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Review Article

Complications of Diabetics in SARS-COVID patients

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ABSTRACT

Diabetes is a significant symptom in a COVID-19 sufferer. This article looks up and gathers information on the pathophysiology of diabetes, the association between COVID-19 and diabetes, and managing diabetes in patients infected with COVID-19. Data was collected using Google Scholar and the Pub Med website, and by entering search terms like COVID-19, SARS-CoV-2, diabetes, and antidiabetic. Patients with COVID-19 may be more likely to have severe diabetes, which could affect their pathophysiology. Controlling blood glucose levels is a critical component for COVID-19 patients as compared to non-COVID patients. Using telemedicine and appropriate diet management are effective controlling approaches.

INTRODUCTION

The number of confirmed cases of severe acute respiratory syndrome (SARS-CoV-2) and associated mortality globally has been progressively rising in 2019 due to the corona virus disease load [1]. Understanding the characteristics of COVID-19-infected diabetics is crucial given the prevalence of diabetes. Due to complete lock-up in the majority of the world and patients' limited ability to reciprocate, this is becoming increasingly crucial. For COVID-19, a sizable quantity of data from all around the world has been included.

When an acute infection attack occurs, people with diabetes and its related comorbidities are more likely to experience an increase in mortality and morbidity because their innate and humoral immune systems are weakened. Glycated hemoglobin (HbA1c) levels above 9% are linked to a 60% rise in hospitalization and pneumonia-related severity in cases of bacterial infection [2]. Patients with diabetes have a higher risk of death and morbidity due to previous viral pandemics. Diabetes-related complications and mortality were present during the 2002–2003 SARS outbreaks [3]. Similarly, diabetes tripled and quadrupled a patient's likelihood of hospitalization and admission to the intensive care unit (ICU) during the 2009 influenza A (H1N1) outbreak [4]. Diabetes was common during the 2012 Corona virus Middle East respiratory syndrome outbreak.

The objective of this publication is to conduct a systematic review and analysis to assess the risk of drugs and the COVID-19 infection-related death of diabetes patients.

DIABETES IS ASSOCIATED WITH COVID-19 PATIENTS

According to information available, COVID-19 is very prevalent in people with hypertension, diabetes, and cardiovascular disease (CVD), albeit prevalence estimates vary by area and country-based data. Information on the co-morbidities and COVID-19 features from 15 Chinese studies (n = 2209), Singh et al. found that 11%, 21%, and 7% of patients, respectively, have a high prevalence of diabetes, hypertension, and cardiovascular disease (CVD) [5]. In the same way, Yang et al reported 8 trials studies including 46,248 COVID-19 patients revealed that the prevalence of diabetes, hypertension, and cardiovascular complications was 8%, 17%, and 5%, respectively [6]. Similarly, the Chinese Center for Disease Control and Prevention's Epidemiology Working Group has identified and examined 20,982 COVID-19 patients. It has been noted that hypertension raises the risk of stroke, and that diabetes and CVD are associated with roughly 13%, 5%, and 4% of hospital admissions, respectively [7]. On the other hand, diabetes was found in almost 36% of patients in the Italian COVID-19 trial by Onder et al. Additionally, cardiovascular complications were linked to nearly 44% of the 369 hospital admissions for COVID-19 [8]. Similarly, Bhatraju et al. found that 58.69% of patients in USA had diabetes in relation to COVID-19. The COVID-19 response team of the Centers for Disease Control and Prevention (CDC), USA, reported a prevalence of approximately 11% based on data from 7,162 COVID-19 patients [9]. The study of the Italian surveillance group COVID-19 (n=481) revealed that nearly 34% of patients with COVID-19 had diabetes [10].

SPECIAL ASPECTS OF DIABETES PATHO-PHYSIOLOGY AND THE RELATIONSHIP BETWEEN THE ANTI-DIABETIC DRUGS IN CONTEXTS OF COVID-19

Cell entrance is accomplished by SARS-CoV-2 and SARS Corona virus ACE-2 receptors [11]. Type I and type II epithelial alveolar cells of the lungs and upper respiratory tract, as well as endothelium, the heart, renal tubular epithelium, intestinal epithelium, and the pancreas, are likely to contain ACE-2 receptors. SARS-CoV-2 surfaces include S-glycoprotein, which interacts to the ACE-2 receptor. This results in a conformational shift in S-glycoprotein. This gives the host cell the ability to initiate proteolytic digestion, which is carried out by the proteases TMPRSS2 and Furin, allowing the virions to enter [12]. When a virus infiltrates a cell, helper T cells that generate gamma interferons are drawn in to aid in the inflammatory response. In severe circumstances, this process might result in organ failure due to a 'cytokine storm,' which is caused by the production of more inflammatory cells. In Wuhan, a study was conducted on 161 COVID-19 samples, and the virus cleared faster in patients with diabetes [13]. Therefore, a few variables including the severity of SARS-CoV-2 infection in diabetes can be blamed for the higher risk.

