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Nutritional Guidelines for Hospitalized Mucormycosis patients

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Abstract
Mucormycosis is an infection that is caused by a fungus named *Rhizopus oryzae* in immune-compromised patients, post-covid patients or patients who have uncontrolled blood sugar levels. As there were no dietary guidelines on mucormycosis, therefore present study was planned to study fifty mucormycosis positive cases critically and develop dietary guidelines on the basis of their biochemical profile, clinical signs & symptoms, medication and ability to have diet during hospitalization. In present study, it was found that patients whose diet intake was upto their nutritional requirements recovered fast in comparison to patients who were not able to have proper meals. As patients had problems of dryness in mouth, acidity, inflammation, high infection, nausea, low hemoglobin level, therefore small frequent liquid / liquid + soft with oral nutritional supplements were given to fulfill their requirements. Complex carbohydrates were given to control hyperglycemia. Iron supplements and multi vitamin were also recommended. Potassium rich food with kesol infusion was decided to increase potassium levels and dietary guidelines were developed after deep observation of patient's biochemical, clinical profile, medication and eating pattern.

Keywords
Mucormycosis, Rhizopus oryzae, nutrition, diet, hospitalized patients, diabetes

Introduction
Mucormycosis is a fatal angio-invasive fungal infection that mostly occurs in persons who are already suffering from other health ailments like diabetic ketoacidosis or who have undergone organ transplant or cancer patients who have neutropenia. Medications given for all these health ailments cause a reduction in immunity. Due to this immune compromised state, the severity and mortality is very high despite of giving antifungal therapy or surgical debridement (Ibrahim *et al*. 2012).

Fungal spores spread through air and affect our sinuses and lungs after inhalation. Mucor infection can be classified clinically into rhinocerebral, gastrointestinal, cutaneous or pulmonary on the basis of its manifestation. It's rare forms are endocarditis, renal, peritonitis, osteomyelitis etc. The disease was first described in 1876 by Furbinger. He found hemorrhagic infarct in the presence of fungal spores in lungs of a patient who died due to cancer in Germany [Furbringer , 1876; Hibbett *et al*., 2007]. Etiologic factor for the infection of mucormycosis is *Rhizopus oryzae* (McBride *et al*., 1960) that is a cause of infection in around 70% of mucor cases [Ribes *et al*., 2000; Spellberg *et al.,* 2005; Roden *et al*., 2005]. Patients having high serum iron are more prone to mucormycosis infection.

Symptoms of mucormycosis: These are pain, redness around eyes or nose, fever, headache, cough, shortness of breath, hemetemesis and altered sensorium. One should get himself tested if having symptoms of sinusitis, facial pain, hemoptysis, numbness or swelling, blackish sign over nasal bridge or palate, toothache, blurred vision, chest pain or respiratory problems.

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The greatest risk factors for mucormycosis are uncontrolled diabetes mellitus as well as systemic corticosteroid medications. The most prevalent manifestation was rhino-orbital cerebral type with mortality rate as high as 49%. It was followed by pulmonary and disseminated types of mucormycosis. Very less cases of cerebral involvement were seen. A markedly high number (46%) of recovered patients underwent irreversible morbidity of vision loss. A number of diseases or disease treatments became risk factors for mucormycosis. These included metabolic acidosis, trauma and burns, blood related malignancies and deferoxamine therapy in hemodialysis patients [Spellberg *et al.,* 2005; Sugar, 2005; Ibrahim et al., 2003]. As per study of Singh et al., (2021) majority of patients affected with mucormycosis were males (78.9%), in active (59.4%) as well as in recovered COVID -19 patients (40.6%). Eighty percent of cases showed pre-existing diabetes mellitus with 14.9% patients underwent diabetic ketoacidosis (DKA).

As per Spellberg *et al.,* 2005 and Gleissner, 2004 the mortality rate due to mucormycosis was noted more than 50%, which reached to 100% in patients with neutropenia or blood malignancies inspite of giving intensive therapies of surgical debridement and antifungal treatment. Understanding of pathogenesis of mucormycosis can only facilitate development of preventive and curative strategies. As per Advisory by ICMR
During treatment course of mucormycosis, main targets were –

1. To manage hyperglycemia,
2. Judicious use of antibiotics with aim to discontinue rapidly,
3. Discontinue immune modulatory drugs

In extensive surgical debridement, medical treatment involved –

1. Install peripherally inserted central catheter,
2. Maintain adequate systemic hydration,
3. Infuse normal saline before amphotericin infusion,
4. Antifungal therapy for 4-6 weeks,
5. Use sterile water for humidifiers during oxygen therapy,
6. Use antibiotics and antifungals judiciously
7. Monitor patient clinically and with radio imaging to check response and disease progression.

Although there were medical treatment guidelines but no guidelines were there for nutritional management of patients. With this mindmap, the present study was planned to develop nutritional guidelines for mucormycosis patients.

Research Methodology

Fifty hospitalized mucormycosis patients were taken for study.

Sample selection

All in- patients diagnosed with mucormycosis were taken until required number (50) was not completed.

