



## VULNERABILITY OF PEDIATRIC POPULATION TO COVID-19 ASSOCIATED MUCORMYCOSIS: AN INDIAN PERSPECTIVE

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### ABSTRACT

The coronavirus disease 2019 (COVID-19) infection caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) involves a wide range of symptoms, varying from mild to serious pneumonia. Gradually, with time and experience as we learn more about this novel Covid-19 pandemic, cases are appearing with a multitude of manifestations and newer complications. After a shocking second wave, India and the world is advancing slowly toward stability; another threat has emerged as a challenge in the form of coronavirus disease-associated mucormycosis. During the second wave of Covid-19, we observed a surge in the number of infections in the pediatric population, who were silent carriers till then. This time children were equally prone to the Coronavirus and manifested mixed symptoms. With India having large population of children suffering from type 1 Diabetes Mellitus, it makes them more prone to developing mucormycosis post-COVID-19. To handle the future situation, there is an urgent need to set up special task forces, issuing guidelines, arranging separate Pediatric patient wards in hospitals for mucormycosis, and obtaining a sufficient number of medicines. This article tries to focus on a situation Post COVID Mucormycosis, which if not controlled can be severely devastating.

**Keywords:** COVID-19, Diabetes, Immunocompromised, Mucormycosis, Pediatric.

### 1. INTRODUCTION

The coronavirus disease 2019 (COVID-19) infection caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2); involves a wide range of symptoms, varying from mild to serious pneumonia. Gradually, with time and experience as we learn more about this novel Covid-19 pandemic, cases are appearing with a multitude of manifestations and newer complications [1, 2]. Like SARS-CoV and the Middle East Respiratory Syndrome Coronavirus (MERS-CoV), SARS-CoV-2 is accountable for lower respiratory tract infection and may also lead to acute respiratory distress syndromes (ARDS). Across the globe, COVID-19 patients are showing diffused alveolar damage along with suppression of immunity with decrease in CD4 T and CD8 T cells [3-5].

The picture in India is no different with a steep rise in the number of cases of COVID-19 during the second wave as well as secondary complications associated with the infection. As the world advances toward stability, another looming threat has emerged as a challenge in the form of coronavirus disease-associated mucormycosis.

Mucormycosis is an uncommon but potentially fatal disease if not managed on time. This acute infection occurs due to the Phygomycetes, subclass Zygomycetes, order Mucorales, family Mucoraceae, an opportunist and universal fungi. This disease usually occurs through inhalation or by the ingestion of fungal spores and get implanted in the oro-nasal cavity or conjunctiva [6].

The number of patients with Mucormycosis also referred to as black fungus, has risen more rapidly during the second wave in India. As of July 2021, the government data has reported over 40,845 cases of mucormycosis or black fungus so far, a majority of which affected the brain and sinuses of patients with a history of Covid -19 infection [7-9]. The prevalence of acute cases continues to be more prominent in the states of Maharashtra, Kerala, Tamil Nadu, West Bengal and Odisha. The reporting growth rates in these states are more than the national covid-19 growth rate. Of the total numbers of mucormycosis cases, 34,940 patients had covid-19 (85.5%), 26,187 (about 64.11%) had associated diabetes mellitus, while 21,523 (52.69%) of those infected were on steroids.7-9

## 2. PREDISPOSING FACTORS

The only drug that has shown success in the treatment of COVID-19 is Glucocorticoids, which is low-cost, easy to procure, and have been shown to curtail fatality in Covid-19 patients with hypoxemia [10]. Nevertheless, the risk of secondary infections becomes more with glucocorticoids therapy. Moreover, the immune dysregulation induced by the virus and the simultaneous use of immunomodulatory drugs such as tocilizumab could further increase the possibility of opportunistic infections in COVID-19 patients [11].

A variety of bacterial and fungal co-infections may occur and be linked to prior systemic conditions such as diabetes mellitus, pulmonary disease or may arise as a hospital-acquired infection such as ventilator-associated pneumonia. Patients inflicted with COVID-19 disease have also reported severe opportunistic secondary infections such as oropharyngeal candidiasis, pneumocystis jiroveci pneumonia, pulmonary aspergillosis, bloodstream candida infections [1, 2, 5, 10].

## 3. GLOBAL SCENARIO OF FUNGAL CO-INFECTIONS AND MUCORMYCOSIS IN COVID-19 PATIENTS

Looking back on SARS in 2003, we found the incidence of fungal infection in SARS patients was 14.8-27%, which was even higher in severely ill ones, up to 21.9-33% [12], meanwhile, fungal infection was the chief cause of mortality in SARS patients, accountable in 25-73.7% of death [13].

In a lab culture evaluation of COVID-19 patients, Chen et al. [14] reported 5 cases of fungal infection, in addition, one case of *Aspergillus flavus*, one case of *Candida glabrata* and three cases of *C. albicans* in all 99 patients admitted with Covid -19.

Yang et al. [3] found three out of 52 critically patients (5.8%) had fungal co-infection, including *A. flavus*, *A. fumigatus* and *C. albicans*. Besides, few Chinese researchers have also reported a higher occurrence (8-15%) of secondary infections in COVID-19 patients, which could be bacterial or fungal [5]. Based on the analysis of the clinical data, 2.8% (31/1099) cases required antifungal treatment, involving 1.9% (18/926) non-severe cases and 7.5% (13/173) severe cases, but there was no etiological indication of fungal co-infection [15].

