

VIEWPOINT/ COMMENTARY



The Mucor Mycosis Epidemic: A Call for Heightened Surveillance of Pregnant COVID-19 Women

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Abstract

As India was struggling with the second coronavirus wave, a new epidemic in the form of Mucormycosis came as a challenge all of a sudden. The overburdened health care system suffered a complete set back. At this moment, we cannot forget the vulnerable pregnant population of the country. With India being the capital of gestational diabetes, she stands the greatest risk of suffering the brunt of its aftermath. Prevailing malnutrition, anemia and micronutrient deficiencies which are rampant during pregnancy make the women of low-middle income countries more vulnerable to this fungal epidemic. All efforts must be undertaken to improve antenatal care and strengthen vigilance, detection and treatment of gestational diabetes across the country.

Keywords: COVID-19, Mucor Mycosis, Diabetes Mellitus, MucoCovi

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1 | INTRODUCTION

As India battles the furious second coronavirus wave, it is facing another challenge in the form of surge in mucor mycosis, or “black fungus” in common parlance. This outbreak has scourged an already overtaxed health care system in the country. Mucor mycosis is a rare but aggressive fungal infection caused by molds of mucoraceae family. Though ubiquitous, this invasive fungus mainly infects individuals who are susceptible due to dwindled immunity. Though several cases of mucor mycosis have been increasingly reported

worldwide after the surge of COVID-19 infection, India alone contributed to 82% of the reported cases of mucor mycosis during this pandemic, with 14872 cases reported till late May 28 2021 (1). Intracranial

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and rhino-cerebral involvement increases the fatality rate to as high as 90% (2). Moreover, rapid dissemination of this fungus is proving fatal even in cases where diagnosis is delayed by 12 hours only (3).

It is worth noting that even before the emergence of this explosive outbreak, India was consistently showing an increase in mucor mycosis cases. There is a lack of population based estimates, even hospital reporting majorly coming from a single tertiary center in North India which has shown a steady rise in cases from 24.7 cases per year (1990–2007) to 89 cases per year (2013–2015) (4). The Leading International Fungal Education (LIFE) portal has computed the disease burden to be 140 cases per million people, over 80 times higher than in developed countries (5). So, though the magnitude of the recent devastation is unexpected, the stage was set much before the dawn of the pandemic.

There are epidemiological differences in the predisposing factors amongst Asia and the West. Diabetes mellitus is implicated in over half to $2/3^{rd}$ of the cases in India, with solid organ transplant, and hematological and solid organ malignancies being the major predisposers in USA and Europe.

While long-term use of corticosteroids is known to be a culprit, even short courses of steroids are leading to emergence of this deadly fungal infection during recent times, especially in patients with underlying diabetes (3). The MucoCovi study across 16 centres in India has now established a firm evidence based link between COVID cases, diabetes and steroid use with 62.7 % cases being uncontrolled diabetics and 78.7% having received glucocorticoids as part of COVID management. Newly diagnosed diabetes, diabetic ketoacidosis and inappropriate glucocorticoid use have been especially implicated (6).

In this context, we must not forget the vulnerable pregnant population of our country. With a growing semi-allogenic fetus within, and the altered CD 4+/CD8+ cell ratio obtunding the maternal immune responses, the pregnant women is a ripe target for this emerging infection. We cannot ignore the fact that, with malnutrition, anemia and micronutrient deficiencies rampant during pregnancy in low income countries, pregnant women stand at the highest risk of opportunistic infections, whether they acquire

mild, moderate or severe COVID-19 disease. The CDC in May 2021 added 'pregnancy and recent pregnancy' to list of medical conditions that increase the risk of severe COVID-19 infection, highlighting once again the gravity of the situation (7).

