

Review of Published Case Reports of COVID-19 Associated Mucormycosis with Search of Therapeutic Potential in Ayurveda and Homeopathy

Danish Javed¹, Ashish Kumar Dixit¹, Himanshi Vats², Sana Anwar³, Nibha Giri⁴

¹Department of AYUSH, All India Institute of Medical Sciences, Bhopal, Madhya Pradesh, India

²Department of Shalya, BMK KLE University, Belgavi, Karnataka, India

³Department of Oral Pathology & Microbiology, Institute of Dental Sciences and Technology, Modinagar, Uttar Pradesh, India

⁴State Homeopathic Dispensary, Jakhania, Gazipur, Uttar Pradesh, India

Corresponding Author: Danish Javed

ABSTRACT

Background and Objectives: Infection with COVID-19 has been linked to fungal diseases. The sudden increase in mucormycosis cases has sparked the scientific community interest. In this review, we attempted to investigate the role of Ayurveda and Homeopathy in the treatment of mucormycosis.

Methodology: The research was carried out in three stages; first step, studies on COVID-19 and mucormycosis were searched on various databases such as PubMed and Google Scholar until May 21, 2021, second step was to search authentic Ayurvedic and Homeopathic text books for the context of mucormycosis and symptoms were repertorised to find homeopathic medicines and finally, in the last step, findings were analysed and concluded in order to arrive at a factual solution.

Result: We found total 16 search results from bio-medical databases of which 14 articles were included. Except source books, no studies with respect to Ayurveda and Homeopathy were found in above databases. In Ayurveda, *Rajyakshama* and *krimijshirorog* has close similarity to COVID associated mucormycosis. *Vrinhana*, *vata-pitta nashakmadhuraushadhi*, *gritpaan*, *dugdha*, *nasya*, *dhum*, *kawal*, *gandush*, *mriduvirechan* may be beneficial along with immune boosting drugs like *ashawagandha*, *giloya*, *tulsi*, *vidanga* etc. Rhino-orbito-cerebral mucormycosis (ROCM) can be treated with *Arsenic album*, *Kali bichromicum*, and *Merc solubilis*, while pulmonary mucormycosis (PM) with *Arsenic album*, *Phosphorus* and *Acalypha indica*. Similarly, gastrointestinal mucormycosis (GM) and cutaneous mucormycosis (CM) can be combated with *Arsenic album*, *Lachesis*, *Merc Corrosivus* etc. and *Anthracinum*, *Arsenic album*, *Lachesis*, *Sulphur*, *Secale cornutum*, and so on in Homeopathy.

Conclusion: In the absence of rigorous trials, the review results found no conclusive comment on the efficacy of CAM in mucormycosis, but anecdotal evidence suggests in favour. To demonstrate its role, rigorous, exploratory, pilot, randomised control trials should be conducted in the future, either alone or as an add-on.

Key Words: COVID-19; Mucormycosis; Black Fungus; Post-COVID-19 care; Rehabilitation; Ayurveda; Homeopathy

1. INTRODUCTION

Coronavirus disease has become a global challenge as the SARS COV-2 virus is changing itself day by day through multiple mutations and new variants are

becoming troublesome [1]. COVID-19 infection has been seen to be associated with fungal diseases. Sudden upsurge of mucormycosis cases has focused the attention of the scientific community.

Mucormycosis is caused by a group of fungi belonging to the order Mucorales. It is an angioinvasive disease mainly involves *Rhizopus*, *Mucor*, *Rhizomucor*, *Cunninghamella* and *Absidia*. The frequent disease causing organism is *Rhizopus* species, which has been reported 46% mortality in patients [2]. Mucormycosis is not a new disease; however the sudden rise in these cases has been seen during COVID-19 time. Its prevalence in India has been noted 0.14 cases per 1000, which is 80 times more as compared to developed countries [3]. Total 8,848 cases of COVID-19 associated mucormycosis have been reported in India till May 22, 2021.

Many theories are being correlating the link of this incidence with COVID 19. Its prevalence in immune-compromised post-COVID-19 patients, who were on long term steroids, remdesivir, tocilizumab, oxygen support especially on industrial or contaminated sources of oxygen, contact with dirty hospital linen etc, has wide room for research. The complicated cases of orbital and cerebral involvement are more related to uncontrolled diabetes and diabetic ketoacidosis along with the unjustified use of high dose steroids. In India, diabetes mellitus is the most common risk factor related to mucormycosis [4]. As India has higher prevalence of mucormycosis and diabetes, it has become world capital of COVID-19 associated mucormycosis. Hyperglycemia has been found to augment the endothelial receptor GRP78, consequently leading to PMN cells dysfunction, impaired chemotaxis and defective intracellular death. High blood levels of zinc and iron have also shown intracellular affinity of fungal agents.

Immuno-compromised state of COVID-19 patients is susceptible to many opportunistic fungal infections. Till date in India, cases of Black fungus, white fungus and yellow fungus have been reported. Antifungal treatment is available in very limited amounts. Liposomal Amphotericin B, Isavuconazole and Posaconazole are being currently used as antifungal agents for

its treatment along with the extensive surgical debridement.

