

## Review Article

### Relation between COVID 19 and Diabetes Mellitus

#### ABSTRACT

The coronavirus disease 19 (COVID-19) is a highly contagious virus that emerged on January 29, 2020, as a result of ~~a brand the new coronavirus,~~ severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), ~~which was discovered identified~~ by the World Health Organization on January 29, ~~and responsible for the outbreak leading to the and the pandemic that was declared COVID 19 outbreak become distinctive a virus on~~ March 11, 2020.

Senescence, ~~expanded excess~~weight, ~~expanded high~~blood pressure, diabetes mellitus, and **CVS** abnormalities are the most well-known factors ~~visibly~~ associated with **COV** disease.

~~In~~infection with the coronavirus 2 of the intense acute respiratory syndrome has been associated to 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 main access receptor (ACE2).

~~DPP4 (D~~Dipeptidyl peptidase four(DPP4) might be a binding target, ~~on the other handbut~~. initial research suggests that hypoglycemic DPP4 inhibitors ~~don't 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 are able to have negative consequences in COVID19 sufferers. inside the combat in opposition to excessive blood sugar, insulin have to now be the first line of defence.

This ~~evaluate~~ article ~~aims to discuss the is a nascent attempt to recognize into probable relation eorrelation~~ between ~~the~~ COVID ~~eontamination infection~~and diabetes mellitus.

**Keywords:**covid-19,SGLT2, hyperglycemia

**Comment [EAMP1]:** What does this acronym mean? As per usual rules, abbreviations must always come after a first instance where the meaning is written in full... Abbreviations should be avoided in abstracts.

**Comment [EAMP2]:** Again, another abbreviation that is not previously explained.

**Comment [EAMP3]:** This paragraph must be rewritten, as its meaning is not clear.

**Comment [EAMP4]:** Again, this paragraph is very confusing. English needs to be reviewed.

## INTRODUCTION

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

**Comment [EAMP5]:** This paragraph lacks proper referencing, as it is an important statement and must be supported in the literature.

~~Before~~ before the end of December 2019, ~~localised~~ localized outbreaks of pneumonia of unknown cause have been recorded in China. Corona Virus illnesses 2019 ~~became was~~ named after a preliminary clinical investigation of lower respiration 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~~ mortality rate. 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)

**Comment [EAMP6]:** Unsure what the authors mean; English must be reviewed.

**Comment [EAMP7]:** Unsure if it's what the authors intend;

**Comment [EAMP8]:** The entire paragraph should be referenced properly. Is the reference provided by the authors (1) the source of all the information in this paragraph? It shouldn't be, as the cited paper should be used when talking about diabetes...

SARSCoV2 is 82 percent corresponding to human SARSCoV 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 by using droplets containing the virus. Sufferers infected with COVID 19 exhibit signs five to six days after contamination. SARSCoV2 contamination, like SARSCoV and the associated middle East breathing Syndrome (MERS) CoV, causes slight signs for 2 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). Patients with severe COVID 19 or a high risk of death 22 have certain characteristics, such as age and male gender, as well as underlying cardiovascular disease (CVD), weight lproblems, and diabetes. The critical care unit, according to preliminary study, 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.

## DESCRIPTION

Early studies indicate that the fulminant instances with COVID have passed off in human beings of older age or in patients with comorbidities, specially diabetes mellitus, CVDs, , continual disorder of the lung 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 an statement that the chance of contamination with multiplied disease severity is likewise very excessive.(1)

Diabetes is persistent metabolic disease with high degree of contracting infections independently regardless of the alternative ~~assosciated~~associated diseases.,~~mechaism~~mechanisms which would possibly result in this are

- (a) Hyper-coagulable state
- (b) inflammation
- (c) dysregulation of 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 to 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 patients. In vitro studies have shown that excessive glucose level enhance influenza virus contamination and replication in pulmonary epithelial cells, indicating that hyperglycemia is probably a vital position in viral replication in vivo. A 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 in 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, stronger 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 aend result, it's questionable whether COVID-19-affected diabetics should retain their ACEi and ARB medicines or not. The downside is if the drug is stopped all at once, the affected person may additionally die of high blood pressure as opposed to COVID-19 (Pan fire to Bon fire 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 to not be halted due to the fact there is presently no medical agreement based totally on research on whether or now not to utilise ACEi and 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. As a result, we can claim with high degree of certainty that diabetes-brought about target organ harm can be in

charge for 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 with giant vigilance. (6)

