

“STUDY OF CLINICAL PRESENTATION AND MANAGEMENT OF MUCORMYCOSIS IN SECOND WAVE OF COVID 19 IN A TERTIARY CARE CENTER”

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ABSTRACT

Background :Mucormycosis is an Angioinvasive disease caused by mold fungi of genus Rhizopus, Mucor, Rhizomucor, Cunninghamella and Absidia of order Mucorales , Class Zygomycetes. Rhinocerebralmucormycosis is a rare but fatal infection of nasal cavity and paranasal sinuses.During second wave of Covid -19 in India (i.e from April 2021 to September 2021) there was sudden surge in number of Mucormycosis cases in patients of Covid- 19.

Objective :To study the demographic data, risk factors for development, clinical presentation, intervention and management of mucormycosis.

Methodology : An observational study was conducted on 48 cases, over 3 months (May 2021 to July 2021). Detailed history, Clinical presentations, Investigations, Management, Outcome noted and analysed.

Result : Mean age of presentation was 54.35 ± 10.55 years with male preponderance (64.6%). 72.9% having history of Covid-19, 89.6% were diabetic. 52.1% were hypertensive, 56.3% received oxygen therapy and 79.2% received steroids. 91.7% were having nasal symptoms, 52.1% having orbital symptoms, 56.3% were having dental symptoms, 4.2% having unilateral facial palsy. 69.8% showing maxillary sinus involvement, 52.1% showing ethmoid, 32.3% sphenoid, 27.1% having frontal sinus involvement, 16.6 % showing intracranial extension on CT PNS and Brain. FESS with debridement was done in 95.8%, Maxillectomy in 57.4% Orbitalexenteration in 10.4%. Amphotericin-B was administered in 91.7% cases and posaconazole in 52.1%. 95.8% cases were alive and 4.2% succumbed to death.

Conclusion : Prompt diagnosis, early initiation of treatment with Amphotericin-B, surgical debridement of PNS, and orbital exenteration, where indicated, are essential for successful outcome.

INTRODUCTION

Mucormycosis is a term used to refer to any fungal infections of the order mucorales, which belongs to class zygomycetes. Rhinocerebralmucormycosis is a rare but fatal infection of nasal cavity and paranasal sinuses. In pre covid era the incidence of mucormycosis was approximately 1.7 cases per 1000,000 inhabitants per year[1] . Mucormycosis was rarely affecting otherwise healthy people[2]. It is a disease of patients with pre-existing debilitating disease (Diabetes Mellitus) or is receiving immunosuppressive therapy.

Phycomycosis or zygomycosis was first described in 1885 by Paltauf[3] and later coined as Mucormycosis in 1957 by Baker[4] an American pathologist for an aggressive infection caused by Rhizopus. Mucormycosis is an uncommon but fatal fungal infection that usually affects patients with decreased immunity. It is an Angioinvasive disease caused by mold fungi of genus Rhizopus, Mucor, Rhizomucor, Cunninghamella and Absidia of order Mucorales, Class Zygomycetes[5]. The RhizopusOryzae is most common type and responsible for nearly 60 % of Mucormycosis cases in humans and also accounts for 90% of the Rhino-Orbital-cerebral (ROCM) form[6]. Mode of Contamination occurs through the inhalation of Fungal spores.

Rhino-Orbito-Cerebral Mucormycosis is known to exist in two forms, the well known Acute form and less known well recognised Chronic form. Acute Rhinocerebral Mucormycosis is an opportunistic but fulminant fungal infection of nose, paranasal sinuses, orbit and Cranial structures. It aggressively spreads to Orbits and cranium within days [7]. In advanced disease Chemosis, Ptosis, Proptosis, Ophthalmoplegia and blindness and Multiple cranial nerve palsies (Function of the cranial nerves 2nd, 3rd, 4th, 5th & 6th may be lost or impaired) [8] [9].

During second wave of Covid-19 in India (i.e from April 2021 to September 2021) we had witnessed a sudden surge in number of Mucormycosis cases in patients of Covid-19.

The primary reason that appears to be facilitating Mucorale spores to germinate in people with Covid-19 is an Ideal environment of low oxygen (Hypoxia), High blood glucose (Diabetes Mellitus, New onset hyperglycemia, and Steroid induced hyperglycemia), Acidic Medium (Metabolic Acidosis, Diabetic Ketoacidosis D.K.A.), High Iron levels (increased Ferritins), and decreased Phagocytic activity of W.B.C.s due to Immunosuppression (SARS-COV-2) mediated, Steroid mediated or background comorbidities coupled with several other risk factors including hospitalisation with or without ventilators [10].

In this study we found the incidence of mucormycosis was suddenly raised during the second wave of Covid-19, especially in the month of May 2021 to July 2021. In Covid- era we found several risk factors example oxygen therapy, use of steroids, uncontrolled diabetes mellitus, etc., responsible for the development of mucormycosis.

MATERIALS AND METHODS

An observational retrospective study was conducted in a tertiary care centre, Bundelkhand medical college, sagar, Madhya Pradesh. A total of 48 confirmed cases of mucormycosis fulfilling the inclusion criteria were selected. A thorough research was done keeping the research question, proposed hypothesis, aims and objectives in mind, the data analysis was done.

Descriptive analysis was carried out to present the distribution of study participants, various risk factors, clinical presentations, clinical findings, laboratory findings, radiological findings, different medical and surgical complications, management protocols and their clinical outcomes was done in the form of frequency, range, mean, standard deviation and percentage.

RESULTS AND OBSERVATIONS

The majority of the participants in the present study belonged to 51- 60 years of age (45.8%), followed by age group of over 60 years (20.8%), followed by age group of 41-50 years (18.8%), followed by age group of 31-40 years (14.6%). The mean age of the study

participants was 54.35 ± 10.55 years. No participants were found below 30 years and pediatric age group.

		Count	Column N %
Age Group	31 - 40 years	7	14.6%
	41 - 50 years	9	18.8%
	51 - 60 years	22	45.8%
	> 60 years	10	20.8%

Table No. 1 : Age wise distribution of study participants

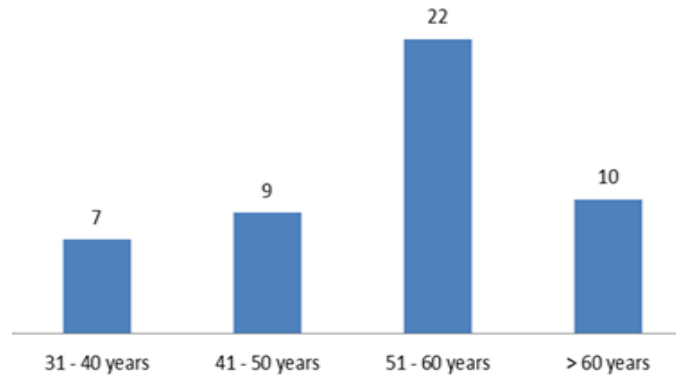


Fig. 1 : Bar graph showing distribution of various age groups of patients

In the present study out of total 48 participants, 31 were male (64.6%) and 17 were females (35.4%)

		Count	Column N %
Gender	Male	31	64.6%
	Female	17	35.4%

Table no.2 showing gender wise distribution among participants.

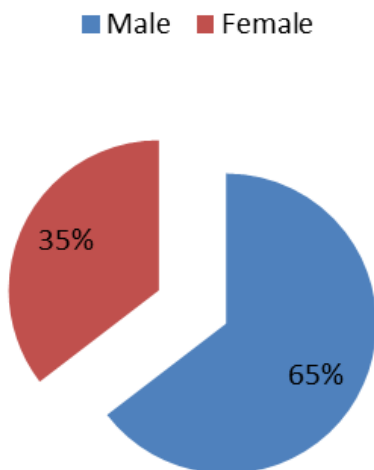


Fig 2 : Pie-chart showing Gender distribution among the study participants.

