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PRACTICAL CONSIDERATIONS FOR DIABETES CARE DURING COVID-19 PANDEMIC

Medicine

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ABSTRACT

The ongoing COVID-19 pandemic has affected healthcare delivery adversely across the globe. Reports estimate that care for chronic diseases such as type 2 diabetes mellitus (T2DM) has been hugely impacted as a result of the pandemic. The need of the hour is to ensure optimized management of T2DM with a view of reducing the risk of exposure in this cohort. People with diabetes, are at high risk of a severe disease course and adverse outcomes. It is essential to maintain the basic measures such as good hygiene, social distancing measures and importantly blood glucose monitoring regularly, as chronic hyperglycaemia can lead to immune dysfunction. People with diabetes should be encouraged to continue medication prescribed for hypertension, diabetes or dyslipidaemia. It is essential to assess the severity of the COVID-19 infection and plan the management protocol for diabetes. This review looks at some practical considerations for optimizing diabetes care in the ongoing pandemic.

KEYWORDS

T2DM, Diabetes Care, Telemedicine, COVID-19.

INTRODUCTION

The World Health Organization (WHO) announced the COVID-19 outbreak as a pandemic on 11 March 2020, after the virus had affected more than 120,000 people and resulted in 4,000 deaths globally. As of 10 May 2021, more than 15.6 million cases of COVID-19 had been reported in over 188 countries, resulting in more than 32,56,000 deaths. [1]

Viral diseases have always had a negative impact on persons with cardiovascular disorders. Cardiovascular disorders were a common risk factor associated with previous viral epidemics, including the severe acute respiratory syndrome (SARS) coronavirus and Middle East respiratory syndrome coronavirus (MERS).[2] Similarly, diabetes mellitus was an independent risk factor for increased morbidity and mortality in previously reported viral pandemics, including the H1N1 influenza, SARS coronavirus, and Middle East respiratory syndrome coronavirus (MERS). [3]

Individuals with diabetes are at increased risk for serious COVID-19 and its complications due to various factors, with up to 50% higher mortality rates reported. [4] In view of the pandemic, lockdowns have been imposed time and again with different durations to contain the spread of the infection. However, such a situation affects patients with diabetes at fronts like diet, exercise, availability of medicines, stress, which lead to uncontrolled glycemia and worsening of comorbidities. [1] This review looks at some practical considerations for optimizing diabetes care in the ongoing pandemic.

Link between hyperglycemia, COVID-19 infection and immunity

It is commonly acknowledged that chronic hyperglycemia may lead to immune dysfunction and a subsequent susceptibility to infections. Thus, innate immunity is an inadequate first-line barrier against SARS-CoV-2. Furthermore, an exaggerated immune response with cytokine overproduction, such as interleukin 6 (IL-6), as well as increased levels of C-reactive protein and ferritin, could possibly explain the vulnerability of diabetic patients to the cytokine storm, shock and COVID-19-related fatal complications. In addition, high D-dimer levels in patients with diabetes and COVID-19 may serve as a marker for the over-activation of the coagulation cascade, which increases mortality through major thromboembolic events.[1]

Impact of COVID-19 pandemic on people with diabetes

While the high cost of antidiabetic drugs is one of the major stumbling blocks in managing diabetes, its impact on the health of diabetic patients during the COVID-19 epidemic season remains a matter of concern. Diabetes, especially type 2 diabetes, is a chronic inflammatory state that can lead to an ineffective immune response. Patients with COVID-19 and poorly controlled diabetes have an increased risk for medical complications and even mortality. A meta-analysis of more than 45,000 patients from Wuhan, China, showed diabetes to be the second most common comorbidity, with a prevalence of 8%.[5] Also from Wuhan, among 1099 patients with COVID-19, those with diabetes were more than twice as likely to have severe disease and 3.5 times more likely to require intensive care unit (ICU) care, mechanical ventilation, and/or to die. [6] A recent meta-analysis of 30 studies enrolling 6452 patients showed significantly increased severity, mortality, acute respiratory distress syndrome, and disease progression. [7]

