Diabetes; The Bidirectional Face of COVID-19

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Although COVID-19 hypothetically, is to cause lethal respiratory disease, yet it led to many metabolic co-morbidities including hyperglycemia. New-onset diabetes was observed as one of the more frequent co-morbidities of COVID-19. The subjects, who had developed hyperglycemia with raised HbA1c, neither had previous diabetes nor had a family history of diabetes, with normal levels of HbA1c.

Diabetes, during the COVID-19 pandemic, particularly, type 2 diabetes mellitus, was among the major comorbidities and carried a high-risk factor, showing poor prognosis with COVID-19 infection leading to severe complications including acute respiratory distress syndrome, multi-organ failure, and death. These studies suggested that due to the underlying increased level of inflammation, in the lungs and other tissues, there is an overexpression of receptor ACE2; angiotensin-converting enzyme 2, the entry port of COVID-19, leading to a more aggressive viral attack[1]. New-onset diabetes observed after COVID-19 infection illustrates a bidirectional picture of the virus-disease relationship. This COVID-19 and diabetes bidirectional relationship depicts diabetes as a risk for severe COVID-19 infection and alternatively, confirms a new onset of diabetes in previously non-diabetic patients.

Studies have hypothesized that disruption in glucose homeostasis was maybe due to Cytokine release during COVID-19 infection precipitating in the form of metabolic alterations in patients who did not have a history of diabetes. The abnormalities included insulin resistance, disturbed glycol-metabolic control, and beta cell function.[2] Secondly, (ACE2) receptors are widely expressed in the body and give access to viruses at multiple sites complicating the pathophysiology of pre-existing diseases or disrupting other mechanisms leading to new diseases. Viruses evolve when they come in contact with the human body. Taking the example of HPV which has many genotypes in which HPV 16 and 18 genotypes are oncogenic and cause oral submucous fibrosis (OSF) and oral squamous cell carcinoma (OSCC). Its E6 and E7 oncoproteins enter the human genome and inactivate p53 and pRb, deregulating the cell cycle[3].

COVID-19 enters the host cells by attaching to a variety of receptors including ACE2, it has 4 major proteins including S (spike glycoprotein), N (nucleocapsid protein), M (membrane protein), and E (envelope protein), and some accessory proteins (ORF3, ORF6, ORF7a, ORF7b, ORF8, and ORF9b)[4]. Thus, it can be hypothesized that the COVID-19 genome via its proteins alters the function of genes related to diabetes. Currently, verification data is not available to confirm the action of COVID-19 but it is possible that COVID-19 may have a pleiotropic activity regarding metabolism of glucose. COVID-19 can easily enter the pancreas through the ACE2 receptor. Once inside, COVID-19 may cause polymorphism in genes changing the gene function and modifying the beta cell function, and may facilitate insulin resistance and beta cell hyper-stimulation. To confirm the action of COVID-19 on beta cell function genes related to diabetes are required to be studied in new-onset diabetes after COVID-19 to verify the function of its proteins.

These manifestations of diabetes pose challenges in clinical management and suggest a complex pathophysiology of Covid-19 related diabetes which needs to be checked at a genetic level.

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