Majority of the participants in the study were having complaint of pain and numbness over face (91.7 %), followed by complaint of nasal blockage/ discharge (66.7 %). Dental complaints were seen in 56.3 % participants followed by orbital complaints were seen in 52.1%. Unilateral facial palsy was observed in 2 cases (4.2%).



Photograph showing (a)Right Facial Nerve Palsy, (b)Right Periorbital Swelling, (c) Palatal Ulcer

Clinical features	Count	Column N %
PAIN AND NUMBNESS OVER FACE	44	91.7%
NASAL BLOCKAGE /DISCHARGE	32	66.7%
ORBITAL COMPLAINTS	25	52.1%
DENTAL COMPLAINTS	27	56.3%
Facial palsy	2	4.2%

Table No. 3 showing distribution of clinical presentations in the study participants.

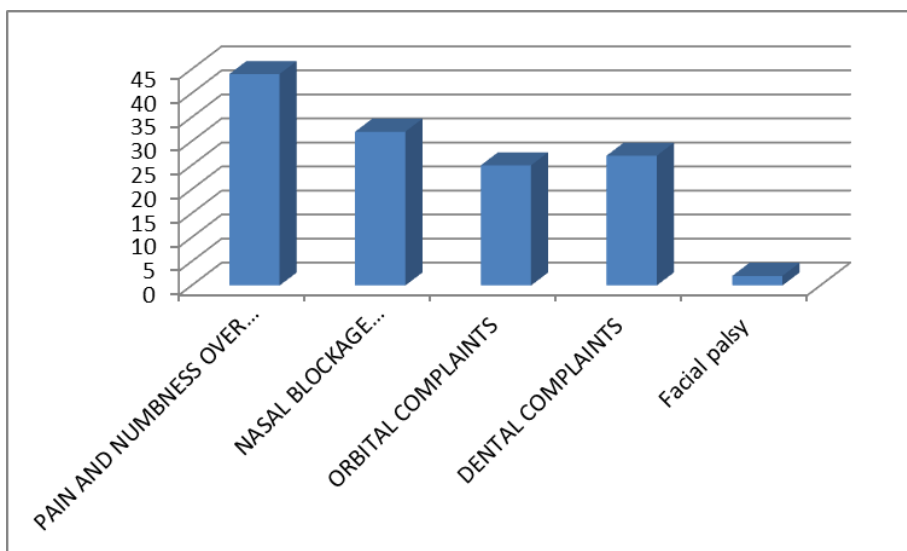


Fig no. 3 Bar graph showing distribution of clinical presentations among study participants.

Among 48 participants, 35 cases were having history of covid-19 (72.9%), 13 cases were having no history of covid-19 (27.1%)

		Count	Column N %
H/O COVID 19	Yes	35	72.9%
	No	13	27.1%

Table no. 4 showing history of covid-19 among study participants.

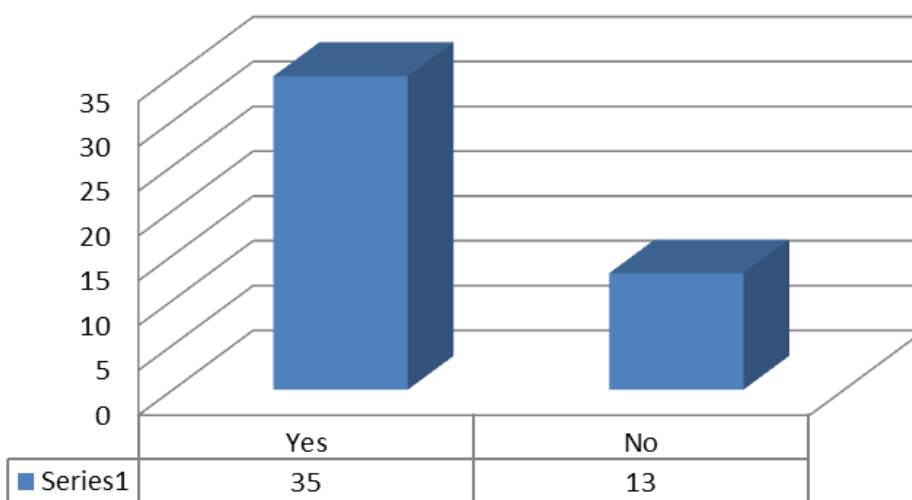


Fig 4 Bar graph showing distribution of H/O covid-19 among study participants.

Out of total 48 participants, majority of patients, 43 were having diabetes mellitus (89.6%), 25 patients were having H/O hypertension (52.1 %) and 1 patient was having H/O renal disease (2.1%).

	Count	Column N %
H/O DIABETES	43	89.6%
H/O HYPERTENSION	25	52.1%
H/O RENAL DISEASE	1	2.1%

Table no. 5 showing distribution of risk factors, H/O DM, H/O HTN, H/O renal disease among study participants in the present study.

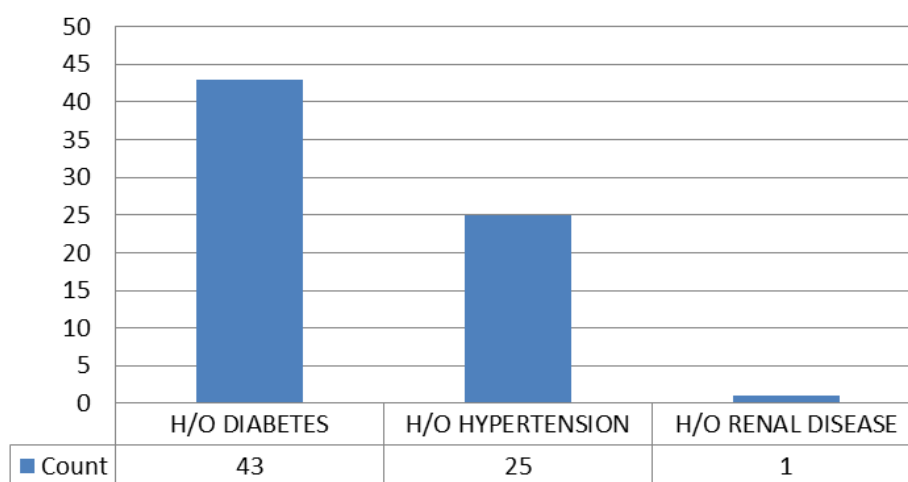


Fig no. 5 Bar graph showing distribution of various risk factors.

Out of total 48 patients, 28 were having H/O hospital admission (58.3%), 27 patients were giving H/O oxygen support (56.3%) and 38 patients were having H/O steroid intake (79.2%).

	Count	Column N %
H/O HOSPITAL ADMISSION	28	58.3%
H/O OXYGEN SUPPORT	27	56.3%
H/O STEROID	38	79.2%

Table no. 6 showing distribution of various risk factors H/O hospital admission, H/O oxygen support and H/O steroid intake during covid-19.

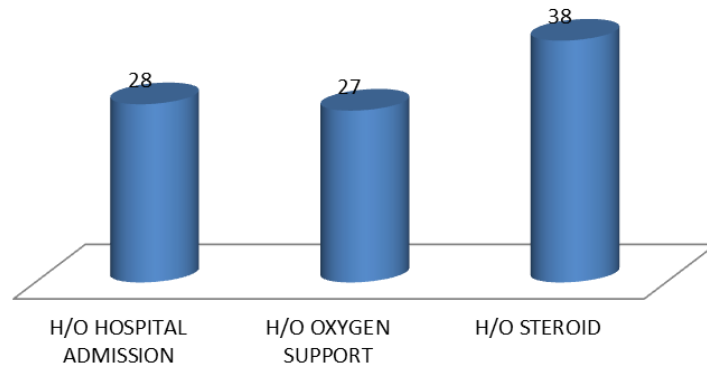


Fig 6 bar graph showing distribution of risk factors

Out of total 48 patients, 8 patients were having H/O steroid intake for less than 1 week, 30 patients having H/O steroid intake for more than or equal to 1 week of duration, 10 patients were having no H/O steroid intake.