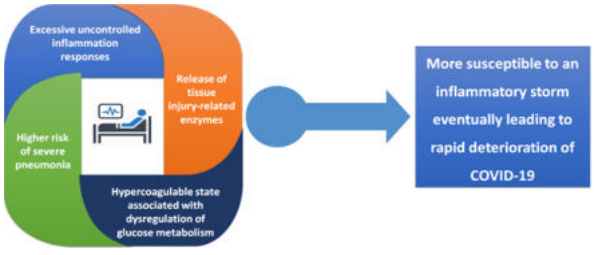

Fig 1: Diabetes and COVID-19: A vicious cycle

Although diabetes has been associated with poor outcomes in persons with COVID-19, the susceptibility to SARS-CoV-2 infection is not higher in people with diabetes. There is not enough data to show whether people with diabetes are more likely to get COVID-19 than the general population. The American Diabetes Association (ADA) has also issued statements that people with diabetes are not more prone to COVID-19 than the general population [8]

The potential risk factors that may increase morbidity among inpatients with COVID-19 and diabetes include corticosteroid therapy, altered and less-frequent glucose monitoring, isolation from physicians, and inappropriate discontinuation of angiotensin-receptor blockers and angiotensin-converting enzyme inhibitors. [9] Thus, there is an urgent need for an effective management of diabetes during this pandemic.

Management approach in person with diabetes not Infected by COVID-19

Tight glucose control needs to be ensured during the COVID-19 pandemic, as poorly controlled diabetes can negatively affect prognosis and promote the risk of any infection [10] In general, social

distancing, good hygiene, avoiding non-essential travel, quarantine measures should be the norm of an effective prevention strategy. Routine medication prescribed for hypertension, diabetes or dyslipidemia are not to be discontinued. Regular intake of antidiabetic drugs and insulin is indicated. [Fig 2] Although many theories suggesting that chronic use of ACE inhibitors and angiotensin 2 receptor blockers (ARBs) may increase the risk and the severity of SARS-CoV-2 infection, The Cardiological Society of India (CSI) has also issued a position statement in this regard, stating that guideline directed drug therapy including ACEI/ARB/ARNI is to be continued in patients with pre-existing heart failure. CSI also says that health care professionals should continue using these drugs to prevent mortality due to heart failure and myocardial infarction, until further research on SARS-Cov-2 interaction with ACEi/ARB's shows a strong reason to stop these drugs**. [11]**

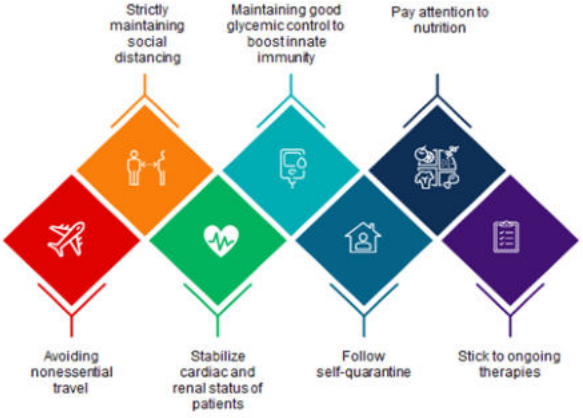

Fig 2: General considerations for persons with diabetes during COVID-19 Pandemic

Accessibility to healthcare providers, availability, and affordability of the resources like medications during the COVID-19 pandemic is the need of the hour. [Table 1] The crisis calls for an innovative approach towards dealing with the lack of resources. 'Resource husbandry', an emerging concept that needs to adopt in this current crisis, which refers to the judicious use of available resources to combat the shortage while simultaneously providing effective treatment to the patients [12]

Table 1: Challenges in current scenario of and possible solutions by resource husbandry.

