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COVID-19 INFECTION AND DIABETES: A CURRENT ISSUE

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Abstract

The Covid-19 outbreak renders managing diabetes mellitus problematic. Infection with Covid-19 predisposes infected individuals to hyperglycemia, leading to hyper glycosylation of ACE2 and increased viral proliferation. Worsening of hyperglycaemia induces inflammation, endothelial dysfunction, and thrombosis via the generation of oxidative stress driving the dysregulation of glucose metabolism and hypercoagulability. Severe infection in the individuals predisposed to vasculopathy and impaired immunity may accentuate thrombotic and ischemic complications associated with multiorgan failure and increased mortality rates. Covid-19 poses a major risk to the diabetes patients. This risk in diabetes patients could through cytokine storm. Some inflammatory cytokines especially interleukin 6 should be monitored.

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Introduction:-

The Covid-19 outbreak renders managing diabetes mellitus problematic(Landstra and de Koning, 2021). In actuality,(Landstra & de Koning, 2021), there aren't many data sources in the literature, and some studies have simply taken prognostic variables based on theory into account. One small retrospective single-center observational study in China that looked at the clinical traits and prognoses of 48 severely ill Covid-19 patients with diabetes discovered that the prevalence of associated comorbidities, such as hypertension, cardiovascular disease, and chronic pulmonary disease, did not significantly vary between Covid-19 surviving victims with diabetes and non-survivors with diabetes(Landstra and de Koning, 2021).

Scheen et al.(2020)said infection with SARS-CoV-2 in the setting of Diabetes initiates a flywheel of cascading effects that result in increased mortality. Infection with Covid-19 predisposes infected individuals to hyperglycemia, leading to hyper glycosylation of ACE2 and increased viral proliferation. Worsening of hyperglycemia induces inflammation, endothelial dysfunction, and thrombosis via the generation of oxidative stress driving the

dysregulation of glucose metabolism and hypercoagulability further(Scheen et al., 2020). Severe infection in the individuals predisposed to vasculopathy and impaired immunity may accentuate thrombotic and ischemic complications associated with multiorgan failure and increased mortality rates(Li et al., 2020).

In Covid-19(Singh et al., 2020), diabetes is regarded as a risk factor for a poor outcome. Numerous theories have been put up to explain why diabetics have a worse Covid-19 prognosis, however as of the writing of this article, these theories are still speculative. These mechanisms include impeded neutrophil degranulation and complement activation, elevated glucose concentration in airway secretion, which significantly boosts viral replication, heightened proinflammatory cytokine response in diabetes, decreased viral clearance, and a more prominent presence of associated clinical features(Singh et al., 2020).

In contrast to individuals without diabetes(Nassar et al., 2021), the proportion of diabetes patients hospitalized in intensive care units for Covid-19 is approximately two to three times greater, and the death rate is at least twice as high. The widely varied diabetic community makes it crucial to identify the characteristics that increase the likelihood of developing the more serious, life-threatening COVID-19 infection(Scheen et al., 2020). The frequency of diabetes in Covid-19 (Coronavirus Disease 2019) patients has varied between nations, ranging from 5-20% in China, 17% in Lombardy in Italy, to 33% in the US(Klonoff and Umpierrez, 2020). Covid-19 is an infection with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Diabetes can alter host-viral interactions and host-immune responses through a number of ways, which may potentially have negative effects(Klonoff and Umpierrez, 2020).

One of the key elements of the association between Covid-19 and Diabetes is that the HbA1c is less useful for predictive purposes than the information on the hyperglycemia at the time of hospital admission(Ceriello, 2020). Angiotensin-converting enzyme 2 (ACE2), the natural viral receptor on the host cell surface, is considered to become hyperglycosylated in infected persons as a result of COVID-19 infection(Guan et al., 2020). Through the creation of oxidative stress, the acute hyperglycemia in these individuals causes inflammation, endothelial dysfunction, and thrombosis(Yang et al., 2010). This might increase viral virulence, pathogenicity, and susceptibility to severe infections. It also could improve viral penetration into cells and tissue tropism(Yang et al., 2010). According to a theory put up by researchers(Guan et al., 2020), the Covid-19 may interfere with the ability of pancreatic B-cells to make insulin, which would exacerbate the underlying lack of glycemic control seen in Diabetes.

