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# Bangladesh Endocrine Society (BES) Position Statement for Management of Diabetes and Other Endocrine Diseases in Patients with COVID-19

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**Background:** The year 2020 witnessed a largely unprecedented pandemic of coronavirus disease (COVID-19), caused by SARS COV-2. Many people with COVID-19 have comorbidities, including diabetes, hypertension and cardiovascular diseases, which are significantly associated with worse outcomes. Moreover, COVID-19 itself is allied with deteriorating hyperglycemia. Therefore, Bangladesh Endocrine Society has formulated some practical recommendations for management of diabetes and other endocrine diseases in patients with COVID-19 for use in both primary and specialist care settings.

**Objective:** The objective of the article is to develop a guideline to protect the vulnerable group with utmost preference – the elderly and those with comorbid conditions. Therefore, to ensure the adequate protective measures and timely treatment for COVID-19 patients with diabetes, other endocrine diseases or any other comorbidities.

#### Considering and Monitoring Issues:

- The risk of a fatal outcome from COVID-19 may be up to 50% higher in patients with diabetes than in non-diabetics.
- Patients with diabetes and COVID had CFR 7.3–9.2%, compared with 0.9–1.4% in patients without comorbidities.
- Diabetic ketoacidosis may be one of the causes of mortality in COVID-19.
- There is wide fluctuation of blood glucose in these patients, probably due to irregular diet, reduced exercise, increased glucocorticoids secretion, and use of glucocorticoids.
- HbA1c should be <7.0% for the majority of the patients, this target may be relaxed in appropriate clinical settings.
- More emphasis should be given on day-to-day blood glucose levels. Hypoglycemia (<3.9 mmol/l) must be avoided.
- Frequent monitoring of blood glucose is needed in critically ill patients.

**Conclusion:** The fight against COVID-19 has been proven to be a challenging one. Therefore, all healthcare personnel should make the best use of updated knowledge and skills to ensure adequate protective measures and timely treatment for COVID-19 patients with diabetes, other endocrine diseases or any other comorbidities.

**Keywords:** COVID-19, diabetes mellitus, SARS COV-2, antidiabetic medications, endocrine diseases and COVID-19, thyroid disease and COVID-19

## Preamble

The purpose of guidelines and recommendations is to summarize and assess available evidence to help healthcare professionals in appropriate decision making in the management of an individual patient with a given condition. The Bangladesh Endocrine Society (BES), as a professional body, has been publishing its recommendations for the last few years. In response to the global COVID-19 pandemic, BES formed a task force comprising experts in this field to formulate practical

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recommendations for the management of patients with diabetes mellitus and/or other endocrine disorders with COVID-19. The members of this task force comprehensively reviewed the available evidence for the specific conditions. Search engines such as Google Scholar, PubMed and Scopus were used, with keywords including

COVID-19 and Diabetes Mellitus, SARS COV-2, Antidiabetic Medications, Endocrine diseases and COVID-19, Thyroid disease and COVID-19, Adrenal disease and COVID-19, Pituitary disease and COVID-19.

Each section of the recommendation was drafted by one member, followed by rigorous review and modifications by other members. During selection of the articles, interventional studies were given highest preference, but due to the scarcity of sufficient randomized trials in this field, observational studies, case studies and expert recommendations were also included. Therefore, this recommendation is a combination of expert opinions and narrative summary of the available evidence regarding management of COVID-19 patients with diabetes mellitus and/or other endocrine diseases.

## Introduction

The year 2020 witnessed a largely unprecedented pandemic of coronavirus disease (COVID-19), caused by SARS COV-2. Many people with COVID-19 have comorbidities, including diabetes, hypertension and cardiovascular diseases, which are significantly associated with worse outcomes.<sup>1</sup> Moreover, COVID-19 itself is associated with worsening of hyperglycemia. Depending on the global region, 20–59% patients in the COVID-19 pandemic had diabetes.<sup>2</sup> In Bangladesh, one in every 12 adults has diabetes, with a prevalence of 8.4%.<sup>3</sup> Data suggest that only 22.5% of patients with diabetes have good glycemic control.<sup>3</sup> Therefore, the Bangladesh Endocrine Society has formulated some practical recommendations for management of diabetes and other endocrine diseases in patients with COVID-19 for use in both primary and specialist care settings.

