

isolation precaution for immunocompromised patient is being considered. After discontinuation of isolation precautions, HCP use standard precautions in the general medical units when caring for COVID-19 patients. HCP are prospectively followed for the development of COVID-19 symptoms and an RT-PCR for SARS-CoV-2 is performed if COVID-19 symptoms develop. Transmission-based precautions (eg, contact precautions for multidrug-resistant pathogens) are also used, if indicated.

Prior to the initiation of the discontinuation of isolation precaution policy, we performed a workshop to share the evidence base for the policy and the elements of the policy with nursing staff throughout the general medical units. Then we collected data including HCP and patient demographics, underlying disease data, classification of COVID-19 severity,⁵ immunocompromised status among COVID-19 patients, development of COVID-19 symptoms in HCP over 2 weeks after the end of patient care, evidence of SARS-CoV-2 RT-PCR among HCP (if performed), as well as complaints and barriers reported by HCP after the policy was implemented.

From April 1, 2021, to July 4, 2021, 25 COVID-19 patients were admitted to the general medical units and 69 HCP were involved in the care of COVID-19 patients. The median age of these HCP was 32 years (range, 22–49 years), and 59 (86%) of these 69 HCP had no underlying disease(s). For these 25 COVID-19 patients, the median age was 59 years (range, 24–79); 15 patients (60%) were female; their median body mass index was 28 kg/m² (range, 24–32), and 23 (92%) had underlying disease(s). Also, 15 patients (60%) received ICU care: 13 of these were classified as severely ill and 2 were immunocompromised. Furthermore, 10 patients (40%) were considered moderately ill and received care in a general medical unit. None of the patients had test-based clearance prior to discontinuation of isolation precaution. HCP and patients demographics are summarized in Table 1. During the follow-up period, none of the HCP reported COVID-19 symptoms or had a SARS-CoV-2 RT-PCR performed. Finally, 2 severely ill COVID-19 patients (8%) died from sepsis with multiorgan failure in the ICU. HCP reported no significant complaints or limitations in the care of COVID-19 patients in the ICU and in general medical units throughout the hospital during this period.

In this study, a time-based policy for discontinuation of COVID-19 isolation precautions for infected patients in COVID-19 ICUs and general medical units was feasible and safe for HCP who cared for these patients. Such policies have become important because increasing COVID-19 cases that require acute care may exceed

the maximum hospital capacity to care for these patients in COVID-19 units. In addition, once the policy was established, no significant barriers arose and no resistance to this policy by HCP occurred. Notably, although patients in our cohort were obese, had underlying diseases, and were mostly classified as severely ill or immunocompromised, none of our cases had repeat SARS-CoV-2 RT-PCR tests to help guide discontinuation of isolation precautions. Our data support the recommendation by the US Centers for Disease Control and Prevention to avoid test-based clearance, given that persistently PCR-positive patients are not contagious.^{1–4} A limitation of our study is that we cannot exclude the possibility of asymptomatic infections in our HCP because routine SARS-CoV-2 testing was not performed. However, because we have no evidence of an outbreak of COVID-19 among our HCP, we believe that the time-based strategy of discontinuation of COVID-19 precautions was both effective and safe. Additional studies with larger sample sizes, from various settings, and with various COVID-19 strains are needed to reassure the feasibility and safety of such policies in acute-care facilities across all continents.

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A look into the relationship between outdated coronavirus disease 2019 (COVID-19) treatment protocols and the overwhelming rise of mucormycosis in COVID-19 patients in India

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To the Editor—India, the second most-affected country by coronavirus disease 2019 (COVID-19), recorded one of the worst second waves across the world, with >400,000 daily cases reported in early

May 2021.¹ In addition, the second wave brought with it a dramatic increase in mucormycosis cases amongst recovering and active COVID-19 patients. A recent update shows that by June 2021 India had recorded >40,000 mucormycosis cases, of whom 35,000 suffered from COVID-19.²