Inclusion criteria

1. Patient should be mucormycosis positive
2. Patient should be cooperative

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3. Patient should be 18 - 65 years of age
4. Both male and females were taken for the study

Exclusion Criteria

1. Those <18 years and > 65 years of age
2. Those who were not cooperative
3. Those who were not diagnosed with mucormycosis

Data collection

1. Patient's general information was collected using a standard performa that included name, age, sex, IP no., educational status, occupation, religion, marital status etc

2. Patient's medical data was recorded by in patient records, patient and attendant for present complaints, signs & symptoms, medical diagnosis, family history; medications were recorded from the in patient record.

3. Nutritional assessment: Patient's nutritional assessment was done as per subjective global assessment. For this anthropometry, biochemical profile, clinical signs and symptoms and diet recall was recorded. In anthropometric measurements, height was measured in centimeters using heightometer, where patient was in standing position; otherwise length was taken in lying down position using measuring tape. Digital weighing scale was used for taking weight of the patient. Body mass index (BMI) was calculated by the formula [Weight (Kg)/ Height (M^2)].

Biochemical reports were recorded from patient's file as per ordered by treating doctors. Clinical signs & symptoms of blackened nasal bridge/ swollen eyes/ redness in eyes/ blackening of tongue/ loss of muscle mass/ weight loss/ loss of appetite were recorded for each patient.

Dietary history was noted from patient or attendants for their 24 hour dietary recall. It was recorded for three consecutive days including two working days and one holiday (if working). After nutritional assessment of patients, their nutritional diagnosis was derived & requirements were calculated as per Mehta *et al*., (2018); which recommended 25 Kcal / kg BW/day for energy requirements + stress factor of 1.5 was considered. Protein was given 1.2- 1.5 g/ kgBW/ day. Besides this antioxidants tablet and 1 multi vitamin tablet with 1 probiotic supplement was also considered.

After calculating requirements, nutritional intervention was planned as per patient's diagnosis, biochemical reports and patient's eating condition. Of patient was able to eat orally, liquid/ soft/ full diet was considered and in more critical condition, Ryle's tube feed was designed.
Patient's condition was carefully monitored for biochemical changes, clinical signs and symptoms and diet compliance.

Statistical analysis

Mean, Standard deviation and ANOVA was applied to know any significant difference of in the results obtained of 50 patients. For this data obtained has been described in two stages -

1. Data obtained at the time of admission &
2. Data obtained at the time of discharge

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Results and Discussion

Out of 50 patients, 40 patients (80%) were diabetic. 10% patients were on immunosuppressant as these underwent renal transplant. Male and female were 50 – 50 percent, i.e. 25 male & 25 female patients were admitted who were selected for the study.

Results and discussion part is divided into following subheads for convenience of understanding:

1. Anthropometric changes at the time of discharge in comparison to time of admission
2. Biochemical profile at the time of admission and discharge
3. Clinical signs at the time of admission & at the time of discharge
4. Diet and nutrients intake at the time of admission and discharge

1. **Anthropometric changes at the time of discharge in comparison to time of admission**

		At the time of admission	At the time of discharge	P value
Males	Average Height (cm)	165 cm	165 cm	NA
	Average weight (Kg)	65	64	P<0.05 (NS)
	Average BMI of 50 patients	23.89	23.53	P<0.05 (NS)
Females	Average Height (cm)	162	162	P<0.05 (NS)
	Average weight (Kg)	61	60	P<0.05 (NS)
	Average BMI of 50 patients	23.28	22.9	P<0.05 (NS)

* NS – Not significant

Average height of male patients was 165 cm & average height was 65 kg, therefore average BMI was 23.89 kg/ M^2. In females also average BMI was found 23.28 kg/M^2. Change in patient's weight and BMI at the time of discharge was not statistically significant when compared to weight and BMI at the time of admission as inspite of patient's poor condition to take full diet, they were given liquid + soft diet with supplements so that their weight did not degrade.

2. **Biochemical profile at the time of admission and discharge**

	At the time of admission	At the time of discharge	P value
Serum Creatinine (mg)	1.9	1.6	p>0.05 (s)
Sodium (mMol)	134	135	P<0.05 (NS)
Potassium (mMol	3	2.9	P<0.05 (NS)
RBS (mg/dl)	300 – 400	150 – 180	p>0.05 (s)
Haemoglobin mg/dl	7.7	10.1	p>0.05 (s)
WBC count	15 x 10^9/L	Normal 6 x 10^9/L	p>0.05 (s)
Platelets	550000/µL	550000/µL	P<0.05 (NS)

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s-significant, ns-not significant

Patient's serum creatinine levels were on a higher side at the time of admission that declined to 1.6 mg that was statistically significant. For this, patients were given low vegetable protein to decrease branch chain amino acid protein load on kidneys. Sodium levels were found normal. Potassium levels were found below normal range both at the time of admission and discharge even after continuous infusion of IV potassium and in diet also potassium rich foods were provided. Uncontrolled diabetes was observed at the time of admission that was achieved towards normal level at the time of discharge due to hypoglycemic drugs and control of simple carbohydrates in diet. Haemoglobin was observed less at the time of admission that increased to a significant level at the time of discharge due to iron supplements and iron rich foods in diet. WBC count was very high that came to normal range at the time of discharge because of antibiotics and antibacterial agents given. Higher thrombocytes in mucormycosis patients can be attributed due to infection and because of iron supplements given to enhance haemoglobin levels.

