Open Access Article

STUDY OF SOME THERAPEUTIC STRATEGIES FOR DIABETIC PATIENTS
AFFECTED FROM COVID 19

Soumya Tripathi
Assistant Professor, NIET Pharmacy Institute, Plot no. 19, Knowledge park-2, Greater Noida,

Ketki Rani
Assistant Professor, NIET Pharmacy Institute, Plot no. 19, Knowledge park-2, Greater Noida,

Richa Shakya
Assistant professor, NIET Pharmacy Institute, Plot no. 19, Knowledge park-2, Greater Noida

Sonia Chauhan
Assistant professor, NIET Pharmacy Institute, Plot no. 19, Knowledge park-2, Greater Noida

Dr.Avijit Mazumder
Director, NIET Pharmacy Institute, Plot no. 19, Knowledge park-2, Greater Noida, 201310

Dr.Rupa Mazumder
Dean, NIET Pharmacy Institute, Plot no. 19, Knowledge park-2, Greater Noida, 201310

Abstract

One of history's greatest human crises is the 2019 Coronavirus Pandemic (COVID-19). Patients with diabetes and related comorbidities have a higher chance of developing COVID-19 problems and dying. The severity of the condition, which makes it more vulnerable to severe symptoms and higher mortality rates in patients, especially those with high blood pressure, cardiovascular illnesses, obesity or diabetes, is causing increasing concern about the consequences of this pandemic. In the early stages of research, it is not apparent if diabetes, or diabetes-related comorbidities, or treatment strategies, lead to a COVID-19 result that is more severe. SARS-CoV-2, which may impair diabetics, can be combated by identifying a novel therapeutic strategy. Diabetic and COVID-19 connection: Potential pathogenic mechanisms and therapeutic suggestions It is impossible to draw definite conclusions based on the currently available insufficient data.

Keywords: COVID-19, SARS-CoV-2, Diabetes, Therapeutic treatment
2019 年冠状病毒大流行 (COVID-19) 是历史上最大的人类危机之一。患有糖尿病和相关合并症的患者出现 COVID-19 问题和死亡的可能性更高。这种疾病的严重程度使其更容易出现严重症状，并且患者死亡率更高，尤其是患有高血压、心血管疾病、肥胖症或糖尿病的患者。这引起人们越来越关注这种流行病的后果。在研究的早期阶段，糖尿病或糖尿病相关的合并症或治疗策略是否会导致更严重的 COVID-19 结果并不明显。SARS-CoV-2 可能会损害糖尿病患者，可以通过确定一种新的治疗策略来对抗它。糖尿病与 COVID-19 的联系：潜在的致病机制和治疗建议 根据目前可用的数据不足，无法得出明确的结论。

关键词：COVID-19，SARS-CoV-2，糖尿病，治疗

INTRODUCTION

Globally, severe acute coronavirus syndrome 2 (COVID-19) infected more than 126 million people and resulted in more than 2.76 million deaths, according to this research. SARS-CoV (the 2003 SARS pandemic virus) is a new, single-stand beta-coronavirus with 82% genetic similarity to this virus. Due of its increased reproduction rate compared to beta-coronaviruses like the SARS-CoV and the Middle East Respiratory Syndrome-CoV, the threat to global health is greater. SARS-CoV-2 The COVID-19 pandemic is causing more deaths (2.76 million deaths until 28 March 2021) than the preceding respiratory coronavirus syndromes (2.54 million deaths until 28 March 2021). (8096 cases with 774 deaths totaled during the 2003 outbreak of SARS and 2519 confirmed cases with 866 deaths totaled in the 2012 MERS outbreak). Because of the exponential increase in the number of confirmed cases and fatalities, epidemiological data may be used to characterize COVID-19 patients and to develop therapies. When a respiratory virus infects the body, it damages several organs, including the heart and kidneys.

Diabetes per se or co-morbidities that lead to a worse prognosis, however, remain unknown. The goal of this research is to discover potential risk factors for COVID-19 individuals with diabetes. COVID-19 and diabetic patients have different therapy options, which are also addressed.

