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An Integrative Approach for management of Mucormycosis along with Ayurveda.

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Across the globe and mainly in India, several cases of *mucormycosis* in people with COVID-19 have been increasingly reported. The rise in the number of cases, the emergence of new risk factors and causative agents, mortality associated with mucormycosis in India is considerably high and the challenges in managing the disease.

Mucormycosis (*Zygomycosis*, *phycomycosis*) is an acute opportunistic infection caused by a saprophytic fungus that belongs to the class of Phycmycetes. *Rhizopus arrhizus* is the most common etiological agent of mucormycosis in India, and globally but other variants are also found as *Rhizopus microsporus*, *Rhizopus homothallicus*, and *Apophysomyces*.

The primary reason found for mucormycosis in people with COVID-19 is an ideal environment of low oxygen (hypoxia), high glucose (diabetes, new-onset hyperglycemia, steroid-induced hyperglycemia), acidic medium (metabolic acidosis, diabetic ketoacidosis, high iron levels (increased ferritins) and decreased phagocytic activity of white blood cells (WBC) due to immunosuppression. Immunosuppression is due to SARS-CoV-2 mediated, or steroid-mediated or other comorbidities present in the body. Several other risk factors including prolonged hospitalization with or without mechanical ventilators is another cause for immunosuppression.¹

Symptoms of mucormycosis include pain and redness around the eyes and nose, fever, headache, cough, vomit with presence of blood in it, black and bloody nasal discharge, pain over one side of the face and in the sinuses, blackish discoloration over the nose, toothache,

and painful and blurred vision, double vision, protrusion of the eyeball. The majority of mucormycosis infections have been seen in covid patients with diabetes or those with underlying and undetected high blood sugar.²

Although mucormycosis is a rare disease and it is associated with high morbidity and mortality ;it is being detected relatively frequently among Covid-19 patients after the second wave of the covid pandemic. It has become rampant throughout India and killed more than half of those infected. Patients most vulnerable to mucormycosis are those who have been treated with steroids and other drugs for Covid 19 to reduce inflammation. Diabetes is the major risk factor for fungal infection, along with other types of immunosuppressive conditions and also overuse of steroids.

Uncontrolled diabetes mellitus can alter the normal immunologic response of patients to infections. Such patients have decreased granulocyte phagocytic ability with altered polymorphonuclear leukocyte response. Reports have suggested that the ability of serum of immunocompromised patients to inhibit *Rhizopus* invitro is reduced, which makes them suitable hosts to opportunistic fungal infections.^{3,4}

The treatment of mucormycosis involves the early initiation of therapy, the surgical debridement of infected tissue, antifungal therapy, and managing the underlying disease. Amphotericin B (AmB) is the first-line drug of choice; subsequently, posaconazole and isavuconazole are prescribed. The major drawbacks in managing mucormycosis in India are a gap in treatment protocol and the financial constraints of patients that they cannot afford liposomal AmB. ⁵ In the absence of surgical removal of

the infected focus, antifungal therapy alone is rarely curative. Even when surgical debridement is combined with high-dose antifungal therapy, the mortality associated with mucormycosis is >50%. The unacceptably high mortality rate, limited options for therapy, and the extreme morbidity of highly disfiguring surgical therapy provide a clear mandate to understand the molecular mechanisms that govern pathogenesis with the hopes of developing alternative strategies to treat and prevent mucormycosis.⁶

In this context of prevention and effective management of mucormycosis; Ayurveda has got significant methods. The recommended Ayurvedic management protocol consists of personal hygiene, preventive medications, rasayana drugs, and antifungal medications. The protocol can be effectively managed with an integrative approach or standalone as per the clinical analysis of severity.

Personal hygiene

Oral hygiene: This include procedures like *Danta-dhavana* (brushing the tooth), *Pratisarana* (Massaging the teeth and gums), *Jivha nirlekhana* (tongue cleaning), *Gandoosha* and *Kavala* (gargling), etc can act as a special care on common route of spread of mucormycosis ; nose, oral cavity, and eyes. Neem (margosa or Azadirachta indica), fresh stems of *Yastimadhu* (*Glycyrrhiza glabra*), Arjuna (*Terminalia arjuna*), *Vata* (*Ficus bengalensis*), *Vijaysara* (*Pterocarpus marsupium*), *Arka* (*Calotropis gigantea*), *Khadira* (*Acacia catechu*), etc can be used for *Danta-dhavana* (brushing the tooth). *Pratisarana* (Massaging the teeth and gums) is done with paste or powder of herbs or by honey/oil along with herbal powder. The commonly used drugs for *Pratisarana* are *Triphala*, *Trikatu* and *Trijata* mixed with honey. Recent researches have proved gum massage is good for dental and oral hygiene. These medicinal plants have a role in the maintenance of oral health and are proven as a potent antibacterial, antifungal, antiviral, and antioxidant in their properties.

