Regulating Diabetes During COVID-19 – A Review

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Declaration

It is hereby declared that

1. The thesis submitted is my/our own original work while completing degree at Brac University.
2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
4. I/We have acknowledged all main sources of help.

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Approval

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Ethics Statement

This study does not involve any human or animal trial.

Abstract

Inspite of having no significant relationship with SARS CoV-2 infection, diabetes takes to disease severity which tends to mortality often. Patients having poor blood glucose management are susceptible to death more in COVID-19. The threshold of decreased death risk is between6 3.9 and 10.0 mmol/L. According to investigations, due to infections of COVID-19, diabetic patients had major problems and died. Diabetic patients have to experience significant COVID-19 problems including severe symptoms and consequences. So, scientists say that well-controlled diabetes can decrease getting ill from COVID-19. So, diabetic patients have to take foods, fruits and liquid, sweetened drink, honey in the time of increasing blood sugar and dropping blood sugar respectively. Anyway, for diabetic patients, insulin and metformin are commonly used to regulate blood glucose in COVID-19 individuals. Few applications of drugs are also used for diabetic patients which may affect the course of the COVID-19. GLP-1R agonists, SGLT2 inhibitors, DPP4 inhibitor and PPARs are included here. However, For the COVID-19 environment, diabetes treatment should be provided adequately.

Keywords: Glucagon-like peptide-1 (GLP-1); Sodium-glucose Cotransporter -2 (SGLT2); Dipeptidyl peptidase 4 (DPP4); Peroxisome proliferator - activated receptor (PPAR); Severe Acute Respiratory Syndrome (SARS); Corona Virus Disease (COVID).

Dedication

Dedicated to my parents.

Acknowledgement

I would like to thank first the Almighty Allah, our creator, the source of our existence. To complete the project, Allah helped me to get support from the people who are recognized here. Then I would like to express my deepest gratitude to my supervisor, Dr. Mohd. Raeed Jamiruddin sir, Associate Professor, School of Pharmacy, Brac University for his guidance and suggestions and for giving me all kinds of support and encouragement at my harder times. After that, I would like to thank some of my friends for supporting me. Last but not the least, I would like to thank my family for supporting me and praying for me in every phase of life.

Table of Contents

Declaration.....ii

Approval..... iii

Ethics Statement.....iv

Abstract.....v

Dedication.....vi

Acknowledgement.....vii

Table of Contents.....viii

List of Figures.....x

Chapter 1 Introduction.....1

1.1 Context of COVID-19.....1

1.2 Diabetes and COVID-19.....3

1.3 Effects of Diabetes on COVID-19.....5

1.4 Effects of COVID-19 on Diabetes.....8

1.4.1 Effects of COVID-19 on Glycemic Control..... 8

1.4.2 Effects on Diabetes of the Limitations Due to the COVID-19 Pandemic..... 9

1.5 Aims of the Review.....12

1.6 Objectives of the Review.....12

Chapter 2 Process, Risks & Relation.....13

2.1 Methodology.....13

- 2.2 Epidemiology …… 13

2.3 Risks with Diabetes and Covid 19 13

2.4 Mechanism 14

2.5 Relation Between Covid-19 and Diabetes 16

Chapter 3 Treatment 17

3.1 Drugs 17

3.1.1 GLP-1R Agonists…… 17

3.1.2 SGLT-2 Inhibitors …..……...17

3.1.3 ACE2 and DPP4 ……18

3.1.4 Insulin Therapy……...18

3.2 COVID-19 Diabetes Plan 19

Chapter 4 Conclusion 20

References 22

List of Figures

Figure 1. 1 Relationship in both directions between COVID-19 and diabetes (E. Varghese et al., 2021) 2

Chapter 1

Introduction

1.1 Context of COVID-19

An instance of severe acute respiratory distress resulted from a new coronavirus was appeared in Wuhan, Hubei Province, China in late December 2019 (*Listings of WHO's Response to COVID-19*, n.d.). Coronavirus Disease 2019 (COVID-19), that ambushed the airway and led to acute respiratory distress syndrome (ARDS), pneumonia along with mortality in critically worked on persons, was connected to the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in the following weeks. As of May 16, 2021, the worldwide SARS-CoV-2 epidemic finds contaminated over 162,000,000 persons including putting an end to over 3.3,000,000 (*Home - Johns Hopkins Coronavirus Resource Center*, n.d.).

Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS), as well as most lately, Covid-19, come about all instances of human infections caused by zoonotic coronavirus transmission (Z. Zhu et al., 2020). The time between exposure and symptoms for the COVID-19 is generally between 7 and 14 days, and it is transmitted through the respiratory system (Z. Zhu et al., 2020). Wheeze, fever, drawing breath along with sore throat difficulties were common symptoms of SARS-CoV-2 infection, albeit their rigidness assorted from one patient to another. Higher mortality rates and more severe outcomes were related with older generation as well as threats like obesity, diabetes, cardiovascular disease, hypertension, along with chronic long term renal disorders in the COVID-19 cohort (Singh & Singh, 2020).