1. Research has shown that the expression of ACE-2 is enhanced in the liver, pancreas, and RC of diabetic mice [14]. A Mendelian randomization investigation of phenotypes revealed a relationship between diabetes and ACE-2 expression [15]. The significance of these findings is currently unknown because higher ACE-2 expression may result in hyperglycemia and SARS-CoV-2 infection. An increase in Furin is the source of various type I diabetes-related health concerns. Proteins are transformed into polyproteins belonging to the Subtilisin/Kexin family (PCSK) by membrane-bound protease. This item is linked to the coronavirus; diabetes has been linked to an increase in Furin, which may facilitate viral replication [16].
2. Reduced T cell function: animal models of Middle East Respiratory Syndrome (MERS) have been shown to exhibit changes in T helper cells [17]. Lymphocytopenia is also utilized as an indicator for prognosis in COVID-19 patients [18].
3. Elevation of Interleukin-6 (IL-6): COVID-19 infection is associated with an increase in several cytokines, including Interleukin-6, whose level is elevated in diabetes, and which is more harmful to COVID-19 studies [19]. Studies on COVID-19 are also using monoclonal antibodies against the IL-6 receptor (tocilizumab) [20].

SARS-COV-2 EFFECT ON BLOOD GLUCOSE

When a person does not have diabetes, ACE-2 receptor expression is seen in the pancreatic islets, and SARS-CoV infection causes hyperglycemia. After three years of recovery from SARS, hyperglycemia has been demonstrated to

continuously occur, suggesting transient beta cell injury [21]. Nevertheless, COVID-19 has not shown comparable results, therefore it's critical to monitor blood glucose levels while the disease is still acute.

THE ROLE OF ANTI- DIABETIC DRUGS IN THE CURRENT SITUATION

There is no information on the differences in how oral anti-diabetic medications affect the progression of COVID-19 disease. Due to its suppression of AMP-activated protein kinase, metformin has immunomodulatory and proliferative effects and has been found to protect against pneumonia in mice models [22]. In a study involving a patient with tuberculosis, it was discovered that those on metformin had a greater survival rate than those who were not [23]. Mending and associates [24], 6.2 years of follow-up of 5269 patients with diabetes revealed that metformin decreased the risk of both diabetes and death in patients with lower respiratory tract disorders (HR: 0.30, 95% Cl, 0.10 to 0.93), even though the adjustment resulted in a few confounding factors. According to a study by Ho et al. which involved 4321 patients over the course of a 2-year follow-up, patients who received metformin had a lower risk of death (HR, 0.46; 95% Cl, 0.23 to 0.92) than patients with diabetes and chronic obstructive pulmonary disease who did not take the medication [25]. By upregulating the expression of ACE-2 in liver tissue, pioglitazone effectively inhibited steatohepatitis in experimental experiments [26]. According to the study, liraglutide, a GLP-1 receptor agonist, improves ventricular hypertrophy and raises the expression of ACE-2 in the lungs of rats infected with type 1 diabetes [27].

SPECIAL FEATURES OF COVID DIABETES MANAGEMENT-19

Glycemic Control

For COVID-19 patients, glucose management is becoming increasingly crucial. Blood glucose levels and COVID-19 are not well-studied, but prior illnesses like SARS and influenza H1N1 have demonstrated that patients with poor glycemic control are more likely to have diabetes, which increases the risk of complications and mortality [28]. Due to inadequate fluid intake and dehydration resulting in euglycemic ketosis, patients are recommended to stop taking SGLT-2 inhibitors. If vomiting happens, stop taking metformin right away and ensure that it is taken orally. The dosage of antihyperglycemic medications, such as insulin and sulfonylurea, should be adjusted based on the blood glucose level. COVID-19 Hospitalized patients experiencing respiratory distress can need insulin, but those who have an infection on their oral antidiabetic medication need.