As a result of respiratory secretions, COVID-19 is extremely contagious from one individual to the next. As the virus infects mucous membranes, it damages the lung. As a result of pulmonary infiltrations of >50% of radiologically imaging lung regions, some people have dyspnoea, respiratory rate 30 breaths per minute, saturation of blood oxygen of 93 percent, and/or low paO2:fiO2 levels. Individuals with severe septic, respiratory, and/or multi-organ illnesses are in the minority. It is believed that less than 5% of those infected develop a serious or life-threatening illness, although this number is likely exaggerated, considering the unknown frequency of subclinical infections in the general population A subsequent pneumonic bacterial infection may also be a problem.
LITERATURE REVIEW

Pegah Ahmadi Sarbarzeh, et al. (2020), Pneumonia One of the world's newest diseases, COVID-19, is rapidly spreading throughout the globe, causing numerous impairments and deaths. This study tries to synthesize evidence on diabetes and the COVID-19 pandemic using a systematic review and meta-analysis approach. Checklists such as PRISMA aided in data collection, analysis, and interpretation. The symptoms of diabetic and COVID-19 patients are not substantially different from those of COVID-19 patients alone, according to certain study studies. In the following meta-analysis, 14.5 percent of the patients had diabetes. In addition, COVID-19 patients have a higher death rate because they are at higher risk for ARDS. Antibiotics, antivirals, and HCQ are also recommended for diabetic patients. Diabetes, according to this study, is a risk factor for COVID-19 patients.

Miriam Longo, et al. (2020), Global health organizations have declared COVID-19 (COVID-19) a pandemic that is causing significant morbidity and mortality globally. Type 2 diabetes, hypertension, and cardiovascular disease significantly increase hospitalization and death risk in COVID-19 patients. For inpatient patients, hypoglycemia and hyperglycemia are predictors of adverse outcomes. Optimal glycemic control is needed in individuals with diabetes and SARS-CoV-2 infection in order to reduce the probability of COVID-19 severity. Patients with Type 2 diabetes who were treated with insulin and GLP-1RAs had optimum glucose and inflammatory effects, suggesting that they may be used to treat COVID-19 diabetics with asymptomatic and non-critical illnesses.

Soo Lim, Jae Hyun Bae, Hyuk-Sang Kwon and Michael A. Nauck (2021), Individuals with diabetes mellitus seem to be more susceptible to coronavirus disease 2019 (COVID-19), which is caused by severe acute respiratory coronaviral illness 2 (SARS-CoV-2). Angiotensin-converting enzyme 2 (ACE2), a component of the renin-angiotensin-aldosterone pathway, is the main receptor for SARS-CoV-2. To the contrary, DPP4 may act as a binding target for SARS-CoV-2. Insulin should be the first line of defense against acute glycaemia. There is a significant incidence of type 2 diabetes mellitus in the majority of existing data. COVID-19 and type 1 mellitus diabetes are presently poorly understood. This information is preliminary and additional study is required to determine the best therapy for people with diabetes.

Lei Li, Ranran Li, Xianghong Yang, Mingyan Zhao, Dechang Chen and Jiao Liu (2020), It become a worldwide clinical issue by the end of 2019 with the 2019 novel coronaviral disease (COVID-19) epidemic in Wuhan, Hubei Province, China. ICU intensive care for critically ill patients infected with the novel coronavirus (2019-nCoV) consumes a lot of medical resources. As a result of our previous experience treating various viral infections and influenza, we evaluated the promising medications, extra medicines, respiratory and circulatory supportive techniques, multiple organ monitoring, and appropriate food options for treating COVID-19 in ICU. Prior to the vaccine, several treatments are available, and COVID-19 specific medications are available.

