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# A CRITICAL REVIEW ON POST COVID-19 DIABETES AND ITS ASSOCIATED COMPLICATIONS WITH THEIR NEWER THERAPIES FOR ITS MANAGEMENT

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## ABSTRACT

An anticipated 216 million cases of 2019 coronavirus illness (COVID-19) have been confirmed, with 4.49 million deaths. The development of diabetes and its associated consequences have been described in persons with and without a family history of the disease. Some researchers have found that focusing on wearable technology is the most effective strategy for spotting cases of newly diagnosed diabetes. The COVID-19 pandemic prompted a flurry of activity as scientists sought for the virus's distinguishing characteristics in the hope of developing a treatment or vaccine.The reported high frequency of infections in people with diabetes mellitus is one of the difficulties and challenges that have surfaced (DM). Patients with COVID-19 often suffer from other conditions, with diabetes ranking second to hypertension. COVID-19-related infectious illness has evolved into a major international health concern. Patients with diabetes and their doctors faced a formidable obstacle during the COVID-19 epidemic. Better patient-provider communication may aid in treating diabetes in this era of social distance, isolation, and quarantine. Patients with diabetes need specialized treatment due to the correlation between their condition and more severe symptoms and consequences. Most modern chronic illnesses, including diabetes mellitus, are controllable by a combination of medical treatment and dietary improvements. Adults over 65 have an increased risk of developing and living with diabetes-related complications. As a result of the COVID-19 pandemic, patients with diabetes may be at a higher risk of infection, serious complications, and even death. A patient's risk for problems after a diabetes diagnosis may rise if their viremia is already high, immunologic deregulation, pulmonary and endothelial, and increased systemic coagulation.

**Keywords:** Covid-19, Diabetes Mellitus, Comorbidity, Isolation, Diabetic Management.

## Introduction

The 2019 corona virus illness (COVID-19) worldwide pandemic has already claimed the lives of more than 4.49 million individuals. The development of diabetes and its associated consequences have been described in persons with and without a family history of the disease (Chavda, Kapadia, Soni et al., 2022). The exact kind of diabetes that this virus produces is unknown. It may be a unique atypical form of diabetes or cause type 1 or 2 diabetes. Some researchers have found that focusing on wearable technology is the most effective strategy for spotting cases of newly diagnosed diabetes. (Budhiraja , Soni , Jha ,2022 or Metwally et al. 2021)

The global spread of COVID-19 has added numerous additional obstacles to managing diabetes. The reported high frequency of infections in people with diabetes mellitus is one of the difficulties and challenges that have surfaced (DM). Hypertension, chronic renal disease, and coronary artery disease are common comorbidities that compound the effects of diabetes (Steenblock et al., 2021; Kunti et al., 2021). We have an obligation as diabetic care providers to counsel our patients in this regard. Both the early diagnosis of new instances of diabetes and the prompt identification of hyperglycemic increases in people already diagnosed with diabetes is crucial. Amid the current global pandemic of chronic respiratory virus infection caused by influenza A (COVID), it is essential that we not only aim for and make every effort to attain excellent glycemic control but that we also detect and treat diabetic consequences as early as possible (Da et al., 2021).

To combat the COVID-19 pandemic, medical professionals need a reliable way to detect new cases of diabetes or hyperglycemic increases in those who currently have the disease (Pettus and Skolnik 2021)). Accurately determining which antidiabetic drugs are best for a given patient has been another significant obstacle in treating diabetes mellitus. When it comes to maintaining healthy blood sugar levels, insulin looks to be a viable alternative (Semwal et al., 2022). The Drugs, Devices, and Cosmetics Agency (DGCI) has authorized hydroxychloroquine (HCQ) use for DM. Since the COVID-19 pandemic began, there has been a great deal of research on its qualities that have the potential to aid

in the treatment and prevention of this unique virus (Sahu et al., 2021).

Until then, this approach will remain hypothetical at best, with the most promise for halting the onset of a hyperinflammatory response in cases of severe COVID infection. Since pioglitazone is an effective insulin sensitizer, it stands to reason that it would also considerably lessen inflammation caused by insulin resistance (Alshahawey et al., 2022). It seems like it may work, but we need to see how it performs in clinical studies before we can use it. The effectiveness of HCQ combined with azithromycin in treating mild to moderate instances of COVID-19 is currently being studied. More extensive randomized clinical trials (RCTs) are encouraged to confirm effectiveness, particularly in diabetic individuals (Raghav et al., 2021).

Because of the drug's established safety profile in DM, it may be worth exploring its usage for glycemic control more often under the present circumstances because of the potential for unintended benefits (Rao et al., 2021). Patients with COVID-19 coinfection may benefit from taking statins. Although there are strong reasons to conduct clinical trials, there is yet no clinical proof that these advantages materialize (Ghazi et al., 2021). Patients with diabetes are often offered statins and angiotensin-converting enzyme (ACE) inhibitors. Let's prepare to face the new post-COVID obstacles in diabetes treatment while keeping an eye out for the ever-evolving lessons we need to know. (Krishnakumar et al., 2022 Madhu, 2021)

**Report of World Health Organization (WHO)**

The World Health Organization (WHO) declared a pandemic on March 11, 2020, due to the fast global spread of the sickness caused by this virus, known as coronavirus disease 19 or COVID-19 (Hoenigl et al., 2022). Oxygen therapy, antivirals, steroids, HCQS, and antibiotics are used as supportive care since a viable vaccine has yet to be developed. HRCT chest scans are highly sensitive and specific, yet there is currently no reliable antibody test for quick diagnosis. COVID-19-related infectious illness has evolved into a major international health concern. A positive swab test doesn't always mean the patient is sick; they may exhibit no symptoms, mild flu-like sickness, or severe symptoms that need hospitalization (Girdhar and Manocha, 2022; Parasher, 2021). Patients with

COVID-19 often suffer from other conditions, with diabetes ranking second to hypertension. Older adults and those with chronic diseases such as diabetes have greater severity of symptoms and problems. The spread of disease has resulted in the quarantine or mandatory indoor isolation of millions of people. Diabetes is linked to higher death rates and frequent visits to critical care units (Gupta et al., 2021).

