

Dr. Pankaj Kumar Pandey, IAS
Secretary



Government of Uttarakhand

Department of Medical, Health and
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Room No. 1, Vishwakarma Bhawan,
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Dehradun, Uttarakhand

Letter No. 402/PS-sec/2021
Dated: 17 May 2021

Sub: Minutes/Recommendations of the Expert Committee reg. Mucormycosis prevention/ management in COVID 19 patients.

Madam/Sir,

As you are aware that an expert committee was constituted by the State Government vide Letters No. 426/SEC-MH/2020 dated 26.05.2020 and 430/SEC-MII/2020 dated 28.05.2020 regarding technical inputs and decision support for COVID 19 response.

In this regard, the minutes of the latest meeting of the expert committee dated 13th may 2021 and the recommendations contained therein aimed at effective prevention and management of Mucormycosis in COVID 19 patients are being attached for necessary actions in this regard.

Yours Sincerely,

Encl: As above


(Dr. Pankaj Kumar Pandey)

1. District Magistrates, All districts of Uttarakhand
2. Chief Medical Officers, All districts of Uttarakhand

Cc:

1. Secretary (Medical, Health and Family Welfare, Govt. Of Uttarakhand)
2. Director General, Medical Education, Uttarakhand
3. Mission Director, National Health Mission, Uttarakhand
4. Director General, Medical Health and F.W., Uttarakhand
5. Chief Operations Officer, COVID 19 control room, Uttarakhand


(Dr. Pankaj Kumar Pandey)

Recommendations of Committee constituted vide Letter No. 426/SEC-MH/2020 dated 26.5.2020 and Letter No. 430/SEC-MH/2020 dated 28.05.2020 regarding technical inputs and decision support

(Date 13th May 2021)

A committee has been constituted vide Letter No. 426/SEC-MH/2020 dated 26.05.2020 and Letter No. 430/SEC-MH/2020 dated 28.05.2020 regarding technical inputs and decision support for informed policy making for Covid-19 in Uttarakhand State. A meeting was held on 13.05.2021 at 11 a.m. in the presence of the Prof. (Dr.) Hem Chandra, Vice Chancellor, Hemwati Nandan Bahuguna Uttarakhand Medical Education University, and Prof. (Dr.) Ashutosh Sayana, Principal, Govt. Doon Medical College & Coordinator of committee through video conferencing with following expert representatives from different hospital/organization of State of Uttarakhand.

1. Prof. (Dr.) M.K. Pant, Deputy Director, Medical Education, Uttarakhand.
2. Prof. (Dr.) Anurag Agarwal, Nodal officer Covid-19, GDMC, Dehradun.
3. Prof. (Dr) NarayanJeet Singh, Prof & Head, Medicine Department GDMC, Dehradun.
4. Dr. Girish Sindhvani, Prof. & Head Pulmonary Medicine, AIIMS, Rishikesh.
5. Dr. Sadhna Awasthi, Prof. & Head Deptt. of Community Medicine, GMC, Haldwani.
6. Dr. Nidhi Uniyal, Associate Professor, Medicine Department, GDMC, Dehradun.
7. Dr. Atul Kumar Singh, Associate Professor, GDMC, Dehradun.
8. Dr. Madhur Uniyal, Nodal Officer COVID-19, AIIMS, Rishikesh.
9. Dr. Paramjeet Singh, Associate Prof. Deptt. of Medicine, GMC, Haldwani.
10. Dr. Sanjoy Das, Representative from HIMS, Jollygrant, Dehradun.
11. Dr. Pradeep Chandra Sharma, Assistant Nodal Officer, COVID-19, GDMC, Dehradun.
12. Dr. Rahul Prasad, Representative from Max Hospital, Dehradun.
13. Dr. Ajay Kumar, Assistant Professor, Deptt. of Dermatology, GMC, Haldwani.
14. Dr. Sadiq Umar, Consultant Dermatology, GDMC, Dehradun.

The matter of exponential growth of positive cases and rapidly increasing mortality of Covid patients in the state of Uttarakhand is a serious concern. In addition, it has come to notice of the committee cases of **Mucormycosis (Black Fungus) are increasing in**

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different parts of our country. To the best of our knowledge, no case has been reported in the state of Uttarakhand till date. However this is the right time to discuss the subject and make recommendation before any case detected in Uttarakhand. Therefore, in view of above, the State Advisory Committee has discussed and deliberated followings:-

