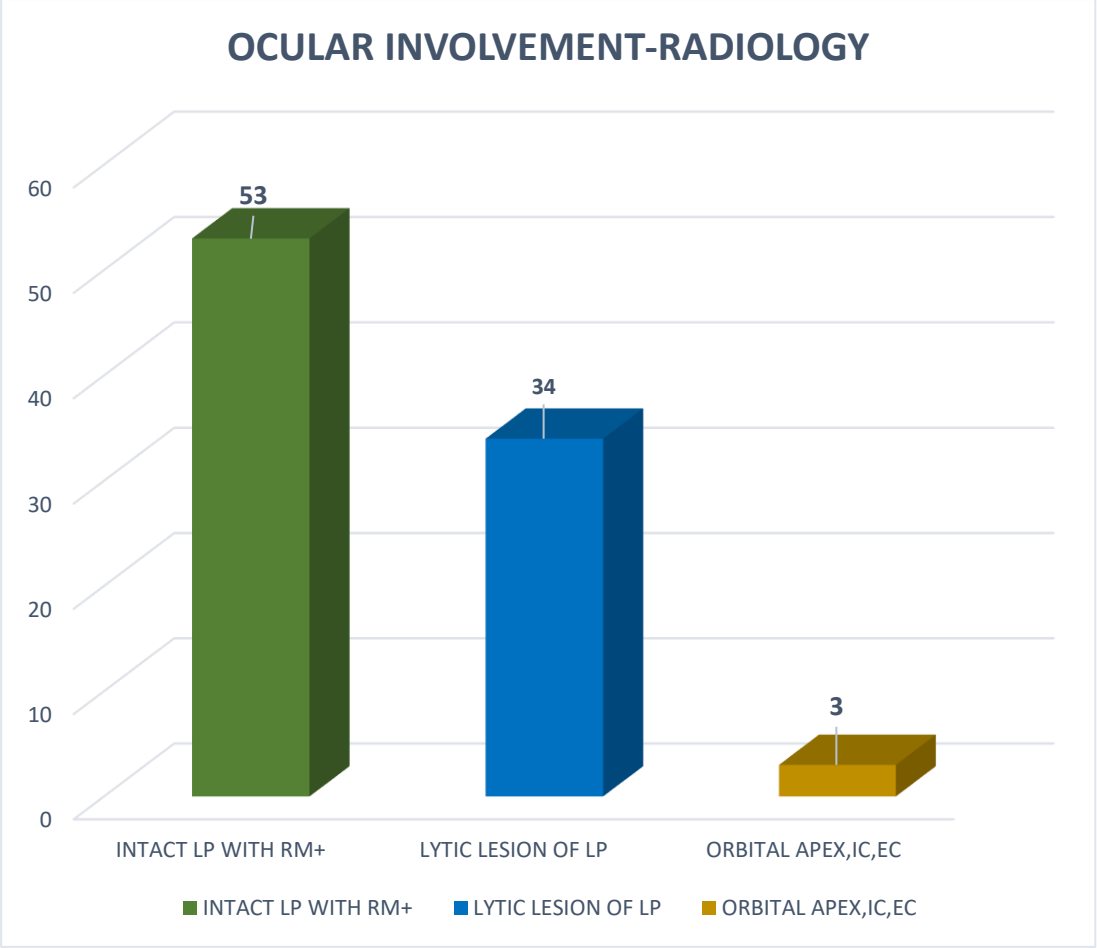
	NO OF PATIENTS	FUNGAL KOH/HPE	RADIOLOGY
ESCHAR	2	2	> 2 SINUS,BONE EROSION
PALLOR	43	42	2 SINUS +
SECRETIONS	20	16	2 SINUS +

Pateints presenting with Early symptoms like Nasal stuffiness ,discharge

2 Patients showed Eschar in DNE with evidence more than 2 sinus involvement with bone erosion radiologically .

Pallor and secretion showed isolated involvement of atleast one or two sinus without bony and pre & retromaxillary fat stranding involvement.

5 Patients with negative mycology and HPE with radiologically positive findings were admitted showed post debridement positive results .



In our study , orbital involvement was found in 90 patients.

53 patients had intact lamina papyracea with the presence of retromaxillary fat stranding

34 patients had lytic lesion which includes erosion ,thinning of lamina papyracea

3 patients had orbital apex involvement ,intraconal, extraconal involvement

HISTOPATHOLOGICAL FINDING:

In our study biopsy was taken from middle turbinate, pale mucosa or eschar itself.

Biopsy	*Frequency*	*Percent*
POSITIVE	144	62.6
NEGATIVE	86	37.4
Total	230	100.0

Table: Showing frequency of HPE positive in our study

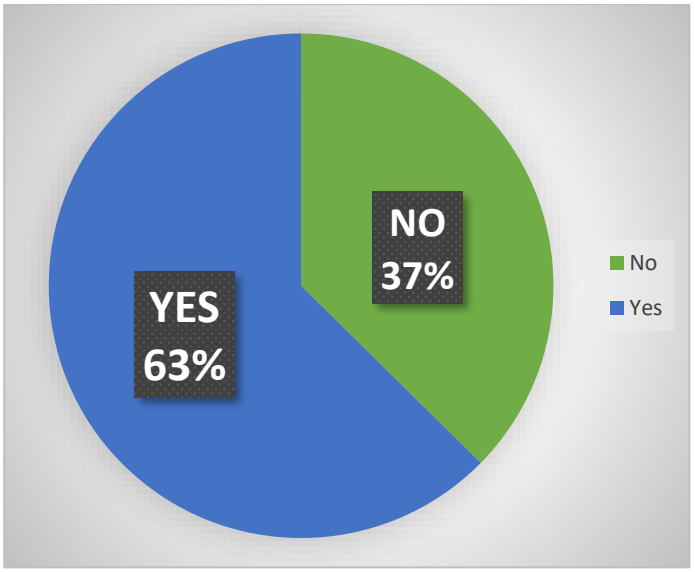


Fig: Pie chart showing histopathological finding in our study

DISCUSSION

The emerging catastrophic situation due to a dual attack by delta variant and black fungal invasion continues to drive a worsening of COVID-19 pandemic with highest cases of mucormycosis recorded in Tamilnadu . Mucormycosis **(ICD-10: B46.5)** is more devastating in its disease progression, and emerged as a epidemic in this pandemic situation.

Following the surge of CAM, the government of India Directive,made Mucormycosis as "**NOTIFIABLE DISEASE"** in several states of India and Tamilnadu is one among them . Tamilnadu government was swift enough in declaring this mucormycosis epidemic a and constituted a task force advisory committee to deal with this epidemic .

