



## Relation between COVID 19 and Diabetes Mellitus

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### Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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## ABSTRACT

The coronavirus disease 19 (COVID-19) is a highly contagious virus that emerged on January 29, 2020, as a result of a brand new coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which the World Health Organization discovered on January 29; and the COVID-19 outbreak became distinctive a virus on March 11, 2020.

The most well-known factors visibly associated with COV disease are senescence, expanded weight, blood pressure, diabetes mellitus, and CVS abnormalities.

Infection with the coronavirus 2 of the intense acute respiratory syndrome has been associated with a better severity of coronavirus infection (COVID19) in sufferers with diabetes (SARSCoV2). Infected folks who are inflamed with COVID19 may also broaden hyperglycemia. While paired with other chance elements, hyperglycemia can also affect immune and anti-inflammatory responses, making sufferers extra sensitive to excessive COVID 19 and its likely deadly results. Angiotensin changing enzyme 2 (ACE2) is SARSCoV2's central access receptor (ACE2).

DPP4 (dipeptidyl peptidase four) might be a binding target, on the other hand. Initial research suggests that hypoglycemic DPP4 inhibitors haven't any impact on SARSCoV2 susceptibility. for the reason that in their pharmacological traits, sodium-glucose cotransporter-2 inhibitors (SGLT2) aren't encouraged because they can have negative consequences in COVID19 sufferers. In opposition to excessive blood sugar, insulin has to be the first defense line inside the combat.

This evaluation article is a nascent attempt to recognize the probable correlation between COVID contamination and diabetes mellitus.

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## 1. INTRODUCTION

Coronaviruses are single-stranded RNA viruses with a strand that can be found in both people and animals everywhere in the world. The diseases caused in humans by coronavirus are primarily mild, even though massive outbreaks of two beta coronaviruses, SARS-CoV and Middle East respiratory syndrome coronavirus (MERS-CoV), have precipitated deadly pneumonia before.

Before December 2019, localized pneumonia outbreaks of unknown causes were recorded in China. Corona Virus illnesses 2019 became named after a preliminary clinical investigation of lower respiratory tract samples from those affected diagnosed a unique coronavirus, which changed into named extreme Acute breathing Syndrome-Coronavirus-2 (SARS-CoV-2) because the maximum likely reason (hereafter known as COVID-19). Regardless of its evolutionary history and clinical similarities to SARS-CoV, SARS-CoV-2 seems to be more communicable and has a lower loss of life price. The World Health Organization (WHO) proclaimed the COVID-19 outbreak a Public Health Emergency of Worldwide Concern on January 30, 2020, and the quickly worsening epidemic was escalated to pandemic status on March 11 due to its global effect and fast-growing cases [1].

SARSCoV2 is 82 percent corresponding to human SARS-CoV and causes severe acute breathing syndrome (SARS) [2]. Angiotensin-converting enzyme 2 (ACE2), that's drastically expressed in alveolar cells, cardiac cells, vascular endothelial cells, and other cell types, is the fundamental invading receptor for SARSCoV2 [3]. SARSCoV2 is usually disseminated via the respiratory system using droplets containing the virus. Sufferers infected with COVID 19 exhibit signs five to six days after contamination. SARSCoV2 contamination, like SARS-CoV and the associated middle East breathing Syndrome (MERS) CoV, causes slight signs for two weeks on average. However, significant problems such as systemic inflammatory response syndrome (SIRS) and acute respiratory distress syndrome might occur. Acute respiration is one of the possible effects [4,5]. Patients with severe COVID 19 or a high risk of death 22 have specific characteristics, such as age and male gender, underlying

cardiovascular disease (CVD), weight problems, and diabetes. According to a preliminary study, the critical care unit has a high risk of cardiovascular diabetes. Because T2DM is generally a condition of the elderly, diabetes is not considered a risk factor for presenile COVID19.

## 2. DESCRIPTION

Early studies indicate that the fulminant instances with COVID have passed off in human beings of older age or patients with comorbidities, especially diabetes mellitus, CVDs, a continual lung disorder, and disease associated with the kidney, cancer, and hypertension. It is uncertain still whether sufferers who have diabetes would have increased probabilities to come to be COVID positive; there's also a statement that the chance of contamination with multiplied disease severity is likewise very excessive [1].