1. INTRODUCTION:

- A) - Mucormycosis is a group of fungal infection caused by group of genera of class ZYGOMYCETES. It is also known as phycomycosis in lay man's language. Most common species causing disease is RHIZOPUS ARRHIZUS. These fungi are commonly found in soil and in environment and are responsible for initiating and decaying most organic material in environment.
- B) - In general infections with mucormycosis are rare in living beings. An infection develops because of some unusual circumstance that places the fungi in contact with the compromised or injured animal or human tissue. But once established it rapidly multiply in blood vessel walls where it effectively reduces the blood supply to the tissues, resulting in organic decaying and widespread tissue destruction. This fulminant spread if not stopped proves fatal and death is an outcome.
- The Rhino - Cerebral Mucormycosis and Pulmonary Mucormycosis are the commonest one in admitted patient.
- C) - The Risk Factors for Mucormycosis in reference to covid -19 are as follows:
1. Diabetes Mellitus- most importantly high and uncontrolled diabetes (Diabetic ketoacidosis).
 2. Patients receiving steroids (especially high doses and for longer duration) as a part of Covid-19 treatment are at risk.
 3. Patients who have received immunomodulatory drugs e.g. Tocilizumab.
 4. Previously immunocompromised patients on cancer treatment or with autoimmune conditions, on steroids for other medical condition, organ transplant, impaired renal functions or Renal failure.
 5. Patients on long term oxygen therapy and on ventilators
 6. Patients with neutropenia
 7. Haemochromatosis or iron overload
 8. Voriconazole therapy (causes breakthrough mucormycosis.)

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Note: High degree of suspicion should be maintained in all covid-19 patients as some patients are diagnosed with diabetes for first time during covid-19 infection and number of patients are treated with steroids.

Route of entry

- Sinuses or lungs of such individuals get affected after fungal spores are inhaled from the air.
- Trauma -vehicular accidents, natural disaster, warfare etc.

WARNING SIGN AND SYMPTOMS:

- **Facial findings :**
 - Facial pain
 - Unilateral facial swelling
 - Discoloration of skin (necrosis / infection over face)
- **Nasal finding :**
 - Foul smelling / Blood-stained nasal discharge
 - Nasal congestion
 - Red / Black necrotic area in nasal cavity
 - Nasal crusting
 - Black lesions on bridge of nose or upper inside of mouth that rapidly becomes severe.
 - Pain and redness around nose
 - Discoloration of nose.
- **Intraoral findings :**
 - Foul smell from mouth
 - Intraoral pus discharge
 - Ulceration & Blackening of mucosa
 - Palatal discoloration, loosening tooth
- **Orbital findings :**
 - Vision loss
 - Eye swelling, eyelid swelling, vision loss, diplopia, restricted eye movement, retro-orbital pain, ptosis.
 - Pain and redness around eyes
- **CNS findings:**
 - Headache, unilateral paraesthesias being earliest symptoms.
 - Cranial nerve involvement.
 - Rapidly progressive neurological deficit.
 - Altered mental status

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- **Pulmonary findings :**

- Fever may be absent in upto half of cases
- Coughing
- Shortness of breath

- **Gastrointestinal findings :**

Abdominal pain, Nausea, Vomiting and gastrointestinal bleeding.

- **Cutaneous manifestation:** Skin discoloration at trauma site, painful swelling, erythema, black discoloration.

IMPORTANT POINTS

- Rapid progression can occur, so high degree of suspicions to be kept.
- Early diagnosis is important for treatment and better outcomes
- Rational use of steroids
- Proper glycaemia control

RECOMMENDATIONS:

The committee made following recommendations for prevention and treatment -

PREVENTION-

As Mucormycosis associated with very high mortality (70 - 80%)_and cases may be associated with injudicious use of steroids without any supervision of Physician. Therefore public should be made aware about this disease, its clinical features, progression and possible outcome. Use of steroids must be after Physician consultation. Public should also follow the guidelines related to Mucormycosis (**Black Fungus**). This will help in early identification, diagnosis and timely shifting of patients to Dedicated Covid Hospitals. By adopting these policies, we can prevent/reduce the occurrence of Mucormycosis (**Black Fungus**) in community.

- **A Clinician / health care provider should look as a routine for following findings in regards to fungal infection:**

Any evidence of redness / swelling / blackening / pustule / ulcer in -

- 1- Oral cavity
- 2- Nasal cavity
- 3- Over facial region
- 4- Other features such as headache, altered mental status, vision loss etc along with other features suggestive of Covid - 19 infection.

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PREVENTION AT PUBLIC LEVEL -

- Always use masks specially if you are visiting dusty construction sites
- Wear shoes, long trousers, long sleeve shirts and gloves while handling soil (gardening), moss or manure
- Maintain personal hygiene including thorough scrub bath
- Proper control of blood sugars
- Regular saline gargles and douching with betadine solution
- Avoid water damaged areas, foods that have spoiled and construction or excavation sites
- Clean your refrigerator and pantry regularly and dispose of spoiling foods without delay.

- Avoid taking unnecessary risk if one is immunocompromised, have an underlying disease or have had a surgery or transplant recently.

- Frequent post-recovery evaluation of high risks individuals.

