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A POPULATION BASED PREVENTIVE APPROACH ON MUCORMYCOSIS IN AYURVEDA - A REVIEW

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ABSTRACT

Mucormycosis a severe often fatal invasive fungal infection has entered public consciousness in response to case outbreaks in India. Thousands of Mucormycosis cases were reported in the wake of India's 2nd wave of COVID 19 cases, bringing global attention to this deadly yet neglected disease since past. Mucormycosis which was previously known as Zygomycosis and now commonly known as black fungus is a serious fungal infection that comes under fulminant fungal sinusitis caused by a group of mold called mucormycetes. The conventional line of treatment usually adopted is towards the higher end and requires a long course of treatment. Thus implementation of this treatment modality in a mass population may turn out to be difficult. In this article, an Ayurvedic preventive approach for Mucormycosis has been discussed based on the evidence based data collected from experiential data, experimental and clinical research findings.

KEYWORDS: Mucormycosis, COVID 19, *Krimighna dravyas,* Ayurvedic medicines.

INTRODUCTION

Across the globe and especially in India, several cases of *mucormycosis* associated with COVID-19 have been increasingly reported. The increase in the number of cases, the emergence of various risk factors and causative agents and the mortality associated with the *mucormycosis* in India was considerably high. In this article, various traditional therapeutics for mucormycosis from a holistic standpoint as well as the potential Ayurveda Profiling has been discussed, as it offers to be a cost effective one with more likely available.

METHODOLOGY

As a part of the study, various systematic reviews and Meta – analyses regarding mucormycosis for the last 10 years were conducted and different word combinations were tried out for searching. Even though COVID-19 had been active since 2019, mucormycosis was active before it. The terms such as mucormycosis covid Ayurveda (n=3), mucormycosis covid India (n=343), mucormycosis covid (n=477), covid associated mucormycosis (n=268), opportunistic infection covid-19 (n=382), Mucormycosis covid 19 (n=468), Mucormycosis covid 19 India (n=334), systematic review mucormycosis covid 19 (n=20) in PubMed, out of which only (n=144) were selected. Mucormycosis covid 19 India n=2130, systematic review mucormycosis in covid 19(n=21) in Google scholar, out of which (n=162) were useful, and different comprehensive resources (n=19), 325 potential and additional titles were identified and 205 articles from all sources were scrutinized. Out of these (n=120) were removed for duplicates or not appropriate for inclusion, only full text studies assessed for eligibility and quality (n=69), those studies concerning about Indian Sociology were enclosed within the study.

The studies verifying association of COVID -19 along with the comorbidities and immune compromised patients as well as the studies demonstrating mucormycosis with the aid of biopsy, imaging or histology were also included in the evaluation of the study. The information regarding the disease is gathered based on demographics, mortality, risk factors, causes, kinds, predisposing factors as well as clinical manifestations.

Causative Agent

Mucormycosis (*Zygomycosis, Phycomycosis*) is an acute opportunistic infection caused by a saprophytic fungus belonging to the class of Phycomycetes. While considering the etiological agent of mucormycosis, *Rhizopus arrhizus* is the most common agent in India, and globally variants like *Rhizopus microspores*, *Rhizopus homothallicus* and *Apophysomyces* are found. Mucormycetes are thermo tolerant molds found in the environment. Certain environmental sampling studies have indicated that mucormycetes are commonly found in the soil rather than the air. Transmission mainly occurs through inhalation, inoculation or ingestion of spores.