DURATION OF STEROIDS IN DAYS	Count	Column N %
< 1 week	08	16.6%
> 1 week	30	62.5%

Table no. 7 showing distribution of duration of steroid intake during covid-19.

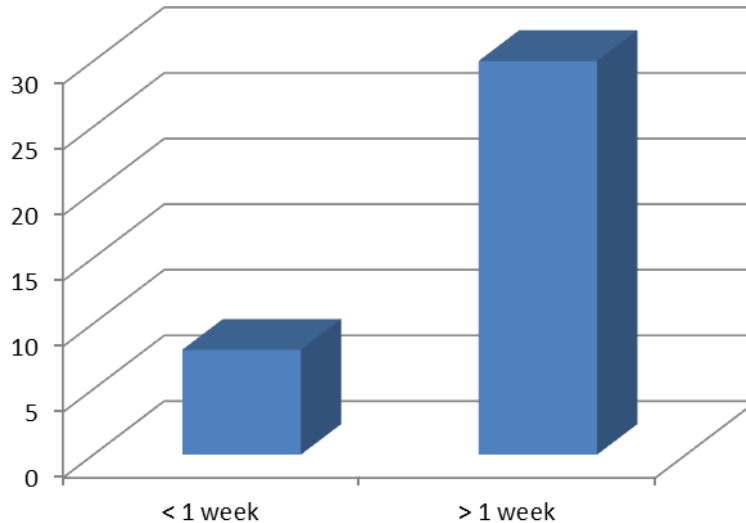


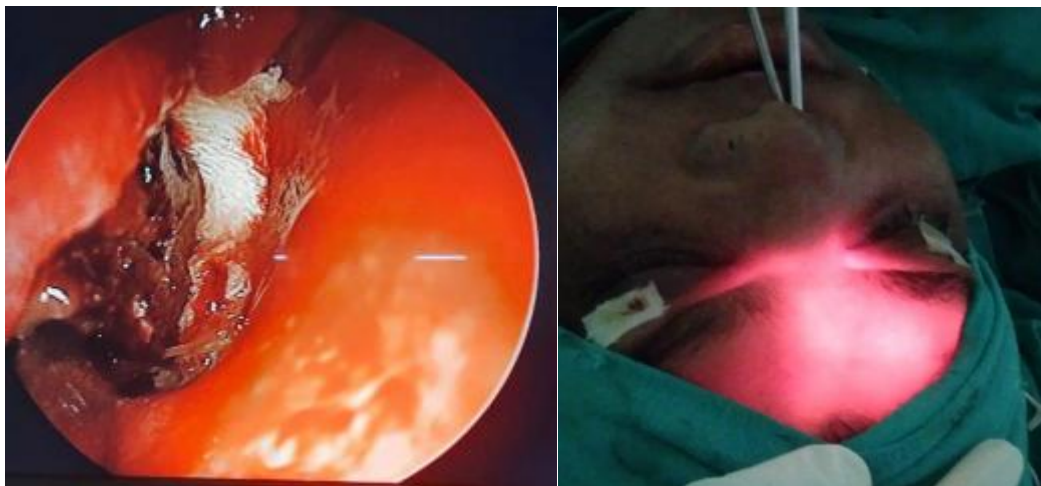
Fig 7 bar graph showing distribution of duration of steroid intake among study participants.

On Right side DNE, most commonly II pass (posterior part of middle turbinate, sphenoethmoidal recess, superior turbinate and meatus, openings of posterior ethmoid cells and opening of sphenoid sinus in the posterior wall of sphenoethmoidal recess) was involved in 27 patients (56.3%) followed by III pass(uncinate process, bulla ethmoidalis, hiatus semilunaris, sinus of the turbinate and the frontal recess) was involved in 26 patients

(54.2%), least common involved was I pass(margins of choana, posterior ends of turbinatesinferior meatus, opening of eustachian tube, opening of nasolacrimal duct and walls of nasopharynx) in 10 patients (20.8%).

Similarly on Left side DNE, most commonly II pass was involved in 28 patients (58.3%) followed by III pass was involved in 27 patients (56.3%), least commonly involved was I pass in 9 patients (18.8%).

Overall most commonly II pass was involved in 57.3% of patients and least commonly I pass was involved in 19.8% patients.



Photograph Showing (a)Black Necrotic Areas on DNE, (b) Frontal Glow on DNE

		Count	Column N %
DNE R I PASS	Involved	10	20.8%
	Normal	38	79.2%
DNE R II PASS	Involved	27	56.3%
	Normal	21	43.8%
DNE R III PASS	Involved	26	54.2%
	Normal	22	45.8%
DNE L I PASS	Involved	9	18.8%
	Normal	39	81.3%
DNE L II PASS	Involved	28	58.3%
	Normal	20	41.7%
DNE L III PASS	Involved	27	56.3%
	Normal	21	43.8%

Table 9 showing distribution of involvement of I , II, III pass of DNE among 48 study participants.

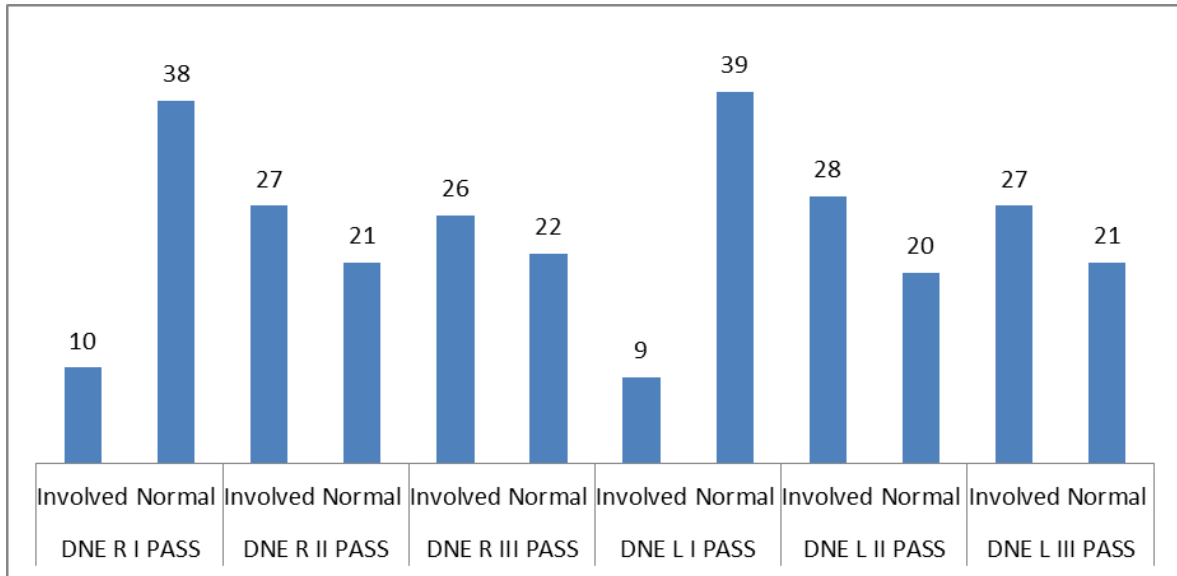


Fig no. 9 bar graph showing distribution of involvement of I, II and III pass of DNE.

Among 48 study participants orbital involvement of Right eye vision was normal in 35 patients (72.9%), decreased in 8 patients (16.7%) and lost in 5 cases (10.4%). Right eye extra ocular muscle involvement was observed in 14 cases (29.2%) and right side peri-orbital swelling was seen in 19 cases (39.6%).