## Diabetes and COVID-19

The risk of a fatal outcome from COVID-19 may be up to 178–221% higher in patients with diabetes than in non-diabetics.<sup>4–6</sup> Data show that patients with diabetes and COVID had CFR 7.3–9.2%, compared with 0.9–1.4% in patients without comorbidities.<sup>7,8</sup> Diabetic ketoacidosis may be one of the causes of mortality in COVID-19.<sup>9</sup>

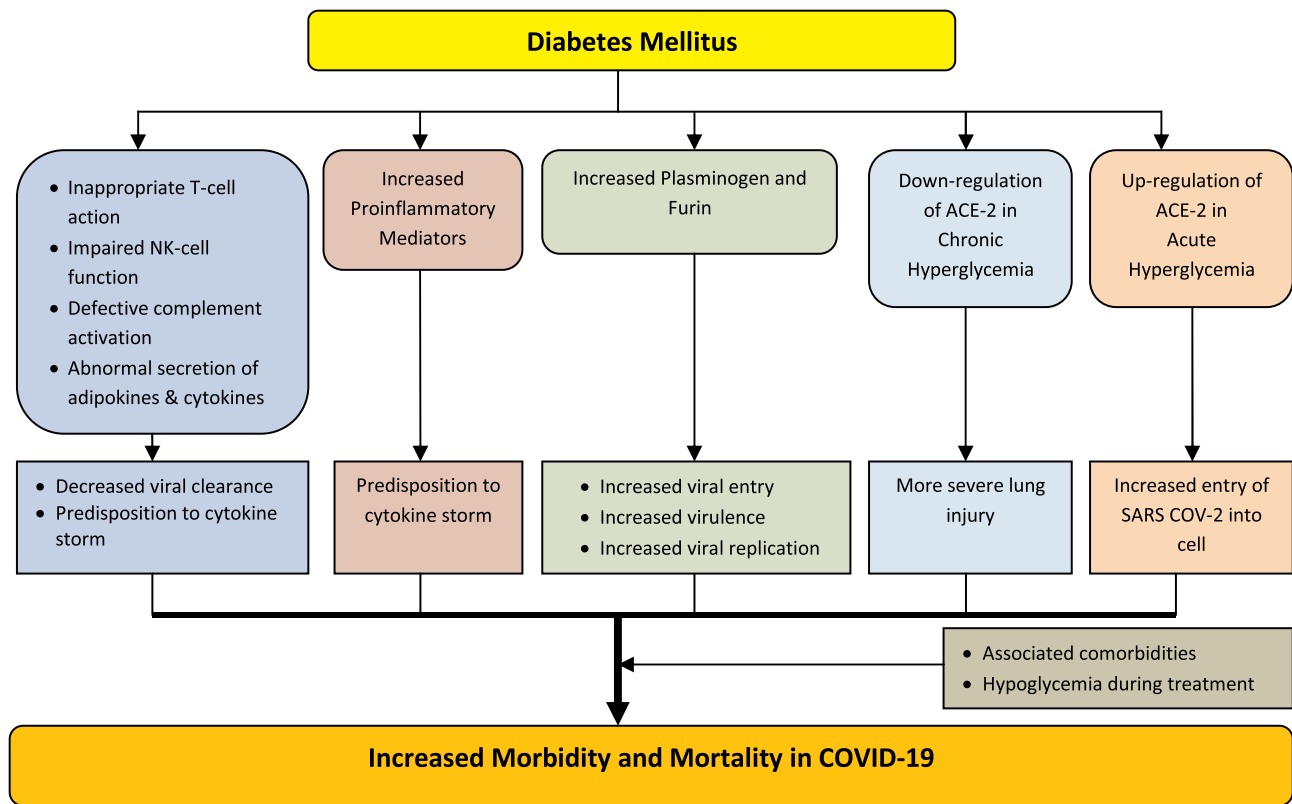
There is wide fluctuation of blood glucose in these patients, probably due to irregular diet, reduced exercise, increased glucocorticoids secretion, use of glucocorticoids etc. Also, COVID-19 can induce a large number of inflammatory cytokines leading to severe insulin resistance.<sup>10</sup> The reason behind increased severity of COVID-19 in diabetes is complex. Gupta et al. noted that poor glycemic control impairs several aspects of the immune response to viral infections. Inappropriate T-cell action, impaired NK cell activity and defects in complement action can reduce viral clearance. Diabetes and obesity are associated with abnormal secretion of adipokines and cytokines such as TNF- $\alpha$  and interferon, predisposing to severe infection. Plasminogen is increased in diabetes, increasing the virulence of SARS CoV-2.<sup>11</sup> Higher levels of IL-6, ESR, CRP, ferritin, fibrinogen and D-dimer were reported in patients with diabetes compared with non-diabetics.<sup>12</sup> Furin, a membrane bound protease involved in the entry of coronaviruses into the cell, is increased in diabetes, which may promote viral replication. Comorbidities such as hypertension, CAD and CKD further worsen the prognosis.<sup>11</sup> Figure 1 shows a summary of postulated mechanisms of increased severity of COVID-19 in diabetic patients.