Ayurveda is catching its attention in this scenario and may provide some better outcome if used along with standard treatment. Recently, some authorities jointly started an initiative to manage the cases of mucormycosis with the help of Ayurveda medicines [5]. The high risk of mucormycosis or black fungus on recovering COVID-19 patients can be taken the edge off with prophylactic AYUSH medicines to strengthen their immunity. It was also proposed to prepare an adjuvant Ayurveda medicines kit for such patients and will be recommended in hospitals along with the standard care after getting proper approvals [6].

Here, we have performed wide search and analysis of various literature including journal articles, texts available in ayurveda, and homeopathy related and analogous to mucormycosis. The possibilities of integration of AYUSH with mainstream has been tried to explore in this pandemic situation that may open the new path of success and knowledge.

2. METHODOLOGY

The study was performed in three steps. In the first step, studies related to COVID-19 and mucormycosis was searched on various database including PubMed, Google Scholar till 21st may, 2021 using key words “COVID-19”, “mucormycosis”, and “Black fungus” with Boolean operators “AND”/ “OR”. Their findings were analyzed and symptoms, diagnostic methods, presentation, available treatment methods of COVID-19 associated mucormycosis were assessed in systematic manner. In the second steps, authentic text books of Ayurveda and Homeopathy were also searched to find the context of similar features of post COVID-19 mucormycosis. Repertorisation of symptoms was performed to find out the possible solution through Homeopathic medicines with the help of software Homoeopathic Repertorium version 3.9.5.7. In the third step, all the

findings were analyzed and concluded in a manner to put some factual solution.

3. RESULT

3.1 Studies related to COVID-19 and mucormycosis

Table 1: Details of Case Reports/Series of mucormycosis

SN	Study	Subject	Case presentation	Associated co-morbidity	Diagnosis	Investigation	Fungus	Anti-fungal Treatment	Surgical management	Outcome
1	Maini A et al.2021 (7)	1	38-year-old male with swelling and pain in the left eye	Inj.Remdesivir +InjMethylprednisolone +Inj.Dexamethasone	Sino-orbital mucormycosis	MRI	Rhizopus oryzae	Inj.Fluconazole 200 mg-12hourly & Inj. Amphotericin B 300 mg/day,	Functional Endoscopic Sinus Surgery (FESS), Surgical debridement	Improved
2	Payam Tabarsi, 2021 (8)	1	50-year-old woman with facial swelling, facial numbness, periorbital edema, headache and erythema	Type 2 DM and hypertension, five years ago +gastric bypass surgery +remdesivir +dexamethasone	Rhinosinusitis	Nasal endoscopy, PNS CT, tissue biopsies, PCR and DNA sequencing	Rhizopus oryzae	Inj. liposomal amphotericin B	Surgical evaluation	Improved
3	Khan N, et al, 2020 (9)	1	44-year-old woman with COVID 19 pneumonia	Type 2 DM +remdesivir +methylprednisolone	Pulmonary mucormycosis	CT Chest, Bronchoscopy, Endobronchial biopsy and bronchoalveolar lavage (BAL)	Candida albicans, glabrata, and krusei along with Aspergillus flavus and niger	Voriconazole 250 mg IV, Micafungin 150 mg IV		Death
4	Mishra N, 2021 (10)	10	Mean age 55.8 years (37 to 78), 9 male 1 female with Eye pain, facial pain and nasal block	DM (8), and/or HTN, CKD +steroids(6) +tocilizumab (1) +Remdesivir(5)	Rhino-orbital-cerebral mucormycosis	CT PNS, MRI brain, HPE and fungal smear	Rhizopus species	IV Amphotericin B	FESS, debridement, Orbitalexenteration, Endoscopicmaxillectomy and ethmoidectomy	Death(4)
5	Kirill A, et al 2021 (11)	1	41-year-old man hospitalized for COVID 19	T1DM +diabetic ketoacidosis +steroids +hydroxychloroquine	Rhino-cerebral-mucormycosis	CT,MRI Brain	Rhizopus species	Amphotericin B (abelcet)	Partial septectomy and bilateral maxillary antrostomy, total ethmoidectomy and sphenoidotomy followed by more extensive surgeries	Improved
6	Garg d, et al, 2021 (12)	1	55-year-old man with severe COVID 19	diabetes 10 years, end-stage kidney disease on hemodialysis 1 year +dexamethasone +remdesivir	Pulmonary mucormycosis	Chest radiograph, CT chest, matrix-assisted laser desorption/ionization time of flight (MALDI-TOF), in vitro antifungal susceptibility testing (AFST)	Rhizopus microsporus	Liposomal amphotericin B		Improved

Table 1 Continued...