Kavala and Gandoosha (Oil pulling):

Kavala and *Gandoosha* (Oil pulling) consists of medicated oil and fluid wic are proven to protect the oral cavity from infection and inflammation by their antioxidant properties. Research has shown that oral

mucosa does not act as a semi-permeable membrane to allow toxins to pass through.⁷

Pratimarsha Nasya

Pratimarsha Nasya is indicated as a daily regimen to maintain the health of nasal passage Commonly oils are advised for *Nasya* which have antimicrobial activity and prevent the entry of infections in the respiratory tract and have a potent role. *Anjana* is indicated as a daily regimen to maintain the health of the eyes by applying medicated collyrium to the inner part of the eyelid.

Dhoopana Karma

Dhoopana Karma- The drugs advised for the dhoopana karma possess antimicrobial and antifungal activity. Commonly used as drugs are *Guggulu*, *Neem*, *Haridra*, *Kustha*, *Jatamansi*, *Sarjarasa*, *Karanja*, *Vacha*, etc . *Aparajita Dhuma Churna* showed that flora before fumigation were rich in coliforms and many saprophytic fungi and after fumigation, the data showed a considerable reduction in microbes. It has significantly higher inhabitation of various *Aspergillus* species ;overall activity was more pronounced against bacteria as compared to fungi.⁸

Rasayana drugs

Administration of Rasayana (Immunomodulators) drugs like *Amalaki*, *Guduchi*, *Vasa*, *Pippali*, *Ashwagandha*, *Haridra*, etc. is beneficial to prevent the associated complications.

Common preparations which act as respiratory immunomodulators are *Chyavanprasha avleha* *Agastya Haritaki Rasayana*. *Naimittika Rasayana* like *Shilajatu* correct the hyperglycaemic episodes and produce their effect by enhancing the *Agni and Ojas* status in the patients, thereby improving metabolic and immune status. If primarily disease is present in the Nasal route then the Panchakarma procedures *Nasya and Dhoom* have beneficial effects. In the case of eye involvement, *Ashchotan /eye* drops can be advised.

Diabetic Patient Management

If the patient is diabetic then fair control of Diabetes is one of the important concern and can be effectively managed by various herbs and herbo- mineral preparations as *Trivanga Bhasma*, *Shiva gutika*, *Shilajeet*, *Triphala Churna*, *Nimbapatra*, *Haritaki*(*Terminalia chebula*), *kahadir*(*Acacia arabica*), *Mangifera indica*,

Eugenia jambolana, *Allium cepa*, *Allium sativum*, *Aloe vera*, *Tinospora cordifolia*, mentioned in Ayurvedic texts.

Antifungal Management

Krimihara Chikitsa is useful to prevent and manage microbes and fungi in Ayurveda. *Rakta shodhaka*, *Raktaprasadaka* drugs, and drugs for *Pranvaha srotas /Urdhajatrurujata roga* may have a significant role in Mucormycosis. The drugs like *Panchanimba Churna*, *Amrita Bhallataka / Rasamanikya/ Talasindhura / Talakeshwara Rasa /Mallasindhura / Gandhaka Rasayana*, *Mahalaxmi Vilasa Rasa* can be recommended orally according to the patients *Dosha*, *Bala*, and other parameters. *Gandhaka Rasayana* solution in higher concentration showed similar antifungal activity compared to Fluconazole against *Candida albicans* and *Cryptococcus neoformans*. It was more significant against *Trycophytum rubrum* and *Aspergillus Niger* than Fluconazole.⁹ Medicinal plants having antifungal properties like *Allium sativum*, *Zingiber officinalis*, *Glycyrrhiza Glabra*, *Curcuma longa*, *Mentha piperita*, *Azadirachta indica* *Withania somnifera*, *Acorus calamus*, *Piper betel*, *Adhatoda vasica*, *Solanum xanthocarpum*, *Aloe Vera*, and *Ocimum sanctum* have antifungal activity.¹⁰ Methanolic extracts of *Solanum xanthocarpum* and *Datura metel* inhibited the growth of *Aspergillus fumigatus*, *A. flavus*, and *A. niger*. *Datura metel* showed significant activity against *Aspergillus*. Similarly, *Solanum xanthocarpum* exhibited similar activity.¹¹

Conclusion:

Personal hygiene, preventive medications, *Rasayana* drugs, and *Krimighna* medications are preventive and curative aspects from Ayurveda. A rigid protocol along with Ayurveda is a special integrative approach for the effective management of Mucormycosis. Further observational evidence based studies and clinical trials are recommended to evaluate the effectiveness of Ayurvedic medicine and therapy against Mucormycosis.

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