

Mucormycosis in COVID-19: Is Zinc a Silent Killer in India?

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The second wave of coronavirus disease 2019 (COVID-19) in India has hit the country hard with over 6.6 million people infected just in the month of April 2021.¹ Recently, a particular concern in COVID-19-affected patients has been the rising incidence of mucormycosis.²

The estimated prevalence of mucormycosis in India is around 70 times higher than the rest of the world. Diabetes mellitus is the most common risk factor, followed by hematological malignancy and solid organ transplant.³ The immune dysregulation due to reduced numbers of T lymphocytes, CD4+T, and CD8+T cells in COVID-19 may alter the innate immunity that facilitates opportunistic fungal growth in these patients. The recent surge in cases of mucormycosis has been linked to rampant usage of corticosteroids, hyperglycemia, broad-spectrum antibiotics, and monoclonal antibodies on a background of an already suppressed immune system in these patients.⁴ However, one particular factor that has been commonly overlooked is the uncontrolled and unmonitored use of zinc in COVID-19. Zinc, which was initially thought to be helpful in the prevention and treatment of COVID-19 owing to the hypothesized antiviral activity, was later found to be ineffective for the same.⁵ Long-term use of large doses of zinc has concerns of serious adverse effects like copper deficiency and neurological deficits, and major guidelines have recommended against the use of zinc in doses above its recommended dietary allowance for the treatment of COVID-19.⁶ However, many regional guidelines in India continue to include high dose zinc as a common treatment across several categories of COVID-19.^{7,8} Zinc being available as an over the counter medication has facilitated general population to consume it in large quantity with hope of protection against COVID-19 due to widespread circulation of such guidelines through social media.

Zinc is known as a common growth factor for different pathological fungi, including Mucorales.⁹ Zinc influences diverse mechanisms of fungal pathogenesis by directly regulating fungal proteins required to infect mammalian hosts.¹⁰ Zinc deprivation by the host is an important antifungal mechanism,¹¹ and zinc chelators have been shown to inhibit different fungal growth, including Mucorales, both *in vitro* and *in vivo*.^{12,13} It is possible that the excess availability of zinc in the body owing to its incessant use by COVID-19 patients might be adding to the risk of fungal infections like mucormycosis in these patients.

To determine whether Zinc has a constant and significant association with mucormycosis in COVID-19-affected patients, further studies are needed. But since zinc is a definite facilitator of fungal infection, in the absence of its clear-cut benefit against the COVID-19 disease, authorities and expert panels in India should read out words of caution and raise awareness against rampant usage of high

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doses of zinc and should exercise measures to prevent uncontrolled availability of zinc tablets over-the-counter in the country.

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