Particular care should be given to this subset of individuals because of the complexity of managing their diabetes. Due to the complexity of diabetes treatment in these cases, these individuals need extra care. Researchers looked at the health records of 909 Italian COVID-19 patients who had gone away and discovered that diabetes was the second most common comorbidity, behind only hypertension (73.5%) (Kesavadev et al., 2021). In this time of increasing social distance, isolation, and quarantine, improved communication between patients and healthcare providers may be helpful in managing diabetes. Even while having diabetes makes you more vulnerable to the severe health consequences brought on by COVID-19, there is hope (Eswaran et al., 2021).

Furthermore, the European Society of Cardiology suggests that incretin-based medicines may be helpful in type 2 diabetes patients and diabetic patients with hypertension (Chawla et al., 2021). Patients with diabetes need specialized treatment due to the correlation between their condition and more severe symptoms and consequences. Although the COVID-19 epidemic presents a significant issue for diabetes patients and diabetologists, it also presents an opportunity to enhance communication between doctors and their patients (Rajueni et al., 2021; Stoian et al., 2020). During the COVID-19 epidemic, managing diabetes was very difficult. Diabetes treatment was swiftly provided, including follow-up phone calls with doctors. A plan for telemedicine and a group of non-clinical physicians was developed. Projects of a similar kind may now be devised for dealing with other chronic diseases. Since medical professionals are now committed to

COVID control, an approach including telemedicine and a group of para-clinical physicians was developed (Hoenigl et al, 2022, Joshi et al., 2020).

**Diabetes Mellitus**

Infected individuals with diabetes mellitus have an increased risk of mortality and severe complications from COVID-19 (DM). People with DM may effectively control their condition with the help of a variety of different treatments. Even though the number of people diagnosed with diabetes decreases annually, the disease has remained the deadliest for decades. Most contemporary chronic disorders, such as diabetes mellitus, are manageable with the help of medicine and good dietary habits. (Girdhar and manoch a2022; Dk, 2022).

Coronavirus cases in India first occurred because of outside connections rather than domestic spread. The Ministry of Health and Family Welfare (MoHFW) issued travel advisory limitations in an effort to halt the epidemic, as it had done during previous pandemics such as SARS, Ebola, and bubonic plague. On March 22, Indian Prime Minister Narendra Modi urged everyone to observe the Janata curfew for 14 hours (Gupta et al., 2021). Similarly, the Epidemic Disease Act of 1897 mandated quarantine restrictions in India. On January 30 and February 3, the first three infected people were identified upon their return to Kerala from Wuhan, China (Kesavadev et al., 2021).

Over 1071 cases and 29 fatalities have been reported in India as of March 30. If social isolation and the quarantine measures outlined by the Indian Council of Medical Research (ICMR) are implemented successfully, the number of cases is expected to drop by 62% in India. (Eswaran et al., 2021; Ghosh et al., 2020).

People with diabetes who also have COVID-19 have a more dire prognosis and fatality rate. Because of its syndromic character, diabetes is associated with a worse prognosis for those who suffer from it (Chawla., 2021). When treating a patient with diabetes, a doctor must consider not just the patient's current health but also strike a delicate balance

between glucose-lowering medications and those designed to combat the viral infection (Rajueni et al., 2021).

According to the data, older individuals did worse in COVID-19, and it's reasonable to assume that this correlation is much stronger among people who already have diabetes (Rubino et al., 2020). To begin, those over 65 have the highest diabetes prevalence. Additionally, problems from diabetes tend to be more severe and persist for longer in persons over 65. Third, diabetes and old age often co-occur with other conditions such as cardiovascular disease, hypertension, and obesity (Elnaem and Cheema 2021).