Varghese E, Samuel SM, Liskova A, Kubatka P, Bu¨sselberg D (2021), An outbreak of severe acute respiratory syndrome coronavirus 2 has been declared by the World Health Organization
(WHO) on March 11, 2020. (SARS-CoV-2). It was found that COVID-19-related problems, ICU admission, and mortality were more likely to occur soon after their emergence in late December 2019. Using insulin and/or other oral anti-diabetic medications (e.g. metformin) to maintain normal blood glucose levels has reduced COVID-19’s harmful effects. Interestingly, Metformin treatment was related to a significant reduction in disease severity and mortality rates among diabetic individuals with COVID-19, whereas insulin therapy was associated with unfavorable outcomes. A great deal of study has been done on metformin in attempt to understand its antioxidant, anti-inflammatory and antiviral effects in COVID-19. As a result of this paper, we describe the various molecular mechanisms that lead to the beneficial effects of Metformin therapy and lay forth the scientific grounds for using Metformin recycling in COVID-19 patients.

**METHODOLOGY**

All patients hospitalized with CO-VID-19 infection and hyperglycemia between March and May 2020 were included in the study. Those who had no diabetes history were excluded from the study. Individuals with diabetes were also prohibited from immunosuppressive therapy, severe renal failure, chronic lung disease, and liver cirrhosis, among other conditions. An observational retrospective chart review of 250 patients from March to May 2020 is being conducted as part of this study.

**Table 1.** Characteristics of all the study subjects 

(N = 250)

<table>
<thead>
<tr>
<th>Gender</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>235 (94)</td>
</tr>
<tr>
<td>Female</td>
<td>15 (6)</td>
</tr>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>Mean age, years</td>
<td>49.6±10.4</td>
</tr>
<tr>
<td>18–35 years</td>
<td>23 (9.2)</td>
</tr>
<tr>
<td>36–50 years</td>
<td>103 (41.2)</td>
</tr>
<tr>
<td>&gt;50 years</td>
<td>124 (49.6)</td>
</tr>
<tr>
<td>Smokers</td>
<td>14 (5.6)</td>
</tr>
<tr>
<td>Mean BMI</td>
<td>28.2±5.1</td>
</tr>
<tr>
<td>Comorbidities present prior to admission</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>81 (32)</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>23 (9.2)</td>
</tr>
<tr>
<td>Onset of symptoms</td>
<td></td>
</tr>
<tr>
<td>Duration in days</td>
<td>5 (3–7)</td>
</tr>
<tr>
<td>Blood group</td>
<td></td>
</tr>
<tr>
<td>Group O</td>
<td>77 (30.8)</td>
</tr>
<tr>
<td>Group A</td>
<td>61 (24.4)</td>
</tr>
<tr>
<td>Group B</td>
<td>62 (24.8)</td>
</tr>
<tr>
<td>Group AB</td>
<td>22 (8.8)</td>
</tr>
</tbody>
</table>
Mean HbA1c 9 (7–11)

Severity of illness

Mild illness with no pneumonia 48 (19.2)
Moderate illness with pneumonia 123 (49.2)
Severe illness with severe pneumonia 79 (31.6)

Oxygen therapy

Required 55 (22)
Not required 195 (78)

Outcome at completion of study

Discharged 172 (68.8)
Transferred 37 (48.8)
Inpatient 16 (6.4)
Deceased 24 (9.6)

Prior to hospital admission, symptoms lasted a median of five days (IQR, 3–7 days). Patients with moderate to severe pneumonia accounted for 49.2% of the study group, whereas 19.4% had minor COVID-19 illness with no pneumonia symptoms. Thirty-six percent of the sample had severe pneumonia, according to the report.
Fifty percent of the oxygen was administered through nasal cannula, while the other 28 percent was administered using non-rebreather masks. Of the patients, 22% were in need of mechanical ventilation. A total of 172 (68.8%) patients had been rejected, 16 (6.4%) were remained in the hospital, and 37 (14.8%) had been transferred to other facilities. Patients that were released had a median stay of 19 days (14.5–28). Table 1 shows the fundamental characteristics of all participants in the study.