A German study found COVID-19 associated invasive pulmonary aspergillosis (IPA) in five (26.3%) of 19 consecutive critically ill patients with moderate to

severe ARDS [16]. Several anecdotal cases are being reported in grey literature, such as print and electronic media. These findings are unprecedented and carry immense public health importance because the fatality rate with mucormycosis is pretty high. Particularly the intracranial involvement of mucormycosis raises the mortality rate to as high as 90%. Prednisone dose of more than 600 mg, a total of 2-7 gms given for a month during the treatment of COVID-19 in immunocompromised patients increases the risk of mucormycosis. It is strange even a brief course (5-14 days) of steroid therapy, especially in people with DM, have resulted in a similar infection. Moreover, mucormycosis exhibits a rare occurrence of expeditious propagation, so a delay of 12 hours in the diagnosis of the disease could be fatal, the reason 50% of cases of mucormycosis have been historically diagnosed only in the post-mortem autopsy series [17].

## 4. INDIAN SCENARIO

There has been a drastic change in our understanding and handling of covid disease. With the advent of new drugs, vaccines in the picture in 2021, the situation looked promising for controlling this disease. After a sharp rise and a considerable amount of dip has come in COVID 19 cases in India, it is mind boggling why an alarming number of patients with mucormycosis are being reported from all over the country. And strangely, the fungal infection is affecting many young people, and even in non-diabetic patients.

India has the highest cases of mucormycosis in the world. Epidemiological data have reported the prevalence of mucormycosis is 0.14 per 1000 in India, which is almost 80 times higher when compared to developed countries, in a recent estimate of the year 2019-2020. (0.005 to 1.7 per million population worldwide) [17].

### 4.1. Indian Pediatric Population and Mucormycosis

During the current second wave of Covid-19, we observed a surge in the number of infections in the pediatric population, who were silent carriers till then. This time children were equally prone to the Coronavirus and manifested mixed symptoms. Not only were more Covid-19 cases in children, but also the infections were more acute in the second wave. There has also been a grave concern over whether the spread of infection was higher in children. Due to these

unexpected turns of events, there is a concern amongst the parents regarding the third wave. Looking at the spread of Covid-19 among children, the absence of the vaccination or a definite therapy, there is an apprehension the upcoming third wave will strike the younger ones the most. It has caused a lot of panic and confusion among the general public. The data gives mixed indications. According to the health ministry, between March 1 and April 4, 2021, approximately 80,000 children from Maharashtra, Chhattisgarh, Uttar Pradesh, Karnataka, and Delhi tested positive for Covid-19, with more than 60,000 children infected in Maharashtra merely in a month. The Indian Academy of Pediatrics (IAP) recently stated children are more vulnerable to infection, but there is doubt that the third wave of COVID-19 will affect the pediatric population [18, 19].

The rapidly spreading mucormycosis, generally termed as black fungus, is now affecting kids as well. Few national print media have cited reports of a 14-year-old girl from Ballari and an 11-year-old boy from Challakere in Chitradurga district of Karnataka infected with mucormycosis. These are the initially reported cases of paediatric mucormycosis in Karnataka [18, 19]. India has the highest global prevalence of diabetes. About 9% of India's adult population is estimated to be diabetic, stated by the World Health Organization. According to the International Diabetes Federation 2015 report, India has the second-largest population of children living with type 1 diabetes mellitus (T1DM) [20]. The Diabetes Atlas 2017 estimates that there are 128,500 children and adolescents with diabetes in India. According to a study published, there is an assumption that India is home to about 97,700 children with type 1 diabetes mellitus [21]. International Diabetes Federation diabetes atlas (6<sup>th</sup> Edition), reports that India has 3 new cases of T1DM/100,000 children of 0-14 years [22]. This prevalence data in India is variable, with 17.93 cases/100,000 children in Karnataka, 3.2 cases/100,000 children in Chennai, and 10.2 cases/100,000 children in Karnal (Haryana) [23-26]. The actual figures might be higher since many cases might not be reported or fail to get diagnosed, making this population more susceptible to developing post-COVID mucormycosis [21, 26, 27]. Immuno-compromised state in children due to various co-morbidities make them an easy target for COVID-19 in the third wave. Hence adequate measures need to be taken beforehand, not only in India but globally.

Suspecting the same, various states of India have started taking measures in advance by setting up special task forces, issuing guidelines, arranging separate Pediatric patient wards in hospitals for mucormycosis, and obtaining a sufficient number of medicines. There will be more emphasis on regular monitoring of the situation and reinforcing education about its spread and prevention amongst the general public. These essential measures might prevent a further rise in the number of mucormycosis cases in patients with COVID-19 and mortality.

## 5. CONCLUSION

Mucormycosis is a known Post COVID-19 complication; which is affecting adults. Of late in the second wave has started affecting children. The non-availability of vaccines make children more prone to getting infected and increases the risk of mucormycosis. The Central government in co-ordination with various states of India are undertaking measures in advance to be able to control the situation by setting up special task forces and groups, issuing specific guidelines, arranging separate Pediatric patient wards in hospitals for mucormycosis, and obtaining a sufficient number of medicines. There is an urgent need to educate parents regarding the severity of the situation. There is no definitive cure for the disease, till the time, we need to follow proper precautions so that our younger generation stays protected.

## Conflict of interest

None declared

## 6. REFERENCES

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