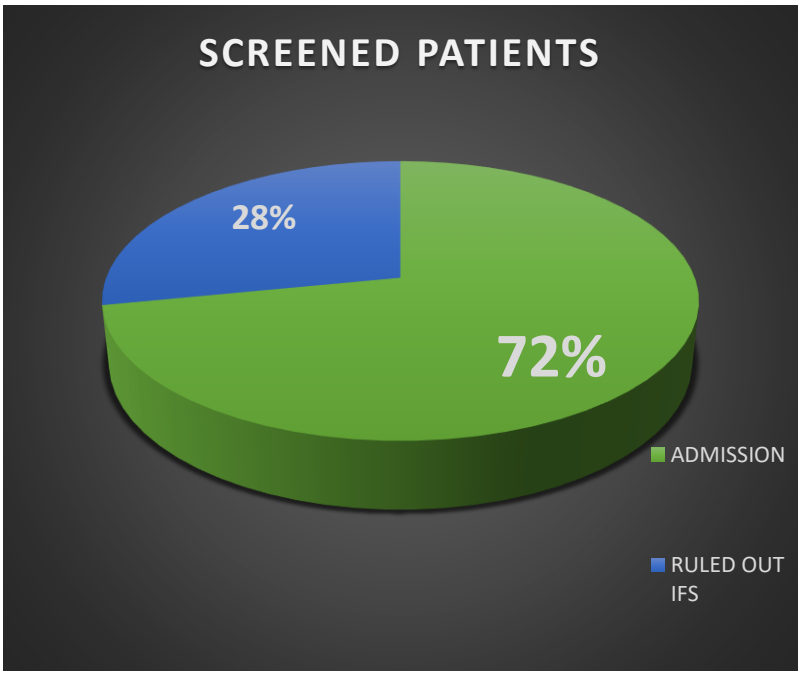
The main job of the mucormycosis task force was

- Prevention
- Early detection
- Formulate proper diagnostic methods
- Formulate treatment protocols
- The main advisory of the task force to detect the disease at the earliest

And as a measure of it mucormycosis special screening clinic was launched.

In our study , conducted in mucormycosis screening OPD , 323 were Walk in patients screened in Mucor OPD. Out of which 230 pateints were admitted from screening OPD ,93 patients thorough evaluations were done and mucormycosis have been ruled out.554 patients were Inpatients who were screened in Mucor OPD for Diagnostic Nasal endoscopy , Fungal KOH and biopsy. So that early confirmation can be made in suspected cases of Invasive Fungal Sinusitis and for intiation of empirical amphotericin.

Many patients who attended mucor OPD had previous history COVID 19 with co-existing Diabetes mellitus, people are so much aware that they enrolled the clinic at the earliest .



Among 323 patients who have been readily screened in mucormycosis clinic 88% had previous history of COVID 19 infection with associated diabetes mellitus .

65-70% of our patients falls under 40 – 60 years , with 70% male predominance noted .

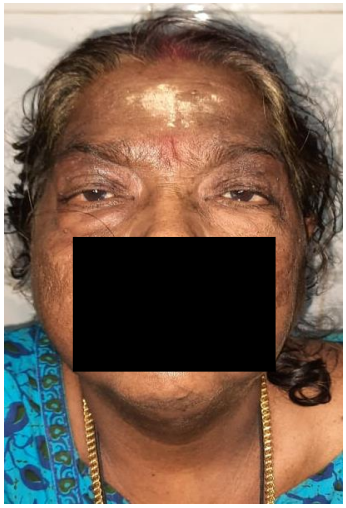
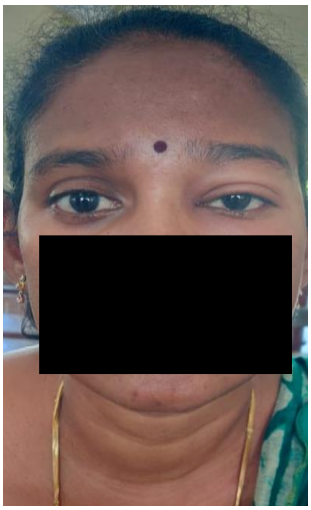
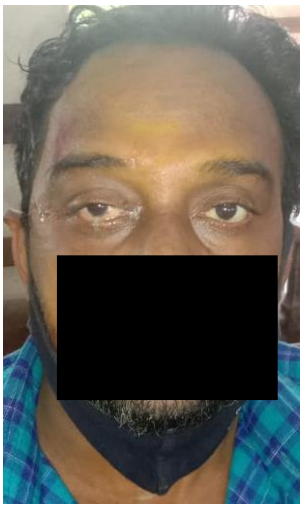
A study by **Yohai et al** done among ROCM patients claims that patients who begin treatment within 6 days have a survival rate of 76-81%,while delay more than 12 days reduces survival rate to 36%. [33]

In our study 62% patients were admitted with less than 7days of onset of symptoms and 38% with more than 7 days of symptoms

Most of the patients belong under Stage 2 and early Stage 3a with preserved vision . Such patients were screened earlier and early intervention was made preventing the further progression of disease. As studies have shown that even a delay of only 6 days can double the morbidity and mortaility from 35 to 70% . Hence identification of disease progression at the earliest is necessary in preventing further devastating effects of mucormycosis. So, patients in early Stage 3a, with vision unaffected should be picked up early and immediate surgical debridement should be carried out with adequate Intravenous Amphotericin.

In our study 31% were in STAGE 2 and 39% in STAGE 3 of which 38 % were in early STAGE 3a with preserved vision and less than 1 % presented with compromised vision. Early cases identified (STAGE I & II) accounts for about 60% and the most common earliest symptom is Nasal stuffiness.

PATIENTS PRESENTING WITH EARLY OCULAR SIGNS WITH VISION UNAFFECTED (STAGE 3a)

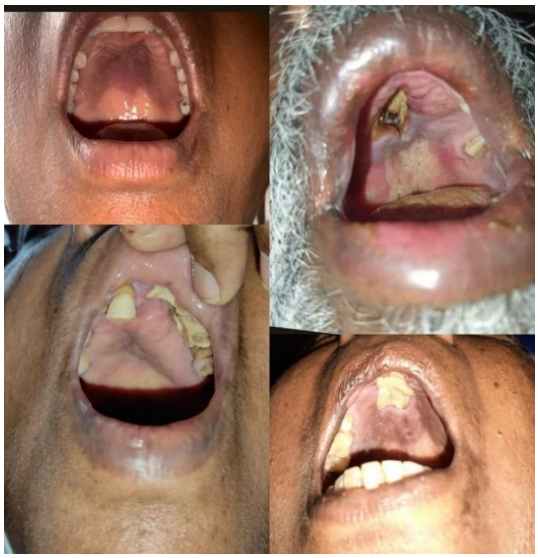
Only one case belongs to Stage 4 presenting with increase in size of intracranial abscess.

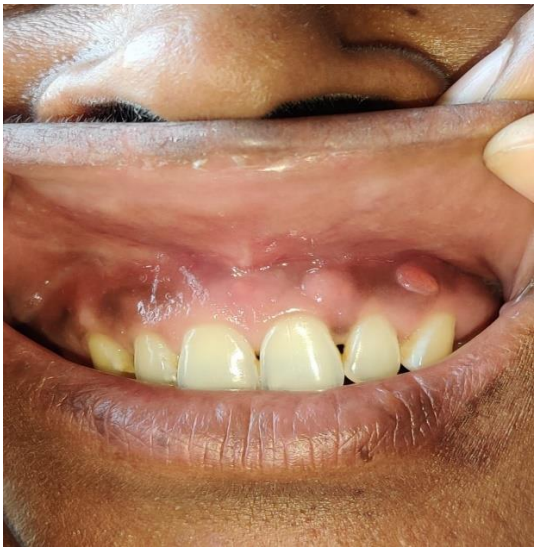
Revision cases admitted is less than 2% of the total cases.