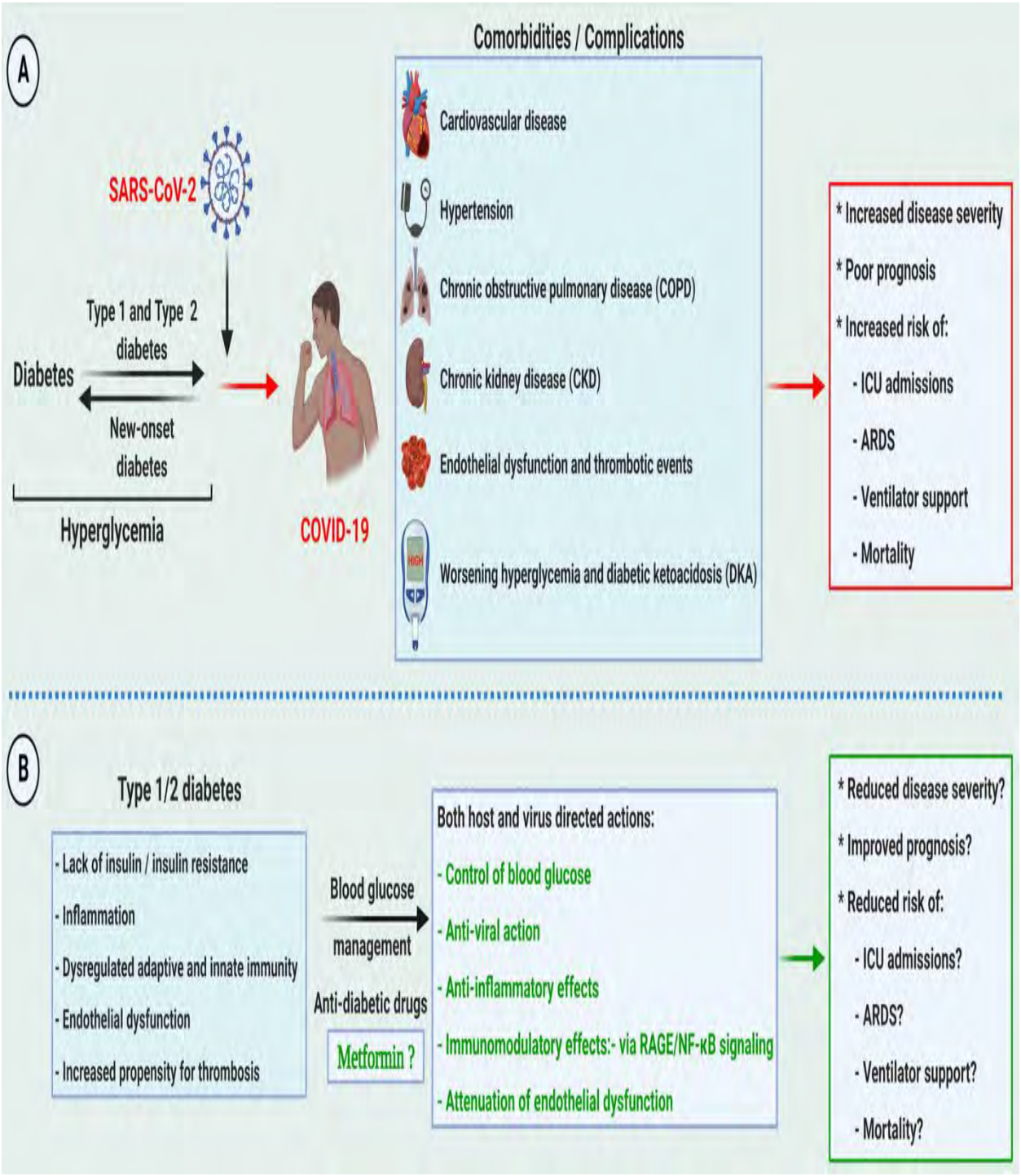

Figure 1. 1 Relationship in both directions between COVID-19 and diabetes (E. Varghese et al., 2021)

To the angiotensin converting enzyme 2 (ACE2) receptor, the irrevocable of SARS-CoV-2 has been recognized as a critical pace in the infective of COVID-19 by molecular studies of viral pathogenesis. By attaching to the host ACE2 labyrinth, that viral spike protein interferes with Renin-angiotensin-aldosterone system (RAAS) control of ACE2, resulting in decreased ACE2 availability (Curran et al., 2020; Samaan et al., 2019). Ultimately, this makes the sickness more severe and raises the risk of death by activating the inflammatory response through the replication as well as conversion of pro-inflammatory cytokines (cytokine storm) intervened by NF-B and JAK/STAT signalling (Samaan et al., 2019), (Curran et al., 2020).