In recent studies(Brufsky, 2020), Chronic hyperglycemia can also lead to changes in innate and adaptive immunity, such as aberrant cytokine responses, a reduction in leukocyte recruitment, and neutrophil dysfunction. In acute viral infections(Yan et al., 2020), the effects of chronic hyperglycemia are exacerbated because systemic insulin resistance and development of hyperglycemia are encouraged by activated immune responses. Significant correlation exists between elevated blood glucose levels and severe Covid-19 development(Cariou et al., 2020). Hemoglobin A1c (HbA1c) had less predictive value in individuals with concurrent SARS-CoV-2 infection and diabetes than blood glucose levels to track increasing hyperglycemia(Cariou et al., 2020). These findings(de Simone, 2020), confirmed that in individuals with pre-existing vasculopathy and endothelial dysfunction, increasing hyperglycemia develops quickly and may lead to fast clinical deterioration.

Regardless of the underlying causes(de Simone, 2020), Covid-19 patients with and without Diabetes tend to have more severe illness and exhibit significantly greater levels of inflammatory markers than non-diabetics (e.g., C-reactive protein, procalcitonin, ferritin, lactate dehydrogenase, and d-dimer). Additionally(Landstra and de Koning, 2021), there is a two- to three-fold greater frequency of diabetes and a death rate that is twice as high in Covid-19 patients admitted to critical care units.

Covid-19 Infection

The method through which human pathogenic coronaviruses(de Simone, 2020), such as the SARS-CoV and SARS-CoV-2, bind to their target cells is angiotensin-converting enzyme 2 (ACE2), which is expressed by epithelial cells of the lung, stomach, kidney, and blood vessels.ACE inhibitors and angiotensin II type-I receptor blockers dramatically increase ACE2 expression in patients with diabetes who are receiving treatment (ARBs)(de Simone, 2020). Hypertension, which upregulates ACE2, is also treated with ACE inhibitors and ARBs. Ibuprofen and thiazolidinediones both cause an increase in ACE2(Fedson et al., 2020). According to previous studies(Fedson et al.,

2020), ACE2 expression is increased in diabetes and is increased when receiving ACE inhibitor and ARB medication. The increased expression of ACE2 would therefore facilitate COVID-19 infection(Fedson et al., 2020). Interestingly(Nassar et al., 2021), More than a million confirmed cases and more than 45,000 fatalities worldwide have contributed to the ongoing rise in the clinical burden of coronavirus infectious disease 2019 (Covid-19) caused by the SARS CoV-2. Because diabetes is so common, it's critical to comprehend the unique characteristics of covid-19 infection in diabetics(Nassar et al., 2021). This becomes even more crucial given that the majority of the world is experiencing limitations on patients' freedom of movement in an effort to contain the epidemic(Nassar et al., 2021). A group(Scheen et al., 2020), just released a paper outlining unique factors to take into account while managing diabetes in the current Covid-19 pandemic era(Hassan et al., 2022; Obeagu, 2022; Obeagu et al., 2023).

The link between diabetes and Covid-19

In the work of(Landstra and de Koning, 2021), Diabetes mellitus is a complex chronic disease characterized by glucose dysregulation caused by an absolute or relative insulin deficiency. Although viruses have long been suspected to influence the risk of type 1 diabetes, the role of respiratory viral infections linked to type 1 diabetes remains obscure(Landstra and de Koning, 2021). A number of factors, such as microbe species, the host's age, and the intensity of beta-cell stress induced by the infection, may affect this association(Filardi and Morano, 2020).

Recently, (Filardi and Morano, 2020) confirmed, there may be a connection between diabetes and infectious diseases. Particularly in older people with type 2 diabetes, lower respiratory tract infections are known to be rather common and severe (T2D). Diabetes has been linked to a higher risk of worse Covid-19 development and outcomes, even though data suggests that diabetes is unlikely to significantly increase susceptibility to SARS-CoV-2 infection(Filardi and Morano, 2020).

