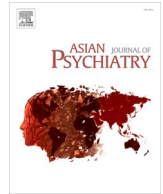




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Letter to the Editor

Finding Horcrux of psychiatric symptoms in COVID-19: Deficiencies of amino acids and vitamin D

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ARTICLE INFO

Keywords

Amino Acids

COVID-19

Neurotransmitters

Psychiatric illness

Vitamin D

Dear Editor

A diverse range of psychiatric complications is involved in patients suffering from COVID-19 (Tandon, 2020). Moreover, psychiatric complications including anxious and depressive disorders are being reported even in those individuals who recovered from COVID-19 (Abrishami et al., 2020). Tandon (2020) has pressed the need for a multidisciplinary approach as a priority to combat ill-effects associated with the COVID-19 pandemic. The world has also been predicted to face a flood of psychiatric illness even in the post-pandemic era (Tandon, 2020). An intervened psychoneuroendocrineimmune (PNEI) response governs the

overall consequences of altered physiological and psychiatric presentation even in COVID-19. (Tandon, 2020; Soni et al., 2020a). Therefore the role of 'physiological spoils' as *raison d'être* for psychiatric sequelae of COVID-19 cannot be overlooked. Physiological offend caused by COVID-19 culminate into gastrointestinal (GI) disturbances; leading to malabsorption. COVID-19 share psychiatric symptoms with Hartnup disorder, a genetic condition with GI expression of defective amino acid transporters (Soni et al., 2020b). The dysfunctional state of angiotensin-converting enzyme-2 (ACE-2), cellular doorway of SARS-CoV-2, downregulates the expression of amino acid transporters.

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Hindered uptake and deficiency of amino acids contribute to multiple psychiatric consequences (Carnegie et al., 2020). Several neurotransmitters including dopamine, epinephrine, gamma-aminobutyric acid (GABA), melatonin, norepinephrine, and serotonin derive from various amino acids (glutamate, glycine, glutamate, phenylalanine, tyrosine, tryptophan, etc); and mental well being is also regulated through metabolic derivatives of amino acids such as tryptophan catabolites (TRYCATs) (Soni et al., 2020b; Carnegie et al., 2020). Deficiencies of amino acids in COVID-19 are expected to modulate physiological as well as psychiatric wellness (Soni et al., 2020b).

Similarly, a significantly lower level of Vitamin D is being invariably reported in COVID-19 patients with severe symptoms (Abrishami et al., 2020). Vitamin D levels have been previously associated with better immunity and mental well being through modulated hematopoiesis and PNEI response (Sarris et al., 2015; Basheer et al., 2017). Reduced outdoor activities and sunlight exposure amid an ongoing pandemic (Tandon, 2020; Abrishami et al., 2020) contributed to a deficiency of this 'sunshine vitamin'. Moreover, a large population in developing and underdeveloped countries already face a low level of vitamin D and associated health consequences (Carnegie et al., 2020; Sarris et al., 2015). Various amino acids and vitamin D serve as precursors and regulators of mental well-being (Carnegie et al., 2020; Basheer et al., 2017). A lower vitamin D level is also associated with neuropsychiatric crises including major depressive disorders (MDD) and Autism (Sarris et al., 2015; Basheer et al., 2017). Moreover, a lower level of serum 25-hydroxyvitamin D has also been linked with psychological distress symptoms in COVID-19 (Di Nicola et al., 2020). Modulation in vitamin D level alters the level of brain serotonin, dopamine, estradiol, etc. Vitamin D stimulates vitamin D receptors (VDR) in CNS; regulates neuronal function. Moreover, proinflammatory cytokines have negative consequences on psychiatric well-being through PNEI response (Soni et al., 2020a); and vitamin D has an inhibitory effect on inflammation (Sarris et al., 2015). The anti-inflammatory effect of vitamin D has been exploited in various pathological conditions including malignancies and cardiovascular disorders. Vitamin D supplementation is expected to provide benefits in the prevention and cure of COVID-19-associated respiratory distress.

To achieve success in the prophylactic and curative treatment of COVID-19, several speculations have surfaced, however, leaving few, most of them are not supported by scientific pieces of evidence. Sahoo et al. (2020) had evaluated several such strategies expected to hold a benefit in COVID-19. Based on known scientific pieces of evidence; Vitamin D was speculated to deliver immunological benefits in COVID-19 (Sahoo et al., 2020). Immunological uphold by Vitamin D will also conjecture to improve the psychiatric well being through PNEI modulation (Tandon, 2020; Soni et al., 2020a).

Collectively, the deficiencies of amino acids and vitamin D can be hypothesized to trigger as well as sustain the psychiatric symptoms in COVID-19. Conditional amino acid supplementation improves the neuropsychiatric state of individuals. Supplementation of Vitamin D has been observed to provide benefits in anxious and depressive disorders including mood disorders and post-traumatic stress disorder (Sarris et al., 2015; Carnegie et al., 2020; Basheer et al., 2017); while few investigations report no benefit in the improvement of psychiatric symptoms (Okereke et al., 2020). Therefore a critical evaluation of the replenishment of these deficiencies for the healing of psychiatric consequences in COVID-19 is warranted. Although, supplementation of micronutrients, precursor amino acids, and vitamins, under supervised medical nutrition therapy (MNT), is speculated to provide neuropsychiatric benefits (Soni et al., 2020b; Sarris et al., 2015; Carnegie et al., 2020); it can also be expected to alleviate the psychiatric manifestations in COVID-19 patients.

Authors' Contribution

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

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of Competing Interest

None.

Acknowledgment

Financial support to AM and YKR [GGU-VRET-Fellowship] and VKS [UGC-SRF] as fellowships are acknowledged. UGC-Special Assistance Program (UGC-SAP) at the Department of Biotechnology (Guru Ghansid Das Vishwavidyalaya) is also acknowledged for necessary facilities in preparation of the manuscript.

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