1.2 Diabetes and COVID-19

The high cost of managing diabetic mellitus (DM), especially when complications arise, has the potential to have far-reaching consequences for both those with the disease and society as a whole. Diabetic patients have a higher possibility to become in patients during a pandemic like COVID-19. variations in exercise, diet along with personal care, as well as deficiency of usual treatment owing to the shutdown of outpatient clinics as well as lack of contact, contribute to a worsening in disease control and make it harder to spot problems. Individuals with DM may have poorer clinical outcomes due to all of the aforementioned factors (Bellido & Pérez, 2021).

Despite the fact that diabetes did not correlate with SARS-CoV-2 susceptibility, it did have a strong relationship with illness severity, the development of ARDS, intensive care unit hospitalizations, and mortality (Apicella et al., 2020; Pinto & Bertoluci, 2020). Other noteworthy findings from Italy, China along with the United Kingdom point to a rise in the incidence of type 1 diabetes amongst infants and young adults beneath the age of 25 ("Summary of Recommendations Regarding COVID-19 in Children with Diabetes: Keep Calm and Mind Your Diabetes Care and Public Health Advice," 2020; Unsworth et al., 2020). Patients with poorly managed blood glucose levels showed a greater death rate in COVID-19

(Z. Zhu et al., 2020) in comparison with those with well-managed blood glucose volume. The risk of death was lowest among patients when the levels of blood sugar were in the middle of 3.9 and 10.0 mmol/L. According to the glycemic characteristics of the clinical outcome, high blood glucose levels are related with a longer hospital stay and a larger risk of death (Bode et al., 2020). Better blood glucose control has been shown to enhance outcomes for individuals with several parts of the body injuries as well as reduce death in people with COVID-19 (Gianchandani et al., 2020; L. Zhu et al., 2020).

Blood glucose in COVID-19 persons is often controlled with a combination of drugs, including insulin and metformin. Metformin (also referred to as "Glucophage") is one of the most widely used medications for treating type 2 diabetes (Samuel et al., 2017; Triggle & Ding, 2017). Metformin's effect on blood sugar reduction is attributed to its effects on glucose absorbing by muscles, breakdown of glycogen, production of glucose from sources other than carbohydrates (gluconeogenesis), and intestinal glucose absorption. Additional benefits of metformin, like as its antioxidant and anticancer characteristics, have been the focus of recent research (S. Varghese et al., 2019). COVID-19's positive prognosis is attributed, in part, to its anti-inflammatory effects (Samuel et al., 2021). Metformin's molecular mechanisms show that it is involved in the pathways that govern inflammatory response, Vascular smooth muscle action, and epidemiologic pathogenesis along with glucose metabolism (Samuel et al., 2021; Scheen, 2020). In this article, we discuss the several ways in which Metformin can benefit people with COVID-19, involving its role like an antiviral, anti-inflammatory, immunomodulatory, cardio-, as well as vasculo-protective agent.

Consequences of the COVID-19 pandemic on the health of patients with diabetes mellitus (DM) are investigated here. There is discussion of how the pandemic's effects on people's lives

and healthcare access could pose a risk to those who already have diabetes (Bellido & Pérez, 2021).

1.3 Effects of Diabetes on COVID-19

Having diabetes is a threat for a bad outcome in peoples infected with COVID-19, although it does not appear to increase the chance of infection. One of the most common co-occurring diseases is diabetes mellitus (Ambrose & Singh,2 015); (Fadini & Colleagues, 2020); (Roncon & Colleagues, 2020). The prevalence of DM among COVID-19 carriers varies greatly from 7-30%, according to published data (B. Li et al., 2020). According to a review of 12 studies on diabetes in China undertaken by Italian researchers, Fadini et al., the overall prevalence was 10.3%. After accounting for age, the prevalence of diabetes in China was similar to or slightly lower than in the United States (Fadini et al., 2020). Diabetes mellitus (DM) was diagnosed in 0.4% of the 61,414,470 living participants in Barron et al.'s whole-population survey in England, 4.7% of the individuals with T2D, and 0.1% of the participants with other DM types. The odds ratios (ORs) for in-clinic COVID-19-relevant mortality were 3.51 (95% CI, 3.16-3.90) in patients with type 1 diabetes and 2.03 (1.97-2.09) in patients with type 2 diabetes after controlling for sex, deprivation age, ethnicity, and geography. Adjusting for previous hospitalizations for stroke, coronary heart disease along with cerebrovascular illness reduced the odds ratios (ORs) for type 1 and type 2 diabetes to 2.86 (2.58-3.18) and 1.80 (1.75-1.86), respectively. Twenty percent of people contaminated with the severe acute respiratory syndrome-causing type 2 coronavirus (SARS-CoV-2) also have diabetes, arterial hypertension, obesity, or cardiovascular disease, according to studies (Barron et al., 2020; Fang et al., 2020; Moazzami et al., 2020; F. Zhou et al., 2020) .