Similarly, among 48 study participants orbital involvement of Left vision was normal in 42 patients (87.5%), decreased in 3 patients (6.3%) and lost in 3 cases (6.3%). left eye extra ocular muscle involvement was observed in 11 cases (22.9%) and left side peri-orbital swelling was seen in 16 cases (33.3%).

		Count	Column N %
R VISION	Normal	35	72.9%
	Decrease	8	16.7%
	Loss	5	10.4%
R EOM INVOLVEMENT	Yes	14	29.2%
	No	34	70.8%
R PERIORBITAL SWELLING	Yes	19	39.6%
	No	29	60.4%
L VISION	Normal	42	87.5%
	Decrease	3	6.3%
	Loss	3	6.3%
L EOM INVOLVEMENT	Yes	11	22.9%
	No	37	77.1%
L PERIORBITAL SWELLING	Yes	16	33.3%
	No	32	66.7%

Table No. 10 showing distribution of orbital symptoms among 48 study participants

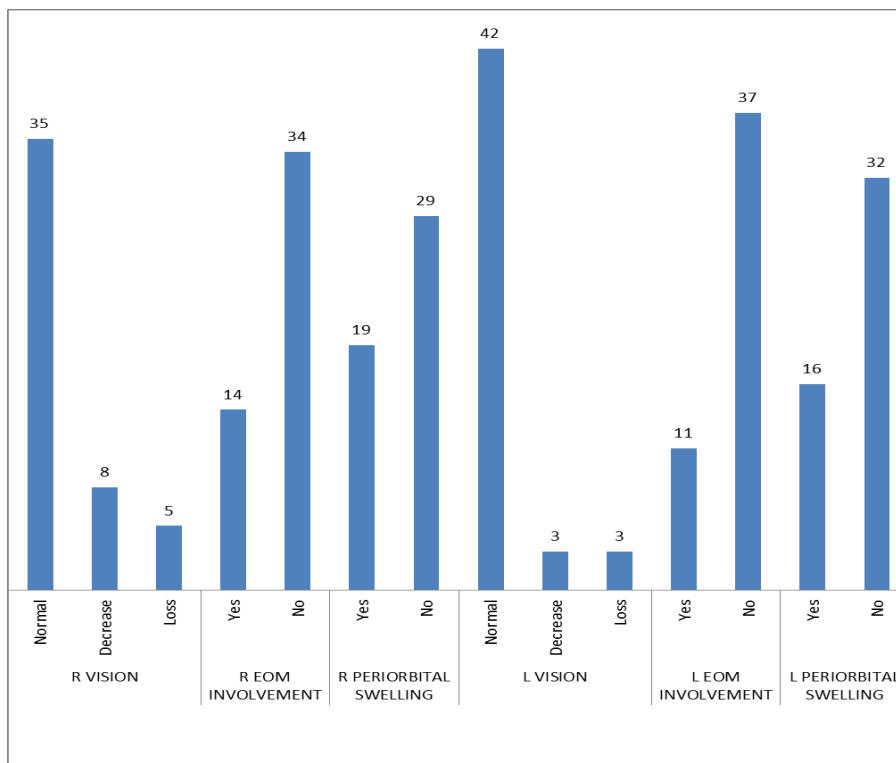


Fig no. 10 bar graph showing distribution of orbital symptoms among 48 study participants.

Among 48 study participants Palatal Ulcer were noted in 16 cases (33.3%) , and Losening of teeth was observed in 26 cases (54.2%).

		Count	Column N %
PALATAL ULCER	Yes	16	33.3%
	No	32	66.7%
LOSENING OF TEETH	Yes	26	54.2%
	No	22	45.8%

Table 11 showing Distribution of dental symptoms among 48 study participants

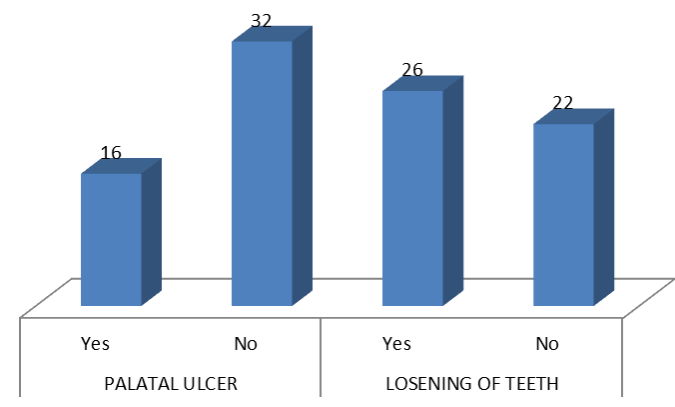
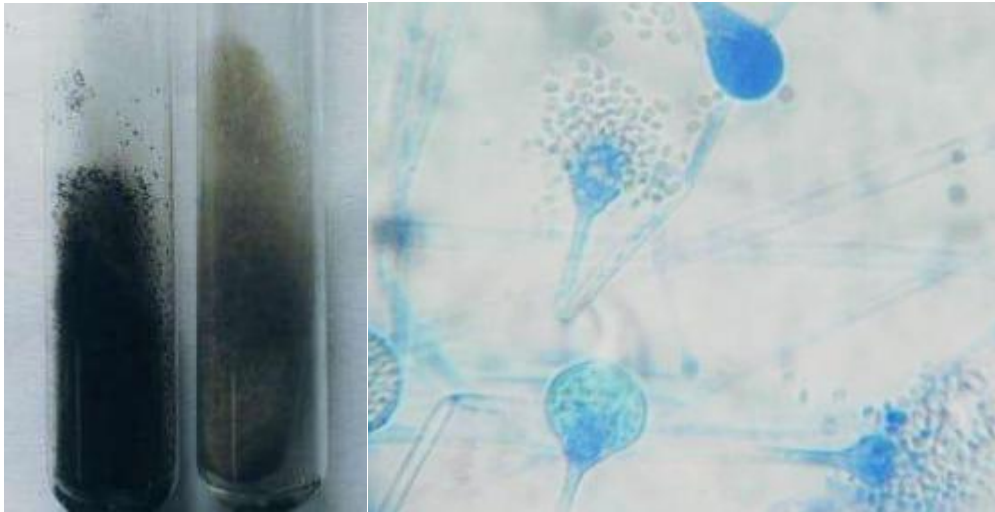


Figure 11 bar graph Showing Distribution of Dental Signs among study participants.

Among total 48 study participants KOH mount was positive in 18 patients (37.5%) , while Fungal culture report was Positive in 21 patients (43.8%).



Photograph Showing (a)Mucormycosis Growth on SDA, (b) Microscopic view

		Count	Column N %
KOH MOUNT	Positive	18	37.5%
	Negative	30	62.5%
FUNGAL CULTURE	Positive	21	43.8%
	Negative	27	56.3%

Table 12 Showing variation in KOH Mount and fungal culture report among study participants.

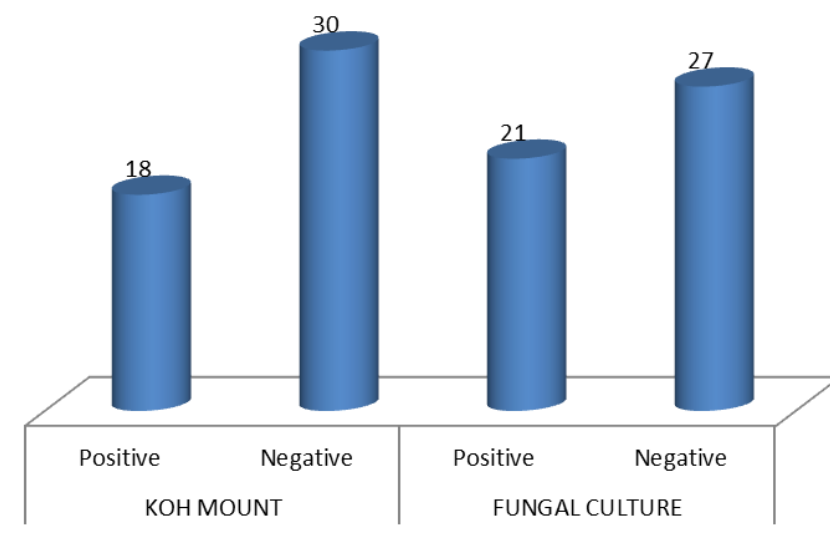


Figure 12 bar graph Showing distribution of result of KOH mount and Fungal culture among study participants

Among 48 study participants The Mean Hemoglobin was 10.3 ± 1.4 gm/dl.