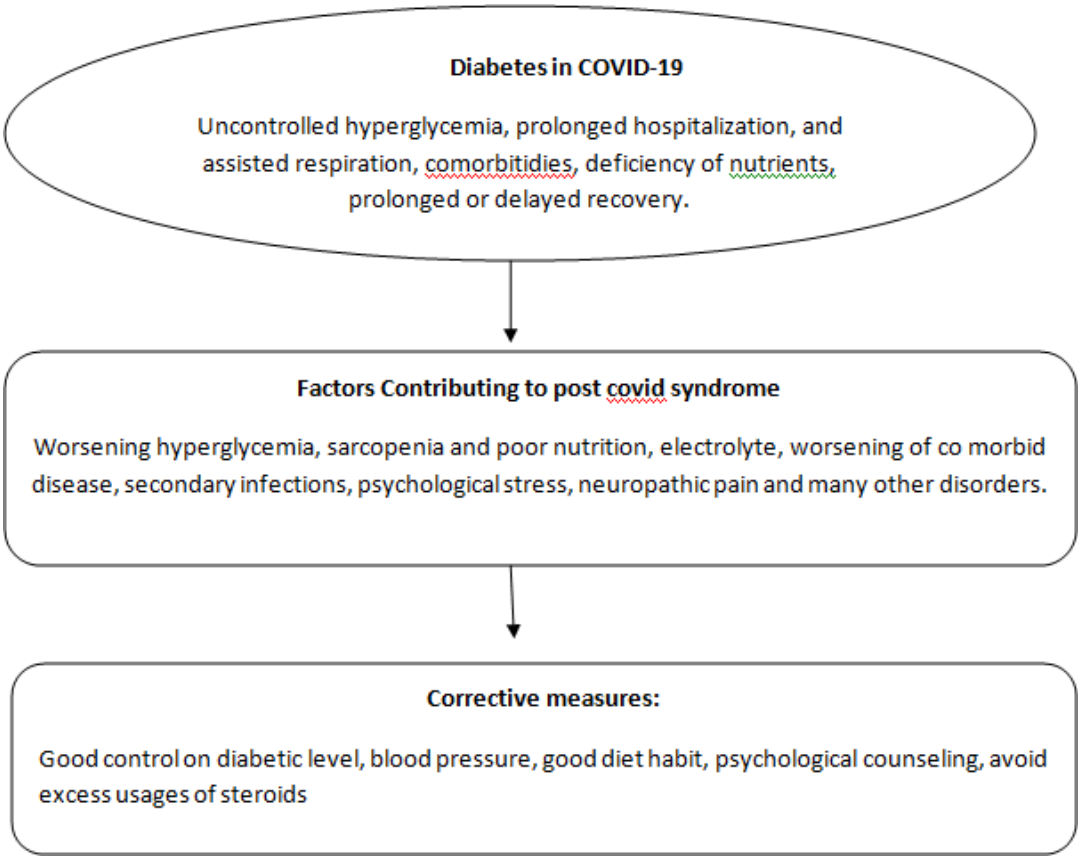



**Fig.1** *Suggest treating diabetes mellitus and its connection to the post-COVID-19 syndrome.*

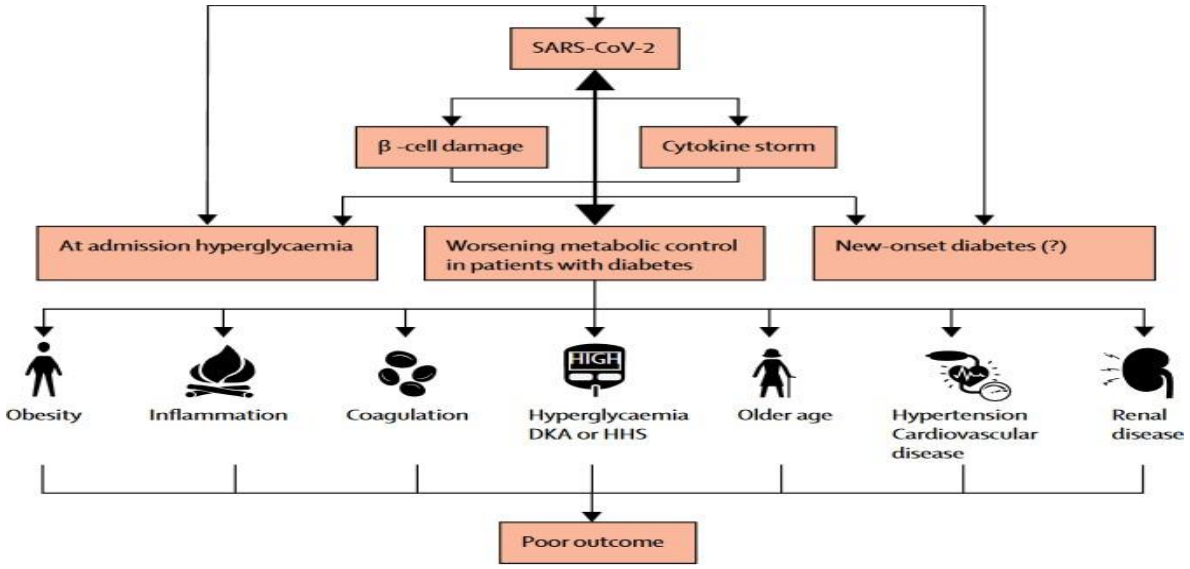



**Fig.2** *Brief overview of the correlation between diabetes and COVID-19*

Inconclusive evidence links diabetes with COVID-19. The fact that people with diabetes often have co-occurring major health problems may contribute to the worse outcomes in this patient population (Singh et al., 2020). CoV-2s that have a SARS tropism for the -cell, on the other hand, might lead to either SUDI or PHG after hospitalization. Inflammatory cytokine storm, counter-regulatory hormone responses, and disruption of -cell function may all contribute to the severity of acute metabolic problems. COVID-19 results may be compromised by comorbidities such as newly diagnosed diabetes, hyperglycemia on admission, and sudden metabolic deterioration (Gupta and mishra, 2021)). DKA, or diabetic ketoacidosis, is the medical name for this state. HHS is the result of hyperglycemia and hyperosmolarity (Lim et al., 2021).

**Diabetes and management (post-covid-19)**

The SARS-coronavirus 2 pandemic, caused by the COVID-19 virus, has infected and killed tens of millions of people. Overweight and obesity are common among those with an inactive phenotype, as well as other medical conditions, such as high blood pressure, diabetes mellitus type 2, heart disease, renal disease, and liver sarcopenia (Caballero et al., 2020). We hypothesize that a lack of physical exercise (and the resulting loss of muscle strength) and an increase in the incidence of obesity both contribute to a bad prognosis for patients. Post-Covidien virus-19 syndrome is widespread, has several causes, and manifests in various bodily systems (Apicella et al., 2020). The cumulative

effect of these restrictive measures has been, at least, a worsening of many people's health, including a decrease in their level of physical activity (Metwally et al., 2021).

Those from low have felt the severe effects of COVID-19- and middle-income countries (LMICs) and those from disadvantaged social backgrounds. Those Asian Indians infected with COVID who have suffered the most also tend to have other lifestyle-related conditions, with type 2 diabetes being mainly linked to severe illness, hospitalization, and mortality (Parasher, 2021). In light of the above, it is tempting to conclude that India's widespread problem of chronic physical inactivity may be responsible for a significant portion of the current situation. Furthermore, some phenotypes have exhibited relatively severe reductions in functional ability (extreme tiredness, difficulties walking) and delays in recovery after COVID-19 (Bedi et al., 2020). These persons often have a history of severe illness and have sarcopenia symptoms, such as weaker handgrip strength.