India ranks second in Diabetes mellitus with a prevalence of 8.9% population and a projected estimate of more than 100 million diabetics in 2030, second only to China (8). In parallel with the increase in diabetes, reporting trends indicate that the prevalence of GDM is also on a steep rise. The available statistics are highly variable due to the heterogeneity of diagnostic criteria and the absence of a national program for GDM surveillance. Reported prevalence ranges from 0% to 41.2%, with the only meta-analysis conducted to-date deriving a pooled prevalence estimate of 8.8% (9). Simply put, at any point of time, it is estimated that about 4 million women are affected by GDM in India (10). Hyperglycemia and ketoacidosis impede the ability of ferritin and transferrin to chelate free iron. The IL-6 rise, endothelialitis and lymphopenia in COVID infections also indirectly elevate free iron in blood. This abundance of free iron, in turn, promotes the germination of mucor spores. It is therefore the need of the hour to implement effective strategies to prevent, timely diagnose and effectively manage GDM, especially in these troubled times, with a third wave expected to hit us in the near future. Each of the first two corona virus waves has affected a different demographic, and with widely different severity. Pregnant women could be next in line!

Treatment of fungal infections including mucor mycosis in pregnancy remains a challenge. It requires a multidisciplinary care which is currently unachievable in a significant part of the country. There are gestation specific challenges such as the effect of the disease on the developing fetus, the risk of fetal exposure with antifungals and altered drug pharmacokinetics due to the physiological changes in pregnancy.

Owing to the extremely limited data regarding safety of intravenous antifungal use in pregnancy, obstetricians will stand at a dilemma if a COVID recovered antenatal lady presents with mucor mycosis. Fortunately, Amphotericin B, which is the first line

treatment for mucor mycosis (along with surgical debridement if needed), is classified as Category B by the US-FDA with sufficient information available to support its safety in pregnancy (11). It is notorious for nephrotoxicity (the incidence being similar in pregnant and non-pregnant women), which can be countered by lipid formulations, though, their safety is not well studied (11).

After the carnage of the second peak, we cannot afford to suffer another devastating blow. It will be, therefore, prudent to ramp up our preparedness in anticipation of the projected third wave. During this time of acute crisis, few important strategies can help us tread the path ahead with greater success and protect the vulnerable pregnant population of our country:

1. Pregnancy must be a call for extra caution and double protection to COVID-19 infection. Displaying COVID appropriate behavior with maintenance of physical distancing, hand and respiratory hygiene, and wearing mask covering the nose and face remains the primary mode of preventing infection.
2. Additionally, multiple national and international obstetric societies are advocating for approving COVID-19 vaccination for pregnant women with appropriate counselling
3. Healthy and balanced nutritious diet shall help in boosting the body's immunity to combat fungal colonization.
4. Avoiding high glycemic index carbohydrate rich diets during pregnancy can reduce rapid surge in blood glucose after meals.
5. Mild to moderate aerobic exercises and yoga during pregnancy will definitely reduce insulin resistance, thereby decreasing susceptibility to GDM
6. More robust national surveillance mechanisms to better understand disease burden and epidemiology of GDM, opportunistic fungal infections such as Mucor.

7. A uniform mandatory national GDM screening and diagnosis program must be set in place
8. Avoiding indiscriminate use of steroids in moderate to severe COVID-19 infected pregnant women
9. Timely diagnosis and prompt initiation of antifungals in affected population
10. Ensuring adequate supply of antifungals and appropriate training of health personnel in their use.

Looking at this rapid surge in cases, various national and international bodies must discuss and formulate best practice guidelines for management of mucor mycosis in antenatal period. Although there are no reported cases of mucor mycosis complicating COVID-19 infected pregnancy till date, yet pregnant COVID population must take extra precautions to boost their immunity against opportunistic infections. All efforts must be undertaken to maintain euglycemia throughout pregnancy. Overuse of corticosteroids must be checked. Healthcare resources are meagre at this moment. Increasing awareness among public is the only remedy that can save healthcare systems of resource limited countries like India from being pushed to the brink of collapse.

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