Challenges in Pandemic	Possible Resource Husbandry solutions
Health care professional's Accessibility	• Adopting telemedicine care • Triaging patients in hospital
Oral Medication Availability	• Change to brand names which is available • Give the drugs separately if Fixed Dose combination not available • Use a different drug from the same class of drug • Use a different class of drug
Insulin Medication Availability	• Substitution with oral drugs, if possible • Use of biosimilar agents/substitutes • Use government resources: insulins from government hospitals
Medications Affordability	• Use of cheaper substitutes/generics • Avoid prescribing non-essential drugs like costly multivitamins
Investigations Affordability	• Reduce the frequency of monitoring. • Focus on only essential investigations

Adopting teleconsultation for diabetes care

The COVID-19 pandemic has created opportunities to revolutionize diabetes care that were not possible before. Given the current situation, there is tremendous scope to rapidly implement, test, and iterate models of diabetes care to achieve various goals of improving clinical outcomes, patient experience, healthcare provider satisfaction, and reducing costs.

Teleconsultation can be a boon to people with diabetes mellitus. Aided by patient specified self-monitoring of blood glucose (SMBG) values, physicians can help fine-tune their antidiabetic medications, thereby avoiding prolonged periods of sustained hyperglycemia as well as recurrent episodes of hypoglycemia.[13] Use of telemedicine has been shown to be associated with a mean Glycated hemoglobin decline of −0.44% as compared to usual care alone.[14] Good glycemic control would in turn strengthen the innate immune system and probably help prevent the gruesome consequences of COVID-19. A recent study conducted by Joshi *et al*. at an Indian tertiary care center showed that the practical approach of providing diabetes care through the yet underused approach of extensively utilizing telemedicine in an Indian set up with engagement of trained para-clinical doctors, proved to be a successful and effective endeavor.[15]

The Indian telemedicine guidelines now facilitate use of this mode of management for chronic conditions. In times of an emergency like the on-going COVID-19 pandemic induced lockdowns, this approach of providing tele-consultations can help people get the much-required basic diabetes follow up advice without the risk of acquiring infection by visiting a hospital.[16]

Table 2: Practical considerations on Good practice and what not to do in teleconsultation

Good Practice Guidelines in Telemedicine Consultation	What Not to Do in Telemedicine Consultations
1. Follow principles of medical ethics 2. Protecting patient privacy and confidentiality 3. Confirm Remote-Tele or Video equipment set-up working properly 4. Practice MCI principles for remote consultations 5. Confirm reason of remote consultation is appropriate for the clinical setting 6. Virtual handshake'-confirm identity 7. Verification of verbal consent for conducting remote consultation 8. Undertake complete assessment of patient's symptoms and virtual signs 9. Summarize the consultation and ensure patient understands the management plan. 10. Allow the patient opportunity to clarify 11. Organize appropriate follow-up arrangements 12. Undertake enhanced documentation 13. Communicate with patient's primary care or referring doctor 14. Ensure and practice information governance, data protection	1. Do not prescribe medicines from the specific restricted list e. g. Opioids without appropriate authentication 2. Never misuse patient images and data 3. Avoiding taking consent 4. Do not prescribe Medicines without an appropriate diagnosis/provisional diagnosis 5. Do not solicit patients for telemedicine through any advertisements or inducements.

New-onset diabetes during COVID-19 pandemic

'New-onset hyperglycemia' is a frequently observed finding especially in admitted patients with COVID-19, who had no history of dysglycemia or diabetes in the past.[17]

New-onset hyperglycemia could be classified as

1. Stress-induced hyperglycemia,
2. New-onset diabetes in previously unrecognized prediabetes,
3. Hyperglycemia possibly related to SARS-CoV-2 direct effect on pancreas
4. Drug-induced (corticosteroids) hyperglycemia or "secondary diabetes" during treatment for COVID-19.

