The Physician
Journal of The British Association of Physicians of Indian Origin

Key Factors Fuelling India's COVID Second Surge

Abstract

Having declared in autumn of 2020, that India had defeated Coronavirus, the steep rise of cases in April-May 2021, caught the authorities unawares. The health care infrastructure was rapidly overwhelmed at every level and equally in the national capital, large and small cities and the vast rural populace. The human catastrophe that was unfolding in front of the digitally connected world was heart-breaking.

The natural ingredients of a battered economy (-23.9% GDP), a large populace (1.34 billion), poor public health, chronic epidemic of disease such as Tuberculosis, diabetes, hypertension or kidney disease, chronic underfunding of healthcare infrastructure (1.8% of GDP), deficiency of healthcare workforce (estimated deficit of 600,000 doctors and 2 million nurses) and disjointed, disordered leadership combined with an incoherent, incohesive healthcare policy led to the disaster.

After relative stabilisation from the first few weeks of the impact of colossal lack of hospital beds, oxygen, supported ventilation, life-saving drugs, safe and dignified disposal of the dead, and any form of coordinated disaster response, there is now the new epidemic of the black fungus. This editorial explores the emergence of this new health challenge for India and issues a call to rally.

Keywords
COVID-19 pandemic; India; mucormycosis; diabetes mellitus;

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Cite as: Chakravorty, I. (2021) Key factors fuelling India's COVID second surge. The Physician Vol 7: Issue 1: epub 23.5.21 DOI https://doi.org/10.38192/1.7.1.9

India faced its second surge of COVID-19 in the spring of 2021. In the third week of May 2021, India crossed 26 million cases and over 300,000 officially recorded deaths, thus reaching third in the world ranking of countries with the largest number of deaths, following USA (>600,000) and Brazil (nearly 450,000). At 218 deaths per million population, India still ranked 108th in the world, while Hungary moved to number one with over 3000. [1] By some estimates, India's real death rate is expected to be 5-10x higher. It is believed that this second surge has been fuelled by the increased transmissibility and virulence of the B.1.617+ variant of SARS-Cov-2. [2]

B.1.617.2 has become the most common variant reported in India. However, the situation varies from state to state. Other variants including B.1.1.7, the P.1 variant first detected in Brazil, and the B.1.351 variant that evolved in South Africa, have also played a part

Article Information
Submitted 22.5.21
Published 23.5.21

ISSN 2732-513X (Print)
ISSN 2732 - 5148 (Online)

in the second wave in India. Some B.1.617.1 viruses have an additional mutation called V382L in the spike protein. This is what is meant by the term “triple mutant”. This mutation has also been found elsewhere, and there is no evidence that these “triple mutant” viruses spread more readily or are deadlier.

Figure showing the worldwide distribution of the B.1.617+ hCOV19 viral variants in May 2021 [3]

Mucormycosis

India was caught unawares. In the same week, there is news of a precipitous drop in vaccination rates and recognition of a new complication of ‘Black fungal’ infection amongst COVID-19 patients in several states. Mucormycosis is an angioinvasive disease caused by saprophytic fungi of the order Mucorales, which are ubiquitous and found in soil, plants, decaying fruits and vegetables and manure. Though Rhizopus arrhizus is the most common etiological agent of mucormycosis in this country, infections due to Rhizopus microsporus, Rhizopus homothallicus, and Apophysomyces variabilis are rising. Occasionally, Saksenaea erythrospora, Mucor irregularis, and Thamnostylum lucknowense are isolated.

Mucormycosis is rare, but the exact number of cases is difficult to determine because no national surveillance exists. Population-based incidence estimates for mucormycosis obtained from laboratory surveillance in the San Francisco Bay Area in the USA during 1992–1993 suggested a yearly rate of 1.7 cases per 1 million population. [4] The exact incidence of mucormycosis in India is unknown due to the lack of population-based studies. The estimated prevalence of mucormycosis is around 70 times higher in India than that in global data. [5,6]

As well as having a detrimental impact on the sinuses, it has the capacity to invade the brain and the lungs, and is potentially life-threatening for individuals with underlying health conditions. The disease is being reported at an alarming frequency over the past decades from India with predominant features of rhino-orbito-cerebral presentation associated with uncontrolled diabetes. Isolated renal mucormycosis has emerged as a new clinical entity.