Although preliminary research suggests that exercise-based therapy may help those with post-COVID-19 syndrome achieve remission and a complete recovery, further research is needed to confirm these preliminary findings. Overall, considering the efficacy of exercise in mitigating SARS-CoV-2 infection and the chronic NCDs (e.g., T2D) that worsen it, it is critical to think about including exercise as a viable preventative approach for COVID-19 and for bolstering rehabilitation during post-COPID-19 illness. Seven days symptom-free may be enough time for risk-stratified individuals to resume activity (with mild effort).( Tiwari et al., 2021; Rao et al., 2021).

| Treatments | |
|---|---|
| Lopinavir-Ritonavir | Do not suggest to treat patients with COVID-19 |
| Umifenovir | May be considered in COVID-19 |
| Interferon | May be considered in COVID-19 |
| Favipiravir | Suggest to treat patients with COVID-19 |
| Remdesivir | Suggest to treat patients with COVID-19 |
| Hydroxychloroquine/Chloroquine | Inconsistent Evidence |
| Combination of Antiviral Drugs | Insufficient Evidence to support or against using two antiviral drugs |
| Interleukin-6 Inhibitors | Insufficient evidence |
| Interleukin-1 Inhibitors | Insufficient evidence |

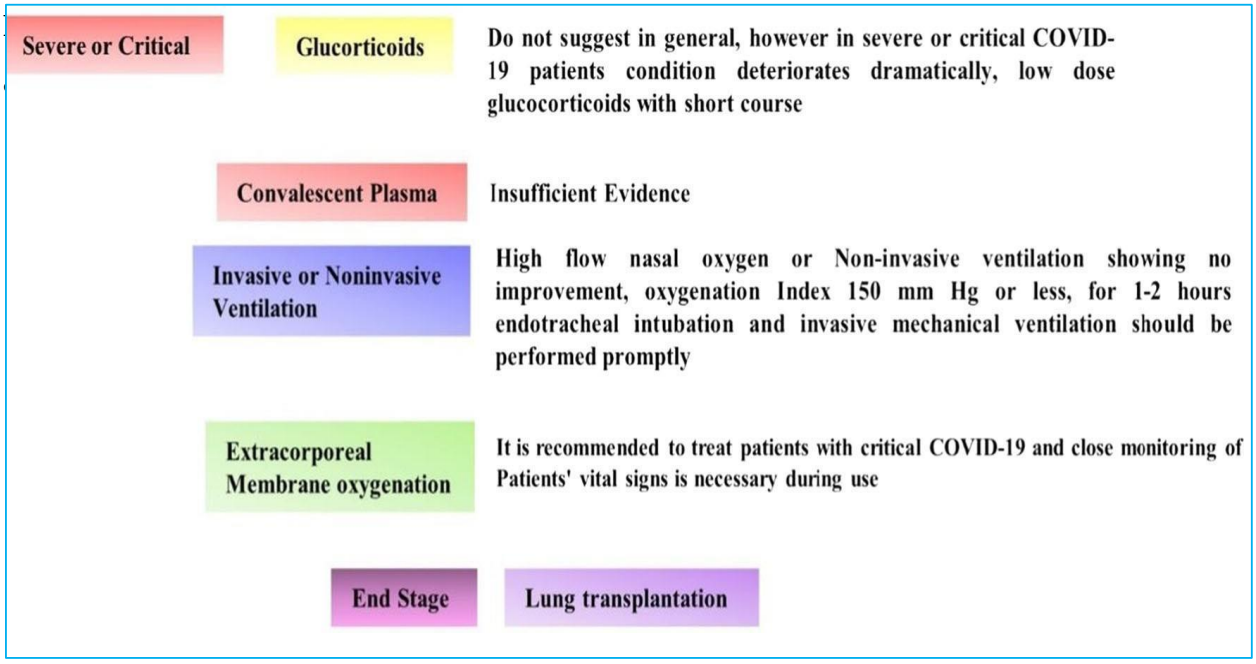



**Fig.4** Drugs and their efficacy in severe SARS-COV-2 infection (Tiwari et al., 2021).

**Possible link between COVID-19 and diabetes**

The risk of getting and dying from COVID-19 is higher in persons who already have a chronic disease, such as diabetes. Still, recent data from Italy shows that diabetes is not often associated with an increased chance of getting COVID-19 infection; instead it is more likely to alter clinical outcomes in those who are already infected (Stoian et al., 2020). This may be because COVID-19-positive diabetics are more likely to have organ failure and an immune-inflammatory response, both of which contribute to worsening clinical outcomes.Some possible alterations for diabetic drugs may be done based on these underlying pathophysiological changes to attenuate the course of the condition (Joshi et al., 2020; Elnaem and Cheema 2021).

**Potential adjustments in the pharmacotherapy**

Patients with diabetes are more likely to have hyperglycemia and the complications that come with it during concomitant illness (Dk et al., 2021). These complications include dehydration, diabetic ketoacidosis (DKA), and hyperosmolar hyperglycemia (HHS).

Therefore, pharmacists should provide patient education to aid in managing these symptoms. Help from pharmacists is essential in lowering patients' odds of having acute problems and subsequent hospital stays (Cascella et.al, 2021).

1. **Insulin**

Acute sickness is associated with a surge in counterregulatory hormones like cortisol, which is thought to raise insulin needs. Patients with type 1 diabetes may need extra injections of rapid-acting insulin if their blood glucose levels suddenly rise. If a patient's blood sugar is already within the normal range, he or she may only need a 10-20% reduction in their insulin dose; if carbohydrate intake is kept to minimum, insulin before meals can even be avoided (Ghosh et al., 2021). Adjustments to insulin doses should be undertaken under medical supervision, and individuals with type 1 diabetes should be strongly encouraged to avoid altogether discontinuing insulin treatment. Additional factors include the necessity for an insulin dose increase of 10-20% in those with type 2 diabetes who have severely increased blood sugar levels (Ghosh et al., 2020). In addition, it may be prudent to consider boosting the frequency with which blood glucose is checked during periods of severe sickness. As a result, adjustments in insulin dosage may be made based on the patient's blood sugar and carbohydrate consumption data (Raveendran and Misra, 2021).