Among 48 study participants The mean of T.L.C. was 7823 ± 2870 / cumm.

Among 48 Study participants the Mean of Platelet count was 3.0 ± 1.0 lakh / cumm.

Among 48 study participants The Mean of HbA1c was $7.5 \pm 1.6\%$

Among 48 study participants the Mean of S. Creatinine is 1.0 ± 1.0 .

Among 48 study participants The mean of S. potassium was 3.45 ± 0.84 mmol/dl.

	Mean	Standard Deviation	Minimum	Maximum
Hb	10.3	1.4	7.3	14.4
TLC	7823	2870	2700	15500
Platelets	3.0	1.0	1.0	5.8
HbA1c	7.5	1.6	4.8	13.5
S. Ferritin	631	163	160	958
S. Creatinine	1	1		4
K+	3.45	.84	1.91	5.50

Table 13.1 Showing Distribution of significant pathological laboratory findings among 48 Study participants.

Among 48 study participants,

S. Hb was found normal in 8 cases (16.7%) and decreased in 40 cases (83.3%).

TLC was found in normal range in 40 cases (83.3%), increased in 7 cases (14.6%) and decreased in 1 case (2.1%).

Platelet count was found normal in 44 cases (91.7%), decreased in 2 cases (4.2%) and increased in 2 cases (4.2%).

HbA1c was found in Diabetic range ($>6.5\%$) in 36 cases (75.0%), pre-diabetic range (5.7-6.4) in 7 cases (14.6%) and in normal range (<5.6) in 5 cases (10.4%).

S. Ferritin was found increased (>336 ng/dl) in 47 cases (97.9%) and normal (24-336 ng/dl) in 1 case (2.1%).

S. Creatinine was found normal range in 37 cases (77.1%) while increased in 7 cases (14.6%).

CRP was found reactive in 47 cases (97.9%).

S. Pottasium was found decreased in 28 cases (58.3%) while normal in 19 cases (39.6%).

		Count	Column N %
Haemoglobin	11.6 - 16.6 Normal	8	16.7%
	Decreased	40	83.3%
Total Leucocyte count	4000 -11000 Normal	40	83.3%
	< 4000 decreased	1	2.1%
	11000 increased	7	14.6%
Platelets	1.5 - 4.5 lakhs Normal	44	91.7%
	<1.5 Decreased	2	4.2%
	> 4.5 lakh Increased	2	4.2%
HbA1c	< 5.6 Normal	5	10.4%
	5.7 - 6.4 Pre diabetic	7	14.6%
	>6.5 Diabetic	36	75.0%
S. Ferritin	24 - 336 ng/ml normal	1	2.1%
	> 336 Increased	47	97.9%
S. Creatinine	0.59 - 1.35 mg/dl Normal	37	77.1%
	< 0.59 mg/dl Decreased	4	8.3%
	> 1.35 mg/dl Increased	7	14.6%
CRP	Reactive	47	97.9%
	Non-reactive	1	2.1%
K+	3.6 - 5.2 Normal	19	39.6%
	< 3.6 mmol/L decreased	28	58.3%
	> 5.2 mmol/L Increased	1	2.1%

Table 13.2 showing laboratory findings of the study participants

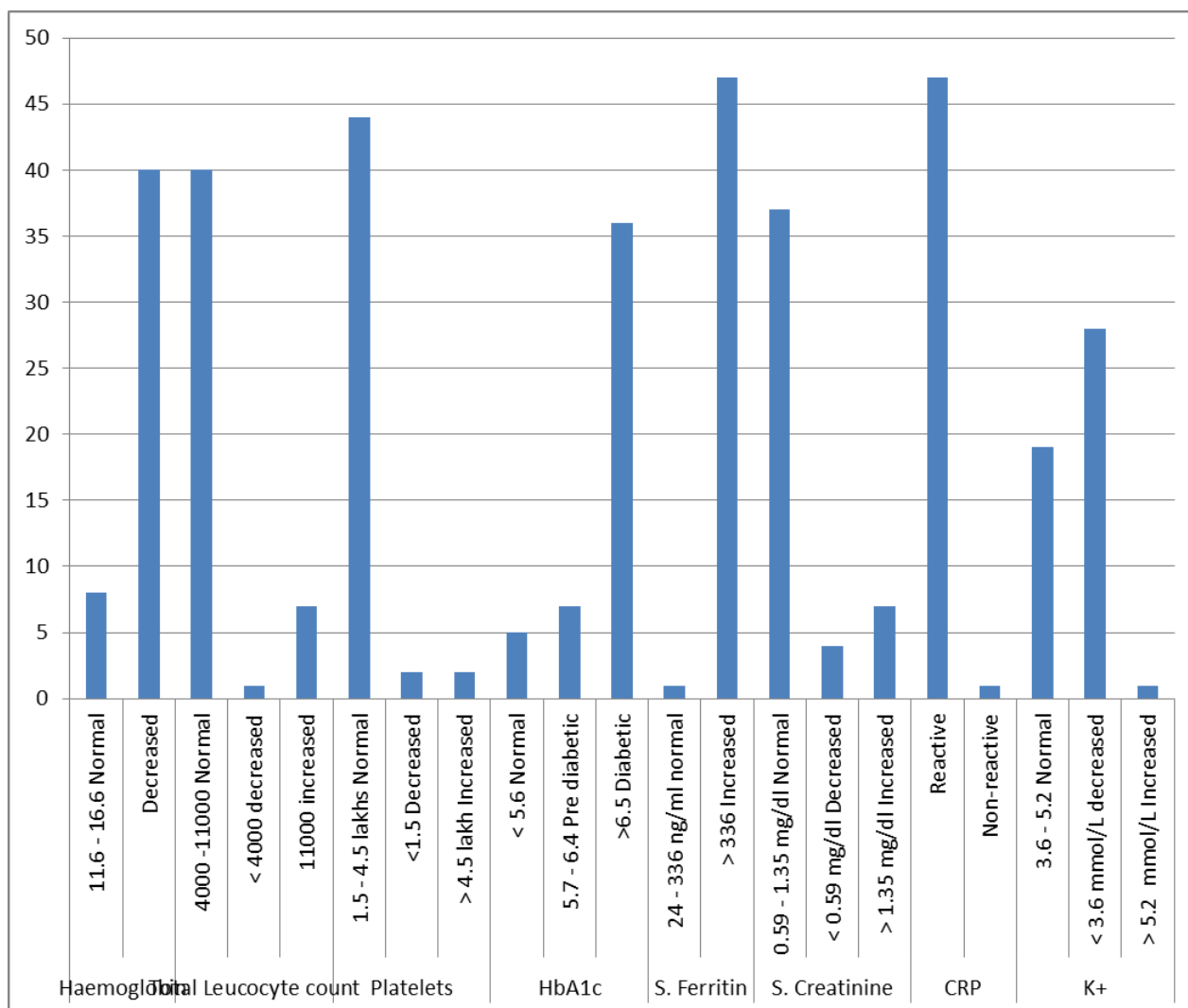


Fig 13 Bar graph showing distribution of laboratory findings of the 48 study participants

Among 48 study cases, on Right side Maxillary sinus was seen involved in 31 cases (64.6%), followed by involvement of ethmoid sinuses was seen in 24 cases (50.0%), followed by involvement of sphenoid sinuses in 14 cases (29.2%) and frontal sinus was involved in 14 cases (29.2%).