Patients whose hyperglycemia or DM is not controlled have an increased possibility of cardiac problems and respiratory failure, and their likelihood of being hospitalized to the intensive care

unit (ICU) is greater than double once COVID-19 infection has occurred. Mortality is increased by a factor of three in those who have diabetes mellitus or uncontrolled hyperglycemia (Barron et al., 2020; Bloomgarden, 2020; Huang et al., 2020; Roncon et al., 2020; Singh et al., 2020). Barron et al. discovered that 30% of COVID-19 mortalities being attributable to DM, and that people with Type 1 and Type 2 Diabetes were nearly three times as likely to die as those without diabetes. The COVID-19 pandemic has both direct health consequences and far-reaching implications for the price and use of healthcare. Direct medical expenses for people with co-occurring conditions like diabetes mellitus were predicted to increase by a factor of two to three in the United States during the course of the contamination (Barron et al., 2020; Bartsch et al., 2020).

It is unknown why people with DM are more susceptible to COVID-19 at this time (Muniyappa & Gubbi, 2020). Increased mortality and morbidity may be attributable to pathophysiological pathways including diabetes mellitus (DM)-related chronic inflammation, impaired immunity, and abnormal coagulation. It is possible that the higher incidence of DM in COVID-19 severe patients reflects the greater incidence of T2D in the aged. Furthermore, DM in the aged is associated with cardiovascular problems as well as fatness both of them contribute to the explanation of the connection between DM and the destructive result of COVID-19. Anyway, the alliance linking DM and worse diagnosis is still present in younger, non-hypertensive people (Huang et al., 2020). During hospitalization, hyperglycemia has been revealed in recent studies to be a predictor of COVID-19-related mortality and other adverse events (Carrasco-Sánchez et al., 2021; Klonoff et al., 2021). According to the COVID-19 register kept by the Spanish Society of Internal Medicine 14, non-critically ill patients who presented with hyperglycemia at admission were more likely to develop complications and die, with the risk increasing with the grade of hyperglycemia (blood glucose >180 mg/dL (or higher)). In a retrospective analysis of 1544 COVID-19 patients from 91 institutions in the United States,

researchers discovered that both hyperglycemia and hypoglycemia were related with worse outcomes (Carrasco-Sánchez et al., 2021; Klonoff et al., 2021). Furthermore, the results imply that maintaining optimal glycemia during hospitalization can be advantageous for patients who have DM and COVID-19 in terms of clinical outcomes, but this evidence is clearly insufficient. A study found about the admission of 59 COVID-19 patients in two Italian hospitals, insulin infusion was sustained as late as the levels of blood glucose were 140 mg/dL (7.8 mmol/L) in 15 patients who have hyperglycemia. The patients' outcomes were better thanks to this treatment than they would have been without the insulin infusion. In addition, when hyperglycemia was managed, both interleukin 6 and D-dimer levels reduced (Sardu et al., 2020).

Two pathways in particular may have a bit part in COVID-19 contamination; angiotensin II-converting enzyme (ACE2) and dipeptidyl peptidase 4 (DPP4) (Iacobellis, 2020; Muniyappa & Gubbi, 2020). The receptor ACE2 for the coronavirus surface protein has been identified. COVID-19 induces respiratory failure, hyperinflammation, and cell damage by suppressing ACE2 expression. There is some speculation that acute hyperglycemia facilitates viral cell entry by raising ACE2 expression in cells (Rao et al., 2020; Singh et al., 2020). Consistent hyperglycemia, however, is admitted to negatively regulate ACE2 expression, leaving cells vulnerable to viral impacts (Bindom & Lazartigues, 2009). Antibodies targeting DPP4 blocked HCoV-EMC infection of primary cells, confirming its role as a working receptor for this human coronavirus (Iacobellis, 2020). It is unknown if the same processes apply to COVID-19 or if the therapeutic ministration of DM with DPP4 impediments has any effect on the progression of the infection.

1.4. Effects of COVID-19 on Diabetes

People with diabetes are doubly impacted by the COVID-19 pandemic; the disease increases the risk of complications for those who already have diabetes and can also worsen or trigger the onset of diabetes in those who don't already have it (Bellido & Pérez, 2021).