Table 2. Subgroup analysis based on diabetes history

<table>
<thead>
<tr>
<th></th>
<th>Newly diagnosed (n = 84)</th>
<th>Known diabetes (n= 166)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Severity of illness</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild illness with no pneumonia</td>
<td>10 (11)</td>
<td>38 (22.9)</td>
<td>0.053</td>
</tr>
<tr>
<td>Moderate illness with pneumonia</td>
<td>41 (48.8)</td>
<td>82 (49.4)</td>
<td></td>
</tr>
<tr>
<td>Severe illness with severe pneumonia</td>
<td>33 (39.3)</td>
<td>46 (27.7)</td>
<td></td>
</tr>
<tr>
<td>------------------------------------</td>
<td>----------</td>
<td>----------</td>
<td></td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Required</td>
<td>25 (29.8)</td>
<td>30 (18.1)</td>
<td></td>
</tr>
<tr>
<td>Not required</td>
<td>59 (70.2)</td>
<td>136 (89.9)</td>
<td></td>
</tr>
<tr>
<td>Outcome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deceased</td>
<td>14 (16.7)</td>
<td>11 (6.6)</td>
<td></td>
</tr>
</tbody>
</table>

In the table 2, the median HbA1c was reported as 9 percent [IQR, 7–11 percent], median C-reactive protein was 95 percent [IQR, 35–159], lactate dehydrogenase was 338 percent [IQR, 249–1452], ferritin was 885, and dimer was 0.88. 30.8 percent of patients have blood type O, whereas blood group AB is the least common (8.8 percent). Ten percent of the research group's participants died (n = 25).

THERAPEUTICS-TREATMENT SPECIFIC TO PATIENTS HAVING BOTH COVID-19 AND DIABETES

Medical teams should maintain appropriate glycemic control in COVID-19 individuals who have diabetes. As a result, any potential therapy issues that are used for these people must be thoroughly assessed.

Insulin is a common treatment for both kinds of diabetes. Insulin treatment should be selected depending on COVID-19 severity, and such patients should be closely monitored. However, this medicine has been recommended for COVID-19 diabetic patients who are in a severe condition. Patients on insulin had poorer clinical
outcomes than those on metformin, according to one study. Patients with respiratory distress, renal failure, or acidosis cardiac insufficiency who are on COVID-19 and metformin should be taken off of the drug. Metformin usage in patients who died, as well as other therapies such as RAAS, b-blockers, and loop diuretics, had been associated with mortality on day 7 in the CORONADO trial by Cariou et al., according to the study's findings. It was hypothesized that this may be related to the fact that people who died had less comorbidities, such as diabetic problems, since insulin and other medicines were prescribed more often. Individuals with COVID-19 have been shown to have much higher postprandial glycemic fluctuations, which are then followed by continuous glucose monitoring. A continuous blood glucose monitoring system should be used throughout the treatment process.

To prevent ketoacidosis and a reduction in fat metabolism, sodium-glucose conveyors 2 inhibitors must also be treated with care. In addition, analogues of glucagon-like receptors-1 (GLP-1R) should be used with caution since diarrhoea, nausea, vomiting, and headaches may develop. It is possible that coronavirus and type 2 diabetes infections have similar disease pathophysiology mechanisms. DPP4 and ACE2 are well-known metabolic signals and inflammatory pathways, cardiorespiratory physiology, and glucose homeostasis transducers for coronaviruses. Glucose-lowering drugs, such as DPP4 inhibitors, which are frequently prescribed to patients with type 2 diabetes, are also known to affect the biological activity of many immunomodulatory substrates.

Glucocorticoids may cause hyperglycemia in people with or without diabetes. To treat patients with very high levels of cytokines and c-reactive peptides despite the fact that the drug may increase insulin resistance, reduce insulin sensitivity, and cause severe hyperglycemia, it was utilized.

**ACE2, SARS-CoV-2 AND DIABETES**

In order to fuse viral membranes and host cells, SARS-receptor CoV-2's binding domain utilizes host ACE2. In the kidney, endothelium, lungs, and heart, ACE2 is a type I integral glycoprotein. As ACE2 is converted by angiotensin I and II into angiotensin (1–9) and angiotensin (1–7), (Fig. 1). A vasodilator, it is effective against inflammation and cardiovascular disease. Studies on animals have revealed that the level of ACE2 expression in lung tissue is low, but increases when lung injury occurs. There is evidence that ACE2 may be used as a therapeutic agent against inflammatory acute lung injury, both in animals and humans. SARS-CoV (the virus responsible for the 2002/2003 SARS pandemic) also seems to regulate the expression of ACE2 in infected cells, and the inflammatory damage is expected to prolong infected cells.
As previously mentioned, the ACE2 transforms both angiotensin I and angiotensin II into angiotensin-1–9 and angiotensin-7. As well as the lung, kidney, heart and pancreas ACE2 serves as a CoVentry facilitator. Increased angiotensin I levels and increased ACE2 gene expression are associated with ACEI/ARB therapy. Hyperglycemia is a result of excessive viral penetration into host cells, which leads to organ damage and insulin insufficiency. It is possible that angiotensin II may be converted to angiotensin via ACE2.

