Diabetes and COVID-19: a bitter nightmare

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Abstract

Initial studies found a bidirectional interaction between coronavirus disease 2019 (COVID-19) and diabetes. In this article we intend to review the association and consequences of COVID-19 in the future of diabetes in case of prevalence and treatment. There is substantial evidence that COVID-19 may result in the new-onset of hyperglycaemia. Therefore, it seems that COVID-19 will change the predictions for the prevalence of diabetes. Moreover, it raises numerous challenges for the clinical management of diabetes. In COVID-19 patients, new-onset hyperglycemia is associated with a poor prognosis. Diabetes mellitus and other comorbidities should be strictly controlled. But, with the emergence of COVID-19 disease, the future of diabetes mellitus in terms of prevalence and treatment will change and policymakers should consider developing new management strategies in this regard.

Keywords COVID-19 · SARS-CoV-2 · Hyperglycemia · Diabetes

Background

The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) virus has quickly spread over the world, resulting in an unexpected pandemic [1].

Diabetes and coronavirus disease 2019 (Covid-19) has a bidirectional interaction. Hyperglycemia or a history of diabetes mellitus (DM) was identified to be predictive factors of morbidity and mortality in Covid-19 patients [2, 3].

According to considerable evidence, COVID-19 may result in the development of DM. It is possible that SARS-CoV-2 will promote pleiotropic changes in glucose metabolism, which could affect the pathophysiology of preexisting diabetes or result to new disease processes. New-onset hyperglycaemia is one of the major metabolic complication of COVID-19, as the new-onset hyperglycemia is not related with any other risk factors, including prediabetes, cardiovascular disease, and obesity [4].

“New-onset” hyperglycemia in COVID era could be classified as (I) “new-onset diabetes” in previously unknown pre-diabetes, (II) “stress-induced” hyperglycemia, (III) hyperglycemia thought to be related to the SARS-CoV-2 direct impact on the pancreas, and (IV) drug-induced hyperglycemia or “secondary diabetes” during the course of COVID-19 treatment, particularly with pervasive use of corticosteroids [4].

American Diabetes Association (ADA) illustrates new-onset hyperglycemia without diabetes when fasting plasma glucose (FPG) is between 100 and 125 mg/dL and/or HbA1c is between 5.7 and 6.4%, in the absence of previous dysglycemia. Similarly, new-onset diabetes would be described in the presence of two abnormal samples either FPG is ≥ 126 mg/dL or HbA1c $\geq 6.5\%$ or a random glucose level

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≥ 200 mg/dL with symptoms of hyperglycemia, in absence of any history of diabetes in past [5].

Even though a chronic stress to an acute viral infection, such as COVID-19, is unlikely to affect HbA1c but may elevate plasma glucose level, thus, in the absence of hemoglobin A1c (HbA1c) $\geq 6.5\%$, a single FPG level of ≥ 126 mg/dL has been characterized by researchers as new-onset hyperglycemia without diabetes. Furthermore, Hyperglycemia in hospitalized patients is characterized as blood glucose levels 140 mg/dL (7.8 mmol/L) [5].

Patients with underlying health issues such as obesity and/or DM, cardiovascular disease (CVD) are at higher risk of severe COVID-19 or worse and higher mortality. Hyperglycemia may promote viral replication. In patients with inadequate glucose regulation or diabetes mellitus, glycemic impairment is a common consequence of COVID-19 [6]. COVID-19 and diabetes mellitus affect on glucose homeostasis, inflammation, activation of the renin–angiotensin–aldosterone system (RAAS) [7].

Infection with SARS-CoV-2 can result in elevated levels of inflammatory cytokines in the blood; SARS-CoV-2 activate the RAAS through increased expression of angiotensin II, which ultimately result in insulin resistance, and hyperglycemia [7].

Patients with new-onset hyperglycemia indicate poorer outcome compared to the normoglycemic individuals [4].

Diabetes is a chronic, long-term disease that has a significant influence on the lives and well-being of individuals, and societies all over the world.

As a result, both the United Nations and the World Health Organization (WHO) have prioritized diabetes as a major global health concern, due to the large global epidemic of this, possibly the most important noncommunicable global disease caused by an unhealthy modern lifestyle [8, 9].

According to WHO noncommunicable diseases (NCDs) kill 41 million people each year, the main types of NCDs are cardiovascular diseases (such as heart attacks and stroke), cancers, chronic respiratory diseases (such as chronic obstructive pulmonary disease and asthma) and diabetes.

The World Health Assembly established the NCD global monitoring framework in May 2013, with nine goals, the first of which was “a 25% relative decrease in total mortality from cardiovascular diseases, diabetes, and other chronic diseases.” NCD management interventions are critical for meeting the global goal of a 25% reduction in the risk of premature death due to NCDs.

It seems that the two-way interaction between diabetes and COVID may increase diabetes prevalence. Findings from the 9th edition of International Diabetes Federation (IDF) showed that diabetes is one of the fastest growing global health emergencies of the 21st century [10]. It is estimated that the number of people with diabetes to reach 578

million by 2030, and 700 million by 2045 but COVID-19 disease is thought to alter all predictions.

COVID-19 has the potential to increase the incidence of diabetes more than that of IDF expectation. Poor glycemic control is a consequence of COVID-19. It predicts a greater need to antidiabetic medications and high rate of mortality. Data shows that insulin and dipeptidyl peptidase 4 inhibitors can be administered safely in diabetes patients and COVID-19; metformin and sodium–glucose cotransporter 2 inhibitors may need to be discontinued in patients who are at risk of severe illness. Hyperglycemia is caused by deficiencies in either insulin production, insulin action, or both, and appears as carbohydrate, lipid, and protein metabolic derangement in a chronic way [5].

According to the IDF Diabetes Atlas ninth edition 2019 [10] which provides the latest information on diabetes worldwide, 79% of adults with diabetes were living in low- and middle-income countries. Therefore, the COVID-19 outbreak may influence in the diabetes prevalence in low- and middle income countries in the coming years because only 2% of people in low-income countries have received at least one dose [11].

On the other hand, the COVID-19 pandemic poses many challenges in the future of diabetes treatment; as whether the need for insulin increase with the destruction of pancreatic beta cells due to COVID-19 disease?

Does inflammation cause by COVID-19 disease increase the need for antihyperglycemic agents with cardiovascular benefit?

What will happen to other anti-hyperglycemic agents? What is the fate of metformin? The most reputable and well-known remedy among diabetologist [12]. However, its long-term cardiovascular protecting effect is under question [13]. Before the pandemic, antihyperglycemic medications were the second most costly therapy class drugs ranked based on per-member-per-year (PMPY) spending in 2018.

In any case scenario, the serious question is whether the COVID-19 disease increases the need for diabetic care and implementation of new technology in this regard?

Conclusions

In conclusion, with this breakthrough we will encounter a huge increase in costs (direct and indirect) and many obstacles in diabetic care. Given the increasing complexity of diabetes care, policy makers and health care providers should implement effective interventions toward areas of greatest needs before the inception of NCD tsunami overwhelming COVID.

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Declarations

Conflict of interest The authors declared that they have no conflict of interest.

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