Etiology

The primary reason for the occurrence of mucormycosis in COVID 19 affected, is an ideal environment of low oxygen (hypoxia), high glucose (diabetes, new onset hyper glycaemia,

steroid induced hyper glycaemia), acidic medium (metabolic acidosis, diabetic ketoacidosis), high iron levels (increased ferritins) and decreased phagocytosis of white blood cells due to immunosuppression. Here the major reason for immunosuppression is the SARS- CoV-2 mediated, steroid mediated or other comorbidities. Other risk factors like prolonged hospitalization with or without mechanical ventilators adds up into as yet another triggering factor.[1]

Pathophysiology

Rapid growth rates occurs in the setting of neutropenia and diabetic ketoacidosis. The acidic pH increases iron content and leads to hyperglycemia which promotes the growth of the organism. Angio invasion is also common, which results in thrombus formation and tissue necrosis. Dead tissue accelerates the growth.[2] GRP78- cell receptors bind to mucorale leading to tissue penetration. Diabetic ketoacidosis that leads to dissociation of iron enhances fungal growth and virulence. Diabetic ketoacidosis – β hydroxyl butyrate increases fungal and host receptors leading to fungal adherence and tissue penetration that finally results on mucormycosis.[3]

High Risk Population

- COVID recovered
- COVID recovering
- COVID in diabetic patient
- Patients undergoing dialysis
- Patients undergoing chemotherapy
- Patients who undergone organ transplantation and taking immunosuppressive drugs

Clinical Features

Mucormycosis can be divided into at least 6 clinical syndromes.[4]

Rhino – orbito – cerebral disease: This is the most common manifestation observed. Most of the cases seen are in the patients with diabetes, especially with glucocorticoid induced diabetes. The major symptoms are pain and redness around the eyes and nose, 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, painful and blurred vision. If left untreated, infection usually spreads from ethmoid sinus to orbit, resulting in the compromise of extra ocular muscle function and proptosis, typically with the

chemosis. From the orbit, infection spreads to the frontal lobe via hematogenous or contiguous dissemination and to the cavernous sinuses via venous drainage.

Pulmonary disease: It is the 2nd most common disease manifestation, where the symptoms include fever, dyspnea, cough and chest pain. Angio invasion results in necrosis, cavitation and hemoptysis. Lobar consolidation, isolated mass, nodules, cavities or wedge shaped infarcts may be seen on the chest radiography.

Cutaneous disease: It usually results from the external implantation of the fungus or from hematogenous dissemination. It can be highly invasive by penetrating muscle, fascia and even bone. The symptoms associated with this condition are blisters, ulcers, pain, warmth, inflammation around the wound.

Gastrointestinal disease: It has been reported as a nosocomial infection following the administration of medications mixed with contaminated wooden sticks. Nonspecific abdominal pain and abdominal distention associated with nausea and vomiting are the most common symptoms.

Disseminated and Miscellaneous forms of Disease: It may emerge from the primary site of infection, where the most common site of dissemination is the brain. Miscellaneous forms may affect any body site, including bones, mediastinum, trachea, kidney and peritoneum.

Diagnosis

Radiology: Endobronchial lesions in diabetes infiltrate wedge shaped consolidation, multiple nodules (≥10), cavitation, mycetoma, lobar collapse and rarely pleural effusion. Halo sign, air crescent sign and Reverse halo sign on HRCT.

Sample Collection: Tissue biopsy and deep nasopharyngeal swab.

Biopsy with histopathological changes: It shows characteristic wide, thick walled, ribbon like septate hyphal elements that branch at right angles.

Treatment

When it comes to the management, Mucormycosis requires three steps:

1. Early initiation of therapy
2. Rapid reversal of underlying predisposing risk factors
3. Surgical debridement

Prevention

Good hygiene, strict sugar control, proper ward protocols and RBS charting.

DISCUSSION

Ayurvedic Treatment Approach

Preventive Guidelines

1. Maintenance of Personal hygiene
2. Environmental hygiene
3. *Pathya Ahara*
4. Usage of preventive medications
5. *Eka moolika prayoga* and other *aushadhis* with *krimihara* properties
6. *Rasayana prayoga* (Respiratory immune modulators)
7. *Yoga* for *Manasika swasthya*

Maintenance of personal hygiene: COVID 19 may be associated with a wide range of bacterial and fungal infections, where one of the most common is Mucormycosis infection, a life threatening invasive fungal infection, with nose, oral cavity and eyes are the common route of spread. Thus maintenance of nasal and oral hygiene is a must as a preventive measure.