Increased expression of the ACE2 receptor and furin, which may encourage SARS-CoV-2 entrance and replication, may be one of the ways by which diabetes raises the risk of serious infection. The viral load rises as a result of more effective virus entry, which has a negative impact on Covid-19's prognosis("Covid-19 and Diabetes," 2022). A raised blood furin level is a sign of developing diabetes and is linked to metabolic irregularities and an increased risk of dying from diabetes-related causes too soon(Reshad et al., 2021). ACE2 acts as the entering site for SARS-CoV-2 to enter into the human body. ACE2 is generally found in the liver and endocrine pancreas with a possible role in developing insulin resistance and reducing insulin secretion. So, there are possibilities that SARS-CoV-2 can affect both pancreas and beta cells, worsening hyperglycemia during acute infection(Reshad et al., 2021).

Covid-19 diabetics may result in increased stress levels and the production of hormones (glucocorticoids and catecholamines) which elevate the blood sugar content and improper glucose fluctuation(Xie et al., 2021). The activation of pro-inflammatory monocyte and the activation of platelets have been related to reducing blood glucose levels, all of which have been linked to a greater cardiovascular risk in diabetic patients. Diabetes mellitus is a chronic inflammatory disease that causes lots of new metabolic and vascular issues that might make it difficult to fight infections(Xie et al., 2021). Additional production of AGEs, interleukins, and tissue necrosis factor (pro-inflammatory cytokines), as well as oxidative stress that drives tissue inflammation, are all promoted by hyperglycemia and insulin resistance. This inflammatory process might be the underlying cause of greater susceptibility to infections, as well as worse infection results in diabetic individuals(Filardi & Morano, 2020).

Also,(Reshad et al., 2021) found that hyperglycemia leads to aggressive glycosylation (disturbance in determining structure, features, and stability of protein) that causes failure in receptor signaling and disrupts the functions of immunoglobulins. This glycosylation disturbance of IgG may cause susceptibility to Covid-19.

Approaches to management of diabetics with covid-19

With Covid-19(Ceriello, 2020), glycaemic management is crucial for all patients. Data from other infections like SARS and influenza H1N1(Basu et al., 2017), have shown that patients with poor glycaemic control have an increased risk of complications and death, even though there is currently little information about the relationship between blood glucose levels and the disease course in Covid-19(Iacobellis et al., 2020). The majority of individuals with moderate infections and normal oral intake can keep using their typical antihyperglycemic drugs. SGLT-2 inhibitors should be stopped, nevertheless, due to the possibility of dehydration and euglycaemic ketosis(Li et al., 2020). In addition(Bozkurt et al., 2020), vomiting or poor oral intake may necessitate stopping the metformin treatment. Depending on the blood glucose levels, the dosages of various antihyperglycemic medications including sulfonylureas and insulin may need to be changed(Fedson et al., 2020).

Furthermore(Ceriello, 2020), A patient visit would be required to change the infusion rates, which would expose more people to the medical staff. Alternative methods of administering insulin must be investigated(Leelarathna et al., 2013). One of these involves the administration of subcutaneous short acting insulin analogues, a strategy that has been used successfully in mild to severe diabetic ketoacidosis, albeit its safety in critically sick patients is less certain(Li et al., 2020). In a trial from Thailand(Leelarathna et al., 2013), it was attempted to provide a single dosage of basal insulin to severely sick patients. As it would drastically minimize interaction with the patient, this would be a desirable alternative; nevertheless, additional study is needed, especially with regard to patients who are severely compromised(Leelarathna et al., 2013). In addition, certain types of an insulin pump or continuous subcutaneous insulin infusion (CSII) offer the benefit of allowing the insulin rates to be changed remotely through Bluetooth(Leelarathna et al., 2013). Patients with COVID-19 may benefit from fully automated closed-loop glucose regulation, which has been tested in critical illness and, if practical, might be beneficial for treating those with the condition(Brufsky, 2020).

It has been demonstrated that(Bozkurt et al., 2020) calcium channel blockers lessen disease severity and death in individuals with pneumonia, probably by preventing calcium influx into the cell. Although the specific function of these substances in COVID-19 has not been investigated(Brufsky, 2020), it is safe to continue using these medications to keep hypertensive patients' blood pressure under control. Some researchers have suggested that(Fedson et al., 2020) calcium channel blocker can be used more often in individuals with Covid-19 and hypertension since it has no effect on ACE2 expression.