Diabetes is a persistent metabolic disease with a high degree of contracting infections independently regardless of the alternative associated diseases, mechanisms that would possibly result in this are:

- (a) Hyper-coagulable state
- (b) inflammation
- (c) dysregulation of the sympathetic nervous machine [6]
- (d) activation of RAAS

Even though the clinical relevance and data of a few in vitro alterations are uncertain, new research and investigations reveal that hyperglycemia is associated with immune system issues. Poorly controlled diabetes is attached to impaired lymphocyte proliferative response to various stimuli, in addition to impaired monocyte and neutrophil activity. Diabetes has also been linked to extraordinary delayed-type allergic reaction responses and complement activation disorder. In vitro studies have shown that excessive glucose levels enhance influenza virus contamination and replication in pulmonary epithelial cells, indicating that hyperglycemia is probably vital in viral replication in vivo. An extensive decline in forced vital capacity (FVC) and forced expiratory volume in a single second (FEV1) has been determined in patients with diabetes mellitus, which has been linked to higher plasma glucose levels. According to

diabetic sufferers, immoderate synthesis of ACE2 might also aid the access of SARS-CoV-2 into host cells, leading to COVID-19. Due to the fact diabetes mellitus and hypertension are handled with ACE2 boosting drug treatments, there's a great chance of COVID-19 [1].

Simultaneously, more robust ACE2 expression aids SARS-CoV-2 access with the aid of permitting the virus to link to the ACE2 enzyme through the virus's envelope surface S protein. As a result, it's questionable whether COVID-19-affected diabetics should retain their ACEi and ARB medicines or not. The downside is that if the drug is stopped all at once, the affected person may also die of high blood pressure instead of COVID-19 (Pan fire to Bonfire syndrome). Even if a diabetic affected person is infected with COVID-19, his medicine must now not be removed due to a lack of medical consensus. Even though a diabetic patient is infected with COVID-19, caution dictates that remedy need not be halted because there is presently no medical agreement based totally on research on whether or not to utilize ARBs [7].

It's nevertheless unknown if diabetes interacts with SARSCoV2 and aids the coronavirus's entry into the frame, as well as the emergence of other issues that cause mortality [8]. As a result, we can claim with a high degree of certainty that diabetes-brought about target organ harm can be in charge of diabetics' heightened sensitivity to this virus. Diabetic patients with excessive inflammatory markers and hypercoagulability have a worse diagnosis. Diabetic people must consequently be constantly monitored and dealt with giant vigilance [6].

## 2.1 Impact of COVID Contamination on Glucose Metabolism

SARSCoV2 replication in human monocytes is directly boosted with the aid of accelerated glucose levels, and glycolysis aids SARSCoV2 replication using generating mitochondrial reactive oxygen species and activating hypoxia-inducing factor 1 [9]. As a result, hyperglycemia may additionally facilitate viral replication. Hyperglycemia, additionally called T1DM and T2DM, has been established to be an unbiased predictor of morbidity and death in SARS patients, indicating that this idea is accurate [10]. Moreover, the immune reaction turned dysregulated in MER CoV-infected mice with type 2 diabetes, causing excessive and sizeable lung damage [11]. Diabetic patients have an

extra intense SARSCoV2 contamination than other patients, and poor glycemic control necessitates additional medicine and hospitalization in addition to an increased chance of mortality. The worsening blood glucose level is an average COVID19 complication in humans with glycemic dysregulation or diabetes. Ketoacidosis is most usually connected with T1DM, but it could also happen in T2DM sufferers with COVID 19. One research found that 77 percent of COVID19 sufferers with ketoacidosis also had T2DM [12].

## 2.2 Gestational Diabetes and COVID Contamination

Regardless of the truth that pregnancy is a delicate duration, mainly considering gestational diabetes mellitus would possibly increase, few studies have checked out pregnant women who've been hospitalized with COVID-19 infection. Four patients with gestational diabetes mellitus and two with hypertension were found in a cohort study of 54 pregnant women with suspected or confirmed COVID-19.; however, there were too few to analyze for a probable hyperlink to contamination severity. However, the researchers observed that having an obese or before BMI before being pregnant became frequent, which they suspected may be a danger for COVID-19 infection. Another small observe (n = 46) performed within the United States of America discovered a high incidence of pre-pregnancy BMI (28.6% overweight, 35.7 percentage overweight [13]. Furthermore, 15% of pregnant ladies who got a severe circumstance advanced, with eighty% of them being overweight or obese. Comparable findings had been acquired in an examination of 427 pregnant ladies in the United Kingdom with confirmed COVID-19, which discovered that thirty-five percent of the patients included in the study were found to have higher BMI values which showed that they were overweight and thirty-four percent of the patients were obese. Although no investigation of disease severity turned into completion, the prevalence of diabetes was 3% compared to twelve% for gestational diabetes mellitus.

The introductory study thus far involved 617 pregnant French ladies. Preexisting diabetes turned into determined in 2.3 percentage of the population, with a 3.8-fold increase within the hazard of severe sickness. GDM, which affects 11.5 percent of pregnant girls, did not affect infection severity results. The researchers did not

explain why there may be a threat between preexisting diabetes and gestational diabetes mellitus. However, it enhances whether or not COVID-19 pathophysiology interacts in another way with gestational diabetes mellitus.