2. **Metformin**

Due to its effectiveness, decreased risk of hypoglycemia, and medication-induced weight reduction, most professional recommendations recommend metformin as a first-line antidiabetic (Madhu, 2020). However, drug-induced GI symptoms may increase the danger of dehydration and may place a risk on renal function, so discontinuing the medication temporarily may be necessary (Iacobellis et al., 2020). In addition, acute infections and shock increase the risk of renal damage and call for a temporary halt to metformin treatment. Pharmacists should instruct patients in preventing and treating dehydration and maintaining excellent glycemic control in the absence of severe illness by teaching them how to manage gastrointestinal symptoms effectively (Zhang et al., 2019).

3. **Gliclazide**

Indications suggest that gliclazide may enhance the danger of hypoglycemia. Hence a dosage decrease may be necessary if appetite is low (Meuller et al., 2021). A further increase in the dosages may be warranted, however, since hyperglycemia is more prevalent during the concurrent illness. In addition, regular monitoring of blood glucose would aid healthcare practitioners in customizing therapy that could be sustained throughout the acute sickness (Coppelli et al., 2020).

**4. Dipeptidyl Peptidase-4 inhibitors (DPP4i)**

Besides the targeted antivirals, anti-inflammatory drugs are of essential relevance because they influence the inflammatory pathway's crucial responses to COVID-19 infection (Reiterer et al., 2021). Diabetic drugs such Dipeptidyl Peptidase-4 inhibitors (DPP4i). They have been demonstrated to have anti-inflammatory properties and are being studied to lessen the acute effects of COVID-19 infection that are caused by inflammation. While it is well established that DPP4 stimulates T-cells and causes inflammation, DPP4i has been linked to an increased risk of sickness (Li et al., 2020). Large-scale, in-depth data are therefore required to confirm hypotheses about the effects of anti-inflammatory diabetes medications on the outcomes and severity of COVID-19 infection (Ebekozien et al., 2020).

**5. Pioglitazone**

Pioglitazone has anti-inflammatory properties, but it also has the potential to promote fluid retention, It may add still another level of difficulty to caring for diabetic patients who are also experiencing cardiovascular problems, such as heart failure. Moreover, it could lead to obesity, which is problematic given that patients throughout a pandemic are already at a greater risk of gaining weight because to their lack of exercise. In light of these issues, pioglitazone should be considered one of the least preferred choices for diabetes control during the next COVID-19 (Unsworth et al., 2020).

**Diabetes care issues in the post-pandemic period**

Health care service delivery in the post-COVID-19 period will need significant changes,

as mentioned in the present negotiations, in order to accommodate the "new normal" for the general public and businesses (Armeni et al., 2020). Self-management and accurate patient monitoring via wearable technology and telemedicine are expected to become mainstream (Lawrence et al., 2021). What was formerly considered complementary treatments for specific populations of patients would instead become standard operating procedures for the vast majority of patients (Tittel et al., 2020).

**How social isolation affects diabetes self-management**

Depression, anxiety, and other psychological disorders that need specialized treatment are likely to be connected with diabetes and lead to disordered eating patterns. These problems are likely to worsen due to fewer opportunities for face-to-face connection and an increase in sedentary behavior due to curbs on outdoor activities (Marchand et al. 2020). Given the negative impact social isolation is expected to have on patients' ability to manage their diabetes on their own, pharmacists will need to provide education to patients to help them cope (Bode et al., 2020).

**The difficulty of maintaining healthy blood sugar levels**

Evidence suggests that persons with poorly managed diabetes are at significantly higher risk of developing infections, making optimal glycemic management a must (Petrie et al., 2021). There isn't enough strong epidemiological data to back up this finding, however. Recent investigations emphasized the possible influence of glycemic management on the unique risk profile of COVID-19-infected patients (Manigandan et al., 2021). Achieving reasonable glycemic control is a complex but essential step in treating diabetes due to the prevalence and severity of diabetes-related complications such as cardiovascular and renal problems (Jamwa et al., 2020).

**Constantly checking your blood sugar levels is essential:**

Patients with diabetes at risk of developing a fever should test their blood sugar levels more often by the sick day guidelines of diabetes until it is clear whether or not they should stop taking their diabetes medications altogether (Kamal et al., 2022). Blood

glucose levels are likely to fluctuate more often as a result of the changes in food and exercise routines. Therefore, pharmacists should regularly advise these patients to check their blood sugar levels (Rosenberg et al., 2020).

**Diabetes patients in the post-pandemic period may rely on pharmacist-led assistance**

Preparedness for the COVID-19 pandemic will benefit significantly from the expertise of pharmacy experts. Following this advice, pharmacists may better assist their diabetic patients both now and in the future when COVID-19 has been implemented (Khuroo et al., 2020; Yasmin et al., 2021).

**Adequate medication supply**

Pharmacists need to take initiative to ensure their patients always have access to a sufficient and secure medicine supply. So as to lessen the frequency with which patients need to visit the pharmacy, pharmacists should increase their use of remote mobile networks, drive-through, and home delivery services (Rao et al., 2021). Pharmacists also have an ethical responsibility to maximize drug use while minimizing waste that might compromise the safety of drug storage and impact patient outcomes (Yasmin et al., 2021).

**Tele-pharmacy counseling and monitoring**

Helping patients over the phone or online with any issues they may be having with their medications would be a great way for pharmacists to demonstrate their compassion, knowledge, and professionalism in an era when personal interaction is frequently restricted (Rodriguez-Morales et al., 2021). Since pharmacists are among the most readily available members of the healthcare team, it stands to reason that their capacity to provide remote counseling services would grow accordingly (Revannavar et al., 2021). New types of remote value-added services in the treatment of diabetes will become increasingly important as evidence mounts in favor of the use of technological solutions to improve disease self-management. The expansion of the use of technological solutions is thus anticipated to give a means of guaranteeing efficient patient monitoring initiatives (Chandley et al., 2022).