7	Mehta S, 2020 (13)	1	60-year-old male patient with bilateral lid edema with right eye prominence	DM +oraloseltamivir, +iv methylprednisolone, +dexamethasone +tocilizumab	Rhino-Orbital Mucormycosis	MRI brain, orbits, and paranasal sinuses, nasal biopsy	Rhizopus species	Amphotericin B	Due to poor vitals debridement could not be done	Death
8	Amirreza V, 2021 (14)	2	40-year old woman with bilateral visual loss and complete ophthalmoplegia of the right eye and 54-year old man with vision loss, proptosis, orbital inflammation, and complete ophthalmoplegia on the left side.	Remdesivir +dexamethasone (both), DM (male)	Rhino-orbital mucormycosis	CT scan, MRI, endoscopic sinus examination, HPE	Rhizopus species	Amphotericin B, oral posaconazole	Daily endoscopic sinus debridement and irrigation with diluted amphotericin B.	1. Death 2. Alive
9	Revannavar SM et al, 2021 (15)	1	Middle-aged woman, mild COVID 19 symptoms with left-sided facial pain, ophthalmoplegia of the left eye and fever of short duration.	Diabetes	Orbital apex syndrome with brain infarction	CT paranasal sinus, MRI brain, HPE, Fungal culture	Rhizopus species	Amphotericin B	FESS	Improved
10	Chennamchettay VK et al, 2021 (16)	1	72-year-old male H/o severe COVID 19 pneumonia, c/o streaky hemoptysis	hypertensive, steroid-induced diabetic, hypothyroid +Ramdevpir +methylprednisolone +convalescent plasma	Pulmonary mucormycosis	PET CT, CT guided biopsy, HPE	Rhizopus species	Liposomal amphotericin B, posaconazole		Improved
11	Ehrenreich AW, 2020 (17)	1	33-year-old female with altered mental status, ophthalmoplegia left eye, proptosis	hypertension, asthma	Rhino-orbital-cerebral mucormycosis	CT head, chest radiograph	Rhizopus species	Amphotericin B	Refused by family	Death
12	Pauli MA. et al, 2021 (18)	1	50-year-old female with mild COVID 19 symptoms and painful lesion in hard palate	type 2 diabetes + Removable partial denture	Painful palatal lesion due to mucormycosis	Incisional biopsy, cone beam computed tomography scan.	Rhizopus species	Amphotericin B	Superficial debridement	Improved
13	Sharma S, et al, 2021 (19)	23	15 male, 8 female old or fresh COVID 19 positive	Diabetes mellitus(21), HTN(12), Renal Failure(1)	Invasive fungal sinusitis (ethmoids (23), Maxillary (12), sphenoid (5), Frontal (1)), Intra-orbital extension (10), intracranial extension (2), Palate (9)	CT, MRI	Not mentioned	Amphotericin B	Not mentioned	Not mentioned

Table 1 Continued...

14	Sungur teki H, et al, 2021(20)	1	56-year-old female COVID 19 patient with proptosis in the right eye, restricted eye movements, edema and color change in the nasal area	Diabetes + MPS	Severe Rhinocerebral Mucormycosis	Biopsy and Paranasal sinus CT,	Rhizopus species, Acinetobacter baumannii	Liposomal amphotericin B, Colimicin	Debridement, Tracheostomy	Death
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We found total 16 search results; out of which one (1) was a letter to the editor and one (1) was a review article. Remaining 14 articles were included in this study. Included twelve (12) articles were case studies, while two (2) were case series. Total forty six (46) patients of different types of mucormycosis were included in these search results. Cases of Sino-orbital, Rhino-sinusitis, Rhino-orbital, Rhinocerebral, Rhino-orbital-cerebral, Intensive fungal sinusitis, Orbital apex syndrome, Brain infection and painful palatal lesion were the presentation of mucormycosis. (Please see Table 1: Details of Case Reports/Series of mucormycosis) [7-20]

In these patients, gender-wise 65.2% (30) male and 34.8% female (16) are seen. Mean age was found 49.9 years age (38-78 years). In this group, diabetes was highly prevalent in 84.8% cases. One patient had type-1 diabetes, while one patient had developed steroid induced. Mucormycosis was seen to highly affect sinuses (54.34%), then nasal part, eyeball, brain (34.8% each), palate (21.74%) and lungs (6.5%).

The most common presenting complaints were eye swelling and pain, periorbital edoema, lid edoema, restricted eye movements, orbital inflammation, eye prominence, visual loss, complete ophthalmoplegia, proptosis, facial swelling, pain, numbness, nasal blockage, edoema and colour change in the nasal area, erythema headache, altered mental status, and painful palatal lesion.

Concerning investigations, in Rhino-orbital-cerebral mucormycosis cases, nasal endoscopy, nasal tissue biopsy, PNS CT, MRI brain orbits and paranasal sinuses, histopathological examination and fungal

smear, PCR and DNA sequencing, matrix-assisted laser desorption/ionization time of flight (MALDI-TOF), and in vitro antifungal susceptibility testing (AFST) were performed while in cases of pulmonary mucormycosis, CT Chest, Bronchoscopy, Endobronchial biopsy, and bronchoalveolar lavage (BAL), PET CT, CT guided biopsy, and HPE were performed. In the case of the palatal lesion, an incisional biopsy and cone beam computed tomography scan were performed. *Rhizopusoryzae*, *R. microsporus*, and other species were mainly recognized in microscopic smears in the form of fungal hyphae. *Candida albicans*, *glabrata*, and *krusei* along with *Aspergillus flavus* and *niger* were also encountered in one case of pulmonary mucormycosis.

