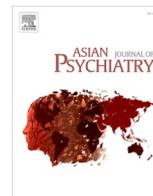




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Letter to the Editor

Fight COVID-19 depression with immunity booster: Curcumin for psychoneuroimmunomodulation



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Dear Editor,

Beyond infection, the COVID-19 pandemic has affected individuals through associated anxiety and stress and caused a collateral damage (Tandon, 2020). Real and perceived fear of infection and distorted daily activities invites psychiatric illness including depression (Banerjee and Viswanath, 2020; Kumar and Somani, 2020; Tandon, 2020). Void for specific therapeutic measures also contributed to this psychotic illness. A 'tsunami of psychiatric illness' will follow as predicted by various organizations and imminent experts (Tandon, 2020). Therefore, attention towards this mental health crisis approaching worldwide is necessary (Tandon, 2020). Along with preventive measures, incorporating 'immunity boosters', including established food ingredients/herbs, are advised. Recently, uncovering the potential of Ayurveda was exigencies to combat COVID-19 outbreaks through modulation of psychoneuro-immune (PNI) response (Rajkumar, 2020). Curcumin is the bioactive component of turmeric, one of the key ingredients of prescribed ayurvedic interventions and spices used in meal preparation in South-East Asia (Rajkumar, 2020; Vishvakarma, 2014). Therefore, critical evaluation of the psychopharmacological potential of turmeric in COVID-19-pandemic-associated psychosomatic disorders is warranted.

The inter-dependent nature of immunity and psychological state is established and decides the outcome of disorders. An immune response can be largely affected by mental well-being, and depression can negatively affect its outcome (Rajkumar, 2020; Zalachoras et al., 2020). Targeting either one of depression or immunity may face insufficiency; dual-acting drug hold promise to improve health amid COVID-19 pandemic. Known for immunoboosting aptitude, curcumin can alleviate the COVID-19 associated ill-effects including cytokine storm (Liu and Ying, 2020). Alleviating psychological stress by curcumin will also adjunct its immunoboosting potential.

Curcumin can avert the anxiety and the stress-driven manifestation of depression through modulation of the monoaminergic troupe (dopamine, glutamate, serotonin, and noradrenaline) by curcumin (Zalachoras et al., 2020). Depression-disorders in COVID-19 prevention measures-driven social distort are possibly brought by oxidative stress (Rajkumar, 2020). Curcumin, through Nuclear factor erythroid-2-related factor 2 (Nrf2), can prevent such stress and improve antioxidant Glutathione (GSH) production (Zalachoras et al., 2020).

GSH prevents the physiological damage to brain cells during stress. Nrf2 also balances the tone of the immune response (Lopresti and Drummond, 2017; Zalachoras et al., 2020). Major depression disorders (MDD) associate with disturbances in the hypothalamus-pituitary-adrenal (HPA) axis. Curcumin can correct the HPA disturbances and avert elevated glucocorticoids, their receptor as well as inducers (cortisone and adrenocorticotropic hormone) (Lopresti and Drummond, 2017).

Along with evident immunomodulator, turmeric component, especially curcumin exhibit antidepressant activity, and improve cognitive/mood function (Lopresti and Drummond, 2017). The potential of curcumin containing nutraceutical in COVID-19 has been predicted both through PNI modulation and 'meaning response' (Rajkumar, 2020). Moreover, curcumin can alleviate the overt inflammatory consequences (Vishvakarma, 2014; Soni et al., 2020), even those associated with COVID-19 (Liu and Ying, 2020), and thus will improve physical well-being. Ayurvedic utilization of turmeric as a concoction, spices and/or golden milk (turmeric in warm milk) provide PNI benefits through alleviated anxiety/depression (Rajkumar, 2020) along with modulation of neurotransmission (through monoamine and gamma-aminobutyric acid) (Zalachoras et al., 2020). Reports indicate the onset of post-traumatic stress disorder (PTSD) in COVID-19 home quarantined healthy individuals. Chronic stress elevates pro-inflammatory cytokines (IL-1, IL-6, TNF- α) which triggers the production of catabolites of tryptophan (TRYCATs) through stimulation of indolamine-2,3-dioxygenase (Naguy and Sabir, 2020). TRYCATs have anxiogenic and depressogenic outcomes through excitotoxicity and neuroprogression (Naguy and Sabir, 2020). In the COVID-19 pandemic, this has created an anxiety-immune-neuropsychiatric-immune loop of health deterioration (Banerjee and Viswanath, 2020). Attempts are being made to better understand the mental health consequences of COVID-19 to promote health and maintain sanity (Tandon, 2020). Curcumin ameliorates inflammation and its regulators like STAT3 in a variety of disorders including COVID-19 (Liu and Ying, 2020; Soni et al., 2020); thus may improve MDD through PNI modulation. High proinflammatory cytokines in MDD individuals wreck the hematopoiesis and weaken the immunity. Diminished immune cell differentiation in COVID-19 patients has also been reported. Curcumin can improve the hematopoietic differentiation of immune cells (Vishvakarma, 2014); and

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thus can mitigate ill effects even through reinstating immune cells number. Moreover, curcumin improves neurogenesis and hippocampus functioning (Rajkumar, 2020; Zalachoras et al., 2020). Curcumin-mediated immunoboosting (Vishvakarma, 2014; Soni et al., 2020), antidepressant effect, and neurogenesis (Zalachoras et al., 2020; Lopresti and Drummond, 2017) may also improve the mood function and ward off anxiety/stress in a covert manner.

Nutraceuticals like curcumin can be a promising option as immunity boosters and antidepressants for PNI response. Traditionally used in medicinal practices, clinical safety of turmeric (and curcumin) is well assessed. Moreover, relative low case fatality rates (CFR) of COVID-19 in South-Asian countries like India are being recorded which can be governed by several factors, including diet and traditional medicine practice.

Although the novel nature of the COVID-19 pandemic makes the efficacy of previously known drugs anonymous, ascertaining the true potential of curcumin through preclinical and clinical investigations will be of immense benefit. Immunoboosting as well as improvement of psychological well-being by curcumin; thus can be hypothesized to facilitate improvement in infected patients, health care workers as well as distantly affected individuals. Psychoneuroimmunomodulation by curcumin, even as an adjuvant, can aid the fight against COVID-19.

Authors' contribution

DS, SK and NKV conceived the idea; VKS and AM compiled the literature; VKS, AM, DS and NKV wrote the manuscript; DS, SK and NKV reviewed the manuscript; all authors have approved the final version of manuscript.

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Declaration of Competing Interest

The authors report no declarations of interest.

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