**Incorporation of new evidence into therapeutic practice**

As a result of the ongoing epidemic, new information on COVID-19 and how to treat it has become available at a dizzying rate. Several antiviral medicines are in development and clinical trials, and more are on the horizon (Janjua et al., 2021). Moreover, after the completion of new studies, several medications once thought to be successful with promising findings were ruled ineffective. Therefore, healthcare providers, including pharmacists, must evaluate, follow, and swiftly incorporate the new data into their patient treatment (Mave et al., 2021).

**Clinical pharmacy support services**

A growing body of research demonstrates that pharmacists in diabetes treatment improve clinical and patient-reported results. However, during the COVID-19 epidemic, pharmacists must give extra help to their diabetic patients to improve their chances of sticking to their medication regimen and, ultimately, better glycemic control (Sim et al., 2021; Shende et al., 2021).

**Epidemiology: (I) Diabetic Patients Are More Likely to Die from COVID-19 Complications.**

According to the COVID-19 cohort, individuals who experience severe morbidity and mortality are more likely to have hypertension or coronary heart disease (26%). (Rudramurthy et al., 2021; Raghav et al., 2021). diabetics often have problems such renal disease, heart disease, and pneumonia (Ghosal et al., 2020; Rao et al., 2021). COVID-19 diabetic patients had a higher mortality rate (20.3% vs. 10.5%) and higher rate of hospitalization for critical care unit admission (17.6% vs. 7.8%). Extreme instances of COVID-19 are associated with a disorder called acute respiratory distress syndrome (ARDS), which is more frequent in diabetes individuals who are hospitalized with COVID-19. In severe cases of ARDS, mechanical ventilation is necessary to prevent death from respiratory failure (Agarwal et al.,2021; Krishnakumar et al., 2022). According to the study, 22% and 31% of people with diabetes with COVID-19 will die from their disease (Hoenigl et al., 2022). UK study finds that 32% of COVID-19 hospital

deaths were attributable to type 2 diabetes, whereas just 1.5% were attributable to type 1 diabetes (Chakaya et al., 2021; Girdhar and Manocha, 2022).

***(II) As things stand, it seems that COVID-19 diabetes patients have much trouble and a high mortality rate.***

In healthy adults, the SARS-CoV-2 virus has been shown to reduce insulin production, increasing the risk of developing diabetes. Twenty SARS patients developed diabetes while hospitalized during the 2003 epidemic. Hospitalized individuals with viral illnesses like human herpes virus 8 and SARS have been demonstrated in clinical studies to have severe hyperglycemia and insulin resistance. These signs and symptoms may represent effective antiviral reactions (Asdaq et al., 2021, Rajueni et al., 2021). However, alterations in glucose homeostasis are linked to these diseases and may increase the likelihood of developing type 1 and type 2 diabetes (Khunti et al., 2021; Rajueni et al., 2021 Unnikrishnan and Misra 2020). Twenty of the 39 SARS-CoV-1 patients in this study acquired diabetes while hospitalized, and two remained diabetic despite glycemic therapy for three years of follow-up. It occurred amid the 2003 SARS-CoV-1 pandemic (Loganathan et al., 2020; Khunti et al., 2021).

**SARC CoV2 : COVID- 19 Associated Effects**

| Disease | Hyperglycemia | Diabetic Ketoacidosis (DKA) | New-onset diabetic |
|---|---|---|---|
| **Introduction** | Acute hyperglycemia in Non diabetic hospitalized COVID-19 Patients | DKA or Hyperglycaemic, hyperosmolar syndrome in diabetic COVID-19 Patients | New-onset diabetic discovered in COVID-19 Patients. |

| | | | |
|---|---|---|---|
| **Level of Disorder** | ICU admission, Mechanical validation, poor chest imaging (CT-Scanning) COVID- 19 Associated Effects | CAD, HTN, ALD, Digestive disorders, ADRs. | ICU Admissions, IMV, ADRs, Acute Kidney disorders, shock, hypoablimenea |
| **Incidences** | Mortality at hospital admission: 41.7% . Morality while hospitalization: 26.8%-40.2% | Diabetic patients): 7.1%-1.5%, Mortality approx 45-50%. | COVID-19 Patients: 20-8%-30%. Mortality: HR: 3.0-10.12% |

**Table 1:** *Diabetes incidence and COVID-19: an epidemiological profile. Epidemiological statistics for COVID-19 cases and fatalities, COVID-19 diabetes prevalence and mortality, and new-onset COVID-19 diabetes are shown in this figure (incidence, complications, and mortality). Ventilation must be performed intermittently (also known as "IMV"). (*Sarveswaran *et al., 2021;* Metwally *et al., 2021).*

**a. Potential Mechanisms**

**i. Canonical Inclusion of SARS-CoV-2**

SARS-CoV-2 is composed of four proteins: the membrane (M) protein, the envelope (E) protein, the nucleocapsid protein, and the spike (S) protein. S proteins aid in viral entrance by interacting with the membrane-bound receptor angiotensin-converting enzyme 2 (ACE2) (Nanditha et al., 2021). ACE2 is found on all respiratory cells. TMPRSS2, a membrane-associated serine protease, cleaves bound S proteins, activating endocytic machinery and allowing the virus to enter the cell and replicate (Giorgino et al., 2021).

**ii. Consequences of SARS-CoV-2 Are Often The COVID-19 Complications Study: Diabetic Patients or Those At Risk For Developing Diabetes**

More cases of newly-onset hyperglycemia and ketoacidosis have been reported, which may indicate that COVID-19 triggered acute T1D via ACE2 expression in b-cell failure (BCF) (Garg et al., 2020). Research has consistently located ACE2 and TMPRSS2 proteins in microvascular endothelial cells and pancreatic ducts. More inflammatory

biomarkers are seen in COVID-19 individuals with uncontrolled glycemia than those without diabetes. Stress on adipocytes and increased chronic inflammation may contribute to the deterioration of IR, hyperglycemia, and other diabetes-related outcomes in SARS-CoV-2-infected individuals (Mohammad et al., 2022).