#### 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 by means of generating mitochondrial reactive oxygen species and activating hypoxia-inducing factor 1. (8). As a end result, hyperglycemia may additionally facilitate viral replication. Hyperglycemia, additionally called T1DM and T2DM, has been established to be an unbiased predictor of morbidity and dying in SARS patients, indicating that this idea is accurate (9). Moreover, the immune reaction turned into dysregulated in MER CoV-infected mice with type 2 diabetes, causing in excessive and sizeable lung damage (10). Diabetic patients have a 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 of 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 additionally happen in T2DM sufferers who have COVID 19. One research located that 77 percent of COVID19 sufferers with ketoacidosis additionally had T2DM (11).

#### 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 womenwho've been hospitalised 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 analyse for a probable hyperlink to contamination severity. However, the researchers observed that having an obese or overweight BMI prior to being pregnant became instead frequent, which they suspected may be a danger thing 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 (12). 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 examine 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 out to have higher BMI value 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%, as compared to twelve% for gestational diabetes mellitus.

The most important study at 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 serious sickness. GDM, which affects 11.5 percent of pregnant girls, had no effect on infection severity results. The researchers did not explain why there may be a distinction in threat among preexisting diabetes and gestational diabetes mellitus, however it does enhance the question of whether or not COVID-19 pathophysiology interacts in another way with gestational diabetes mellitus.

Diabetes mellitus remedy in patients with COVID contamination

Metformin

Metformin may be maintained with common oral ingestion in stable individuals who do not revel in nausea or vomiting. Metformin has these days attracted loads of attention due to its ability in immunomodulation. In animal studies, lengthy-term use of metformin in sepsis turned into related to decreased levels of inflammatory cytokines such tumour 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.(13)

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

A small increase in the prevalence of nasopharyngeal infection and urinary tract infection has been linked to using a dipeptidyl peptidase four (DPP4) inhibitor. There was no statistically significant distinction in the use of 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 (14). 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 or anti-inflammatory cytokine production (15). DPP4 inhibitors can be useful in the treatment of SARS-CoV-2 infection, but similarly research is needed. In strong sufferers with adequate oral consumption, clinicians can keep to apply DPP4 inhibitors.

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

Signaling via the glucagon-like peptide-1 (GLP-1) receptor has been associated with anti inflammatory properties (16). 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 (17). Moreover, due to the fact 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, is common in critically ill sufferers, may additionally restrict the effectiveness of glycemic control. It is frequently contraindicated in

patients with renal impairment. a good way to assist or reject the usage of GLP-1 receptor agonists within the treatment of coronavirus contamination, there's presently insufficient facts.

Thiazolidinedione, sulphonylurea, meglitinide and sodium–glucose cotransporter 2 inhibitors

Latest studies has connected better ACE2 expression to increasing thiazolidinedione use, raising concerns approximately an elevated risk of having SARS-CoV-2 contamination (18). Thiazolidinedione, then again, must be avoided in sufferers with intense contamination because of its adverse effects like fluid retention. In conditions of acute illness, however, sulphonylureas and sodium-glucose cotransporter-2 inhibitors are often contraindicated. Sulphonylureas and meglitinide, when given inadequately, boom the risk of hypoglycemia. With using 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 with use of Sodium Glucose Co-Transporter-2 inhibitors especially in occasions with acute ailment conditions.

### **Insulin**

Insulin is the medicine of preference for improving glycemic manage in individuals with acute infection. numerous breakthrough research have verified that aggressive insulin treatment reduces mortality and morbidity. IV insulin may be given as a continuous infusion, taking into consideration short titration. Furthermore, insulin has the capacity to downregulate the Angiotensin changing enzyme receptor 2(19), even though additional look at is needed to determine the favourable impact of insulin utilization inside the context of COVID infection. Patients with COVID-19 had extended insulin needs, consistent with more observational studies investigations (20-25). This adds to the evidence that the assumption SARS-CoV-2 can also result in  $\beta$ -cell disorder

## CONCLUSION

COVID-19 has rapidly spread and becoming a global catastrophe when you consider that its initial sporadic localized reporting in Wuhan around the turn of the yr and has proven a various spectrum of severity. while scientist 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 cases 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 dire 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. Certain 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.

**Comment [EAMP9]:** These are not conclusions from this paper!

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