Mucormycosis is a rare but serious angioinvasive condition caused by a group of ubiquitous fungi called *Mucormycetes*,³ and it mainly affects immunocompromised individuals. Mucormycosis has an aggressive nature, requiring early diagnosis and treatment. India, often called the global capital of mucormycosis, had an estimated prevalence 70 times higher than the global average⁴ even prior to the COVID-19 pandemic. However, with the arrival of the second wave, India recorded an unprecedented rise in mucormycosis cases among COVID-19 patients, far exceeding the global national average. On July 14, 2021, the number of mucormycosis cases exceeded that of active COVID-19 cases in Delhi, the nation's capital.⁵

Although an official treatment protocol for COVID-19 was published by the Indian Council of Medical Research, protocols among different states varied greatly, with certain states adopting different treatment guidelines. For example, the treatment guidelines published by the Health and Family welfare of the state of Tamil Nadu⁶ included drugs such as azithromycin and zinc for mild COVID-19 cases, despite low certainty of evidence. These medications were absent from the treatment protocol published by the Indian Council of Medical Research.

Despite official treatment protocols using evidence-based therapies, doctors across the country have typically prescribed a cocktail of medications in high doses including azithromycin, doxycycline, vitamin C, vitamin D, zinc, and inhaled budesonide/dexamethasone,⁷ despite the lack of available evidence-based research for some of these medications. This trend of blanket treatment, coupled with the rising incidence of self-medication, due to the wide availability of these medications and poor regulation of prescription-based drugs, may have played a large part in the rise of mucormycosis cases.

Among the different medications prescribed by healthcare professionals, great attention has been given to zinc as a contributory factor in the rise of mucormycosis cases. Zinc has typically been prescribed to patients in India in high doses of 50 mg for a course of 5 days or more.⁶ Although there is no evidence of a direct relationship between zinc and mucormycosis, Staats et al⁸ describe the importance of zinc in the fungal metabolism, observing that zinc starvation places increased stress on fungal development by interfering with zinc-binding proteins that act as transcription factors. Furthermore, Leonardelli et al⁹ described the increased efficacy of amphotericin B and posaconazole against mucormycosis when paired with zinc chelators, thereby demonstrating the vital role of zinc in the growth and development of *Mucormycetes*.

Several experts have questioned the use of antibiotics, such as azithromycin, which is prescribed in India in doses of 500 mg, thrice daily for 3 days for the treatment of even mildly ill COVID-19 patients.⁶ Antibiotics offer little to no benefit and may even be counterproductive. Also, undue use of antibiotics may disturb the normal commensals that would otherwise protect from opportunistic infections such as mucormycosis. A randomized control trial by the RECOVERY collaborative group¹⁰ studied the use of azithromycin in COVID-19 patients across 176 hospitals in the United Kingdom and determined that azithromycin did not improve survival in COVID-19 patients. In addition, the use of such antibiotics has also been questioned by

Dr V.P. Pandey, who studied 210 COVID-19 patients with mucormycosis at MGM Medical College in Indore, India.¹¹ Antibiotics had been used by 100% of the patients.

Perhaps, the most important factor contributing to the rise of COVID-19-associated mucormycosis in India is the nonchalant use of steroids, even across the mildest cases of COVID-19. Glucocorticoid induced hyperglycemia and immunosuppression, together with COVID-19-induced hyperglycemia, lymphopenia, and immune dysregulation (causing decreased T lymphocytes, CD4+ and CD8+ T cells),¹² create a favorable environment for the growth of *Mucormycetes*. These factors are enhanced by the increased use of steroids in large doses, even across the mildest COVID-19 cases, due their easy over the counter availability in India. Furthermore, the current Indian guidelines regarding steroid use advise 0.5–1 mg/kg/day of methylprednisolone in moderate cases and 1–2 mg/kg/day in severe cases of COVID-19. This dosage is far higher than the recommendation by the National Institute of Health, which is 6 mg/day for a maximum of 10 days and only for those on assistive ventilation or supplemental oxygen therapy.¹²

Steam inhalation and the use of nebulizers are also suspected to be contributory agents to the rise in COVID-19-associated mucormycosis cases, due to poor quality of water and unsterilized equipment used in such procedures. Such procedures can facilitate the transport of fungal spores into the respiratory tract via inhalation, where the spores can develop. Furthermore, steam inhalation can also cause scald injuries¹³ to the respiratory tract, thereby reducing the efficacy of local immune responses, which in turn facilitates the development of foreign pathogens. However, despite advisories against steam inhalation due to lack of evidence citing its benefits, it has been used widely as routine treatment across Indian households.