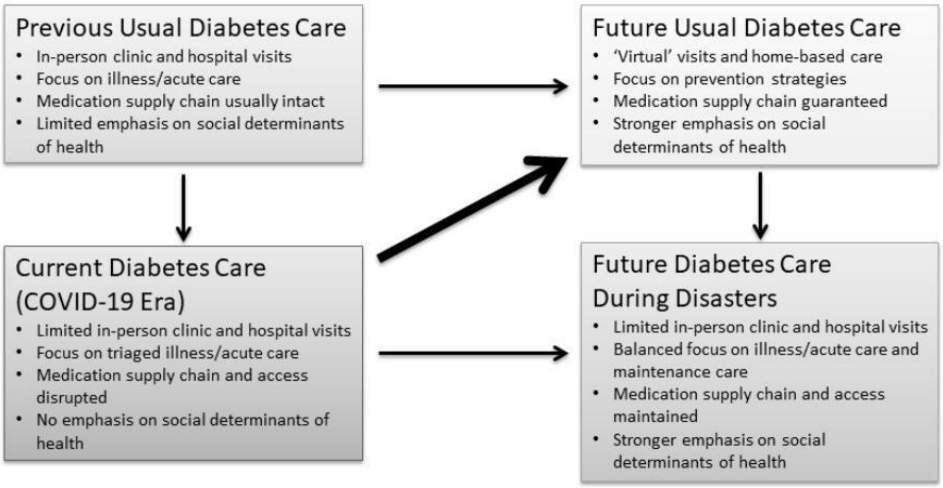



**Fig.6** Key diabetes care characteristics before, during, and after the COVID-19 crisis.

Some of these illnesses, including mucormycosis, are more common among immunocompromised people. Patients having a history of diabetes mellitus are more likely to be affected (Evans et al., 2022). CAM often manifests anywhere from 15 days to a few months after a person has been released from the hospital or fully recovered from coronavirus sickness. High body temperature, tooth loosening, swelling under the eyes, and discomfort in the maxillary sinuses are only some of the symptoms of COVID-19-associated mucormycosis, a life-threatening illness (Jindal et al., 2020; Mahalaxmi et al.. 2021).

**Ramification**: The long-term effects of SARS-CoV-2 infection in individuals who later develop clinically significant COVID-19 sickness are still unknown. The worldwide mortality rate for cases remains between 1% and 2%.(Sun et al., 2021; Cascella et al., 2021).

**The Challenges of Researching Type 2 Diabetes in the Young and a Plan for Studying, Detecting, and Tracking Type 2 Diabetes in the Young**: Due to the delayed

onset of symptoms in COVID-19 infections (usually 7-14 days), it is challenging to recruit individuals with early SARS-CoV-2 infections for investigations of newly diagnosed diabetes. Unraveling the process via which diabetes might suddenly appear is another formidable obstacle (Bhagat et al., 2022). The molecular knowledge of diabetes genesis and progression may be enhanced by deep longitudinal profiling of several omics. Another difficulty in investigating NIDDM is determining whether or if large groups of research participants without a previous history of diabetes are incretin or has hyperglycemia before study participation and also the COVID-19 diagnosis. In the presence of insulin resistance, elevated blood glucose levels outside of normal glycemic ranges characterize the onset of diabetes (Malhotra et al., 2021; Cohen et al., 2020).

While many Americans with prediabetes are at risk for developing type 2 diabetes, many are unaware that they have the condition. The research strategy we plan to use to learn more about diabetes brought on by COVID-19 is summarised in Figure 7 (García-Lledó et al., 2022; Khuroo , 2020).

**Instruments for Micro sampling**

The glucometer, which requires just a few mechanical pricks to acquire a usable blood sample, is the most used microsampling instrument. Despite its usefulness, users may need to do many tests daily to get insight into glucose changes due to the absence of real-time monitoring. At-home HbA1c testing kits help keep tabs on the development of diabetic problems in individuals with COVID-19 who have just been diagnosed with the disease (Giorgi et al., 2020; Marchand et al., 2022).

**Monitoring Blood Glucose Constantly to Treat Diabetes**

Among the many available wearable solutions for managing diabetes, the Eversense CGM gadget is trendy. Continuous glucose monitors (CGMs) are medical devices that take and analyze blood glucose readings in real-time to assist patients in maintaining a healthy glycemic range (Iyengar et al., 2020). Integration with insulin pumps is available in more advanced devices, allowing for automated insulin changes depending on CGM readings. It is possible to find CGM devices suitable for in-hospital or long-term glucose monitoring that do not need surgical implantation under the skin, such as the Senseonics Eversense, which has a sensors life cycle of 90 days (Sanyaolu et al., 2022; Petrie et al.,

2022).Sensors implanted beneath the skin assess interstitial glucose levels every few minutes, and transmitters may either manually scan the sensor or send the data wirelessly to a receiver or smartphone (Jain et al., 2022; Marchand et al., 2020).

## The Use of Stretchable Electronics in Diabetes Monitoring, Control, and Management

Due to their tiny size, adhesiveness, and adaptability to movement, stretchable electronics are a relatively new category of wearable gadgets that may be kept hidden. A stretchable is a flexible electronic device with an integrated electrical circuit and biosensors made of silicon or polymer (Uzunova et al. 2021). Glucose levels are only one of several indications in sweat and blood that may be used to track the development and progression of diabetes, making biosensors an essential tool in the management of this illness. After a diagnosis of COVID-19, new-onset diabetes may be managed with stretchable electronics. Some stretchable devices, like some CGMs, help people with diabetes tend to their condition by automatically administering insulin or metformin when high blood sugar levels are detected (Singhai et al., 2020; Rosenberg et al., 2020; Khuro, 2020).

