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CORONAVIRUS (COVID-19) ASSOCIATED MUCORMYCOSIS IN INDIA

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ABSTRACT
India continued to struggle with the second wave of COVID-19. A variety of etiological factors have been linked to the association of COVID-19 with a recent increase in the incidence of COVID-associated mucormycosis. Mucormycosis refers to a cluster of distinctive mycoses caused by saprophytic fungi, Mucorales. it's typically an airborne infection and is initiated within the upper or lower airways. This paper aim to review current information about the prevalence of COVID-19 associated mucormycosis. A prospective observational study was conducted over five months from February 2021 to June 2021, involving all the official social media and newspapers giving information about Covid associated mucormycosis.

KEYWORDS: COVID-19, Mucormycosis, India, steroids.

INTRODUCTION

The pandemic coronavirus disease 2019 (COVID-19) continues to be a big problem all over the world. Systemic glucocorticoids were shown to enhance survival in COVID-19. Unfortunately, the widespread use of glucocorticoids can cause secondary bacterial or fungal infections out of which mucormycosis is usually suspected in India. The cases of mucormycosis were present with the first wave of covid19 in 2019 but the second wave of the covid has had shown an even worst effect. Mucormycosis refers to a cluster of distinctive mycoses caused by saprophytic fungi, Mucorales. It's typically an airborne infection and is initiated within the upper or lower respiratory tract. The infection in humans starts from the inhalation of spores of and then it enters the respiratory tract. This paper aim to review current information about the prevalence of COVID-19 associated mucormycosis.

METHOD

A prospective observational study was conducted over five months from February 2021 to June 2021 involving all the official social media and newspapers giving information about Covid associated mucormycosis.

PREVALENCE AND INCIDENCE IN INDIA

The overall prevalence of mucormycosis has increased. There is a difference in the epidemiology of mucormycosis between developed and developing countries. In developed countries, the disease remains uncommon and, at the present, is usually seen in patients with Diabetes Mellitus and Hematological malignancies (HMs) undergoing chemotherapy and people who have received allogeneic somatic cell transplants.[1] In contrast, in developing countries, especially in India, mucormycosis cases, although sporadic, occur mainly in patients with uncontrolled diabetes or trauma.[2,3] Chakrabarti et al. showed an increasing trend of mucormycosis from one center at successive periods, with an annual incidence of 12.9 cases per annum during 1990–1999[4], 35.6 cases per annum during 2000–2004[5], and 50 cases per annum during 2006– 2007.[6] the general numbers increased from 25 cases per annum (1990–2007) to 89 cases per annum (2013–2015).[7]

The incidence of mucormycosis is rising in patients recovering from COVID-19 having uncontrolled diabetes and in those who are under over usage of steroids to treat COVID-19. According to the surgeons, mucormycosis is not as infectious as COVID but the mortality rate is 55% and for COVID, it is 1-2%. The second wave of the COVID has had a major effect on the youngster. The 3% high death rate among the age group has shifted from 60-80 years to 40-60 years in a month. While going through data, over 44% of deceased had diabetes while 40% of them had hypertension. According to the figures shared by official media, 13 states and Union territories are majorly affected. Maharashtra state has 1,500 cases of mucormycosis and 90 deaths due to it. Gujarat has 1,163 cases of mucormycosis are detected and 61 people have died. Madhya Pradesh state has 575 cases and 31 deaths. Haryana has 268 cases, eight deaths due to mucormycosis are reported in Haryana. Delhi has registered 203 cases of mucormycosis and one death.

Uttar Pradesh state has registered 169 cases of mucormycosis and eight deaths. Bihar has 103 cases, 2 deaths thanks to mucormycosis are registered in Bihar. Chhattisgarh has 101 cases and one person has died within the state due to it. Karnataka has 97 cases of mucormycosis reported during this southern state. Telangana has 90 cases of mucormycosis detected 10 deaths have also been recorded.[8] Rajasthan, Gujarat, Punjab, Haryana, Karnataka, Tamil Nadu, and Telangana have declared it a "notifiable disease" under the infectious disease Act, making it mandatory to report every mucormycosis case to the government.[9]

PREDISPOSING CONDITIONS

1. Indiscriminate use of steroids: Steroid-induced increase in blood glucose level and suppression of immunity. The predisposing factor can be also due to endothelial damage and thrombosis.
2. Unhygienic way of delivering oxygen to patients: There might be improper cleaning and disinfection of cylinders in which the liquid oxygen is stored. The water used for the humidification of oxygen should be sterile or else can be a potential source of black fungus.
3. Shortage of amphotericin B. The utilization of costly and toxic antifungals like amphotericin B need to be administered for a longer duration adding significantly to the economic burden.
4. Hospitals are overwhelmed, and health workers are exhausted and becoming infected. The sudden increase in COVID-19 cases during the second Indian wave led to the collapse of an already strained healthcare system with a dearth of hospital beds and a low oxygen supply. As a result, patients who had mild symptoms of COVID involuntarily took steroids and other drugs at home which could have led to suboptimal monitoring especially of blood sugar levels and early signs of mucormycosis.