Although diabetes mellitus is the most common risk factor, haematological malignancy and solid-organ transplant are also potential risks, as is scarring from pulmonary tuberculosis and chronic kidney disease. Trauma is a risk factor for cutaneous mucormycosis. Isolated renal mucormycosis in an immunocompetent host is a

unique entity in India. [6] Although most cases are sporadic, outbreaks of mucormycosis are known to have occurred.[7]

In healthcare settings, it can be difficult to determine whether mucormycosis is healthcare-associated or whether the infections were acquired somewhere else. Some examples of sources implicated in healthcare-associated mucormycosis outbreaks include adhesive bandages, wooden tongue depressors, hospital linens, negative pressure rooms, water leaks, poor air filtration, non-sterile medical devices, and building construction. Community-onset outbreaks have been associated with trauma sustained during natural disasters. [8]

Mucormycosis is frequently a life-threatening infection with an overall all-cause mortality rate of 54%, which can vary depending on underlying patient condition, type of fungus, and body site affected. [9] The overall mortality rate was 47% but was observed to be significantly higher in north Indian patients (51%) compared to 32% in south India. Mortality was higher in patients with gastrointestinal (94%, OR: 9.58) and pulmonary (77%, OR: 2.44) mucormycosis. [10]

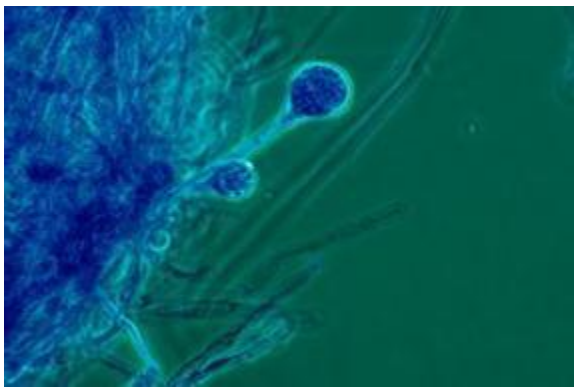

Figure illustrating microscopy of mucormycosis [11]

In the latest outbreak from India, the major risk factors include uncontrolled diabetes (97%) and COVID-19 positivity (61%), with concomitant steroid use in 61% patients. [12,13] Upon the background lung pathology, immune dysfunction and corticosteroid therapy, patients with severe viral pneumonia are likely to develop invasive fungal infections further augmented by steroid induced immunosuppression and hyperglycaemia. [14] Yet, corticosteroids are the only therapy which has been shown to improve symptoms, oxygenation and mortality in COVID-19. Although clinical observational studies reported the improvement in symptoms and oxygenation for individuals with severe COVID-19 who received corticosteroid therapy, case fatality rate in the corticosteroid group was significantly higher than that in the non-corticosteroid group (16% versus 4%).[15]

Rapid consensus guidelines from Vancheeswaran et. al. in this edition recommends corticosteroids (dexamethasone, methylprednisolone and hydrocortisone) in COVID-19 patients with hypoxia.[16] These recommendations are based on the findings from the RECOVERY and REMAP-CAP studies showing survival benefits. [17–19] In the RECOVERY trial, among patients randomised to the dexamethasone group, the incidence of death was lower than that in the usual care group among patients receiving invasive mechanical ventilation (29.3% vs. 41.4%; rate ratio, 0.64; 95% CI, 0.51 to 0.81) and among those receiving oxygen without invasive mechanical ventilation (23.3% vs. 26.2%; rate ratio, 0.82; 95% CI, 0.72 to 0.94) but was probably higher or no different among those who were receiving no respiratory support at randomization (17.8% vs. 14.0%; rate ratio, 1.19; 95% CI, 0.92 to 1.55). [20]

The mortality rate was high when patients with COVID-19 and concurrent mucormycosis were treated with surgery alone (61%) or amphotericin B alone (54%). Patients who were managed with a combination of surgical

debridement and amphotericin B therapy had significantly lower mortality (32%). [10] An average duration of liposomal Amphotericin B treatment can last between 14-21 days, with the cost of therapy being out-of-reach for the majority of patients in resource poor countries, further complicated by the lack of availability. [21]