Injection Fluconazole, Injection Amphotericin B, Injection Liposomal Amphotericin B, Voriconazole, Miconazole, Oral Posaconazole, Colimicin etc were used as primary antifungal agents in various cases. To prevent disease progression, functional endoscopic sinus surgery (FESS), surgical debridement, daily endoscopic sinus debridement and irrigation with diluted amphotericin B, orbital exenteration, endoscopic maxillectomy, ethmoidectomy, partial septectomy, bilateral maxillary antrostomy, total ethmoidectomy and sphenoidotomy, and more extensive surgeries were performed in these cases. Many patients refused surgical procedures, and in some cases, surgery was unable to be performed due to low vitals and technical difficulties. Mortality of available data was 39.13%, whereas 60.87% cases improved with few deformities.

: An alternative and integrative strategy to mucormycosis

3.2.1 : Ayurveda perspective [21, 22]

No such description of mucormycosis is found anywhere in Ayurveda text. However, diseases of head, neck, eyes and mouth are described deliberately in Ayurveda literature. Many symptoms of mucormycosis have close similarity with symptoms as described in Ayurveda. Covid associated opportunistic fungal infection is a result of a weak immune system. In this regard, we may treat the Covid disease on the line of *Rajyakshama* and *Urdhva-jatrugata roga* both simultaneously. *Rajyakshama* has similarity with the disease of the respiratory system which ultimately leads toward poor immune-compromised state (*Oja Kshaya*) of patients. So, in whole scenario, if we join the different pieces of jig-saw puzzle, the picture of Covid and its complications will be clear under the preview of Ayurveda by including *Rajyakshama*, *Oja Kshaya*, *Siroroga*, *netraroga*, *nasarog* and *mukha rog*.

In most of these conditions, which are found quite similar to Covid associated mucormycosis are showing preponderance of *Vata* and *Pitta dosha* exacerbation and *Rakta* and *Mamsa dhatu* are most affected *dushya*. *Akash* and *vayu mahabhut* are mainly affected in sinus and nasal disorders. Substantial *Oja kshaya* in post covid patients results in palpitation, anxiety, overthinking and pain all over the body. In the above condition, *apara-oja* from all over the body gets emaciated by three means i.e. *ojavistransa*, *ojavyapada* and *ojakshaya*. This course leads to symptoms like pain in joints, debility to do work, heaviness and stiffness in body, discoloration, laziness, giddiness, muscle wasting, weight loss, vertigo, delirium and all of sudden death. Here, mainly *vata* aggravation and immune compromised (*vyadhi kshamatva* or *oja*

kshaya) conditions produce vicious events in patients (SU.SU 15/28-33 & CH.Su 17/73).

In *Krimijanya Shiroroga* (pathological headache), *Udarstha krimi* (some microbes) are increased due to various reasons and causes reflex headache and blood mixed pus (*Rakta* and *Puya*) comes out from the nose. As per the *Charaka*, in case of *krimijanya* or pathological headache, *Rakta* and *Mamsa dhatu* get vitiated and cause *Tridosha Prakopa* which leads to the symptoms like Fever, Nasal discharge and Pain over sinuses and teeth (SU.U 25/10 &CH.Chi 26/118). Here, headache is seen to be associated with *krimi* or microbes and the further progression of disease is always resulting in several complications related to eyes, sinus, ear and brain. In nasal disorders like “*Apinasa*, *Aampinasa*, *Nasapuya*, *vyadhirakta* and *Dusthapinasa*”, results dryness, blockage, discharge and pain in nose, eye diseases, blurring vision, facial swelling and problem in functions of respiratory system blood tinged nasal discharge (SU.U 22/6, 22/17 & 24/15-17 &CH.Chi 26/114, 26/116). Symptoms like difficulty in closing of eyes, periorbital swelling, pain in eyeball, discharge, heaviness, blurring of vision redness and discoloration around eyes are seen in *Vartmabandha*, *Klinnavartma*, *Raktaabhishyanda*, *Sashofapaka*, *Amyladhyushita*, *Sirotpata*, *Sirapraharsha* etc described by *Sushruta* and *charaka* (SU.U 3/17, 21 SU.U 6/9,28-30&CH.Chi 26/129). Please see Table 2: Symptoms of mucormycosis compared with symptoms of Ayurvedic diseases

3.2.1.1 : Recommendations: Please see Table 3: Recommendation of ayurveda management