Similarly, Among 48 study cases, on Left side Maxillary sinus was seen involved in 36 cases (75.0%), followed by involvement of ethmoid sinuses was seen in 26 cases (54.2%), followed by involvement of sphenoid sinuses in 17 cases (35.4%) and least involvement was seen in frontal sinus in 12 cases (25.0%).

Among 48 cases, Intracranial Extension was seen in 8 cases (16.66%)

	Right		Left	
	Count	Column N %	Count	Column N %
CT Maxillary	31	64.6%	36	75.0%
CT Ethmoid	24	50.0%	26	54.2%
CT Sphenoid	14	29.2%	17	35.4%
CT Frontal	14	29.2%	12	25.0%
Intracranial Extension	8 cases / 16.66%			

Table 14 showing distribution of CT Scan findings of Para-nasal sinuses and brain

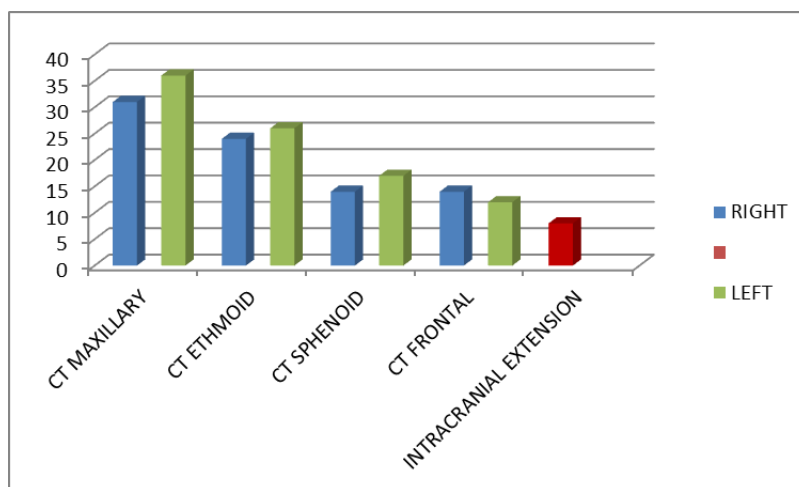


Fig. 14 bar graph showing CT findings of PNS and brain

Among 48 study participants, FESS was done in 46 cases (95.8%), maxillectomy was done in 27 cases (57.4%), eye exenteration was done in 5 cases (10.4%) and transcutaneous retrobulbar amphotericin-B was given in 13 cases (27.08%).



Photograph Showing (a) Left Eye Exenteration, (b) Right Segmental Maxillectomy

		Count	Column N %
FESS	Yes	46	95.8%
	No	2	4.2%
MAXILLECTOMY	Yes	27	57.4%
	No	20	42.6%
EYE EXENTERATION	Yes	5	10.4%
	No	43	89.6%
TRANSCUTANEOUS RETROBULBAR AMPHOTERICIN-B	YES	13	27.08%
	NO	35	72.92%

Table 15 showing distribution of different procedures performed in 48 study participants.

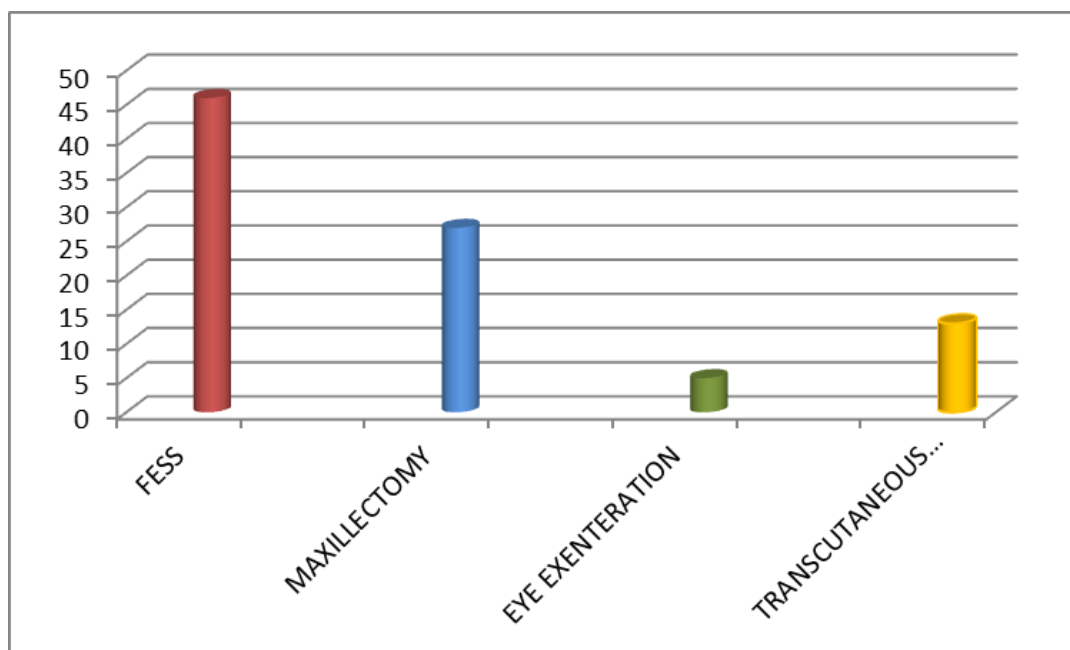


Fig 15 bar graph showing different procedures performed among 48 study cases.

Among 48 cases, 44 were treated with injection amphotericin (91.7%), while 25 cases (52.1%) were given posaconazole.

		Count	Column N %
AMPHOTERICIN	Yes	44	91.7%
	No	4	8.3%
POSACONAZOLE	Yes	25	52.1%
	No	23	47.9%

Table 16 showing distribution of medical management of 48 cases of mucormycosis.

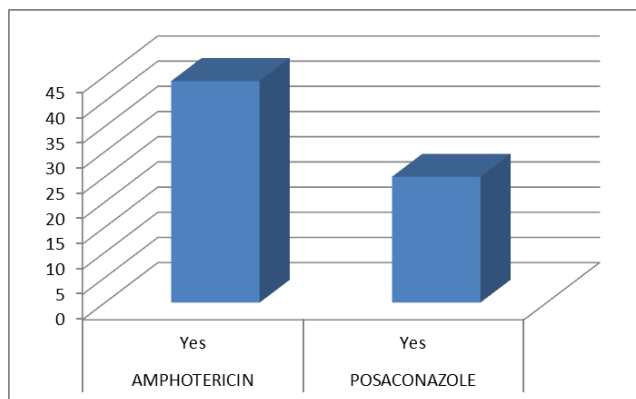


Fig 16 bar graph showing distribution of medical management of 48 cases of mucormycosis

The mean duration of hospital stay in days is 28 with standard deviation of 12.46.

	Mean	Standard Deviation	Minimum	Maximum
DURATION OF STAY IN DAYS	28.19	12.46	3.00	72.00

Table 17 showing duration of hospital stay during course of illness among 48 study cases.

Among 48 cases of mucormycosis, CSF leak was seen in 3 cases (6.3%), hypokalemic palsy was seen in 8 cases (16.7%), acute renal failure was seen in 2 cases (4.2%), chronic renal failure was seen in 1 case (2.1%), unilateral facial palsy was seen in 2 cases (4.2%), oro-antral fistula was seen in 1 case (2.1%). Recurrence of disease was seen in 14 cases (29.2%).