1.4.1. Effects of COVID-19 on Glycemic Control

Although there is limited data on COVID-19-related hospitalizations of people with diabetes, what is available suggests that glycemic control is inadequate (Bode et al., 2020; J. Zhou & Tan, 2020). Hospitalizations with a average blood glucose volume above 180 mg/dL (10 mmol/L) were found in 37.8% of the study population, and 39.1% of values were above that criterion (Bode et al., 2020). One American study found that the target blood glucose volume was not gained by 56% of patients in the intensive care unit (ICU) and 53% of patients outside the ICU throughout the first two or three days; in a separate investigation capillary blood glucose levels were found to be over the recommended target in 56.6% of the Chinese population (140-180 mg/dL) (7.8-10 mmol/L) (Klonoff et al., 2021; J. Zhou & Tan, 2020). Extremely high insulin requirements, up to 201 IU/d (2.2 IU/kg/d) [21], were observed in insulin-dependent people with SARS-CoV-2 infection; these rates are collaborated with elevated volume of inciting cytokines. Decompensation, manifested as diabetic ketoacidosis in patients with T2D and COVID-19, is seen in patients with other critical contamination as well. An extensive review found that 7 of the 10 people with COVID-19 who had glycated hemoglobin levels greater than 9.5% at admission also had underlying T2D (Pal et al., 2020; Wu et al., 2020). Complex mechanisms, including but not limited to the toxicity caused by persistently elevated glucose levels and the familiar anxiety response collaborated with critical sickness, are likely involved in the pathophysiology of many DM symptoms. Significant insulin resistance, and hence a greater demand for insulin, can occur from the proinflammatory

environment triggered by COVID-19. Pancreatic cells express ACE2, thus if the virus makes its way into the islets of the pancreas and damages them, it could cause an insulin deficit. Acute hyperglycemia develops even in persons who do not have diabetes mellitus (Yang et al., 2010). As noted by J. Li et al. in 2020, insulin insufficiency in the presence of significant insulin resistance may account for the frequent occurrence of critical diabetic ketoacidosis and ketosis upon hospitalization. Clinically relevant medicines for COVID-19 patients, like systemic corticosteroids and antiviral medications, are known to aggravate glycemic control and give rise to significant hyperglycemia trips on top of the course of a day (Lim et al., 2021; Perez et al., 2014). Records of a elevated prevalence of hypoglycemia are there in the time of hospitalization, which may have aided the malnutrition caused by COVID-19 and occurred excluding the associated modification of medications that lower blood sugar (Scheen et al., 2020; J. Zhou & Tan, 2020). Finally, there may be barriers to glycemic management in patients with COVID-19 due to the necessity of preventing virus exposure and the certainty that medical staff manage sufferers with COVID-19 who have minimal skill controlling hyperglycemia. Therefore, deficient glycemic control in diabetic patients and hyperglycemia in people without a record of diabetes are COVID-19 consequences.

1.4.2. Effects on Diabetes of the Limitations Due to the COVID-19 Pandemic

Thus, the COVID-19 outbreak, patients with diabetes have had a much more difficult time going about their daily lives due to the need to adhere to social isolation policies. Immediately, it severely limits a person's ability to get medical care, buy medications and supplies for managing diabetes, live a healthy lifestyle, and keep up with friends and family. Data are now becoming available to assess the impacts of the first motion of the COVID-19 pandemic, notwithstanding the lack of information on the indirect effects on DM.

Studies in T1D patients who utilize continuous glucose monitoring (CGM) or flash glucose monitoring (FGM) show that glycemic control did not suffer during lockdown and may have even improved (Capaldo et al., 2020; Fernández et al., 2020). In a current meta-analysis including 3441 people with T1D who used CGM or FGM, it was found that the percentage of time spent in the 70-180 mg/dL range expanded by 3.05% (95% CI, 1.67-4.43%; p 0.0001) during the lockdown period, while the percentage of time spent more than scale (>180 mg/dL and >250 mg/dL) reduced by 3.39% (-5.14 to -1.63%) and 1.96% (2. Possible causes for this enhancement include more time spent on DM, more regular work schedules, and reduced stress during commutes. T1D individuals that are incompetent to manage their ailment, who do not utilize CGM, or of whom communal or work circumstances conflict with the time spent controlling DM may not benefit from our findings. The epidemic has made it more difficult to manage type 2 diabetes for 46% of the 763 people with type 1 diabetes and they took part in the taking hold of Your Diabetes research in the United States. In addition, both episodes of hyperglycemia and variations in blood sugar were 25% more common (Fisher et al., 2020). Among the 603 T1D patients, two-third taking part in an online review in Spain described problems with glycemic management as well as 40% reported weight increase (Tejera- Perez et al., 2021).

