



Research Article

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Bidirectional Relationship between COVID-19 and Diabetes

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To Cite This Article: Ahmed M Abbas. Bidirectional Relationship between COVID-19 and Diabetes. 2020 - 9(6). AJBSR.MS.ID.001442. DOI: [10.34297/AJBSR.2020.09.001442](https://doi.org/10.34297/AJBSR.2020.09.001442).

Received: 📅 July 16, 2020; Published: 📅 July 31, 2020

Abstract

In December 2019, novel coronavirus 2019 has appeared in china, eventually spread to other countries. Many studies on COVID-19 have reported its strong relationship with Diabetes Mellitus (DM). It is discovered that not only diabetes is a key risk factor for developing severe COVID-19, but also the virus might trigger DM in some cases. The aim of this review to show the bidirectional relationship between COVID-19 and DM.

Key words: COVID-19, Bidirectional relationship, Diabetes, Diabetes Mellitus, Single-stranded RNA viruses, Ketoacidosis, Hyperosmolarity, Glucose homeostasis, Renin Angiotensin System, Pathophysiological

Introduction

Coronaviruses are enveloped, positive single-stranded RNA viruses widely distributed in humans and animals worldwide [1]. The outbreak of a new coronavirus, termed officially by the World Health Organization (WHO) coronavirus disease-2019 (COVID-19) and the international committee on taxonomy of viruses has suggested SARS-CoV-2 as the name of the virus that causes COVID-19. There is many cases and deaths especially from its first identifications in Wuhan, china, in December 2019 [2-4]. Because of this continuous increase in numbers, COVID-19 has become the focus of attention of many scientists and researchers. Through the studies done on the cases of COVID-19, it was found that Diabetes Mellitus (DM) is not only a key risk factor for developing COVID-19 [5], but also the virus might trigger DM in some cases and severe metabolic complications of preexisting diabetes such as diabetic ketoacidosis and hyperosmolarity for which exceptionally high

doses of insulin are warranted [6-8]. This is expected for COVID-19 virus, because through our experience in dealing with previous coronaviruses (SARS and MERS), it was found that they also have a relationship with diabetes onset [9].

Diabetes is one of the leading causes of morbidity and mortality throughout the world due to its several macrovascular and microvascular complications that finally impact the overall patient's survival [10] Characteristic feature of DM is hyperglycemia [11]. The most common forms of DM are type 1DM, which is an organ-specific autoimmune disease, schematically comprised of two phases:

- A. An occult phase of pancreatic inflammation that reduces the number and function of insulin-producing β -cells, eventually provoking sufficient damage to result in
- B. The overt phase of DM, when insulin production is

insufficient for proper glucose homeostasis [12], and type 2DM, in which insulin resistance may lead to hyperglycemia [11].

In the Renin Angiotensin System (RAS), ACE is a key enzyme, which converts Angiotensin (Ang) I to the vasoconstrictor Ang II, thought to be responsible for most of the physiological and pathophysiological effects of the RAS. This classical view of the RAS was challenged with the discovery of the enzyme, Angiotensin-Converting Enzyme2 (ACE2) which not only degrades Ang II, but also leads to formation of the vasodilatory and anti-proliferative peptide, Ang 1-7 [13]. The expression of the ACE-2 could increase in patients with DM and it is a major contributor to diabetic complications [13].

Individuals with DM are more likely to be infected and at a higher risk for complications and death from COVID-19 [14-16] due to human pathogenic coronaviruses bind to their target cells through ACE2, which is expressed by epithelial cells of the lung, intestine, kidney, and blood vessels [17], and its expression could increase in diabetic patients as we mentioned before.

If we consider the history of DM with infection, we find there is a recognized relationship between DM and infection a long time ago [18]. Nevertheless, the evidence remains controversial regarding whether diabetes itself indeed increases susceptibility and impacts outcomes from infections, or the cardiovascular and renal comorbidities that are frequently associated with DM are the main factors involved [19]. Diabetes and uncontrolled glycaemia were reported as significant predictors of severity and deaths in patients infected with different viruses, including the 2009 pandemic influenza A (H1N1) [20], SARS-CoV [21] and MERS-CoV [22].

As we mentioned before, SARS-CoV-2 bind to their target cells through ACE2, which is expressed in key metabolic organs and tissues, including pancreatic beta cells, adipose tissue, the small intestine, and the kidneys [17,23], so it is expected that COVID-19 will impact these cells, because when the virus enter the body the immune system is stimulated to kill the virus and this will lead to the destruction of pancreatic cells as an example [24,25]. This will cause pleiotropic alterations of glucose metabolism that could complicate the pathophysiology of preexisting DM or lead to new mechanisms of disease [26]. Ketosis or ketoacidosis and induced Diabetic Ketoacidosis (DKA) are complications of DM that increased with viral infection.

Conclusion

There is a bidirectional relationship between COVID-19 and DM. ACE2 expression increases during DM and COVID-19 uses this enzyme to enter cells, so diabetes is a risk factor for COVID-19. The expression of ACE2 occurs in metabolic organs and cells such as liver and pancreatic beta cells, so when COVID-19 uses this enzyme

to enter the cell this will lead to cell destruction by activated immune system against the virus and trigger DM in non-diabetic patient or worsen the case in diabetic patient.

Conflict of Interest

The authors state that there are no conflicts of interest.

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