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CONTENTS

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From the desk of Editor-In-Chief

Post covid complications: Reminiscences of a novel viral infection

Being a novel infection, SARS-Covid 2 infection frequently is accompanied with an incomplete recovery and cure. Post recovery period of covid infection, more frequently, incompletely recovered patients, often show several composite complications like persistent asthenia, cough, fatigue, dyspnea and more importantly, an intellectual deficiency exhibited by compromised memory and the ability to concentrate. Quite expectedly, these clinical complications are often associated with substantial derangement of the pulmonary, cardiovascular, renal, coagulative, and neurological systems and can be detected by their cognate laboratory investigations. As the SARS-CoV-2 enters host cells mainly through angiotensin-converting enzyme 2 (ACE2) and transmembrane protease serine 2 (TMPRSS2) viral receptors on the respiratory tract alveoli, and the same receptors are expressed on several endocrine tissues, namely, the hypothalamus, pituitary, thyroid, adrenal, gonads, and pancreatic islets, it is obvious that covid virus get their entry into these cells in good number and hence makes them vulnerable to post covid conglomeration of the adverse endocrinological symptoms associated to these organs[1]. Hene, endocrine organs become common targets for the SARS-Covid viruses that result in several types of hormonal imbalances in post covid recovery period and the spectrum of these complications extend to almost every endocrine organ system of the body starting from the brain to the gonads.

Hypothalamic and pituitary tissues are the one of the important cell types that have ACE2 receptors and so are natural targets for the SARSCoV-2[2]. Post covid recovery phase in several patients after 3 months of recovery from previous coronaviruses (e.g., SARS-CoV) infections has been found to be complicated by the associated hormonal dysfunctions namely central hypocortisolism (39%) and central hypothyroidism (5%). These complications are reflected by reduced circulating levels of growth hormone (GH), thyroid-stimulating hormone (TSH). A remarkable similarity between the specific amino acid sequences between the SARS-CoV-2 and the ACTH residues potentiate the inactivation of endogenous ACTH by the cross reacting antibodies[3, 4]. Although, the virus cleverly adopts this homology to avoid the immune attack from the host, it leads to a substantial destruction of endogenous ACTH also by an inevitable host immune response against the infecting virus[5]. Furthermore, the immune mediated attack extends to affecting the other parts of hypophysis also[6] resulting in a broad spectrum of pituitary disorders like a marked cortisol deficiency, diabetes insipidus, oxytocin deficiency, GH deficiency and thyroid deficiency in the post covid period. As oxytocin, in its normal concentration, reduces inflammation and oxidative stress reactions by decreasing cytokines released from activated macrophages, a compromised hypophysis predisposes the post covid patients to more severe attacks by immune activated diseases in future. In the same way post covid growth hormone deficiency increases the chance of cardio-metabolic disorders in patients who have been supposed to recover from covid infections.

In another way hyper immune response in covid patients have been found to increase the chances of auto-immune thyroiditis after the SARS-Cov-2 pandemic. The resulting rise in TSH activate the adipocytes to synthesize and secrete more interleukin 6 that further stimulates the systemic inflammation and related complications.

Due to confinement in house or hospitals during the covid 19 infection, the prevalence of vitamin D deficiency (VDD) among COVID-19 patients has been higher in covid patients than the general population[7], particularly in those who had to be hospitalised for prolonged periods with more severe acute respiratory failure[8]. Furthermore, the pandemic-related lifestyle changes, including the compulsorily reduced time spent outdoors and persistent home confinement among the non covid healthy people also increased the chance of VDD in common population significantly. Vitamin D is such a hormone that may modulate immune system function by modulating the activity of activated antigen-presenting cells (APCs), natural killer (NK), T-cell CD4+, and B-cells through the cognate vitamin D receptors. The active form of this vitamin i.e the 1,25 DHCC or calcitriol has been also found to maintain a good balance in immunomodulation by directly inhibiting the development of T helper-1 and 17 cell types and enhancing the T helper 2 type cells along with their differentiation[9, 10]. Furthermore, calcitriol regulates the expression of class II major histocompatibility complex and controls the hyperimmune reactions by buffering the antigen presenting cells' antigen presenting activity to the T cells[11]. In addition, calcitriol has been reported to reduce the synthesis of pro-inflammatory IL-17 and augment the synthesis of anti-inflammatory IL-10 thus regulating the hyperimmune reactions furthermore[12]. All these anti-inflammatory mechanisms of vitamin D are blunted in post covid patients due to decrease in their vitamin D levels which merits a regular check up for blood levels of this vitamins in post covid patients and taking the appropriate measures thereafter.

The SARS-CoV-2 infection also leaves a potential injury mark on the adrenal gland even after recovery as it has been found to cause significant acute fibrinoid necrosis of small vessels and arterioles in adrenal parenchyma, its capsule and its surrounding tissues which together invite apoptotic death of a significant number of adrenal gland cells. The resultant decreased adrenal functions and reduced cortisol and gonodal steroid synthesis have been reported to cause crypto-azoospermia and a decreased sperm count in about 25% of men who had recovered from COVID-19 infection even after 90 days of recovery[13, 14]. Thus, the studies have indicated the chances of substantial decrease in male fertility among covid infected patients for a substantial longer period even after their recovery.

Thus, the effects of covid -19 are going to be long lasting at least in the context of the endocrinological derangements among human population the concept of which automatically heralds the need of regular clinical and laboratory monitoring among post covid patients and to take appropriate measures timely.

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