Mucormycosis causing cranial nerve plasy was least found in screening OPD ,as it was more evident in advanced disease .Only 2 patients with facial nerve palsy was recorded .

Another important presentation we encounter was Palatal complaints. Palatal signs commonly encountered was

- Discolouration
- Bulge
- Bulge with tooth mobility
- Erosion
- Defect





Patients with early palatal symptoms like discolouration and bulge with no tooth mobility are managed conservatively. Only patients with Palatal bulge with mobility of tooth are managed with alveolectomy , necrosed and defect are taken up for inferior maxillectomy and followed up in mucor clinic watching for further spread of infection.

Isolated palatal involvement is seen in 17 cases , In 15 cases early palatal lesion like bulge and gingival swelling was present . Biopsy take from the nasal cavity is found to be positive .Four cases were post operative

presented to the clinic after primary debridement with palatal symptoms. This shows how latent disease spreads via perineural route with early underlying osteitis which gets controlled for liposomal amphotericin during primary debridement , since Posaconazole was ineffective for osteitis and disease gets flared up ,those patients were intervened early in screening OPD.

Computed Tomography was performed and showed opacification of paranasal sinuses, thinning of lamina papyracea ,erosion of bony walls and to look intracranial involvement

A study conducted by **Seid Mousa Sadr et al** in mucormycosis found that among 11 patients symptomatically presented with facial pain, radiologically all patients had intact posterior wall of maxilla, 9 out of 11 patients had retromaxillary fat stranding stating angio invasion to be occurred earlier than bony invasion and 6 patients had orbital involvement among which 4 patients presented with blindness, all patients showed intact lamina papyracea. None of their patients showed invasion of orbit via ethmoid sinus .They concluded that Pterygoplatine fossa to be the prime source of spread which they proved surgically[34].

In our study 90 patients with orbital involvement 53 patients had retromaxillary fat stranding with minimal sinusitis , 34 had erosion of lamina papyracea, 3 had intraorbital extension . Patients with early

symptoms had isolated involvement of one or more paranasal sinuses in 63 patients.

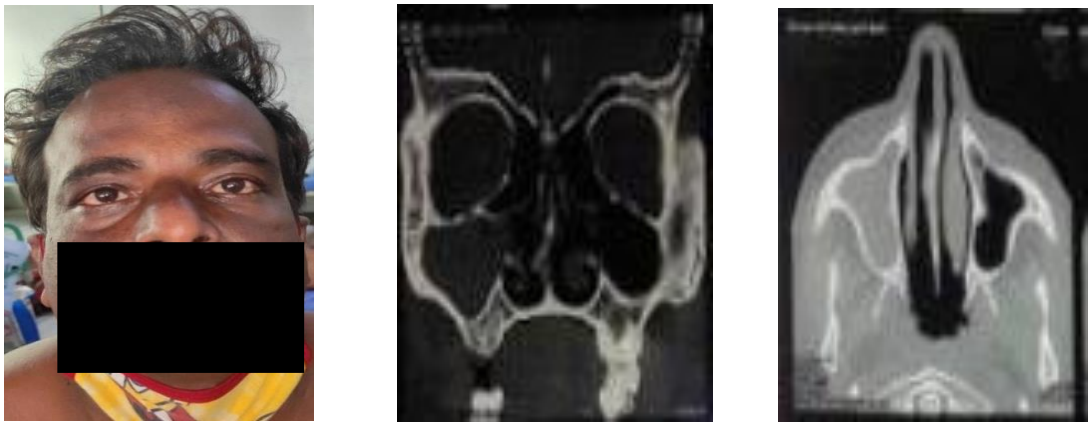
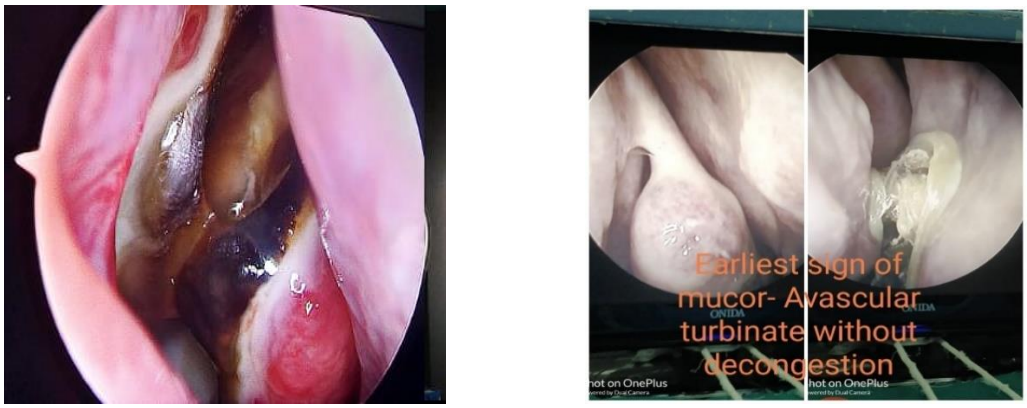


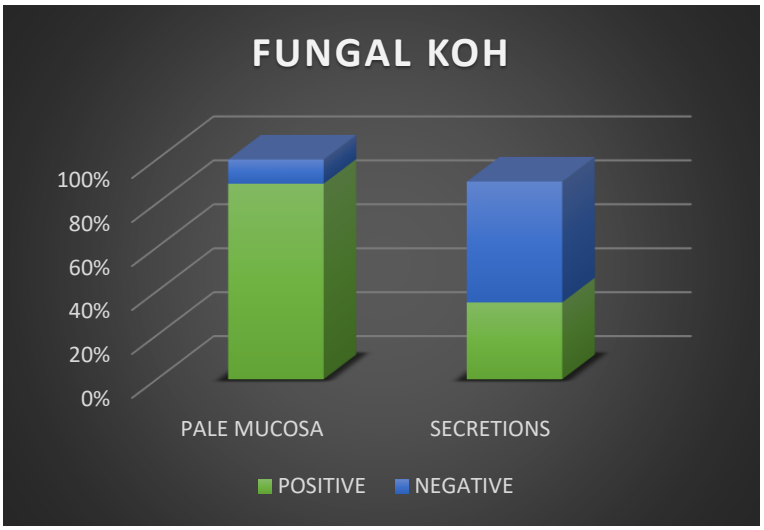
Fig: Patient with Right infraorbital edema with isolated involvement of maxillary sinus with retromaxillary fat stranding without involvement of ethmoid sinus .

Diagnostic endoscopy in mucor clinic reveals that 18% patients presents with typical eschar of middle turbinate which is the most characteristic sign of mucormycosis .

Remaining 82 % had early changes like pallor, mucopurulent secretion of middle turbinate positive for Fungal KOH.



Among 82% patients, 62 to 70% showed positive Fungal KOH. Early pickup of the disease was made out even if the mucosa of the nasal cavity seems to be normal which shows the effectiveness of the screening clinic. Early invasion of fungus resulting in vascular compromise resulting in a Pale middle turbinate is evident in 62% of our cases. Pale middle turbinate showed a positivity rate 89% for fungal KOH.