3. Clinical signs at the time of admission & at the time of discharge

	At the time of admissior	At the time of discharge	P value
Blackening over nasal bridge/ eyes	Yes (In 50% patients)	No	p>0.05 (s)
Nasal bleed	Yes (in 50% patients)	No	p>0.05 (s)
Excess sweating	Yes (in 80% patients)	No	p>0.05 (s)
Joint pain	Yes (in 20% patients)	No	p>0.05 (s)
Blur vision	Yes (in 60% patients)	No	p>0.05 (s)
Redness of eyes	Yes (in 90% patients)	No	p>0.05 (s)
Blockage of nasal cavity	Yes (in 95% patients)	No	p>0.05 (s)
Hyperglycemia	Yes (in 95% patients)	No	p>0.05 (s)
Respiratory symptoms	Yes in (100% patients)	No	p>0.05 (s)
Acidity	Yes (in 100% patients)	No	p>0.05 (s)
Fever	Yes (in 80% patients)	No	p>0.05 (s)
Vomiting	Yes (in 75% patients)	No	p>0.05 (s)
Abdomen pain	Yes (in 65% patients)	No	p>0.05 (s)
Loss of appetite	Yes (in 90% patients)	No	p>0.05 (s)
Loss of muscle mass	Yes (in 20% patients)	No	p>0.05 (s)

As per above symptoms, patients were given different types of medication.

Medication

Patients were on antibiotic, NSAID, antipyretic, anti fungal, anti bacterial, antacid, anti emetic, anti-allergic drugs. Drugs were given to treat Meniere's disease also (symptoms include loss of hearing, ringing in the ears, dizziness due to fluid in the ears), nasowash, eye drop for redness of eyes, eye lubricating drops, medicine to decrease lung fibrosis, Magnesium, potassium, iron, multivitamin supplements were also prescribed to them.

Blackening of nasal bridge, blurred vision, redness of eyes, and blockage of nasal cavity may

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be attributed to fungal infection in sinus area. Joint pain may be due to fever. Loss of appetite, nausea, vomiting, acidity may be due to fever, fungal infection, medications like antibiotics or antifungals, NSAIDs and reduced food intake also.

4. Diet and nutrient intake at the time of admission and discharge

	At the time of admission	**At the time of discharge**	**P value**
Type of diet on an average	Liquid diabetic diet/ RT feed 100 ml/2 hrly	Full high protein diabeti diet + supplement	p>0.05 (s)
Average calorie intake	500- 600 Kcal	1950 Kcal	p>0.05 (s)
Average protein intake	20 -25 g	80 - 90 g protein	p>0.05 (s)
Consistency of food	Liquid	Solid	p>0.05 (s)

Compliance of prescribed hospital diet: Above 90% patients showed diet compliance as diet was planned as per their condition. Initially liquid diet/ RT feeds were started as patient's condition was very miserable, but as they tolerated liquid diet, supplements were added to it and soon they shifted to soft diet to full diet. Nutrient intake wise initially they were given around 500 Kcal and 30 g protein. Then it was increased to 1000 Kcal, 50 g protein by adding supplements. As soon as patient's condition improved, their food intake also increased and calorie and protein intake enhanced to average 1950 Kcal and 80- 90 g protein.

Days of hospital stay: Average hospital stay for 80% was around 7 days although 20% severe cases took long (20- 30 days) to recover as they underwent many surgical debridements.

Conclusion

The present study can be concluded as mucormycosis equally affected both male and female. Majority of patients had similar signs & symptoms like redness & swelling of eyes, blockage in nasal cavity, fever, hyperglycemia, higher WBCs & platelets, low haemoglobin levels, acidity, loss of appetite etc for which patients were on antibiotics, antifungal drugs, antacids, NSAIDs etc. These medications also decreased their diet intake because of gastric upsets, nausea, dryness in mouth. Patient's whose diet intake (in any form, i.e. liquid/ soft/ full/ Rt feed) was upto their requirements, recovered well in less time as compared to patients who were notable to have diet as per their requirements. Therefore some guidelines can be formulated as below:

1. Energy: 25 Kcal/ kg BW/ day * stress factor
2. Protein – 1.2-1.3 g/ kgBW/ day, it can be given 1.5 g/kgBW/ per day in case of surgical debridement.
3. Multivitamin
4. Iron supplement
5. Complex carbohydrates in form of small frequent meals to control hyperglycemia and simple sugars should be restricted
6. At least 3-4 Lt. of fluid in form of water, lemon water, coconut water, dal soup, vegetable soup, buttermilk etc.
7. Don't take much time to add supplements if patient is not able to meet his/ her nutritional requirements through diet alone

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8. Potassium rich foods like lemon water, coconut water, dal soup, kiwi, amla, bell pepper, citrus fruits, banana etc. should be added to diet prescription.

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