- Oral hygiene: *Jihva nirlekhana* (tongue scraping) has a domineering role in eliminating anaerobic bacteria and prevents the microbial growth within the cavity. Application of *Nimba patra* is proven as a potent Antibacterial, Anti-fungal, Anti-viral and Anti-oxidant in property.[5] *Kavala* and *Gandoosha consist* of medicated oil and fluid which are proven to protect the oral cavity from infection and inflammation by their antioxidant properties. Usage of *Tulsi patra, haridra, lavanga* etc. is also preferred for the maintenance of oral hygiene.
- Nasal Hygiene: *Pratimarsha Nasya* is another preventive measure which aids in the maintenance of nasal hygiene. Commonly *Pratimarsha nasya* is carried out with *Anu Taila*, where instillation of oil in the nasal route kills the microorganisms and prevents the entry of spores into the respiratory tract.[6]
- Opthalmic Hygiene: *Anjana* procedure is one of the major preventive measures carried out for the maintenance of ophthalmic hygiene. Daily use of *Srotoanjana* and *Rasanjana* to the inner canthus with the help of *shalaka* or fingertip.[7]

Maintenance of Environmental Hygiene: Airborne diseases may spread while coughing, sneezing etc. which generates droplets and droplet nuclei in the air. Under the concept of *Vayu Shodhana, Ayurveda* have explained *Dhupana Karma* (medicated fumigation), where

Krimihara and *Kushtahara dravyas* like *Guggulu, Vacha, Nimba, Haridra, Kushta, Jatamamsi, Sarjarasa* etc. are used. *Vidanga* and *Khadira* which is advocated for *Dhupana* in skin manifestations can be used.[8] *Aparajitha dhuma churna* which is explained in the context of *jwara* can also be used for *Dhupana* procedure. A study related to Dhupana procedure was conducted where the microbial flora was examined before and after fumigation. The study stated that the microbial flora before fumigation was rich in coliforms and saprophytic fungi, whereas after fumigation there was considerable reduction in the microbial growth.[9]

Principles of Treatment

- Maintenance of Agni with the aid of *Laghu ahara* and *Agni dipaka aushadhis* plays an important role in the prevention of post – COVID complications like mucormycosis.
- Application of *Krimihara chikitsa* is useful for the prevention of spread of the disease. When we analyze the literature, the concept of *Raktaja krimi* can be compared with the pathogenesis of mucormycosis.
- *Shirovirechana* with *Vidanga taila / Shigru taila* and the administration of *Vairechanika dhuma* is highly effective.[10]
- In the case of ophthalmic manifestations, eye drops prepared from *Tankana, Sphatika, Yashada, Panchavalkala* and *Shirisha* can be used effectively.
- *Kapha pitta nashaka* and *Vata avirodhi chikitsa* is the main line of management in Mucormycosis.

Pathya Ahara Vihara

- Followance of 10-30 ml of *Gomutra pana* twice a day on empty stomach.
- Use of *Nimba, Guggulu, Karanja, Gomaya* for fumigation of the room.
- Use of mask regularly.
- Maintenance of blood glucose level.
- Consumption of nutritious food.

Apathya Ahara Vihara

- Avoid excess of *amla, lavana* and *katu ahara.*
- Avoid activities where there will be contact with soil, since fungal spores are richly present in the soil.
- Avoid fatty, heavy, curd and acidic food.

Research Evidence on Antifungal Preparations

A review article has been published on medicinal plants having antifungal properties which included *aushadhi dravyas* like *Nimba, Vasa, Vacha, Yashtimadhu, and Haridra.*[11] Another study related to potential activity against fungi was carried out on 14 Indian plants which were selected based on its therapeutic effect in respiratory related disorders in traditional systems of medicine. The antifungal activity was investigated by disc diffusion, micro broth dilution and percent spore germination inhibition tests against Aspergillus species. According to the study, Dattura metel and Solanum xanthocarpum had significant activity against fungal infections.[12]

Cumin and fennel which comes under the *aharopayogi varga*, its essential oils could be used as alternatives to conventional antifungal drugs for treating edentulous patients with oral candidiasis.