Mycology examination which is readily made out by fixing the specimen with Potassium Hydroxide, where the results are known within 2 hours. It acts as a decision maker in doubtful suspected cases where only middle meatal secretions are present and patient's clinical symptoms are suggestive of mucormycosis. In one patient who is Non Covid, Diabetic with middle meatal secretions on DNE showed presence of *Mucormycosis and Candida*. Among 230 patient admitted one patient showed the

presence of Aspergillus. Isolated candida infection found in screening OPD includes 3 cases and aspergillus 7 cases.

Histopathological examination showed a positivity rate of 62%, with maximum positivity in STAGE II & III. Since Fungal KOH has a sensitivity of more than 90%. Nearly 755 mycology slides have been examined overall. Patients negative for Fungal KOH was admitted based on radiological findings and clinical symptoms had Post operative positive results for Fungal KOH. Negative cases in screening OPD on biopsy/KOH doesnot exclude mucormycosis .Negative results can be due to sample transport time ,tissue destruction .Since Post operative Biopsy showed positive results for more than 98% of patients .So, Surgeons endoscopic view is very important for accurate diagnosis.

FOLLOW UP CLINIC:

Follow up is a part of special mucormycosis OPD, where

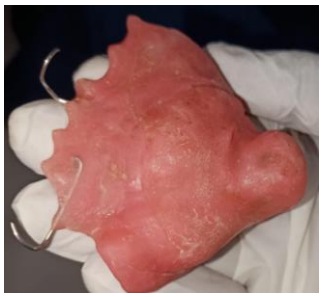
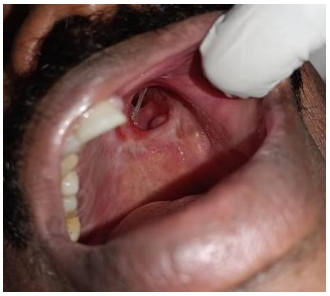
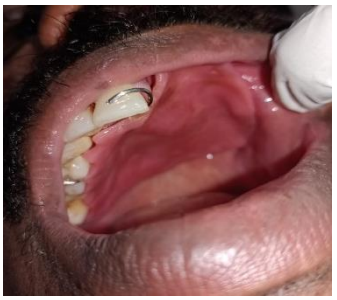
- Post-Operative discharged patients are followed up weekly with Diagnostic Nasal Endoscopy/Ophthalmological Evaluation/ Diabetology and Internal Medicine evaluation.
- Nearly 1813 nasal endoscopy have been done so far with includes diagnostic nasal endoscopy and suction clearance.

- T.Posaconazole is issued for the discharged patients weekly.
- Readmission if necessary (in Disease progression).

Posaconazole is used as a stepdown therapy for patients who have responded to Amphotericin B and it was also provided to patients after surgical debridement , who don't tolerate Amphotericin B . A 8 year study (2003-2011) conducted by **Joerg J.Vehreschild et al** among **96** mucormycosis patients on Posaconazole stepdown therapy showed, Complete response in 62 %, partial response in 7% and stable disease in 1% [31]. The median duration of posaconazole treatment was 5 months.

A 2 year clinical study done by **Tarani et al** in a diabetic girl with stage IIIc Rhino orbital mucormycosis with posaconazole follow up suggests long term safe and beneficial in prevention of relapses and CNS progression[32].

In our study Posaconazole was issued for a period of 2 months - 3 months as a stepdown therapy and stopped thereafter depending on patients symptoms and endoscopic findings on subsequent follow up.

Patients with interim obturator following inferior maxillectomy have been provided with Permanent Obturator with help of prosthodontics , seen to that the prosthesis fits correctly and remnant mucosa is free of disease , so that the patient can be functionally normal .

Post operative diagnostic endo cleaning was very essential for further spread of disease, it. Such intiation helps in regular follow up of the patients and helps to identify the post surgical outcomes of these patients , ultimately reflects the tissue response to antifungal medications and diabeteic control of these patients .

Surgically drained brain abscess and conservatively managed abscess were periodically followed up in mucor OPD for new onset of neurological symptom and deficit , nasal endoscopy and follow up MRI.

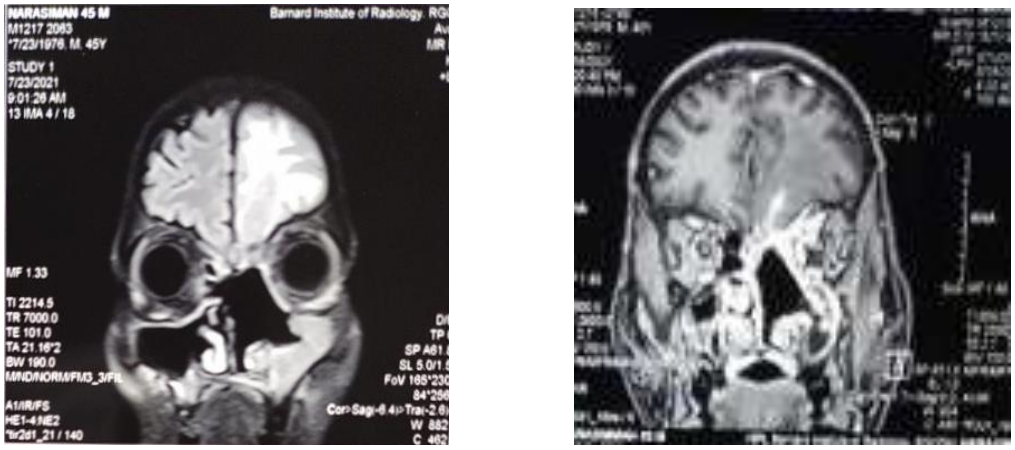


Fig: Pre Operative MRI Showing abscess in Left frontal lobe and Post Operative follow up MRI ,with no residual collection,inflammation.

One case with intracranial abscess managed conservatively ,on follow up had neurological symptoms and repeat MRI showed further progression was admitted from screening OPD, managed effectively with intravenous amphotericin B along with integrated management by neurologist in our ward.

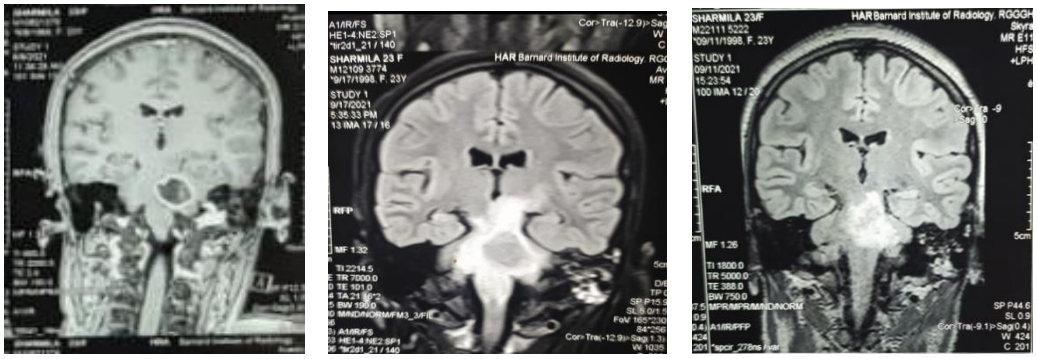


Fig:Cerebellar abscess treated conservatively , second image showing increase in size with associated inflammation on two months follow up, patient admitted and treated where abcess resolved

Cases with frontal Osteomyelitis on conservative management treated with salvage therapy of Tab Posaconazole had no worsening of symptoms and were followed up periodically and so far none of the cases was readmitted.