Hence, COVID-19 treatment guidelines need to be updated, and uniform compliance of these guidelines needs to be ensured across the country to prevent dire complications such as mucormycosis. This is especially important in a country like India, where resources are scarce and life-saving medications for mucormycosis, such as amphotericin B, have been in very short supply in recent months and the cost of such therapies far exceeds the affordability of the common man in India.¹⁴

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Coronavirus disease 2019 (COVID-19) is a healthcare dilemma for human immunodeficiency virus (HIV)–positive individuals in Pakistan

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To the Editor—Coronavirus disease 2019 (COVID-19) has been spreading worldwide since the first case was reported in Wuhan, China, in early December 2019. The outbreak was declared a pandemic by the World Health Organization (WHO) on March 12, 2020. On February 26, 2020, the Ministry of Health, Government of Pakistan, confirmed the first case of COVID-19 in Karachi.¹

According to the Centers for Disease Control and Prevention (CDC), a syndemic is defined as “synergistically interacting epidemics,” that is, 2 or more concurrent or sequential epidemics or disease clusters in a community, which exacerbates the prognosis and burden of disease. Although the Asia and the Pacific region has 5.8 million human immunodeficiency virus (HIV)–positive patients and the coronavirus disease 2019 (COVID-19) pandemic has spread across Asia and the Pacific region, limited data are available on infection among HIV-positive patients. The acquired immunodeficiency syndrome (AIDS) caused by HIV has become a severe public health issue worldwide, particularly in underdeveloped nations. Approximately 37.8 million people are living with HIV, and in 2020, ~680,000 people died from AIDS-related illnesses globally. In Pakistan, ~200,000 individuals are infected with HIV.² The Joint United Nations Program on HIV/AIDS (UNAIDS) is in charge of the global campaign to eradicate AIDS as a public health hazard by 2030. A new report from the

Global HIV Prevention Coalition, which summarizes the state of HIV prevention programs during the COVID-19 pandemic, highlights significant vulnerabilities, dangers, and severe service interruptions. However, HIV service improvements and adjustments are achievable.³

The UNAIDS Global AIDS program provides evidence that HIV-positive persons are more vulnerable to COVID-19, which can be prevented by getting COVID-19 vaccination and HIV treatment. The new report details how lockdowns due to COVID-19 and other restrictions have severely hampered HIV testing, resulting in sharp reductions in HIV diagnoses, care providers, and treatment initiations in several countries.⁴ The UNAIDS Deputy Executive Director for Programs Shannon Hader stated that COVID-19 has disproportionately affected HIV prevention programs and cultural obstacles for the individuals most left behind, such as critical populations, teenaged girls, and young women.³

Despite a global decline in the number of new HIV infections, Pakistan is seeing an increase in the number of HIV cases.⁵ Pakistan has had several HIV outbreaks since 2003, making it Asia’s second fastest-rising HIV nation.⁶ A variety of socioeconomic factors, such as poverty, illiteracy, and unemployment, likely contribute to HIV transmission in Pakistan.⁷ Also, HIV infection involves male sex workers (MSWs) rather than female sex workers, which indicates the variation in regional sex practices in Pakistan. AIDS infections among intravenous drug users (IDUs) are also increasing; IDUs are a potential source of HIV transmission because users share drugs and needles and can pass the virus on to sexual partners, resulting in HIV replication. Pakistan appears to be following the “Asian Epidemic” model as a result.^{7,8}

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