Monitoring of Blood Glucose

It is impossible to stress the significance of constantly checking blood glucose levels, especially in patients who are critically ill and receiving intravenous insulin. There are efforts made to advise minimizing exposure. If the patients don't have any serious illnesses, self-monitoring skills can be taught and a glucose test gadget can be given. Additionally, blood glucose readings can be shared over the phone so that the necessary action can be performed. Continuous glucose monitoring (CGM) has its uses; this is particularly true with systems that allow for remote access without physically seeing or caring for patients. Numerous CGM obtrusions occur with using commonly recommended medications, including as acetaminophen, lisinopril, and atenolol, which have been demonstrated to be beneficial in patients with severe illness [29,30].

Role of ACE/ARB

ACE-2 will be regulated in patients using ACE inhibitors and angiotensin II receptor blockers (ARB) [31]. Treatment with losartan, an angiotensin receptor blocker, improves the lung injury caused by the coronavirus in mice [32]. An earlier examination of pneumonia brought on by an ACE inhibitor-treated virus revealed a drop in mortality and endotracheal intubation rates [33]. The opposing viewpoint maintains that elevated ACE-2 expression may theoretically raise the likelihood of contracting SARS-CoV-2 infection. There was no significant difference seen in the percentage of women or men taking ACEI/ARB medications between survivors and non-survivors in a prior analysis of 112 COVID-19 patients in Wuhan [34]. Based on the recommendations of the European Society of Cardiology section Council on Hypertension, the European Hypertension Society, and the American Heart

Association, it is reasonable to continue using ARB and ACE Inhibition for patients in the absence of strong evidence of either a benefit or harm [35].

Role of Statins, Calcium Channel Blockers and Aspirin

Research has been done on the topic of statins' ability to prevent pneumonia [36]. It is commonly recognized that statins raise the amount of ACE 2, which blocks the entry of SARS-CoV-2 [37]. Additionally, statins prevent nuclear factor kappa B from activating and stop the cytokine storm [38]. By preventing calcium from entering the cell, antihypertensive medications such as calcium channel blockers are known to lower the severity and mortality of viral pneumonia patients [39]. Despite safety precautions, the precise function of these COVID-19 medicines has not yet been determined; hypertensive patients should continue to use these medications to lower their blood pressure. Researchers have found that the preferred use of ACE-2 in COVID-19 and hypertension patients will not be impacted by CCB [40].

TREATMENT IN COVID-19 PANDEMIC

Diabetes therapy is getting more and more difficult in light of the current global pandemic. Numerous locations are under lockdown, making it impossible to work out, go for a stroll, use gyms, or go swimming. Individuals are afraid as a result of some COVID-19-related social media posts, and the majority of individuals are under emotional stress. The body is directly impacted by these changes in routine because there is a greater predisposition to consume packaged foods high in saturated fat and fresh produce is scarce. Because of the partial or total lockdown, access to the medication has also become extremely restricted. The issue with senior citizens is far more complicated. All these conditions could lead to glucose dysregulation and put patients at risk for heart attacks, ketoacidosis, and other conditions.

To guarantee that patients with diabetes have good health, the following steps should be taken:

1) A patient with diabetes must consistently eat a balanced diet and have their calorie consumption appropriately tracked. A healthy balance of fiber, protein, and very little saturated fat is necessary to keep blood sugar levels under control.

2) Continue your indoor exercise regimen, such as using a treadmill, running in one spot, pushups, squats, etc.

3) Regularly using insulin, a medication that lowers blood sugar, is crucial.

4) Patients must receive education when they come to the hospital, same as if they were experiencing dyspnea, dysphagia, weakness, etc.

5) Telemedicine is quite helpful right now. Through telemedicine, patients can consult with their doctor and receive treatment recommendations [41].

Research has been done to monitor or identify the effects of SARS-CoV-2 in individuals with diabetes and the effects of anti-diabetic medications in those with COVID-19. Although a thorough investigation on this topic is lacking, there is enough knowledge to assist COVID-19-positive diabetes individuals. Patients combine a healthy diet and exercise regimen with multiple anti-diabetic medications.

CONCLUSION

COVID-19's increased frequency and angularity are associated with diabetes. There is experimental evidence that diabetes affects both the inflammatory response to the infection and the virus's ability to penetrate cells. The significance of viruses in blood glucose regulation in SARS-CoV-2 patients cannot be emphasized. Diabetes management can be particularly challenging in situations when movement is restricted, however advancements like telemedicine, diet, and exercise can be helpful in these situations.

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CONFLICT OF INTEREST

None

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