Regardless of pre-morbid glycaemic status, severity of disease, or glucocorticoid usage, admission rates of hyperglycaemia are higher in SARS patients. Later, SARS-CoV was shown to damage ACE 2 in pancreatic islet cells, causing abrupt hyperglycemia and perhaps contributing to an elevated mortality rate even in those without diabetes. Infection with SARS-CoV-2 may result in hyperglycemia, severe complications, and death.

Despite the fact that ACE2 and ACE1 have certain similarities, ACE inhibitors do not block ACE2 (ACE1). Treatment with ACEI and angiotensin receptor antagonists increases ACE2 expression. On the basis of these findings, it was speculated that ACEI/ARB use may increase SARS-CoV-2 infection, which would result in a serious disease. En outre, the ACE2 polymorphism is associated with a greater risk of diabetes and cardiovascular disease, which may also protect against severe CoV infection. A rise in angiotensin levels (1–7) due to upregulated ACE2 may, on the other hand, have an anti-inflammatory effect. Angiotensin II levels that are low owing to ACEI inhibition may negate this benefit. It is thus difficult to determine the balance between the benefits and risks of continuing or ceasing ACE inhibitory therapy.

**PATIENTS WITH DIABETES AT RISK OF COVID-19**

As far as medical issues are concerned, the COVID-19 pandemic is far from being a medical issue. People and society are affected on many levels by it. A person's health and lifestyle may be adversely affected by major confinement techniques, such as isolation, social distance and city lockdown. Managing chronic diseases like diabetes, which requires dietary changes, frequent exercise, and excellent adherence to medicines, presents a number of difficult issues.

Because of restricted availability to suitable food, maintaining a balanced diet may be difficult. Particularly for patients on multiple-dose insulin regimens, careful portion selection and regulating mealtime insulin according to carbohydrate consumption remains the optimal approach.

The need of regular blood glucose monitoring cannot be overstated. However, read below under 'Management of patients with diabetes with COVID-19' for potential issues about paracetamol/acetaminophen usage in conjunction with CGM. The monitoring of ketone levels and awareness for the onset of DKA symptoms are essential for individuals with type 1 diabetes.

Routine clinic visits and hospital congestion should be reduced in order to prevent the spread of illness among diabetics. In addition, healthcare professionals should explore measures such as telemedicine consultations or
telephone guidance, the distribution of medicines to caregivers at reduced risk, online coordination of drug delivery, and the distribution of medications for longer durations. As a result of direct interaction between healthcare professionals and patients, regular non-emergency examinations should be postponed. Priority should be given to patients who are at risk of losing a limb or losing their eyesight.

**DIAGNOSIS**

The diagnosis of COVID-19 cannot be confirmed without a microbiological examination. Patients who meet the criteria outlined below should be tested for SARS-CoV2 in addition to other respiratory diseases. Currently, only suspected cases of COVID-19 may be tested. It is possible that local health authorities may create specific priority criteria for case studies with limited resources. RT-PCR is the current COVID-19 standard diagnostic method, despite the fact that many laboratory tests have been performed. Detection of SARS-CoV-2 positive nucleic acid in sputum, throat swabs, and samples of lower respiratory tract secretions.

**Criteria for suspicion and testing**

COVID-19 instances should be recorded in all countries, as well as the transmission route. This is what the WHO and other sources recommend:

**Preliminary observational symptoms**

Infected individuals who have a new fever and/or respiratory symptoms (e.g., cough, dyspnea) or patients with severe lower respiratory tract illness have traveled to a community transmission area without a clear cause and without a history of close contact with a confirmed COVID-19 patient.