Table 2: Symptoms of mucormycosis compared with symptoms of Ayurvedic diseases

Mucormycosis symptoms	Symptoms in ayurveda	As per Sushruta samhita	As per Charaka samhita
Pain around eyes	<i>Toda -needle pricking pain</i>	<i>Vartambhandha-Su.U.3/17, klinnavartama- Su. U. 3/21, Sashofa paka, Su.U.6/21</i>	<i>Vataj netraroga & pittaj netraroga Ch.chi.26/129</i>
Redness around eyes	<i>Lalima present</i>	<i>Raktaabhishyanda Su.U.6/9, Amyladushita Su.U.6/28</i>	
Difficulty in closing of eyes		<i>Siroutpata & Sirapraharsha Su.U.6/29&30 vartambhandha</i>	<i>Same above</i>

Table 2 Continued...			
Blurring of vision and diplopia		Sirapraharsha, Su.U.6/30, Dusthpratishayaupdrava, Su.u.24/17	
Periorbital swelling	Shofa/shotha	Vartambhandha , klinnvartama, Sashofa paka	Krimajshirashoola Ch.su.17/29
Conjunctival infection and chemosis	Kshita, vrana	Vartambhandha, sashofapaka, Arjuna -Su.U.4/7	
Headache	Ugraruja, Ghorruja	Kshayajshiroroga, Su.u.25/9, Krimijanyashiroroga 25/10, Anantvata, 25/13, Ardhavabheda, Su.u.25/15, Nasapuyarakta, Su.u.22/10,	Krimajshirashoola, Ch.su.17/29, Vatajshirashoola, Ch.su.17/19-21, Vatajpratishaya and sannipatajpratishaya Ch.chi.26/105-106, Sahasjanyarajyakshma, Ch.ni.6/4
Bloody vomits/ haemoptysis	Mukha se rakta vaman/strava	Yakshmashadrupa, Su.u.41/13, Urshatajanyashosha, Su.u.41/29-31	Puyarakta, Ch.chi.26/116, Sahasjanyarajyakshma, Ch.ni.6/4, Kshayajanyarajyakshma, Ch.ni.6/8
Nasal discharge-blackish or blood tinged	Nasa se rakta and puyastrava,	Krimijanyashiroroga, Nasapuyarakta, Su.u.22/10, Nasashosha, Su.u.22/17,	Apinasa, Ch.chi.26/114, Puyarakta, Ch.chi.26/116, Sahasjanyarajyakshma, Ch.ni.6/4
Nasal crusting	Shukhaourna abhasa	Raktajanyapratishaya, Su.u.24/13, Apanisha, Su.u.22/6, Aampinasa, Su.u.24/15vimarsha, Dusthpratishayaupdrava, Su.u.24/17	
Blackish discolouration of skin over nasolabial groove			Putinasya, Ch.chi.26/113
Paraesthesia over half of face	Ardhangghata	Anantvata, Su.u.25/14,	
Facial pain	Ekangghata	Ardhavabheda, Su.u.25/15	
Pain over sinuses	Dantashoola	Krimijanyashiroroga 25/10vimarsha,	
Pain in teeth and gums			
Fever	Jwara	Aampinasa, Su.u.24/15vimarsha, Yakshmashadrupa, Su.u.41/13	Sahasjanyarajyakshma, Ch.ni.6/4
Loosening of teeth/ discolouration of palate	Talushosha	Rajyakshamapurvarooopa, Su.u.41/11	
Shortness of breath	Uroghata	Nasashosha, Su.u.22/17,	Sahasjanyarajyakshma,Ch.ni
Chest pain	Ushwasawrodha	Raktajanyapratishaya, Su.u.24/13,	.6/4,
Worsening of respiratory symptoms	Urshata	Dusthpratishayaupdrava, Su.u.24/17, Rajyakshamapurvarooopa, Su.u.41/11, Yakshmashadrupa,Su.u.41/13, Urshatajanyashosha, Su.u.41/29-31, Shokashoshi, Su.u.41/23	Kshayajanyarajyakshma, Ch.ni.6/8
Altered mental status or consciousness	Brahm Mada	Ardhavabheda, Su.u.25/15, Aampinasa, Su.u.24/15vimarsha, Rajyakshamapurvarooopa, Su.u.41/11	Putinasya, Ch.chi.26/113