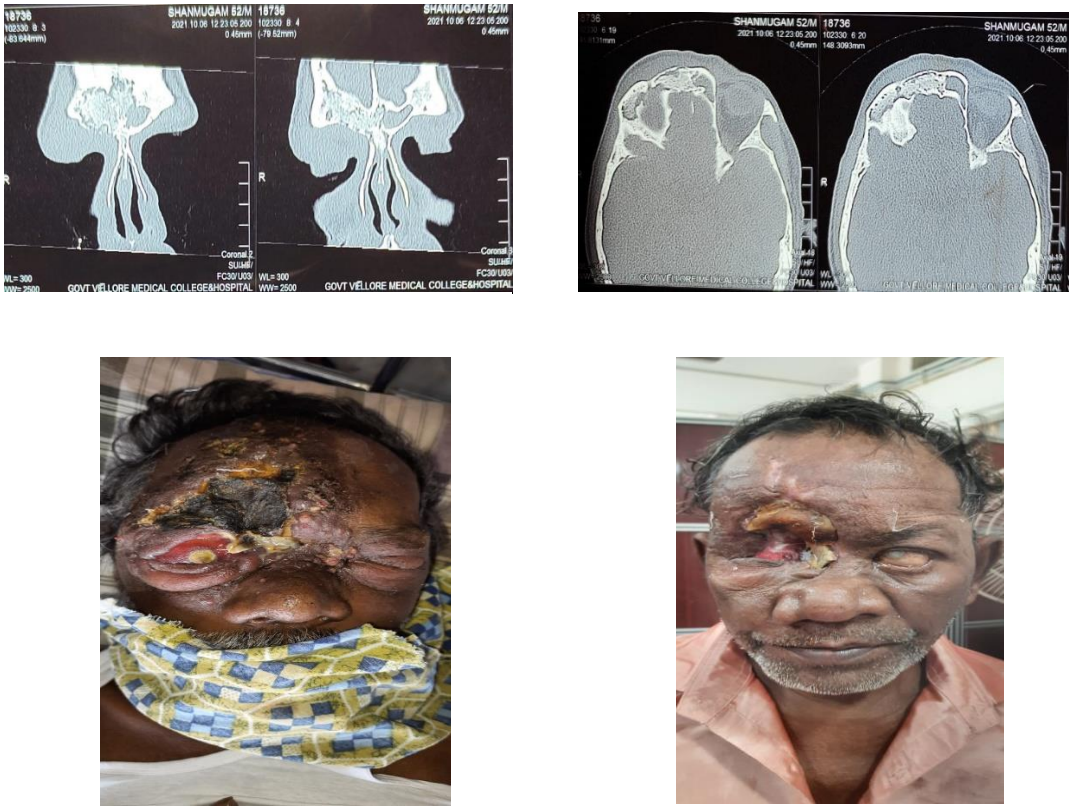


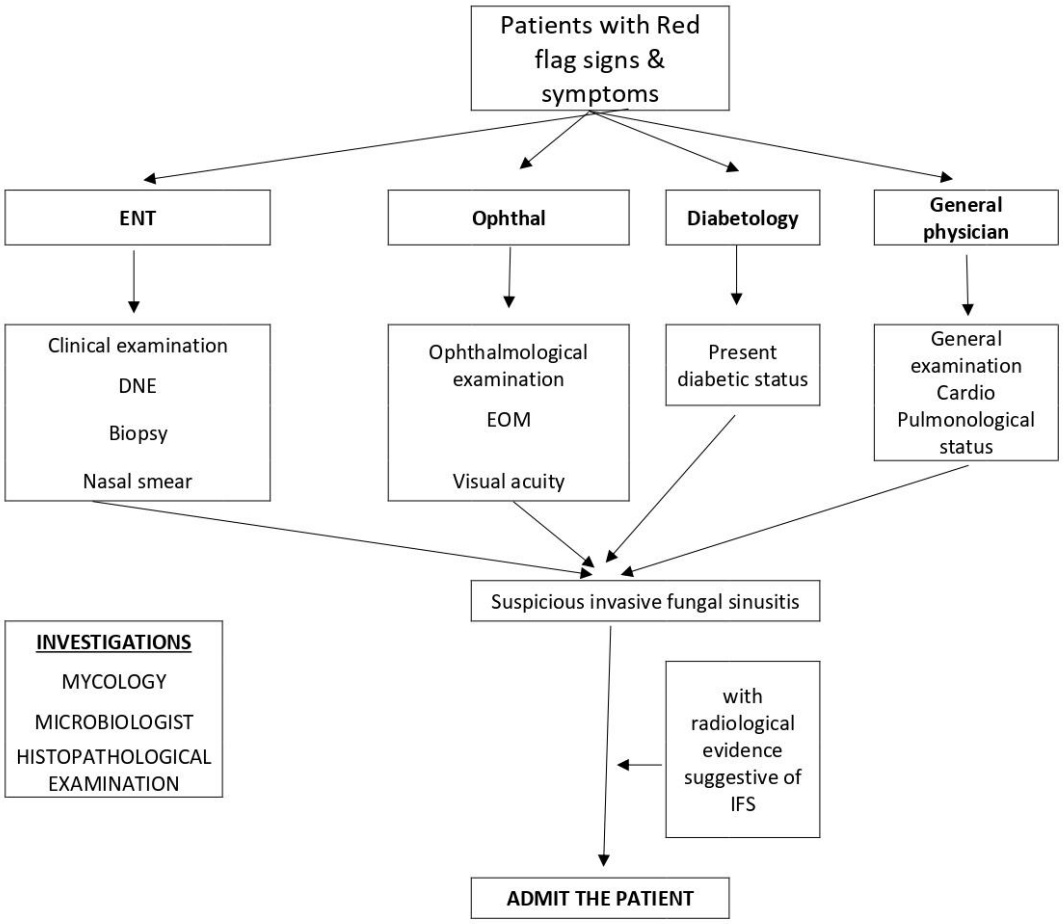
Fig: showing a patient with necrosis of facial skin with vision loss patient underwent early intervention and follow up of the patient with adequate antifungals showed no further progression of disease and intracranial extension .

About 700 – 1000 patients were followed up periodically for a period of 6 - 8 weeks along with nasal endocopy and suction clearance.

So early intervention can be made if there is further worsening of symptoms in the post operative follow up period. So the main goal is to make early disease diagnosis, not missing early signs, Maintaining glycaemic control , Classification of possible, probable, and proven infection , Segregating patients based on COVID-19 disease status and Timely therapy initiation. Screening clinic plays a major role in picking up the case at the earliest, which results in earlier intervention preventing further progression of disease.

Consultation with various experts like General Physician, Otorhinolaryngologist, ophthalmologist, microbiologist, pathologist, pulmonologist, neurologist, , dentist, and radiologists , People who are suspected to have early symptoms of mucormycosis should seek the above specialist at the earliest and this Special Mucor Screening Clinic serves the purpose .

ALGORITHM FOLLOWED IN SCREENING OPD



CONCLUSION

- The COVID -19 aftermath resulting in a wave of mucormycosis epidemic proportion is an unprecedent experience. As the morbidity and mortality was alarming necessiting early detection and control of the disease was a challenging task .