**Tests may be carried out according to resources**

Patients with severe lower respiratory system illness who have visited or gone to the sites of SARS-CoV-2 in communal contact with COVID-19 patients within 14 days and have a new fever or respiratory symptoms (cough, dyspnea, etc.). Testing for those older than 60 should be prioritized, as should tests for people suffering from diabetes, hypertension, cardiovascular disorders (CVDs), chronic renal diseases (CRDs), cancer, and immunological illnesses that cause symptoms like fever, cough, or dyspnea.

**Should be tested**

Long-term exposure to SARS-CoV-2 infected individuals (within 2 metres) or direct contact with infectious fluids without the use of personal protective equipments.

**MANAGEMENT OF PATIENTS WITH DIABETES AND COVID-19**

**Setting and general considerations:** In the majority of cases, COVID-19 patients are suffering from a mild disease that may be treated at home if local guidelines are followed. If a patient has diabetes and COVID-19 symptoms, they should notify their local health care providers as soon as possible about the need for a diagnosis, severity evaluation, isolation and hospitalization. Diabetes patients should be treated ideally in hospitals or locations where thorough monitoring of disease development is possible since the risk of adverse outcomes is higher. In order to identify deteriorating
glycaemic control, hyperglycaemic crises, and/or clinical status deterioration, people treated at home must maintain regular phone contact with healthcare providers.

**Glycaemic control:** During the COVID 19 pandemic, good glycaemic management is essential. Considering that this is a new viral disease, there are few data points and the expert advise is based on methods used in similar epidemics. As long as patients are able to eat and drink appropriately, conventional glucose-lowering medicines may be used to treat mild COVID-19. It is important for patients with diabetes to adhere to the 'sick-day standards', and it is vital to monitor capillary glucose frequently. Severe cases of cancer sometimes need a modification in the course of treatment. Decision-making is affected by several factors, including glycaemic state, hemodynamic stability, nutritional status, renal function and risk of hypoglycemia. For those with COVID-19, glucose-lowering medicines may be problematic (Table 3). Metformin may be stopped in patients who are hospitalized and extremely ill because to the risk of lactic acidosis. Lactic acidosis in severe COVID 19 infection may be exacerbated by hypoxic circumstances.

SGLT2 inhibitors are not advised during COVID-19 infection because of the risk of dehydration and euglycaemic ketoacidosis, as well as the difficulties in maintaining effective perineal hygiene. Glucagone-like peptide-1 receptor agonist therapy should probably be discontinued temporarily in individuals with haemodynamic instability (compromising absorption from subcutaneous sites), renal failure, and gastrointestinal dysfunction (which prevents adequate oral intake). Treatment with GLP-1RAs may cause gastrointestinal side effects, including as volume depletion and aspiration, which can be dangerous. As a result, the dangers of hypoglycemia are low, and a wide range of renal functions are usually safe while using DPP4 inhibitors. Although DPP4 inhibitors do not increase hypoglycaemia risk, they improve glycaemic management even in hospitalized patients. However, these drugs are anticipated to have lesser therapeutic advantages in patients with severe COVID-19. While DPP4 inhibitors may be maintained in patients with mild symptoms, they should be stopped in patients with severe acute illnesses and replaced with insulin if necessary. It is difficult to maintain a tight grip on blood glucose levels while using sulfonylurea during a severe illness state. It is recommended that people with diabetes use insulin instead of sulfonylureas. The use of chloroquine with sulfonylureas should be done with caution owing to the dangers of both.

**Table 3: The utilization of diabetes and associated comorbidities pharmacotherapies during COVID-19**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Considerations for use during COVID-19</th>
<th>Suggestions for practice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin</td>
<td>Risk of lactic acidosis in hypoxia and acute illness</td>
<td>Stop if severely ill with haemodynamic instability or hypoxia</td>
</tr>
<tr>
<td>SGLT2 inhibitors</td>
<td>Increased risk of dehydration and euglycaemic ketoacidosis</td>
<td>Stop if oral intake is not tolerated or severely ill</td>
</tr>
</tbody>
</table>
A growing body of evidence shows that insulin is superior to other glycaemic control medicines for hospitalized patients. Glycaemic management in non-critically ill patients in the hospital is best achieved by subcutaneous insulin therapy with basal or intermediate-acting insulin given once or twice a day, in combination with short- and rapid-acting meal boluses.