Application of *Rasayana Dravyas*

As Post COVID complications are quite common among the patients with Post steroid therapy, immune compromised conditions, patients with diabetes and chronic respiratory diseases etc. Thus the usage of *Rasayana dravyas* like *Amlaki, Guduchi, Vasa, Pippali, Ashwagandha, Haridra* etc. has a beneficiary role in preventing the associated complications. *Rasayana dravyas* are helpful in repairing the lung parenchyma and helps in enhancing the qualitative and quantitative production of T cells.

Diabetic Patient Management

Since diabetes mellitus is a strong predisposing factor for the occurrence of Mucormycosis, a good control over diabetes is of a great concern when it comes to the prevention and management of Mucormycosis. *Naimittika Rasayana* like *Shilajathu* helps in the correction of hyperglycemic episodes.

CONCLUSION

Personal hygiene as well as environmental hygiene along with the preventive medications both *Eka moolika prayoga* and herbal compounds, *Rasayana dravyas* and *krimighna dravyas* can be used as an Ayurvedic preventive approach against Mucormycosis. By considering the treatment principles, a proper treatment protocol based on these treatment modalities should be formulated. Henceforth a cost effective and easily accessible treatment approach could be

implemented as a mass strategy among the population and could be appreciated as a good alternative for the conventional line of treatment.

REFERENCES

1. Singh A K, Joshi S R, Misra A. Mucormycosis in COVID 19: A systematic review of cases reported worldwide and in India. Diabetes Metab Syndr. 2021; doi: 10.1016/j.dsx.2021.05.019
2. Alison Burkett, M.D., Sawanan Saitornuang, B.S., Sixtom.Leal, Jr., M.D., M.B.A. Microbiology and Parasitology.
3. Jameson, Fauci, Kasper, Hauser, Longo and Loscalzo Textbook of Harrison's principle of internal medicine 20th edition 213 chapter.
4. Jameson, Fauci, Kasper, Hauser, Longo and Loscalzo Textbook of Harrison's principle of internal medicine 20th edition 213 chapter.
5. Rudra Prasada Giri, Ajith Gangavane, Suchetha Giri, Neem the wonder herb – A short review. International journal of Trend in Research and Scientific development. https://www.researchgatenet/publication/333683177 Neem the Wonderherb
6. Agnivesha, Charaka Samhita with Ayurveda Deepika commentary of Chakrapanidatta revised by Charaka and Dridhabala, edited by Vaidya Yadavji Trivikramji Acharya, published by Chaukhamba publishers, reprint – 2015, Sutrasthana 5.
7. Acharya Vagbhata, Ashtanga Hridaya elaborated by Vagbhata with joined commentaries of Ayurveda Rasayana by Hemadri and Sarvanga Sundari by Arunadatta, Harisadasiva Paradakara, edition – 2020, Varanasi, Chaukhamba publications, Sutrasthana 2.
8. Agnivesha, Charaka Samhita with Ayurveda Deepika commentary of Chakrapanidatta revised by Charaka and Dridhabala, edited by Vaidya Yadavji Trivikramji Acharya, published by Chaukhamba publishers, reprint – 2015, Chikitsa sthana 7/159-161.
9. Celin C, Sindhu A, Muraleedharan MP. Microbial growth inhibition by Aparajitha dhooma choornam. Anc Sci Life, 2007 Jan; 26(3): 4-8.PMID: 22557234; PMCID: PMC3330879.
10. Vasant C Patil, Textbook of Principles and Practices of Panchakarma, Nasya Adhyaya, 4th edition. Pg.No.534.
11. A.K. Meena, Ramanjeet Kour, Brijendra Singh, A.K. Yadav, Uttama Singh, Ayushi Sachan, Bhavanapal, M.M. Rao. Review on Antifungal activities of Ayurvedic Medicinal Plants (researchgate.net). Drug Intervention Today, 2009; 2(2): 146-148. (PDF) Review on antifungal activities of Ayurvedic Medicinal Plants (researchgate.net).