The clinical sign & symptoms of COVID associated mucormycosis are fever, headache, numbness, facial erythema, black discoloration on the skin, ulcerations and dental pain and the other features are described in Table 1.

The clinical manifestations of mucormycosis are traditionally divided into a minimum of six separate syndromes:

1. Rhinocerebral 2. Pulmonary 3. Cutaneous 4. Gastrointestinal 5. CNS 6. Others (e.g., kidney, heart, bones and mediastinum).

Out of all these types, Rhinocerebral mucormycosis found to be the most common one associated with COVID-19 in India. It is the most common form of mucormycosis in patients with diabetes mellitus.[10,11] The spores enter the paranasal sinuses by inhalation. The infection may then rapidly extend into soft tissues. The fungus invades the palate, sphenoid sinus and reaches cavernous sinus involves the orbits and finally reaches to the brain. The clinical signs and symptoms were sinusitis, facial pain, Periorbital cellulitis followed by vision problems. Other symptoms that suggest mucormycosis in susceptible individuals include multiple cranial nerve palsies, unilateral periorbital facial pain, orbital inflammation, eyelid edema, blepharoptosis, proptosis, acute ocular motility changes, internal or external ophthalmoplegia, headache, and acute vision loss, and a black necrotic eschar. The extent can be defined by preoperative contrast-enhanced CT. Such CT scans show the edematous mucosa, fluid filling the ethmoid sinuses, and destruction of periorbital tissues and bone margins.[12] Magnetic Resonance helps to identify the intracranial and intradural extent and thrombosis of cavernous portions of the internal carotid artery.

MANAGEMENT

The patient should not neglect any symptoms of the disease and should get themselves tested at the centres as early diagnosis can lead to early treatment and saving lives. The Patient should start symptomatic treatment while waiting for sample reports. A team approach is required with infectious disease specialists, ENT specialists, microbiologists, intensivists, neurologists, ophthalmologists, dentists, histopathologists, surgeons & radiologists.

Evidence based advisory had been released by Department Of Health Research Ministry Of Health And Family Welfare Government Of India in the time of COVID-19 for the screening, diagnosis, and management of mucormycosis.[13]

1.	**How to prevent?**	1. Use masks if you are visiting dusty construction sites wear shoes, long trousers, long sleeve shirts, and gloves while handling soil (gardening), moss, or manure. 2. Maintain personal hygiene including a thorough scrub bath.
2.	**When to suspect:**	Congestion, nasal discharge (blackish/bloody), local pain on the cheekbone, numbness or swelling Blackish discoloration over the bridge of nose/palate Toothache, tooth mobility, involvement of jaws blurring of vision or double vision along with pain, fever, lesions on the skin, thrombosis and necrosis (eschar)Chest pain, pleural effusion, bleeding on coughing, worsening of respiratory symptoms

3.	**Management**	For Diabetic or immunosuppressed individuals: Control hyperglycemia. Monitoring blood glucose level. Correct timing and correct dose of steroids if required. Use of sterile water for humidifiers during oxygen therapy Use antibiotics/antifungals judiciously
4.	**Investigations**	Aggressive investigations (KOH staining & microscopy, culture, MALDI-TOF) must be sought without hesitation to rule out fungal etiology.

Table 1: Shows clinical sign & symptoms of COVID associated mucormycosis.

	A. General features	**B. Extraoral**	**C. Intraoral symptoms**
1.	Fever and Headache	Facial erythema	Ulcerations
2.	Numbness	Black discoloration on the skin	Dental pain
3.	Nasal stiffness	Periorbital erythema	Intraoral draining sinuses
4.	Nasal discharge with epistaxis	Orbital pain	Mobile teeth
5.	Problem in vision	Upper lip edema	
6.	Breathing problem	Erythema of nasal mucosa	
7.	Cough with blood	Facial erythema	

DISCUSSION

Covid associated mucormycosis has been associated with high morbidity and mortality, excessive treatment costs and has lead to a shortage of antifungal drugs. The solution is to enforce quality control and compliance for production, storage, and delivery (sterile water, clean system of oxygen) as well as stop indiscriminate use of steroids to minimize this new enemy. The best way to deal with these types of situations is to consolidate the country's healthcare system, close monitoring of glycemic status in patients of COVID-19, close prudent use of steroids, following the guidelines, and a good interdepartmental partnership for management.

CONCLUSION

To summarize, overdosage of steroids, metabolic disease like diabetes mellitus, high levels of iron, Unhygienic way of delivering oxygen to patients are the probable causes for mucormycosis spreading. Lastly, in order to control any fungal disease, we need to identify the sign and symptoms of diseases and need to create awareness about the respective disease.

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