		Count	Column N %
CSF LEAK	Yes	3	6.3%
	No	45	93.8%
HYPOKALEMIC PALSY	Yes	8	16.7%
	No	40	83.3%
OTHER COMPLICATION	ACUTE RENAL FAILURE	2	4.2%
	CHRONIC RENAL FAILURE, HYPOTENSION	1	2.1%
	CVA HEMIPARESIS	1	2.1%
	FACIAL PALSY	2	4.2%
	SYNECHIA FORMATION	1	2.1%
	OROANTRAL FISTULA	1	2.1%
RECURRENCE	Yes	14	29.2%
	No	34	70.8%

Table 18 showing distribution of different complications among 48 cases of mucormycosis.

		FESS				Chi-square	p value
		Yes		No			
		Count	Column N %	Count	Column N %		
CSF LEAK	Yes	3	6.5%	0	0.0%	0.139	0.709
	No	43	93.5%	2	100.0%		

Table 19 : association of FESS with CSF leak

		MAXILLECTOMY				Chi-square	p value
		Yes		No			
		Count	Column N %	Count	Column N %		
ORO-ANTRAL FISTULA	Yes	1	3.7%	0	0.0%	0.757	0.384
	No	26	96.3%	20	100.0%		

Table 20 : Association of Maxillectomy with Oro-antral fistula

		AMPHOTERICIN				Chi-square	p value
		Yes		No			
		Count	Column N %	Count	Column N %		
HYPOKALEMIC PALSYP	Yes	8	18.2%	0	0.0%	0.873	0.35
	No	36	81.8%	4	100.0%		
ACUTE RENAL FAILURE	Yes	2	4.5%	0	0.0%	0.0.190	0.663
	No	42	95.5%	4	100.0%		

Table 21 : Association of Amphotericin and Hypokalemic Palsy and Acute Renal Failure

		POSACONAZOLE				Chi-square	p value
		Yes		No			
		Count	Column N %	Count	Column N %		
HYPOKALEMIC PALSYP	Yes	5	20.0%	3	13.0%	0.417	0.518
	No	20	80.0%	20	87.0%		
ACUTE RENAL FAILURE	Yes	0	0.0%	2	8.7%	2.268	0.132
	No	25	100.0%	21	91.3%		

Table 22 : Association of Posaconazole with Hypokalemic Palsy and Acute Renal Failure

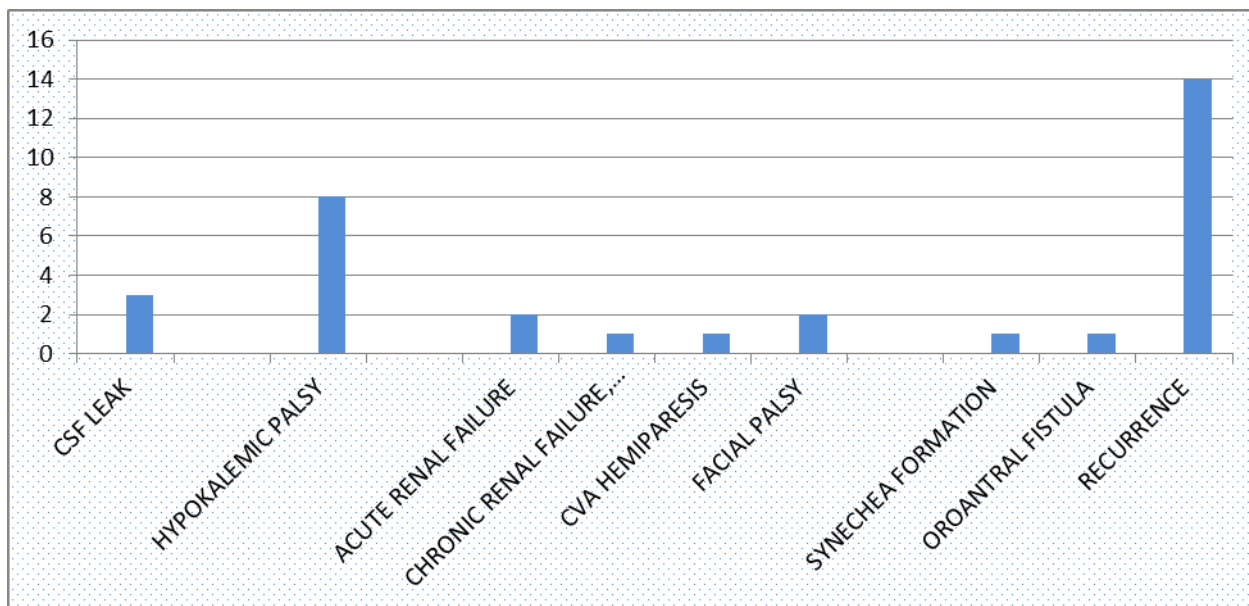


Fig 17 bar graph showing distribution of different complication among 48 cases of mucormycosis.

Among 48 cases of mucormycosis, 44 (91.7%) were alive after 6 months of follow-up, 4 cases (8.3%) patients were succumbed and 8 cases (16.66%) were referred to higher centre for further management.

		Count	Column N %
OUTCOME	Alive	44	91.3%
	Death	4	8.3%
	Refer	8	16.6%

Table 23 showing clinical outcome of 48 mucormycosis cases.

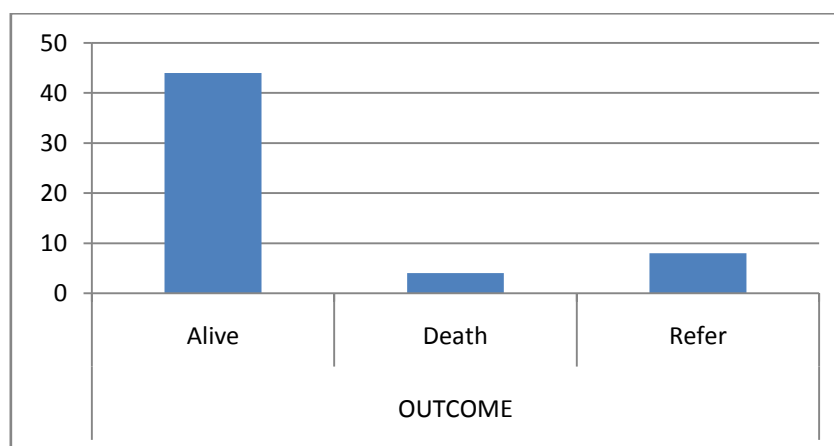


Fig 18 bar graph showing outcomes of 48 cases of mucormycosis

DISCUSSION

Globally, the prevalence of mucormycosis varied from 0.005 to 1.7 per million populations, while its prevalence was nearly 80 times higher (0.14 per 1000) in India compared to developed countries, in a recent estimate of year 2019–2020 [11-13]. In other words, India has highest cases of the mucormycosis in the world. Notwithstanding, India is already having second largest population with diabetes mellitus (DM) and was the diabetes capital of the world, until recently [14]. Importantly, DM has been the most common risk factor linked with mucormycosis in India, although hematological malignancies and organ transplant takes the lead in Europe and the USA [13]. Nevertheless, DM remains the leading risk factor associated with mucormycosis globally, with an overall mortality of 46% [15].

While long term use of corticosteroids has often been associated with several opportunistic fungal infection including Aspergillosis and mucormycosis, even a short course of corticosteroids has recently been reported to link with mucormycosis especially in people with DM. A cumulative prednisone dose of greater than 600 mg or a total methyl prednisone dose of 2–7 g given during the month before predisposes immunocompromised people to mucormycosis [16]. 46% of the patients had received corticosteroids within the month before the diagnosis of mucormycosis in the European Confederation of Medical Mycology study [17].