Stringent infection control should be implemented for COVID-19 patients with diabetes regardless of where they are being treated, due to their vulnerability for secondary bacterial infections with potentially severe consequences.

### SPECIFIC THERAPIES FOR COVID-19 IN PEOPLE WITH DIABETES

There are many organizations that have established management standards and procedures for COVID-19. COVID-19 therapy for diabetics, on the other hand, does not have any particular recommendations. In the majority of recommendations, COVID-19 should only be treated in those who have virologically confirmed COVID-19. Candidate agents' safety concerns should be weighed against their comparative benefit in order to determine which is more important. Individuals with diabetes may be particularly affected by certain of these drugs (Table 4). A comprehensive clinical study including compassionate or off-label anti-COVID-19 therapy is the best way to do this.

**Table 4: Concern for Patients with Diabetes Over The Use Of Planned Covid-19 Therapeutic Agents**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Concerns</th>
<th>Transaminits and Myositis</th>
<th>Risk and Benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td>GLP-1RAs</td>
<td>Gastrointestinal side effects and risk of aspiration</td>
<td>Stop in severely ill patients</td>
<td></td>
</tr>
<tr>
<td>DPP4 inhibitors</td>
<td>Low risk of hypoglycaemia; possible to use for a wide range of renal function</td>
<td>May be continued in non-critically ill patients</td>
<td></td>
</tr>
<tr>
<td>Sulfonylureas</td>
<td>Risk of hypoglycaemia if oral intake is poor or with concomitant use of hydroxychloroquine or chloroquine</td>
<td>Stop if unable to maintain regular oral food intake or at risk of hypoglycaemia</td>
<td></td>
</tr>
<tr>
<td>Insulin</td>
<td>Requires frequent monitoring due to risk of hypoglycaemia</td>
<td>Drug of choice in critically ill patients (see text)</td>
<td></td>
</tr>
<tr>
<td>ACEI/ARBs</td>
<td>Uncertain risk of increased susceptibility for infection and uncertain benefit in mitigating inflammatory injury</td>
<td>Continue use unless a specific contraindication arises (hypotension, hyperkalaemia, acute kidney injury)</td>
<td></td>
</tr>
<tr>
<td>Statins</td>
<td>Possibility of increased risk of transaminitis and myositis</td>
<td>Individualise d decision on</td>
<td></td>
</tr>
</tbody>
</table>
Therapeutic agent | Considerations for people with diabetes
---|---
Chloroquine/hydroxychloroquine | • Hypoglycaemia: caution with insulin and insulin secretagogues • Prolongation of QT interval: caution in people with comorbid cardiovascular disease. Risk increased by azithromycin
Lopinavir/ritonavir | • Hyperglycaemia, deterioration of glycaemic control • Interaction with statins: increased risk of hepatic and muscle toxicity
Glucocorticoids | • Hyperglycaemia • Susceptibility to secondary bacterial infection
Remdesivir | • Hepatotoxicity: caution with statins and pre-existing fatty liver disease

CONCLUSION

The risk of severe infections, poor prognoses, and a higher mortality rate is substantially greater for individuals with COVID-19 and diabetes compared to those without diabetes. Individuals with diabetes with severe prognosis and risk factors include age, gender, high blood pressure, heart disease, obesity, inflammation, and hyperglycemia. A greater risk of serious illness is associated with all the factors mentioned above. SARS-CoV-2 damages pancreatic islets and deteriorates insulin homeostasis, leading to the development of new diabetes. More research is required to discover the specific mechanisms of SARS-CoV-2. There is a pressing need for future research to better understand genetic predispositions, pathophysiological mechanisms that explain the link between COVID-19 and diabetes, and their therapeutic management, across different populations.

REFERENCES