Recent Indian study by Ghosh A et al. suggested that new onset diabetes during COVID-19 had worse glycemic parameters and higher C-peptide levels. The reason for higher magnitude of glycemic parameter could be the panic and fear due to the COVID-19 and

lockdown which resulted in increased stress levels across all sections of society. Fear of contracting the virus, losing friends and family to the disease, losing one's job and livelihood, challenges associated with working from home, change in dietary habits may all together have contributed. [18]

Management approach in person with diabetes Infected by COVID-19

Adults with COVID-19 infection can be categorized into the following severity of illness categories. However, the criteria may overlap or vary across clinical guidelines and clinical trials, and a patient's clinical status may change over time. [19]

1. *Asymptomatic or Pre-symptomatic Infection*: Individuals who test positive for SARS-CoV-2 using a virologic test but who have no symptoms that are consistent with COVID-19.
2. *Mild Illness:* Individuals who have any of the various signs and symptoms of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) but who do not have shortness of breath, dyspnea, or abnormal chest imaging.
3. *Moderate Illness*: Individuals who show evidence of lower respiratory disease during clinical assessment or imaging and who have an oxygen saturation (SpO2) ≥94% on room air at sea level.
4. *Severe Illness*: Individuals who have SpO2 <94% on room air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO2/FiO2) <300 mm Hg, respiratory frequency >30 breaths/min, or lung infiltrates >50%.
5. *Critical Illness*: Individuals who have respiratory failure, septic shock, and/or multiple organ dysfunction.

Mild to Moderate COVID-19 infection in person with Diabetes

In most cases of mild to moderate COVID-19 infection, home or institutional quarantine are advised and their antidiabetic treatment should be continued as usual. Regular monitoring of blood glucose levels to be mandated. Metformin, Modern sulfonylureas & Dipeptidyl-peptidase 4 (DPP4) Inhibitors can be used. Antidiabetic medications, including Sodium–glucose cotransporter-2 inhibitors (GLT2i), Glucagon-like peptide-1 receptor agonists (GLP-1 RA), and Thiazolidinediones (TZD), should be considered for temporary dose reduction or discontinuation.[12] Metformin use was associated with reduction in mortality in people with diabetes and COVID-19. It may provide a protective approach in this high-risk population [12]

Sodium–glucose cotransporter-2 (SGLT2) inhibitors, which may increase the risk of dehydration and diabetic ketoacidosis, demanding careful renal function monitoring. Interestingly, a study has been recently initiated to investigate a possible beneficial effect of dapagliflozin in hospitalized patients with COVID-19-related respiratory failure, and type 2 diabetes, cardiovascular disease and/or chronic kidney disease (DARE-19). [20] Sulfonylurea doses should be adjusted depending on patients' blood glucose levels to assess the risk of hypoglycemia, while discontinuation is suggested in hospitalized patients. Although dipeptidyl peptidase 4 (DPP-4) inhibitors have been linked with upper respiratory infection risk, they do not alter the risk of pneumonia and there is not adequate evidence for or against their discontinuation.[12]

Severe and Critically ill COVID-19 infection in person with Diabetes

Severe and critically ill COVID-19 positive person with diabetes are to be admitted in hospital setting. Insulin therapy seems to be the primary strategy for hospitalized patients. Though various guidelines recommended that hospitalized patients should discontinue all oral antidiabetic medication, the authors opine that certain OADs such as metformin and DPP4 inhibitors, can be considered case to case basis along with insulins whereas other agents like SGLT2 inhibitors to be stopped. Individualized Insulin doses may need to be adjusted, based on the individualized therapeutic plan. In patients who receive basal insulin, fast-acting insulin is used for acute hyperglycemia correction, blood glucose fluctuation during insulin therapy prerequisites strict and frequent monitoring. [17] Effective blood glucose control in hospitalized patients (glycemic variability within 70-180 mg/dl) was associated with reduced mortality compared with poorly controlled patients, in a retrospective, multicenter study in China, [21] In ICU-admitted patients with diabetes and COVID-19, the main challenges remain efficient blood glucose control and high insulin requirements. Continuous tube feeding, the frequent use of intravenous corticosteroids and the prescription of vitamin C or other medications may contribute to an increase of glucose variability.