Mucormycosis is characterized by the presence of hyphae invasion of sinus tissue and a time course of less than four weeks [18,19]. Clinically, rhinocerebral mucormycosis can present with atypical signs and symptoms similar to complicated sinusitis, such as nasal blockade, crusting, proptosis, facial pain and oedema, ptosis, chemosis, and even ophthalmoplegia, with headache and fever and various neurological signs and symptoms if intracranial extension is present [20,21].

A black eschar is often seen in the nasal cavity or over the hard palate region, but is not characteristic [22,23]. Histological features include mycotic infiltration of blood vessels, vasculitis with thrombosis, tissue infarction, haemorrhage and acute neutrophilic infiltrate [23].

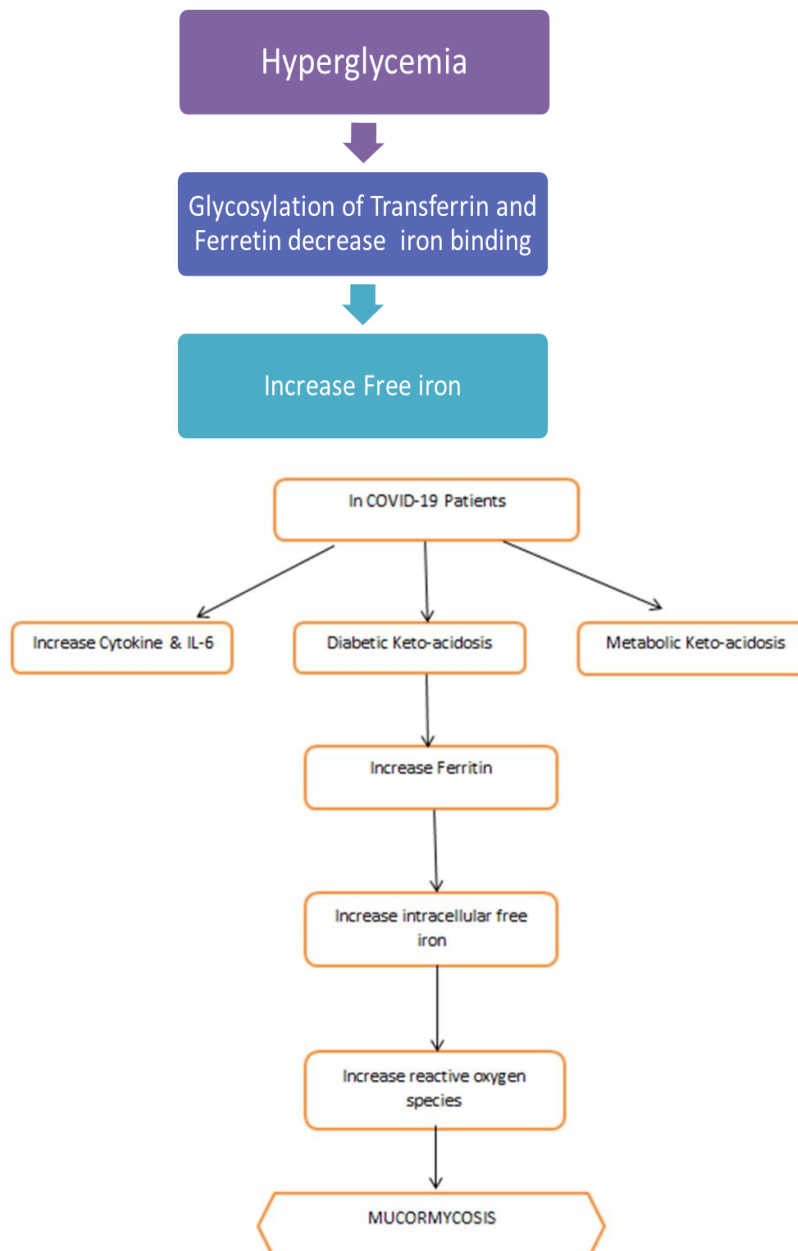
Without early diagnosis and treatment, there may be rapid progression of the disease, with reported mortality rates from intra-orbital and intracranial complications of 50–80 per cent [24]. Even with prompt diagnosis, treatment of underlying diseases, and aggressive medical and surgical intervention, the management is often not effective, leading to an extension of the infection and ultimately death [25].

The Covid-19 infection caused by the novel SARS-CoV-2 has been associated with a wide range of disease patterns, ranging from a mild cough to life-threatening pneumonia [26].

Uncontrolled hyperglycemia and precipitation of DKA is often observed due to corticosteroid intake. Low pH due to acidosis is a fertile media for mucor spores to

germinate. Moreover, steroid use reduces the phagocytic activity of WBC (both first line and second line defense mechanism), causes impairment of bronchoalveolar macrophages migration, ingestion, and phagolysosome fusion, making a diabetic patient exceptionally vulnerable to mucormycosis. COVID-19 often causes endothelialitis, endothelial damage, thrombosis, lymphopenia, and reduction in CD4+ and CD8+ level and thus predisposes to secondary or opportunistic fungal infection.

Free available iron is an ideal resource for mucormycosis. Hyperglycemia causes glycosylation of transferrin and ferritin, and reduces iron binding allowing increased free iron. Moreover, increase in cytokines in patients with COVID-19 especially interleukin-6, increases free iron by increasing ferritin levels due to increased synthesis and decreased iron transport. Furthermore, concomitant acidosis increases free iron by the same mechanism and additionally by reducing the ability of transferrin to chelate iron.



High glucose, low pH, free iron, and ketones in presence of decreased phagocytic activity of WBC, enhances the growth of mucor. In addition, it Journal Pre-proof enhances the expression of glucose-regulator protein 78 (GRP-78) of endothelium cells and fungal ligand spore coating homolog (CotH) protein, enabling angioinvasion, hematogenous dissemination and tissue necrosis[27].

The disease was commonly seen in age group 51-60 yrs, Predominantly seen in males. Significant association with covid-19 infection. The most relevant risk factor found was uncontrolled diabetes mellitus type II. Another significant risk factor found was steroid intake, the extent of disease was proportional to the duration of steroid intake.

The most common clinical symptom was involvement of nose and PNS. Involvement of the brain was not uncommon. Significant extension of disease was seen in adjacent structures like eyes and palate. The extension of disease was proportional to the HbA1c level.

CT scan of nose and PNS + Orbit and brain was the investigation of choice.

Combined surgical approach of ENT, ophthalmology and Dental department was beneficial. Medical management following surgical clearance of disease with amphotericin-B and posaconazole was found beneficial. Surgical complications includes CSF leak, Synechia formation and oro-antral fistula formation. Medical complication that were observed are reversible hypokalemic palsy and acute renal failure.

Variable	Our study (48 cases)	Lev selarka et.al [28] (47 cases)	Pradeep pradhan et al [29] (46 cases)	Ritu arora et.al [30] (65 cases)	Urmil Chawla et al [31] (254 cases)
Mean age	54±10.55	55±12.8	48±10.83	57	50±13.38
M/f	64.6%	74.5%	86.95%	-	64.56%
H/O covid	72.9%	-	100%	-	52%
DM II	89.9%	76.6%	84.8%	88.1%	86%
HTN	52.1%	57.4%	-	23.3%	
CKD	2.1%	-	-	3.3%	-
Hospitalisation	58.3%	-	-	63.3%	35.03%
O2 support	56.3%	80.9%	-	50%	27.55%
H/O Steroid	79.2%	95.7%	89.1%	63.3%	76%
Facial pain	91.7%	100%	46%	80%	32%
Nasal sy.	66.7%	100%	46%	80%	10%
Orbital sy.	52.1%	40%	2.1%	3.3%	40%
Dental sy.	56.3%	-	12%	1.67%	6%
Facial palsy	4.2%	-	-	-	

Table no 24 Showing Comparison of variables between our study and several other studies

Conflict of Interest : Nil

Funding Source : Nil

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