- Tracing the history of RhinoOrbitalCereberal Mucormycosis which usually occur as a stray cases in uncontrolled diabetes patients , this Multidisciplinary speciality diagnostic Mucormycosis Special Screening OPD is a novel approach introduced in Rajiv Gandhi Government General Hospital for the first time in the history of Mucormycosis occurring in such a massive proportion within a short duration to address this problem .

- A total of 885 cases were screened in Mucor OPD which also includes patients from ward so that early intervention can be done ,and nearly 1019 patients who underwent surgical intervention were followed up periodically . Hence early Medical and Surgical intervention has halted the progress to STAGE III & IV, and in 89 patients vision is salvaged in screening OPD .

- Early detection of mucormycosis was possible since more than 60% of cases secured were in STAGE 1 & II, which stands as a testimony in success of Mucor Screening OPD.

- Average time for evaluation is just 30-45 minutes and diagnosis is known to the patients in 2 hours.

- Even though the epidemic is weaning Mucor Screening Clinic is still functioning, follow up of the post-operative patients and rationalizing the dispensary of drugs to these patients according to the severity of the disease and timing of caessation of treatment was effective over a large volume of patients because of this multidisciplinary screening clinic.

- All the facilities are offered under one roof. Patients migrating from one department to the other is avoided.

- Peculiarity of the Mucormycosis epidemic is increased in south east asia as the entire western world is insensitive to this problem as it was free of mucormycosis and there was no proper guidelines to tackle this problem, further the management of mucormycosis occurring in this mass proportion compounded with the availability of liposomal Amphotericin and Posaconazole for this large number of patients.

- The clinic aided in rationalizing the usage of costly drugs like Tablet Posaconazole.

- All these problems faced have been effectively approached and tackled by this novel approach for the 1st time in the country.

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PROFORMA

SOCIO-DEMOGRAPHIC DATA

Name:

Age :

Sex:

Education:

Occupation:

Income:

Family Members:

Clinical details

Covid positive on:

CT grade:

Hospitalization:

Co- morbidities:

h/o Diabetes and duration:

Use of steroids:

Type of steroid used:

Dosage of steroid:

Duration of steroid usage:

O2 requirement

h/o headache

h/o swelling of face

h/o orbital swelling

h/o nasal discharge, if yes whether foul smelling

h/o discoloration inside oral cavity

ANNEXURE III

INFORMATION SHEET- ENGLISH

We are conducting **"ROLE OF SPECIAL MUCOR SCREENING OPD IN THE MANAGEMENT OF POST COVID MUCOR EPIDEMIC"** at the upgraded institute of Otorhinolaryngology, Madras Medical College&Rajiv Gandhi government general hospital, Chennai - 03

In this study, we will be assessing incidence, risk factors and clinical profile of rhinoorbital mucormycosis in post covid patient

in the inclusion criteria. The privacy of the participants in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time. Your decision will not result in any loss of benefits to which you are otherwise entitled.

The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment or prevention.

Signature of investigator Signature of the participant

Date:

ஆராய்ச்சி தகவல் தாள்

ஆய்வு செய்யப்படும் தலைப்பு :

ROLE OF SPECIAL MUCOR SCREENING OPD IN THE MANAGEMENT OF POST COVID MUCOR EPIDEMIC

ஆராய்ச்சியாளர் பெயர் :

பங்கேற்பாளர் பெயர் :

சென்னை ராஜீவ் காந்தி அரசு மருத்துவமனைக்கு, இந்த ஆராய்ச்சியின் நோக்கம்.

நீங்கள் இந்த ஆராய்ச்சியில் பங்கேற்க நாங்கள் விரும்புகிறோம். இந்த ஆராய்ச்சியால் உங்கள் சிகிச்சைக்கு பாதிப்பு ஏற்படாது என்பதை தெரிவித்துக் கொள்கிறோம்.

இந்த ஆராய்ச்சியின் முடிவுகளை அல்லது கருத்துக்களை வெளியிடும் போதோ அல்லது ஆராய்ச்சியின் போதோ தங்களது பெயரையோ அல்லது அடையாளங்களையோ வெளியிடமாட்டோம் என்பதையும் தெரிவித்துக்கொள்கிறோம்.

இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின் பேரில் தான் இருக்கிறது. மேலும் நீங்கள் எந்நேரமும் இந்த ஆராய்ச்சியிலிருந்து பின்வாங்கலாம் என்பதையும் தெரிவித்துக்கொள்ளலாம்.

இந்த ஆராய்ச்சியின் முடிவுகளையும் நோயின் தன்மைப்பற்றியும் ஆராய்ச்சியின் போது அல்லது ஆராய்ச்சியின் முடிவின் போது தங்களுக்கு அறிவிப்போம் என்பதையும் தெரிவித்துக்கொள்கிறோம்.

ஆராய்ச்சியாளர் கையொப்பம் பங்கேற்பாளர் கையொப்பம்

தேதி:

சுய ஒப்புதல் படிவம்

ஆய்வு செய்யப்படும் தலைப்பு :

ROLE OF SPECIAL MUCOR SCREENING OPD IN THE MANAGEMENT OF POST COVID MUCOR EPIDEMIC

ஆராய்ச்சி நிலையம் : இராஜீவ் காந்தி அரசு பொது மருத்துவமனை மற்றும்
சென்னை மருத்துவக் கல்லூரி,
சென்னை - 600 003.

பங்கு பெறுபவரின் பெயர் : உறவுமுறை :

பங்கு பெறுபவரின் எண். :

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களைப் பெறவும் வாய்ப்பளிக்கப்பட்டது.

நான் இவ்ஆய்வில் தன்னிச்சையாகத்தான் பங்கேற்கிறேன். எந்தக் காரணத்தினாலோ எந்தக் கட்டத்திலும் எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்ஆய்வில் இருந்து விலகிக் கொள்ளலாம் என்றும் அறிந்து கொண்டேன்.

இந்த ஆய்வு சம்மந்தமாகவோ, இதை சார்ந்த மேலும் ஆய்வு மேற்கொள்ளும்போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளைப் பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன்.

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையும், பரிசோதனை முடிவுகளையும் மற்றும் சிகிச்சை தொடர்பான தகவல்களையும் மருத்துவர் மேற்கொள்ளும் ஆய்வில் பயன்படுத்திக் கொள்ளவும் அதைப் பிரசுரிக்கவும் என் முழு மனதுடன் சம்மதிக்கிறேன்.

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக்கொள்கிறேன். எனக்குக் கொடுக்கப்பட்ட அறிவுரைகளின்படி நடந்து கொள்வதுடன், இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்றும் உறுதியளிக்கிறேன். என் உடல் நலம் பாதிக்கப்பட்டாலோ அல்லாத எதிர்பாராத வழக்கத்திற்கு மாறான நோய்க்குறி தென்பட்டாலோ உடனே அதை மருத்துவ அணியிடம் தெரிவிப்பேன் என உறுதி அளிக்கிறேன்.

பங்கேற்பவரின் கையொப்பம்..... இடம்..... தேதி
கட்டைவிரல் ரேகை

பங்கேற்பவரின் பெயர் மற்றும் விலாசம்.....