Practical considerations for Basal Bolus Insulin regimen

Basal bolus insulin regimen is key for managing the glycemic parameters for hospitalized COVID-19 positive persons with Diabetes. [22] [Fig. 3]

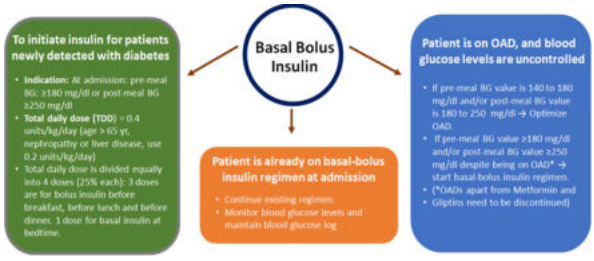

Fig.3 Basal Bolus Insulin regimen – Practical considerations

Post COVID-19 infection management approach in person with diabetes

Mucormycosis: The Black fungus

Mucormycosis also known as black fungus remains a devastating invasive fungal infection, with high mortality rates even after active management. The disease is being reported at an alarming frequency during this COVID-19 Pandemic in India. Rhino-orbito-cerebral presentation associated with uncontrolled diabetes is the predominant characteristic.[23] Major reason for its increased incidence during COVID-19 is thought to be from the increased use of corticosteroids therapy. Steroids render the phagocytic cells dysfunctional. Both neutrophils and macrophages exhibit an impaired chemotaxis and defective killing by both oxidative and non-oxidative pathways under such conditions.

Suspect Mucormycosis when a COVID-19 positive person with diabetes presents with the below [24]

- Sinusitis – nasal blockade or congestion, nasal discharge (blackish/bloody), local pain on the cheek bone
- One sided facial pain, numbness or swelling
- Blackish discoloration over bridge of nose/palate
- Toothache, loosening of teeth, jaw involvement
- Blurred or double vision with pain; fever, skin lesion; thrombosis & necrosis (eschar)
- Chest pain, pleural effusion, haemoptysis, worsening of respiratory symptoms

Clinical Practice points for management of Mucormycosis [24]

- Control diabetes and diabetic ketoacidosis
- Reduce steroids (if patient is still on) with aim to discontinue rapidly
- Discontinue immunomodulating drugs
- No antifungal prophylaxis needed
- Extensive Surgical Debridement - to remove all necrotic materials
- Medical treatment: Install peripherally inserted central catheter (PICC line), maintain adequate systemic hydration, Infuse Normal saline IV before Amphotericin B infusion, Antifungal Therapy, for at least 4-6 weeks.
- Monitor patients clinically and with radio-imaging for response and to detect disease progression

The practical considerations for delivering optimized diabetes care during COVID-19 Pandemic are summarized in Fig 4.

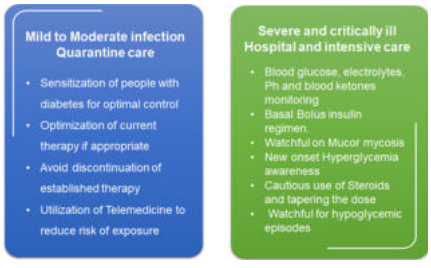

Fig 4: Considerations for care of T2DM patients in COVID-19

CONCLUSION

The advent of COVID-19 pandemic and the subsequent lockdown restrictions has posed new challenges in diabetes care. Thus, management for these patients requires a thoughtful approach to

ensure optimal blood glucose control and minimize risk of infection or of its complications. The implementation of modern technology like teleconsultation, change in medication or of doses, titration of insulin doses, allowing access to healthcare providers can help improve diabetes care during such time of pandemic.

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