Diabetes mellitus

Globally, India has the second largest number of people with diabetes. Diabetic patients have poor immune responses to infections such as bacterial, viral, parasitic, and mycotic infections compared to non-diabetic patients.[22] In the present situation of pandemic, managing diabetes is challenging. The twin enemies of uncontrolled hyperglycemia and unwanted hypoglycaemia pose an ethical dilemma during the decision-making process of diabetic management. [23] Furthermore, COVID-19 has been implicated in the development of new-onset diabetes mellitus, both during the acute phase of infection or during the post-acute COVID-19 phase both in the UK [24] and in India. [25]

With an unfavourable support system against this public health threat, diabetic patients having COVID-19 infection should follow normal course of antihypertensive and antidiabetic drugs prescribed with the exception of sodium glucose cotransporter-2 inhibitors which may increase the risk of dehydration and ketoacidosis.[26]

A cornerstone of management of type 2 diabetes mellitus includes optimum weight management [27] and regular physical activity.[28] Physically active (PA) people have less severe symptoms, shorter recovery times, and are less likely to infect others, besides developing better immunity after an anticipated vaccination and minimize future complications. There are many creative ways to be physically active that do not require specialized technology and equipment. PA guidelines suggest that to decrease sedentary time, adults with type 2 diabetes should interrupt prolonged sitting with bouts of light activity every 30 min. However, the above recommendations are additional to, and not a replacement for structured exercise that include at least 150min/week of combined aerobic and resistance exercise training. Metabolism and immunity are inextricably interwoven since the metabolic state is a critical determinant of immune function. Hence, enhanced public awareness and encouragement for adoption of every practical measure to reinforce public health is critical for glycaemic control and reducing the risk of poor COVID-19 outcomes.[29]

Conclusion

The second surge of COVID-19 pandemic was fuelled in India by all counts, due to a lack of public health infection control measures, the acceptance by the authorities of large religious gatherings, the elections in several states and the emergence of B.1.617 variant. The simmerring firewood of a weakened economy, a legacy of chronic underfunding of public health infrastructure, the lack of coherent and cohesive health policy uniting all the states, poor leadership and lack of public guidance combined with poor general health of the nation (especially diabetes, hypertension and kidney disease) just needed kindling. The final nail in the coffin was the botched vaccine plan, where there was no forward investment, ordering, securing of supplies and no plan to distribute vaccines to all. Even now, the fiasco of individual states paying a premium, tendering from across the world and no clear guidance on cost of vaccination to the individual citizen appears to be utterly short sighted.

The crisis that ensued from April to May 2021, left a whole world and the vast Indian diaspora reeling in disbelief. The rallying of support for India was phenomenal. After recovery from the crisis of lack of hospital beds, oxygen, supported or mechanical ventilation and appropriate medication, India is now facing the double whammy of diabetes, and mucormycosis in COVID-19 patients. Add to this colossal misinformation, lack of a united leadership or strategy is leaving India reeling on the edge of a precipice. Public health experts estimate that the death toll will cross a million. What will be left of the devastated survivors, the non-existent public health infrastructure, demoralised health workers, a mountain of non-COVID disease that has been neglected, a

resurgence of Tuberculosis and a net negative 8% Gross Domestic Product [30] is likely to leave India in an unimaginable state of social and economic depression for decades to come.

This is the time for Indian intelligentsia [31] - intellectuals who are an essential component of an open society who bring their analytical insights to not only scrutinise the society in its immediate form but also help shape the ideas and ideologies of the future. They need to conduct research, deploy critical thinking, reason, teach, author books, challenge dogma and equip us with cognitive tools to engage with the world for the greater human good. India has a rich and ancient tradition of producing such thinkers, teachers and philosophers who have contributed to the creation of new schools of thought that have travelled and established themselves far beyond Indian shores too. [32] Members of the Indian diaspora from across the world need to rally together, drop fundamental differences of caste, creed, colour, religion and unite under the tricolour. A nation of 1.3 billion people cannot be left to crumble. The phoenix must rise again.

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