### **2.2.1 Diabetes mellitus remedy in patients with COVID contamination**

#### *2.2.1.1 Metformin*

Metformin may be maintained with common oral ingestion in stable individuals who do now not revel in nausea or vomiting. Metformin has attracted loads of attention these days due to its ability in immunomodulation. In animal studies, lengthy-term use of metformin in sepsis is related to decreased levels of inflammatory cytokines such as tumor necrosis factor and interleukin-6 (IL-6). Metformin has also been shown to improve survival in Legionella pneumophila-infected mice. Because of the risk of lactic acidosis, metformin should be avoided in critically sick patients with acute renal impairment, hepatic damage, or hemodynamic instability [14].

#### **2.2.2 Dipeptidyl peptidase- four inhibitors**

A slight increase in the prevalence of nasopharyngeal and urinary tract infections has been linked to using a dipeptidyl peptidase four (DPP4) inhibitor. There was no statistically significant distinction in using DPP4 inhibitors among men and women at high threat of upper breathing tract infections, consistent with Kai et al.'s meta-analysis. Every other cohort examine determined no relation between DPP4 inhibitors and the incidence of pneumonia [15]. In the middle East's breathing disease, DPP4 has also been found to be a coronavirus cellular invasion receptor. It's unclear if this will increase susceptibility to coronavirus infections or the severity of such illnesses. In human studies, DPP4 inhibitors have shown no effect on lymphocyte function of anti-inflammatory cytokine production [16]. DPP4 inhibitors can be helpful in the treatment of SARS-CoV-2 infection, but similarly, research is needed. In muscular sufferers with adequate oral consumption, clinicians can apply DPP4 inhibitors.

#### **2.2.3 Glucagon- like peptide- 1 receptor agonists**

Signaling via the glucagon-like peptide-1 (GLP-1) receptor has anti-inflammatory properties [17].

Remedy with GLP-1 receptor agonists is connected to a good-sized discount in inflammatory cytokine production and infection within the respiratory epithelium in mice inflamed with breathing syncytial virus [18]. Moreover, because glucagon forty is suppressed in intensive care units, remedy with GLP-1 receptor agonists is attached to lessen hypoglycemia, glucose fluctuation, and catabolism, all of which may guard those critically unwell patients. However, delayed stomach emptying, which is common in critically ill sufferers, may also restrict glycemic control effectiveness. It is frequently contraindicated in patients with renal impairment. There are presently insufficient facts, which is an excellent way to assist or reject the usage of GLP-1 receptor agonists in the treatment of coronavirus contamination.

#### **2.2.4 Thiazolidinedione, sulphonylurea, meglitinide, and sodium-glucose cotransporter two inhibitors**

Recent studies have connected better ACE2 expression to increasing thiazolidinedione use, raising concerns about an elevated risk of having SARS-CoV-2 contamination [19]. Thiazolidinedione, then again, must be avoided in sufferers with intense contamination because of its adverse effects like fluid retention. However, in conditions of acute illness, sulfonylureas and sodium-glucose cotransporter-2 inhibitors are often contraindicated. Sulfonylureas and meglitinide, when given inadequately, boom the risk of hypoglycemia. With Sodium-Glucose Co-Transporter-2 inhibitors, there's an expanded threat of dehydration and normoglycemia DKA, specifically within the elderly. There is a higher hazard of dehydration and normoglycemia DKA using Sodium-Glucose Co-Transporter-2 inhibitors, especially in acute ailment conditions.

### **2.3 Insulin**

Insulin is the medicine of preference for improving glycemic management in individuals with acute infection. Numerous breakthrough research has verified that aggressive insulin treatment reduces mortality and morbidity. IV insulin may be given as a continuous infusion, considering short titration. Furthermore, insulin can downregulate the Angiotensin changing enzyme receptor 2 [20], even though a different look is needed to determine the favorable impact of insulin utilization inside the context of COVID infection. Patients with COVID-19 had extended

insulin needs, consistent with more observational studies investigations [21-26]. This adds to the evidence that the assumption SARS-CoV-2 can also result in  $\beta$ -cell disorder

### 3. CONCLUSION

COVID-19 has rapidly spread and become a global catastrophe when you consider its initial sporadic localized reporting in Wuhan around the turn of the yr and has proven a various spectrum of severity. While scientists everywhere in the globe are still operating tirelessly to get a human vaccine to get rid of the sickness from the face of the earth, meantime measures of isolation, rapid scientific screening, and early management in each symptomatic and asymptomatic case are our gift shields in arresting the spread of this deadly disease. To sum up, human beings with diabetes mellitus have a better chance of having grave signs and symptoms and bad headaches whilst infected with the virus because of decreased immunity making the restoration method extra challenging. studies to date indicate that the probability of getting contracting COVID is likely to be lower if diabetes is properly managed. Specific research is of excessive importance to well-known the correct hyperlink between novel coronavirus contamination and diabetes and to understand the character to character and geographic diversification of the sickness.

### CONSENT

It is not applicable.

### ETHICAL APPROVAL

It is not applicable.

### COMPETING INTERESTS

Authors have declared that no competing interests exist.

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