ஆய்வாளரின் கையொப்பம்..... இடம்..... தேதி

ஆய்வாளரின் பெயர்.....

ANNEXURE V

INFORMED CONSENT FORM

"**ROLE OF SPECIAL MUCOR SCREENING OPD IN THE MANAGEMENT OF POST COVID MUCOR EPIDEMIC "**

INSTITUTION **:** Upgraded Institute of OtoRhinoLaryngology,

Madras Medical College,

Chennai – 03.

Name of the participant	:	IP NO	:
Age	:	IP PROJECT NO	:
Sex	:	Date	:

I have been explained in detail about the study and its procedure. I confirm that I had completely understood the study and have had the opportunity to ask questions

I understand that my participation in the study is voluntary and that I'm free to withdraw at any time, without giving any reason, without their medical care or legal rights being affected.

I understand that the principal investigator, others working on the investigator's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However I understand that my identity will not be revealed in any information released to third parties or published.

I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s).

I agree to my participation in the above study.

Signature of investigator Signature of the participant

Date: Date:

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI 600 003

EC Reg.No.ECR/270/Inst./TN/2013/RR-16
Telephone No.044 25305301
Fax: 011 25363970

CERTIFICATE OF APPROVAL

To
Dr.T.GAAYATHRI,
III year MS ENT Post Graduate,
Upgraded Institute of Otorhinolaryngology,
Madras Medical College &
Rajiv Gandhi Govt. General Hospital,
Chennai - 600003.

Dear Dr. **T.GAAYATHRI**,

The Institutional Ethics Committee has considered your request and approved your study titled **"ROLE OF SPECIAL MUCOR SCREENING OPD IN THE MANAGEMENT OF POST COVID MUCOR EPIDEMIC"- NO.09082021.** The following members of Ethics Committee were present in the meeting held on **04.08.2021** conducted at Madras Medical College, Chennai 3.

1. Prof.P.V.Jayashankar,MS Orth.,D.Orth.,M.Ch Orth (Liverpool) :Chairperson
2. Prof.N.Gopalakrishnan,MD.,DM., FRCP, Director, Inst.of Nephrology,MMC,Ch. : Member Secretary
3. Prof. K.M.Sudha, Prof. Inst. of Pharmacology,MMC,Ch-3 : Member
4. Prof. Alagarsamy Jamila ,MD, Vice Principal, Stanley Medical College, Chennai : Member
5. Prof.Rema Chandramohan,Prof.of Paediatrics,ICH,Chennai : Member
6. Prof.S.Lakshmi, Prof. of Paediatrics ICH Chennai :Member
7. Tmt.Arnold Saulina, MA.,MSW., :Social Scientist
8. Thiru S.Govindasamy, BA.,BL,High Court,Chennai : Lawyer
9. Thiru K.Ranjith, Ch- 91 : Lay Person

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

Member Secretary – Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003.