Table 3: Recommendation of ayurveda management

General - (Su.u. 26/25-31; 41/35, 41; 24/18; 23/3,6; 10/5)	Specific (Su.u. 25/24-34; 41/44,48,49; 12/15,17,44; 10/14; 13/14) & (Ch.chi. 8/93,94,99,104,105,113,145-147 and 26/144,157,158,159,165,174,175)
Brimhanvidhi, Vata and Pitta nashakaushadhi, Madhurdravyas, Kshaya and Kasanashakaushadi, Kriminashakaushadi	Trikatu ,chavya and vidangachurna with ghrita and madhu,
Ghritapana, Mandushna and MadhurDugdhapaan, goat and sheep milk and ghee, Mamsarasa, ksheersarpi, ksheeranavikriti like malai, ghevar,halua, lapsi etc.	AshwagandhadiChurna, SitopladiChurna, TalishadiChurna, NagbalaChurna with milk MuktaPisthi ,PravalPisthi Vardhmanpippali, ShilajeetVati, Mahalaxmivilas rasa, Saptamritlauha
Shiralepa with vata and pitta nashakdravyas	Vidangadichurna ,vidangadikwatha Shadbindu tail, anu tail, balatail ,ksheersarpi, pradhmanchurna, rasnadi tail for nasya(nasal instillation)
	Chandrodyavarti,Nagaarjunavarti,Yoganjana, jatipushpaanjana, rasanjana, lekhayanjna, takshryaanjana,mustadyaanjanaforanjana
	TrifalaGhrita, Tilwakaghrita, Puranghrita, Dashmooladyaghrita, Rasnaghrita, Balaghrita, Panchpanchmoolghrita, Vasa ghrita ,Shatavarighrita, Jivantiyadighrita, Mayurghrita, Mahamayurghrita, KaumbhagritaforGhritapana Trivrutghrit for mriduvirechana.

3.2.2 : Homoeopathic Perspective

Mucormycosis is no exception to the fact that homoeopathy is a medical system

based on individualisation; each case must be presented in an individualistic manner.

Mucormycosis, or black fungus, can affect the sinuses, eyes, and brain and can occur concurrently with COVID-19 infection or in the early post-recovery phase. Even though mucor is present in the oral and respiratory linings of healthy people, it does not cause infection if the immune system is intact and healthy. In general, this infection occurs in patients with uncontrolled diabetes, undergoing cancer treatment, on long-term steroid therapy, following an organ transplant, and those who have suffered a severe injury such as a burn.

A large number of experimental studies have been carried out to assess the efficacy of homoeopathic drugs against fungal diseases in animals and humans [23-27]. However, there have been many studies on fungal diseases in general, but as of our most recent search, we could not find any in-vitro/vivo or human trial studies on Mucormycosis.

Recently based on literature some anecdotal evidence released in the public interest by state authorities recommending mucormycosis treatment [28]. They proposed treatment for four types of mucormycosis: rhino-orbito-cerebral, pulmonary, cutaneous, and gastrointestinal.

For Rhino-orbito-cerebral Mucormycosis (ROCM), drug prescribed is *Arsenic-Alb, Kali Bich, Merc.Iod. Rubrum, Merc. Iod. Flavum, Merc. Sol, Cinnabaris, Thuja, Carbo Animalis*; 200 potency, daily two times 6 pills each time for 5 days. *Arsenic-Alb, Phosphorous, Bryonia, Carbo Animalis, Ant.Tart*; 200 potency, daily two times 6 pills each time for 5 days has been advised for Pulmonary mucormycosis (PM).

Likewise, in case of Cutaneous Mucormycosis (CM), it is *Arsenic-Alb, Sulphur, Merc. sol, Anthracinum*; 200 potency, daily two times 6 pills each time for 5 days while for Gastrointestinal Mucormycosis (GM), it is *Arsenic-Alb, Phosphorous, Nitric Acid*; 200 potency, daily two times 6 pills each time for 5 days.

← Result of repertorization											
12 symptom(s)	1	2	3	4	5	6	7	8	9	10	11
Name of remedy	Merc	Ars	Hep	Phos	Acon	Bell	Caust	Kali-bi	Kali-i	Apis	Puls
Symp. covered	9	6	6	7	6	5	5	6	5	4	6
Totality	14	14	12	11	10	11	11	10	11	11	9
1. CHEST, HAEMO..											
2. CHEST, PAIN, ...											
3. EYE, CHEMOSIS,..											
4. EYE, INJECTED, ...											
5. EYE, SWOLLEN, ...											
6. FACE, PAIN, exte..											
7. FACE, PAIN, exte..											
8. FACE, PAIN, one-..											
9. MOUTH, SOFTE..											
10. NOSE, DISCHA..											
11. NOSE, DISCHA..											
12. TEETH, LOOSE..											

Figure 1: Repertorisation sheet

Another advisory for homoeopathic practitioners, though not based on any specific trial, has been released for the management of mucormycosis by the Drug Policy Section of the Ministry of AYUSH, Government of India, in consultation with senior physicians and researchers [29].

Based on symptoms guided by ICMR, repertorisation was carried out with the help of Homoeopathic Repertorium [30] and details of rubrics considered for repertorisation and results are being given. (Please see-Figure 1: Repertorisation sheet) and (See-Table 4: Details of Repertorisation sheet with medicines)