When compared to type 1 diabetics, people with type 2 diabetes have a much wider range of treatment options, monitoring, self-adjustment of treatment, and the ability to use remote consultation technology. Comparable results on the effect of lockdown on diabetes treatment were found in the survey of hold of your diabetes participants (763 people with T1D and 619 with T2D) (Fisher et al., 2020). Patients tended to be non-Hispanic White, highly educated, and in control of their blood sugar. Moreover, 46% of T2D patients received insulin therapy as well as 25% utilized CGM. Lockdown resulted to lower metabolic control in the short term for 26% of patients who had previously had good metabolic control, according to a study of 114

T2D patients being followed at a major Italian institution (Biancalana et al., 2021). These numbers are not representative of the type 2 diabetes population as a whole since they do not include patients who are actively engaged in healthcare for purposes of control monitoring and therapy intensification. Furthermore, we may expect that treatment intensification and lack of monitoring will usually result in worse control in the long term because of the short time periods of published data and the fact that T2D is a progressive disease. A total of 13,352,550 patients were tracked between March 2020 and April 2020 at 1709 primary care centres in the United Kingdom, and their electronic medical records were analysed (Carr et al., 2021). This is especially worrisome since it points to a drop in glycated haemoglobin testing and the prescription of metformin and insulin, particularly in older persons with T2D (a decrease of 77–84%). Between January and July 2019 (N = 79,268) and January and July 2020 (N = 85,046), patients in Germany with type 2 diabetes reported making similar changes to their treatment plans for decreasing blood sugar. Here is a breakdown of the number of people who switched only one drug from 2019 to 2020: DPP4 inhibitors (15%), SGLT2 inhibitors (-3%), other oral hypoglycemics (-6%), GLP-1 receptor agonists (0%), insulin (21%), and sodium-glucose co-transporter 2 (SGLT2) inhibitors (-3%). Another unintended outcome of the COVID-19 epidemic in type 2 diabetes patients is that it complicates the process of diagnosing diabetic mellitus, that needs particular distinctive techniques that can only be executed in a impersonal surroundings. More than 45,000 new cases of type 2 diabetes in the UK were either not diagnosed or delayed during the first four months of the lockdown (Carr et al., 2021). Overall, these numbers are cause for worry because misdiagnosis or inadequate monitoring of DM might cloud evaluations of treatment determined boosting metabolic command and putting a stop to the escalation of undoubtedly life-threatening problems.

1.5 Aims of the Review

The motive of the study is learning how COVID-19 affects diabetic individuals and how to treat these patients so that their death rate decreases in the future.

1.6 Objectives of the Review

The motive of the study is synthesizing the remaining studies and provide new insight into the topic at hand.

Chapter 2

Process, Risks & Relation

2.1 Methodology

Managing diabetes during covid 19 is the topic of this review. Primary and secondary sources, including PubMed, Scopus, Science Direct, and Springer, as well as authoritative websites, provided all the data and material used in this study. In order to approach the evaluation methodically, first, an outline was created. We searched for relevant articles using terms like "diabetes" and "covid 19." After sifting through a large number of studies, about 50 that included the necessary information were selected for inclusion in the study.

2.2 Epidemiology

Preliminary research indicates that over 25% of hospitalized individuals with severe COVID-19 infections also suffered from diabetes. Patients with diabetes were more likely to experience severe complications and ultimately succumb to the infection. When blood sugar levels are excessive, the body's defenses weaken and infection becomes more likely. (Diabetes and Coronavirus: What People Should Know About COVID-19, n.d.).

2.3 Risks with Diabetes and Covid 19

Infections of the skin, bones, eyes, ears, digestive tract, urinary tract, and respiratory system are all significantly more common in people with diabetes, as can hospitalizations for these conditions and even death (Erener, 2020). However, there is not enough data to say whether or not people with diabetes are more likely to contract COVID-19 than the general population. Diabetic people do not have a higher risk of contracting the virus, but they are more likely to experience serious complications as a result of infection. Significant COVID-19 repercussions are also more likely to occur in the presence of numerous other health conditions (such as

diabetes and heart disease). People above the age of 65 who get the virus also have a greater chance of developing problems (Erener, 2020).

Patients who have diabetes are at enlarged possibility for severe complications related to COVID-19. People who have diabetes are at an expanded possibility to experience critical symptoms along with effects after contracting any virus. Scientists say that it is possible to get beneath possibility of serious illness from COVID-19, if our diabetes is adequately managed. Having multiple health disorders at once weakens the immune system, increasing the likelihood of being severely ill with COVID-19 and other viral infections. This includes diabetes (Erener, 2020).

Patients with type 1 or gestational diabetes can be at a higher possibility of serious ailment from COVID-19, according to current CDC data. It is important to recognize that people with diabetes may vary in age, comorbidities, and glycemic control. Poorer outcomes after diagnosis of COVID-19 have been observed in those with diabetes who have a record of diabetes-related health concerns differentiated to those patients that have diabetes who are generally healthy (Erener, 2020).