The preventive effect of statins in pneumonia has been studied extensively(Fedson et al., 2020). It is well known that statins raise ACE-2 levels and that they may offer protection against SARS CoV-2 entrance. It could be illogical in the given situation, nevertheless, for ACE-2 to grow. Statins, however(Fedson et al., 2020), are known to prevent Nuclearfactor kappa B (NF-B) activation and may be able to calm the cytokine storm.

Given that it necessitates frequent bedside visits(Basu et al., 2017), blood glucose monitoring provides a specific challenge, particularly if the patient is critically ill and receiving IV insulin. To lessen exposure, nevertheless(Basu et al., 2017), actions could be taken. A glucose test kit and instructions for self-monitoring may be given to the patient if their condition does not pose a threat to their life(Leelarathna et al., 2013). Sharing blood glucose levels over the phone allows for the following taking of the necessary action(Ceriello, 2020). The use of continuous glucose monitoring devices, particularly those that provide data access without having to physically visit the patient, may be beneficial(Ceriello et al., 1985). Although there is some evidence that several commonly prescribed medications, such acetaminophen, atenolol, and lisinopril, can interfere with continuous glucose monitoring, it has been established that these people who are critically sick benefit from(Fedson et al., 2020).

Recently, SGLT2 inhibitors, such as dapagliflozin, canagliflozin, empagliflozin, and ertugliflozin, should have a low threshold for discontinuation in Covid-19 patients who are unable to eat and stay hydrated(Iacobellis et al., 2020). The renal excretion of glucose is aided by SGLT2 inhibitors(Brufsky, 2020). They heighten calorie losses, volume contraction and dehydration risks, and genitourinary tract infections. Patients with type 1 diabetes (during off-label usage) and type 2 diabetes who were using SGLT2 inhibitors have also been documented to experience euglycemic DKA(Scheen et al., 2020). In individuals with SGLT2 inhibitor-associated DKA(Basu et al., 2017), glucose levels may only be somewhat increased. SGLT2 inhibitors may still be used in individuals with very minor illnesses as long as they continue to consume a regular diet and amounts of fluids(Basu et al., 2017).

Moreover, knowing the function of the "cytokines storm" in the Covid-19,(Guan et al., 2020) it is obvious that this impact has to be minimized. Another factor that appears to be highly unique to COVID-19 is connected to SARS-attachment CoV-2's to ACE2(Guan et al., 2020). The ACE2 must be glycosylated, a step that can be triggered by hyperglycemia, in order for the virus to attach to this cellular receptor(Ceriello, 2020). Therefore, elevated and abnormally glycosylated ACE2 in the tissue under uncontrolled hyperglycemia might promote the cellular entrance of SARS-CoV2, increasing the likelihood of Covid-19 infection and the severity of the illness(Landstra & de Koning, 2021). Furthermore(Yan et al., 2020), it's possible that the quantity of the glycosylated ACE2 receptor, rather than just the quantity of ACE2, is what causes the binding and fusion of viruses. However, it is well known that the glycosylation process associated with hyperglycemia is initially reversible, passing via the so-called "labile glycosylation" that is likewise reversible in vivo(Ceriello et al., 1985).

In reality(Singh et al., 2020), Covid-19 diabetes patients must manage their blood sugar levels in a setting with more unpredictable and frequently reduced food intakes while simultaneously dealing with a severe illness that is typically accompanied by fever and an insulin-resistant condition caused by cytokine activation. Additionally, as was already indicated(Yang et al., 2010), it's also feasible for the SARS coronavirus to enter pancreatic islets and harm beta cells, which would worsen diabetes and cause acute hyperglycemia.Therefore(Singh et al., 2020), Covid-19 poses a dual risk to diabetic patients.

Conclusion:-

The Covid-19 outbreak renders managing diabetes mellitus problematic. Infection with Covid-19 predisposes infected individuals to hyperglycemia, leading to hyper glycosylation of ACE2 and increased viral proliferation. Covid-19 poses a major risk to the diabetes patients. This risk in diabetes patients could through cytokine storm. Some inflammatory cytokines especially interleukin 6 should be monitored.

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