Table 4: Details of Repertorisation sheet with medicines

S. No.	Rubrics	Medicines (Short name full name) with S-Symptoms covered, R-Total marks
1.	CHEST, HAEMORRHAGE, ...	1. Merc MercuriussolubilisHahnemanni S:9 R:14
2.	CHEST, PAIN, ...	2. Ars Arsenicum album S:6 R:14
3.	EYE, CHEMOSIS, ...	3. Hep Heparsulphuriscalcareum S:6 R:12
4.	EYE, INJECTED, ...	4. Phos Phosphorus S:7 R:11
5.	EYE, SWOLLEN, ...	5. Acon Aconitum napellus S:6 R:10
6.	FACE, PAIN, extending to, teeth	6. Bell Belladonna S:5 R:11
7.	FACE, PAIN, extending to, temples	7. Caust CausticumHahnemanni S:5 R:11
8.	FACE, PAIN, one-sided	8. Kali-bi Kali bichromicum S:6 R:10
9.	MOUTH, SOFTENING, GUMS	9. Kali-i Kali iodatum S:5 R:11
10.	NOSE, DISCHARGE, bloody, ...	10. Apis Apismellifica S:4 R:11
11.	NOSE, DISCHARGE, brownish	11. Puls Pulsatillanigricans S:6 R:9
12.	TEETH, LOOSENESS, painful	12. Rhus-t Rhustoxicodendron S:5 R:10
		13. Bry Bryonia alba S:5 R:9
		14. Ferr Ferrummetallicum S:5 R:9
		15. Ferr-ar Ferrumarsenicum S:5 R:9
		16. Lach Lachesismuta S:5 R:9
		17. Nux-v Nux vomica S:5 R:9
		18. Kreos Kreosotum S:5 R:8
		19. Mez Mezereum S:5 R:8
		20. Nit-ac Nitricumacidum S:4 R:9
		21. Am-c Ammonium carbonicum S:4 R:8
		22. Con Conium maculatum S:5 R:7
		23. Ip Ipecacuanha S:4 R:8
		24. Kali-c Kali carbonicum S:4 R:8
		25. Sep Sepia succus S:4 R:8

Table 5: Indications of Homoeopathic medicines suggested for Mucormycosis (31,32,33,34,35)

S. No.	Types of Mucormycosis	Medicines	Indications
1.	Rhino-orbito-cerebral	<i>Arsenic Alb</i>	Hemicrania relieved by cold, Periodical burning pains, with restlessness; with cold skin. Oedematous eyes, inflamed, with extreme painfulness; burning, hot, and excoriating lachrymation. Thin watery excoriating discharge from nose, blocked feeling with burning and bleeding.
		<i>Kali Bich</i>	Septum ulcerated; round ulcer. Fetid smell. Discharge thick, ropy, and greenish-yellow. Tough, elastic plugs from nose; leave a raw surface. Inflammation extends to frontal sinuses, with distress and fullness at root of nose. Coryza, with obstruction of nose. Violent sneezing. Loss of smell. Unilateral headache in small spots, and from suppressed catarrh. Frontal pain; usually over one eye.
		<i>Merc.Iod. Rubrum</i>	Coryza and dull hearing; right side of nose hot. Hawks mucus from posterior nares. Turbinate bones swollen. Boggy mucus membrane of nose and throat; closure of Eustachian tube, opening with a pop.
		<i>Merc. Iod. Flavum</i>	Small ulcers on posterior pharynx. Easily detached patches on inflamed pharynx and fauces; worse on right tonsil; much tenacious mucus. Constant inclination to swallow.
		<i>Merc. Sol</i>	One-sided, tearing pains. Catarrhal headaches; much heat in head. Lids red, thick, swollen. Profuse, burning, acrid discharge.
		<i>Cinnabaris</i>	Severe shooting pain in bones of orbit, especially running from inner to outer canthus in the bone. Redness of whole eye. Lids granulated; canthi and lids red. For ciliary neuralgia and ulceration upon a syphilitic base.
		<i>Thuja</i>	Catarrh; thick, green mucus; blood and pus. On blowing nose, pain in teeth. Ulceration within the nostrils. Dryness of nasal cavities. Left-sided headache.
		<i>CarboAnim alis</i>	Headache, as if head had been blown to pieces. Rush of blood with confusion. Sensation as if something lay above eyes so that she could not look up.
2.	Pulmonary	<i>Arsenic Alb</i>	Burning in chest. Suffocative catarrh. Cough worse after midnight; worse lying on back. Expectoration scanty, frothy. Darting pain through upper third of right lung. Wheezing respiration. Haemoptysis with pain between shoulders; burning heat all over.
		<i>Phosphorus</i>	Cough worse, cold air. Sweetish taste while coughing. Hard, dry, tight, racking cough. Congestion of lungs. Burning pains, heat and oppression of chest. Tightness across chest; great weight on chest. Sharp stitches in chest; respiration quickened, oppressed. Pneumonia, with oppression; worse, lying on left side. Sputa rusty, blood-colored, or purulent.
		<i>Bryonia</i>	Dry, hacking cough from irritation in upper trachea. Cough, dry, at night; must sit up; worse after eating or drinking, with vomiting, with stitches in chest, and expectoration of rust-colored sputa. Frequent desire to take a long breath; must expand lungs. Difficult, quick respiration; worse every movement; caused by stitches in chest. Croupous and pleuro-pneumonia.
		<i>CarboAnim alis</i>	Pleurisy, typhoid character, and remaining stitch. Ulceration of lung, with feeling of coldness of chest. Cough, with discharge of greenish pus.
		<i>Ant.Tart</i>	Great rattling of mucus, but very little is expectorated. Rapid, short, difficult breathing; seems as if he would suffocate; must sit up. Oedema and impending paralysis of lungs.
3.	Gastrointestinal	<i>Arsenic Alb</i>	Gastralgia; Burning pain in stomach, Great thirst; drinks much, but little at a time. Vomiting of blood, bile, green mucus, or brown-black mixed with blood.
		<i>Phosphorus</i>	Pain in stomach; relieved by cold food, ices. Stomach painful to touch. Inflammation of stomach, with burning extending to throat and bowels. Vomiting; water is thrown up as soon as it gets warm in the stomach and Haematemesis.
		<i>Nitric Acid</i>	Pain in cardiac orifice. Haemorrhages from bowels, profuse, bright. Diarrhoea, slimy and offensive. After stools, irritable and exhausted.
4.	Cutaneous	<i>Arsenic Alb</i>	Ulcers with offensive discharge. Gangrenous inflammations.
		<i>Sulphur</i>	Itching, burning; worse scratching, washing, warmth and in evening.
		<i>Merc. sol</i>	Glands swell every time patient takes cold. Buboec. Ulcers, irregular in shape, edges undefined. Excessive odorous viscid perspiration; worse, night.
		<i>Anthracinum</i>	Ulceration, sloughing and intolerable burning. Haemorrhages, black, thick, tar-like, rapidly decomposing.