PREVENTION AT HEALTH CARE /HOSPITAL FACILITY -

- Do not miss warning symptoms and signs – to be inspected and examined regularly.
- Control hyperglycemia.
- Monitor blood glucose level post COVID-19 discharge and also in diabetics
- Use steroid judiciously – correct timing, correct dose and duration
- Use clean, sterile water for humidifiers during oxygen therapy. Frequent changes of humidifier solution to be done
- Tubing of oxygen to be changed frequently and not to be used frequently.
- Use antibiotics/antifungals judiciously
- Do not consider all the cases with blocked nose as cases of bacterial sinusitis, particularly in the context of immunosuppression and/or COVID-19 patients on immunomodulators
- Do not hesitate to seek aggressive investigations, as appropriate (KOH staining & microscopy, culture, MALDITOF), for detecting fungal aetiology
- Do not lose crucial time to initiate treatment for Mucormycosis.
- Avoid using Voriconazole as antifungal prophylaxis .
- Maintain safe distance from pet animals.

DIAGNOSIS:

1. Requires high degree of suspicion in vulnerable population (with warning symptoms and signs) in home care treatment/ Hospitalized patients.
2. Nasal endoscopic examination for early diagnosis and biopsy
3. Positive cultures from sterile site like needle aspirate, tissue biopsy specimen, pleural fluid aspirate- for confirmatory diagnosis.
4. Probable diagnosis-by culture from non-sterile site like Broncho alveolar lavage, sputum etc
5. Biopsy with histopathology remains the most sensitive and specific diagnostic tool.

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6. CT Scan Head or MRI Brain for corroborative finding and extension of disease

Note- Initiate empirical antifungal therapy once mucormycosis is suspected.

Treatment:

- Control Diabetes and Diabetic Ketoacidosis
- Doses and duration of steroid given to be monitored in view of covid-19 treatment and to be reduce accordingly
- Conservative approach for RBC transfusion- avoid iron overload
- Discontinue immune-modulating drugs
- Extensive Surgical Debridement - to remove all necrotic materials
- Install peripherally inserted central catheter (PICC line)
- Maintain adequate systemic hydration
- Infuse Normal saline IV before Amphotericin B infusion
- **Antifungal Therapy: for at least 4-6 weeks**

➤ **1ST LINE ANTIFUNGAL THERAPY : Inj Liposomal Amphotericin B (LSmB):**

Dosages : 5 mg/kg per day and in CNS mucormycosis dose is 7.5-10mg/kgper day. Less nephrotoxic, better CNS penetration than AmB or ABLC.-to be continued till the patient starts showing improvement and start taking orally-switch to step down treatment.

➤ **Step-down treatment : Isavuconazole & Posaconazole are broad spectrum azoles available in oral formulations**

- **Isavuconazole oral equivalent to 186 mg of Isavuconazonium sulphate: loading dose - 2 capsules q8h for 6 doses (48 hrs.) followed by maintenance dose of 2 capsules once daily via PO route**

OR

- **Posaconazole - 200 mg four time per day after food**

OR

Alternatively, Posaconazole delayed release tablets(300 mg every 12 hrs. on first day followed by 300 mg once daily) taken with food

➤ **SALVAGE THERAPY: To Be used in patient in whom Amphotericin -B is contraindicated or who cannot tolerate Amphotericin -B**

- **Isavuconazole: Loading dose: 1 vial of 200 mg of Isavuconazole (372 mg of Isavuconazonium sulphate), q8h x 6 doses (48 hrs.) followed by maintenance dose of 1 vial once daily per IV route- drug of choice with impaired renal function**

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OR

- Posaconazole IV Loading 1st day- 300 mg 12 hourly duration followed by 300 mg 24 hourly IV Posaconazole to be avoided inpatient with moderate to severe renal impairment and creatinine clearance less than 50 ml / minute.
- Patient can be switched to oral therapy once he shows sign of improvement and can take orally.

Duration of the therapy:

- Antifungal, 4-6 weeks or more depending on complete cure
- Overlap of injectable & oral antifungals for 3-4 days followed by oral antifungals.
- Oral anti fungal to be continued one week after biopsy is negative.
- Regular follow up initially monthly for three months then SOS

NOTE: Situation where patient is improved / treated for COVID-19 infection, but IV antifungal therapy for Mucormycosis continued, patient will remain admitted in hospital.


Patient can only be discharged once oral antifungals are started.

✳ Currently, there are no recommendations to use prophylactic antifungals therapy for preventing Mucormycosis.

- Monitor patients clinically and with radio-imaging for response and to detect disease progression
- Team Approach Works Best-Microbiologist, Internal Medicine Specialist, Intensivist, Neurologist, ENT Specialist, Ophthalmologist, Dentist Surgeon (maxillofacial/plastic), Biochemist.



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