Numerous studies have shown that obtaining COVID-19 increases one's risk of developing diabetes. More than 30 days after contracting COVID-19, infants who are less than the age of 18 have a higher possibility of developing diabetes (Erener, 2020).

2.4 Mechanism

Even though obesity, hypertension, and CVD are all more common in people who have diabetes, this is still confusing if or not diabetes itself is solely in charge of the increased despair and death connected with COVID-19. Scientists found that people with cardiometabolic multimorbidity do worse on the COVID-19 than those with either diabetes or CVD alone. However, plasma glucose levels and diabetes independently predict SARS patients' mortality

and morbidity. It is likely that DM patients are more susceptible to COVID-19 due to a stronger chemical attraction along with effective virus appearance. Viral approval is hampered, T-cell function is impaired, vulnerability to cytokine storm disorder is increased as well as cardiovascular disease is present as additional mechanisms. Pneumocytes and other lung cells in the lungs are the principal sites of coronavirus entrance and inflammation. Proteins like ACE2 (Angiotensin-converting enzyme 2), TMPRSS2 (transmembrane protease serine 2), furin as well as DPP4 (dipeptidyl peptidase-4) are expressed, which are critical for the entry of coronaviruses. DPP4 inhibitors are commonly used in the management of diabetes, and both ACE2 and DPP4 have been connected to the pharmacologic as well as anatomical power of cardiovascular and glucose homeostasis (Abu-Farha et al., 2020).

Enlarged ACE2 expression in kidney, heart, pancreas along with pulmonary cells may increase the frequency with which SARS-CoV-2 binds to cells. It is widely noted that in diabetic animal models, Angiotensin-converting enzyme 2 is overexpressed in numerous tissues. Insulin therapy reduces ACE2 expression, but glucagon-like peptide-1 (GLP-1) agonists, thiazolidinediones (pioglitazone), antihypertensive medicines including statins, and ACE inhibitors all increase ACE2 expression. Lately, researchers have been investigating lung illnesses and characteristics which can be connected to expanded ACE2 appearance. They used "phenome-wide Mendelian randomization analysis" and found that diabetes was linked to expanded appearance of ACE2 in the lungs. It has also been found that the cellular protease furin is elevated in the blood of patients with T2D. The results of the above-mentioned investigations provide credence to the idea that the outlook for diabetics with COVID-19 is dismal. In addition, recent studies show that people with diabetes had a longer clearance time for SARS-CoV-2. However, aforementioned result requires confirmation by further extensive investigation (Abu-Farha et al., 2020).

2.5 Relation Between Covid-19 and Diabetes

People infected with Covid-19 typically experience a moderate form of diabetes that can be managed at home with minimal care. Uncontrolled glycemia, which may be exacerbated by Covid-19, which is a leading reason of demise in people who have Diabetes. When compared to hospitalization to an ICU, the risk about cardiac complications and respiratory failure doubles. Researchers found that 30% of fatalities in Covid-19 were attributable to diabetic individuals. Therefore, the most important thing a patient can do is to get checked regularly in order to detect any anomalies or evaluate their current clinical situation. Optimizing glycemic management, in particular through regular monitoring of blood glucose levels, can reduce the chance of developing serious disorders. Glycemic management by food and medication adjustments is also essential (Bellido & Pérez, 2021).

Chapter 3

Treatment

Due to the lack of effective and targeted medications, treating Covid-19 infection in diabetic patients presents a number of difficulties. Metformin, GLP-1R agonists, SGLT2 inhibitors, DPP4 inhibitors, insulin treatment, and PPARs are only few of the medicines that may alter the Covid-19 course in diabetic patients. However, there was insufficient data to conclude that (Abu-Farha et al., 2020).

3.1 Drugs

3.1.1 GLP-1R Agonists

These medications work to lessen systemic inflammation in diabetic animals by targeting a variety of pathways. As they mitigate lung immune cytokine replies and lessen lung harm in animals following respiratory virus infection, they may be effective in treating Covid-19 patients (Bloodworth et al., 2018).

Restoring cell glucose sensitivity requires its participation in both intracellular glucose metabolism and cAMP signaling. Therefore, the process concurrently reduces the blood glucose level to maintain control and ensures a relatively low risk of hypoglycemia. If the patient's condition does worsen, however, these medications can be stopped quickly (Futatsugi et al., 2020).

3.1.2 SGLT-2 Inhibitors

These medications work by blocking the reabsorption of filtered glucose via the sodium-glucose cotransporter 2 (Heerspink et al., 2016). Several studies showed that in addition to improving glycemic control, SGLT-2 inhibitors had a protective effect on various organs. Caution is advised before taking these inhibitors, however, as increased glucose excretion may increase the risk of dehydration and Diabetic Ketoacidosis. If the patient has a severe case of

SARS-CoV-2 contamination or has threatening respiratory failure or thrombosis, treatment must be stopped (Abu-Farha et al., 2020).