Further, indications of these possible groups of medicines are given in consultation with different Materia Medica Books as directed from the above-mentioned advisories and from repertorisation results. (Please see-Table 5:Indications of Homoeopathic medicines suggested for Mucormycosis (^{31,32,33,34,35}])

4. DISCUSSION

Although no such robust study was found in our search, a study of the authentic books of Ayurveda and Homeopathy has revealed some possible medicine that can be used. However, the approach while treating such cases may be multiple. As reported, mucormycosis cases are having poor immunity and hyperglycemia, an integrated plan of treatment may be beneficial. A team from different departments of modern medicine and AYUSH is vastly required to treat these cases. Simultaneously, role of AYUSH in these cases must be well defined.

Complementary and alternative medicine (CAM) may delivers additive effect to standard treatment in the form of immunomodulation (*rasayana*), hyperglycemic control through diet and therapy, purification treatment (mild purgation, nasal cleaning, oral and throat cleaning), fumigation therapy, oil pooling treatment etc. Prevention, communication, motivational guidance, personal and environmental hygiene, yoga and meditation, supportive treatment to those who are not fit for surgery or refusing are the significant domains to be covered by AYUSH experts. A proper protocol may be framed to provide AYUSH care. Experts of different field can bring significant change if they work in coordination. Fumigation (*dhupan*) with dry herbal medicines; oral hygiene by neem, clove, turmeric, basil, maushri etc; *kawal* and *gandush* for oral and pharyngeal cleaning; nasal cleaning by *anu tail*, *shigru oil*, *vidanga oil* etc.; eye care by *Maha triphala ghrī*, *anjana* etc. may be facilitated to all the post COVID-19 patients

as a prophylactic measure. Use of fresh mask especially impregnated with herbal decoctions and essential oil may work as anti-microbial as well as mood elevators. Regular practice of slow deep breathing pranayama, bhramari, Shitali etc. will give add-on benefit on respiratory parameters.

Homeopathy treatment is mainly based on symptoms; in this unwanted disease also the help of this AYUSH system can be taken. However, in our search, no such test was found directly related to this disease in which this medicine is infallible in its treatment, yet as it is known that if the homeopathy medicines are discovered by keeping the symptoms at the centre, then it is possible to get favourable results. Symptoms of ROCM; Facial pain, headache, lethargy, visual loss, proptosis, and/or palatal ulcer, nasal discharge (blackish/bloody), blurred or double vision with pain may be combated chiefly through *Arsenic album*, *Kali bichromicum* and *Merc solubilis*. Difficult breathing, cough, chest pain, pleural effusion, haemoptysis, worsening of respiratory symptoms (PM) managed by *Arsenic album*, *Phosphorus*, *Bryonia*, *Acalypha indica* etc. Similarly, GM and CM can be combated with *Arsenic album*, *Lachesis*, *Merc Corrosivus* *Phosphorus* etc and *Anthracinum*, *Arsenic album*, *Lachesis*, *Sulphur*, *Secale cornutum* etc respectively [28-29, 31-35]. Homeopathic therapy is significantly less expensive than conventional pharmacological therapy [36]. Patient satisfaction is also higher in the homeopathic group than in the conventional treatment group [37]. Homeopathic remedies are generally thought to be safe [38]. However, it is not without risk, and a few mild adverse events were reported in the studies reviewed [39].

5. CONCLUSION

In the absence of rigorous trials, we found no conclusive comment on the efficacy of CAM in mucormycosis, but anecdotal evidence offers possibilities of CAM. To demonstrate its role, we

recommend that rigorous exploratory pilot randomised control trials be conducted in the future, either alone or as an add-on.

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