Curiginal

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RANI	40/F	LEFT NASA	-	-	10	L NASAL CA	-	NORMAL	NORMAL	1	-	-	-	+	-	+	-	-	POSITIVE	POSITIVE	LEFT M,E, BONY EROSION
SURESH KU	38/M	LEFT NASA	-	-	7	L NASAL CA	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	NEGATIVE	POSITIVE	LEFT M,E
BAKTHAVA	75/F	RIGHT NAS	-	-	14	R NASAL CA	-	-	NORMAL	1	-	-	-	-	-	-	+	-	POSITIVE	POSITIVE	RIGHT M,E,S
RAGHUPAT	40/M	RIGHT NAS	-	-	14	R NASAL CA	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	NEGATIVE	NEGATIVE	RIGHT M,E,S
PALANI	45/M	RIGHT ORB	-	-	7	R NASAL CA	-	DISCOLOU	NORMAL	1	+	-	-	+	-	+	-	-	POSITIVE	POSITIVE	B/L M,E,S,BONY EROSION
VACHALA	46/F	RIGHT NAS	-	-	14	R NASAL CA	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	POSITIVE	POSITIVE	RIGHT M,E,S
RAYAN	64/M	RIGHT NAS	-	-	10	R NASAL CA	-	-	NORMAL	1	-	-	-	-	-	-	+	-	NEGATIVE	NEGATIVE	RIGHT M,E,S
BAKIYAVAT	35/M	RIGHT NAS	-	-	14	R NASAL CA	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	POSITIVE	POSITIVE	RIGHT M,E,S
CHINNASA	63/M	LEFT NASA	-	-	10	L NASAL CA	-	-	NORMAL	1	-	-	-	+	-	-	-	+	NEGATIVE	POSITIVE	LEFT M,E,S
KUMARAN	37/M	RIGHT NAS	-	-	14	R NASAL CA	-	-	NORMAL	1	-	-	-	-	-	-	+	-	POSITIVE	NEGATIVE	RIGHT M,E,S
AMBIKA	48/F	LEFT NASA	-	-	14	L NASAL CA	-	-	NORMAL	1	-	-	-	+	-	-	-	+	NEGATIVE	POSITIVE	LEFT M,E,S
GOTHAND/	62/M	LEFT NASA	-	-	10	L NASAL CA	-	-	NORMAL	1	-	-	-	+	-	-	-	+	NEGATIVE	POSITIVE	LEFT M,E,S
SUMATHI	54/F	RIGHT NAS	-	-	14	R NASAL CA	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	POSITIVE	POSITIVE	RIGHT M,E,S
ANANDHA	45/M	RIGHT NAS	-	-	14	R NASAL CA	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	POSITIVE	POSITIVE	RIGHT M,E,S
BALAJI	33/M	RIGHT NAS	-	-	20	R NASAL CA	-	-	NORMAL	1	-	-	-	-	-	-	+	-	NEGATIVE	NEGATIVE	RIGHT M,E,S
SHAKILAM	37/F	LEFT NASA	-	-	5	L NASAL CA	-	-	NORMAL	1	-	-	-	+	-	-	-	+	NEGATIVE	POSITIVE	LEFT M,E,S
POTHIYAM	39/F	RIGHT NAS	-	-	15	R NASAL CA	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	POSITIVE	POSITIVE	RIGHT M,E,S
SHANKAR	62/M	LEFT NASA	-	-	10	L NASAL CA	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	NEGATIVE	POSITIVE	LEFT M,E
SHAINA	54/F	RIGHT NAS	-	-	14	R NASAL CA	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	POSITIVE	POSITIVE	RIGHT M,E,S
SIVAKUMA	39/M	RIGHT NAS	-	-	7	R NASAL CA	-	-	NORMAL	1	-	-	-	-	-	-	+	-	NEGATIVE	NEGATIVE	RIGHT M,E,S
CHANDRAI	53/M	LEFT NASA	-	-	20	L NASAL CA	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	NEGATIVE	POSITIVE	LEFT M,E
THIRUMOO	42/M	LEFT NASA	-	-	20	L NASAL CA	-	-	NORMAL	1	-	-	-	+	-	-	-	+	POSITIVE	POSITIVE	LEFT M,E,S
KARPAGAN	56/F	LEFT NASA	-	-	14	L NASAL CA	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	NEGATIVE	POSITIVE	LEFT M,E
SHANTHI	58/F	RIGHT NAS	-	-	20	R NASAL CA	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	POSITIVE	POSITIVE	RIGHT M,E,S
KARUNAKA	50/M	LEFT NASA	-	-	14	L NASAL CA	-	-	NORMAL	1	-	-	-	+	-	-	-	+	NEGATIVE	POSITIVE	LEFT M,E,S
SUGUNA	34/F	RIGHT NAS	-	-	5	R NASAL CA	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	POSITIVE	POSITIVE	RIGHT M,E,S
LOURDUSA	46/M	LEFT NASA	-	-	14	L NASAL CA	-	-	NORMAL	1	-	-	-	+	-	-	-	+	POSITIVE	POSITIVE	LEFT M,E,S
SRIDHARAI	49/M	LEFT NASA	-	-	10	L NASAL CA	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	NEGATIVE	POSITIVE	LEFT M,E
MANGAI	52/F	RIGHT NAS	-	-	7	R NASAL CA	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	POSITIVE	POSITIVE	RIGHT M,E,S
ASHOK	60/M	RIGHT NAS	-	-	5	R NASAL CA	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	POSITIVE	POSITIVE	RIGHT M,E,S
SELVI	54/F	LEFT NASA	-	-	14	L NASAL CA	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	POSITIVE	POSITIVE	LEFT M,E
DHANDAPA	54/M	LEFT NASA	-	-	14	L NASAL CA	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	NEGATIVE	POSITIVE	LEFT M,E
UDHAYACH	54/F	LEFT NASA	-	-	20	L NASAL CA	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	POSITIVE	POSITIVE	LEFT M,E
KUMARI	47/F	LEFT NASA	-	-	10	L NASAL CA	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	NEGATIVE	POSITIVE	LEFT M,E
SIVASHAKT	42/M	RIGHT NAS	-	-	20	R NASAL CA	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	POSITIVE	POSITIVE	RIGHT M,E,S
MANIVANI	38/M	RIGHT NAS	-	-	20	R NASAL CA	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	POSITIVE	POSITIVE	RIGHT M,E,S
DHARSHIN	29/F	B/L NASAL	-	-	7	DISCHARG	-	NORMAL	NORMAL	1	+	-	-	-	-	-	+	-	NEGATIVE	NEGATIVE	B/L M,E
GUNAPRAS	29/M	LEFT NASA	-	-	14	L NASAL CA	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	NEGATIVE	POSITIVE	LEFT M,E
NITHYA	30/F	RIGHT NAS	-	-	10	R NASAL CA	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	POSITIVE	POSITIVE	RIGHT M,E,S
MANI	57/M	LEFT NASA	-	-	10	L NASAL CA	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	NEGATIVE	POSITIVE	LEFT M,E
DHANDUKI	65/M	RIGHT FAC	-	-	10	R NASAL CA	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	POSITIVE	POSITIVE	RIGHT M,E,S
RAMESH	30/M	RIGHT NAS	-	-	20	R NASAL CA	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	POSITIVE	POSITIVE	RIGHT M,E,S
KALAISELV	47/F	RIGHT NAS	-	-	7	R NASAL CA	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	POSITIVE	POSITIVE	RIGHT M,E,S
JOTHI	68/F	RIGHT NAS	-	-	14	R NASAL CA	-	-	NORMAL	1	+	-	-	-	-	-	+	-	POSITIVE	POSITIVE	RIGHT M,E,S
CHOKKALIN	50/M	RIGHT NAS	-	-	14	R NASAL CA	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	POSITIVE	POSITIVE	RIGHT M,E,S
SHAKILA	31/F	RIGHT NAS	-	-	10	R NASAL CA	-	-	NORMAL	1	+	-	-	-	-	-	+	-	POSITIVE	POSITIVE	RIGHT M,E,S
ARUMUGA	47/M	RIGHT NAS	-	-	14	R NASAL CA	-	-	NORMAL	1	+	-	-	-	-	-	+	-	POSITIVE	POSITIVE	RIGHT M,E,S
SURESH KU	41/M	RIGHT NAS	-	-	30	R NASAL CA	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	POSITIVE	POSITIVE	RIGHT M,E,S
GEETHA	45/F	RIGHT NAS	-	-	14	R NASAL CA	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	POSITIVE	POSITIVE	RIGHT M,E,S
SUMATHY	54/F	LEFT NASA	-	-	10	L NASAL DI	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	NEGATIVE	POSITIVE	L M,E,
MURUGAN	38/M	RIGHT NAS	-	-	14	R NASAL CA	-	-	NORMAL	1	-	-	-	-	-	-	+	-	NEGATIVE	NEGATIVE	RIGHT M,E,S
KUMAR	53/M	LEFT NASA	-	-	10	L NASAL CA	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	NEGATIVE	POSITIVE	LEFT M,E
SARASSAM	MAL73/F	LEFT NASA	-	-	10	L NASAL DI	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	NEGATIVE	POSITIVE	L M,E,
MAHALAKS	45/F	RIGHT NAS	-	-	20	R NASAL CA	-	-	NORMAL	1	+	-	-	-	-	-	+	-	POSITIVE	POSITIVE	RIGHT M,E,S
MALLIGA	56/F	LEFT NASA	-	-	14	L NASAL DI	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	NEGATIVE	POSITIVE	L M,E,
BALA	41/M	LEFT NASA	-	-	7	L NASAL CA	-	NORMAL	NORMAL	1	+	-	-	+	-	-	+	+	NEGATIVE	POSITIVE	LEFT M,E
LATHA	68/F	RIGHT NAS	-	-	5	R NASAL CA	-	-	NORMAL	1	-	-	-	-	-	-	+	-	NEGATIVE	NEGATIVE	RIGHT M,E,S
GANESAN	65/M	RIGHT NAS	-	-	7	R NASAL CA	-	-	NORMAL	1	-	-	-	-	-	-	+	-	NEGATIVE	POSITIVE	RIGHT M,E,S
YASODHA	65/F	RIGHT NAS	-	-	20	R NASAL CA	-	-	NORMAL	1	-	-	-	-	-	-	+	-	POSITIVE	POSITIVE	RIGHT M,E,S
SUMATHI	40/F	RIGHT NAS	-	-	7	R NASAL CA	-	-	NORMAL	1	-	-	-	-	-	-	+	-	NEGATIVE	NEGATIVE	RIGHT M,E,S
THENMOZI	60/F	RIGHT NAS	-	-	20	R NASAL CA	-	-	NORMAL	1	-	-	-	-	-	-	+	-	NEGATIVE	POSITIVE	RIGHT M,E,S
NANDAGO	73/M	RIGHT NAS	-	-	5	R NASAL CA	-	-	NORMAL	1	+	-	-	-	-	-	+	-	NEGATIVE	POSITIVE	RIGHT M,E,S
SURESH	39/M	RIGHT NAS	-	-	14	R NASAL CA	-	-	NORMAL	1	-	-	-	-	-	-	+	-	NEGATIVE	NEGATIVE	RIGHT M,E,S
LAKSHMI	54/F	RIGHT NAS	-	-	20	R NASAL CA	-	-	NORMAL	1	-	-	-	-	-	-	+	-	NEGATIVE	POSITIVE	RIGHT M,E,S
KANAGA	48/M	RIGHT NAS	-	-	5	R NASAL CA	-	-	NORMAL	1	-	-	-	-	-	-	+	-	POSITIVE	POSITIVE	RIGHT M,E,S