**Technologies to Monitor Hyperglycemia pre/post COVID-19 Diagnosis**

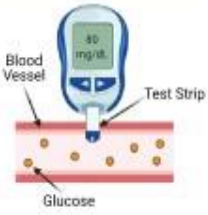
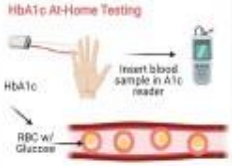
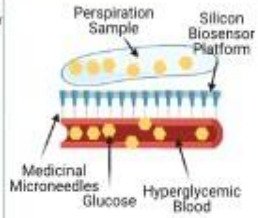
| Device | Glucometer | At-home HbA1c Testing | CGM | Stretchables |
|---|---|---|---|---|
| Illustration |   |   |   |   |
| Cost | Cheap | Moderate | Expensive | In research phase; projected low cost |
| Ease of Use | Painful | Easy | Easy | Easy |
| Information | Static measure of current blood glucose level | Average blood glucose levels for the last three months | Continuous measure of blood glucose level | Continuous measure of perspiration/blood glucose level |

**Fig.7** Diabetes management and monitoring tools. Continuous glucose monitoring (CGM), glucometers, HbA1c at-home testing, and smartphone apps for diet, exercise, sleep, and stretchable electronics are only some of the technologies available for controlling diabetes and its problems. Perspiration samples may be used via stretchable glucose monitoring to check blood sugar levels. Patients with diabetes may use micro needles to take sweat samples, monitor their blood sugar levels, and inject drugs like

insulin and metformin.

***iii. Dietary habits and blood sugar levels of diabetics may be monitored using mobile apps.***

There are a number of smartphone apps designed to track and control a person's diet if they are at risk. Meals, carbohydrate levels, insulin dosages, HbA1c, heart rate, and weight are just some of the factors that algorithms may help users better understand and manage (Monik et al.. 2022). Newly diagnosed diabetics may benefit from the guidance of a number of mobile apps that provide advice on how to maintain a balanced diet and lifestyle (Kumar et al., 2021).

**Studies Investigating the Two-Way Connection Between COVID-19 and Type 2 Diabetes that Are Currently Underway**

The optimal way to treat newly discovered cases of diabetes in infected persons is still largely unclear, despite the rise in reported cases of COVID-19 and the start of international adoption of vaccination methods. That's why many of medical investigations are looking into how COVID-19 relates to diabetes and other diseases that can be monitored with similar gadgets. Thanks to support from Hospital of South West Jutland, researchers in Denmark and Portugal may analyse how COVID-19 affects the prevalence and phenotype of persons with newly diagnosed Type 1 Diabetes (Manchanda et al., 2021; Shin et al., 2020). Patients over the age of 18 with type 1 diabetes who are currently being treated at hospitals in Denmark or Portugal are eligible to apply, regardless of whether or not they have been infected with SARS-CoV-2. B-cell functionality will be evaluated and compared on an annual basis for two years in clinical studies and epidemiological follow-ups. Data like these may help scientists predict the growth of the number of people with type 1 diabetes who test positive for COVID-19 each year (Nouhjah et al., 2020; Rao et al., 2021).

As part of the COVID-19 and T1D Multicenter Study, researchers are keeping tabs on newly diagnosed cases of diabetes in both Denmark and Portugal. CoviDIAB is an international registry established by researchers at King's College London and Monash University to better understand the global spread of this kind of diabetes. The

participants' b-cell performance will be monitored and evaluated over a two-year period by administering a battery of tests annually (Wadhawan et al. 2021).

**Future Recommendations**

Epidemiological and interventional strategies are encouraged for follow-up research. This novel occurrence of COVID19-related new-onset diabetes allows for longer-term follow-up of affected individuals. The CoviDIAB Project, coordinated by academics worldwide, has already created a worldwide registry of patients with COVID-19-related diabetes (Das, 2020; Samuel 2021). To combat mucormycosis infections cost-effectively, it is crucial to gather relevant epidemiological data. All medical centers should follow uniform guidelines for reporting outbreaks as soon as possible. The use and monitoring of corticosteroids and other immunosuppressive drugs are recommended. Phage treatment and potential combinations of antifungal medications are two alternatives for treating these infections (Weissberg-Benchell et al., 2007). It has been estimated that a significant number of cases of COVID-19 have been reported in most countries since December 2019. No vaccines or treatments are available to prevent infection at that time. Pathological circumstances, physiological mechanisms, clinical symptoms, diagnostics, and public health crises will drive research forward until suitable therapeutic candidates and vaccines are identified (Tripathy et al., 2021). Now there are various vaccinations are available on the booster dose for showing more effective immunity toward COVID.

**Conclusion**

A higher prevalence of infection, serious consequences, and death in people with diabetes have been linked to the ongoing COVID-19 pandemic. According to the most recent studies, these dangers may also result in more severe problems such as ketosis, ARDS, a maladaptive immunological response, and increased mortality. The RAS hormonal system may be affected by SARS-CoV-2 spike proteins, and they can also enter the host cell via tying up ACE2 receptors. Diabetes patients may be at high risk of severe consequences upon diagnosis due to elevated viral load, immunological dysregulation, alveolar and endothelial dysfunction, and elevated systemic coagulation. Adequate care for these illnesses is crucial as researchers work to understand better the implications of

type 2 diabetes in those diagnosed after the release of Covid-19. An emerging public health issue of growing significance is COVID-19-related new cases of diabetes. Although data are few, there is reason to believe that individuals with diabetes and other comorbidities are at increased risk for complications. This paper provides an overview of the current understanding of new-onset diabetes and COVID-19, including mechanisms, epidemiology, and technology, and argues that research into metabolic and physiological aspects of these illnesses should be given full attention. There are some encouraging but inconclusive data that individuals with concomitant diabetes are more likely to have problems, indicating that measures should be taken to avoid and better manage this comorbidity.

**List of abbreviations:**

DM; Diabete Mellitus

COVID: Corona Virus Disease

HCQ: Hydroxychloroquine

RCTs: Randomized Clinical Trials

MoHFW: Ministry of Health and Family Welfare

ICMR: Indian Council of Medical Research

DKA: Diabetes Ketoacidosis

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