3.1.3 ACE2 and DPP4

DPP4 functions like a coreceptor for a member of coronaviruses, together with MERS-CoV, and it does so via regulating the activity of a wide variety of chemokines and cytokines that have an immunomodulatory effect. DPP4 inhibitors increase the levels of the incretin hormones GLP-1 and GIP in the blood by blocking their degradation. There is no indication that these drugs can regulate the pathway related to coronavirus infection, despite the fact that DPP4 is both a receptor of the MERS-Cov and a helper in the suppression of DPP4 (Futatsugi et al., 2020). However, DPP4 inhibitors are linked to the enhancement of Covid-19 in a number of ways (Solerte et al., 2020). In addition, ACE2 receptors aid in blocking viral entrance into cells, albeit the metabolic factors involved have not yet been explored (Monteil et al., 2020). Linagliptin was shown to be effective in a research for lowering blood sugar and stopping the decline of Covid-19 patients (Iacobellis, 2020).

3.1.4 Insulin Therapy

When it comes to lowering blood sugar levels, insulin continues to be the solution of cure for treated Covid-19 patients (Bornstein et al., 2020). Patients with severe infections get a continuous intravenous insulin infusion with a selected glucose level of 7.8-10.0 mmol/L (Association, 2019). Moreover, insulin therapy indicated superior outcomes in the treatment of hyperglycemia and Covid-19, with the reduced possibility of serious disease compared to treatment without insulin (Sardu et al., 2020). A key difficulty in the prescribing of insulin therapy is the fact that several reviews have shown that insulin raises each risk of mortality and catastrophic outcomes by three times the normal rate (Chen et al., 2020). Close monitoring of blood glucose levels may alleviate these difficulties (Umpierrez & Korytkowski, 2016) and

thereby minimize mortality rates in patients, which may be attributable to hypoglycemia crises. Insulin is still the best choice for the cure of diabetic patients infected with Covid-19 because there is no evidence that other medications show better results.

3.2 COVID-19 Diabetes Plan

Patients with diabetes should always have ready access to:

- A variety of healthy foods, including whole-grain crackers, vegetable or noodle soups, and unsweetened applesauce.
- Patients with diabetes should keep honey, sugary drinks, fruit juice, and hard candies on hand in case their blood sugar levels dip, and they should be able to get more refills on their insulin and other medications.
- Extra glucagon and ketones on a strip.

Chapter 4

Conclusion

One of the most common comorbidities in individuals with COVID-19 and a predictor of poor outcome is diabetes mellitus. Although the reasons why diabetics patients are bound to get admitted in the hospital because of COVID-19 remain unknown, the scant data available suggests that poor glycemic control may be to blame. The necessity to limit exposure to the virus and the fact that most COVID-19 patients are seen by doctors who aren't well-versed in diabetes management both provide challenges to maintaining good glycemic control in these individuals. Education, monitoring of control and consequences, and screening for the condition in those at risk are all important parts of effective clinical therapy. Analyze how COVID-19 affects diabetes in terms of glycemic management and the challenges that this epidemic presents. Think about things like exercise, diet, checking blood sugar levels, and medication. Hospitalized patients and those with life-threatening illnesses are given priority. Finally, we talk about the present and future of telecare in the care of dibeteic patients infected with COVID-19 (Bellido & Pérez, 2021).

Treatment for diabetes needs to be modified appropriately for the COVID-19 scenario. This article can set out like an instruction for health field contributors to make sure progression of treatment for diabetic patients by providing a summary of guidelines for managing diabetes under several COVID-19 pandemic scenarios. Further analysis is required to determine the short- and lengthy result of COVID-19 in this inhabitant. These recommendations, together with the application of technological developments in telemedicine and the treatment of diabetes in inpatient as well as outpatient settings, need to be assessed for their efficacy (Bellido & Pérez, 2021).

Diabetes expands the possibility of serious COVID-19 and illness, together with admittance in the ICU along with fatality and it is suggested through evidence, including ICU admission and fatality. Diabetes mellitus is a common comorbidity with the COVID-19 virus. Elevated blood glucose volume and social deprivation are connected with unpleasant COVID-19 scores. To prevent critical COVID-19 from progressing in patients with diabetes, it may be necessary to maintain tight control over blood sugar levels. However, there is a lack of information about the efficacy of anti-diabetic drugs that do not contain insulin. In order to lessen the severity of diabetes-related problems, it is crucial that patients maintain their usage of diabetic facilities and accepts adequate impersonal care, such as conceal, instruction, and observation of diabetes management as well as difficulties in the time of personally or distant visits (Bellido & Pérez, 2021).

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