Angiotensin-converting-enzyme 2 (ACE2) has been identified as the receptor for the coronavirus spike protein. COVID-19 infection decreases ACE2 expression, increasing the risk of cellular damage, hyperinflammation and respiratory failure.<sup>13</sup> Chronic hyperglycemia downregulates ACE2 expression making the cells vulnerable to the inflammatory effect of the virus. But acute hyperglycemia upregulates ACE2 expression, facilitating viral cell entry. It is also postulated that COVID-19 can induce new onset diabetes via its direct effect on pancreatic  $\beta$  cells which express ACE2 receptors.<sup>14–16</sup>

## Glycemic Targets and Glucose Monitoring

HbA1c should be <7.0% for the majority of the patients, this target may be relaxed in appropriate clinical settings.<sup>17</sup> More emphasis should be given on day-to-day blood glucose levels. Hypoglycemia (<3.9 mmol/l) must be avoided (Table 1).<sup>17,18</sup>

In the case of continuous glucose monitoring/flash glucose monitoring, time-in-range (3.9–10.0 mmol/l, 70–180 mg/dL) should be >70% of the time (or >50% in frail and older people and moderate to severe cases).<sup>2</sup> For severe and critically ill patients who are on intravenous insulin infusion, the glycemic target should be 7.8–10 mmol/L (140–180 mg/dL).



**Figure 1** Suggested mechanisms of increased severity of COVID-19 in diabetes.

**Glucose Monitoring**

Self-monitoring of blood glucose (SMBG) is an acceptable alternative to laboratory plasma glucose estimation in the present scenario. SMBG should be checked at any clinical suspicion of hypoglycemia.<sup>19–21</sup> Frequent monitoring of blood glucose (every hour or every 2 h) is needed in patients with very poor oral intake or those in ICU or non-ICU who are on mechanical ventilation who would require intravenous insulin infusion.<sup>19–21</sup> Table 2 shows the recommended frequency of SMBG in COVID patients.

Continuous glucose monitoring (CGM) may confer additional benefit in terms of glycemic control in patients receiving multiple dose insulin injections, continuous subcutaneous insulin infusion (CSII) or insulin pump or intravenous insulin syringe pump.<sup>19–22</sup>

**Nutrition Management and Physical Activity in COVID-19 and Diabetes**

Some conditions may interfere with a healthy regular diet, such as anorexia and anosmia, gastrointestinal symptoms such as diarrhea, vomiting, dehydration, irregular schedule, lack of care in isolation ward, stress, anxiety, insomnia etc.<sup>23</sup> During sick days, the patient should follow the regular calorie and schedule given before. To maintain hydration at least half a cup (100 mL) of water or unsweetened drinks should be taken hourly. The patient should not miss meals and should not fast. If unable to eat much, he/she should try snacks or drinks with carbohydrates. A regular meal schedule should be maintained. Glucose

**Table 1** Plasma Glucose Targets

	<b>Strict Control (Mild and Moderate Illness in Young)</b>	<b>Medium Control (Mild and Moderate Illness in Elderly, or Patients on Glucocorticoids and in Resource-Poor Inpatient Care Settings)</b>	<b>Low Control (Severe Illness, Hypoglycemia Intolerable Patients, or Patients Having Organ Dysfunctions or Serious Cardiovascular or Cerebrovascular Diseases)</b>
Fasting (mmol/L)	4.4–6.1 (80–110 mg/dL)	6.1–7.8 (110–140 mg/dL)	7.8–10.0 (140–180 mg/dL)
2 h post-prandial (mmol/L)	6.1–7.8 (110–140 mg/dL)	7.8–10.0 (140–180 mg/dL)	7.8–13.9 (140–250 mg/dL)

**Note:** Data from Cemiyeti.<sup>18</sup>

**Table 2** SMBG Frequency

Type of Diabetes	Patient Category	Recommended Frequency of SMBG
Type 2 DM	On Sulphonylureas or Meglitinides On other OADs On Insulin ± OADs	<ul style="list-style-type: none"> <li>• Four times/day and should include preprandial, post-prandial and bedtime levels.</li> <li>• In well-controlled diabetes, daily fasting and after the major meal may be justified.</li> <li>• Fasting and post-prandial capillary blood glucose once or twice a week.</li> <li>• At least 4 times/day and should include preprandial, post-prandial and bedtime levels.</li> </ul>
Diabetes in pregnancy	On lifestyle modifications	<ul style="list-style-type: none"> <li>• A day profile once a week FBG and 3 post-prandial values at least once a week or staggered over the week.</li> </ul>
	On insulin	<ul style="list-style-type: none"> <li>• At least 4 times/day (FBG and 3 post-prandial values).</li> </ul>
Type 1 DM	On multiple dose insulin injection	<ul style="list-style-type: none"> <li>• Pre- and post-meals, at bedtime, at 3am (if nocturnal hypoglycemia).</li> </ul>

**Note:** Data from Banerjee et al,<sup>19</sup> Basu et al,<sup>20</sup> and Rao et al.<sup>21</sup> **Abbreviations:** OAD, oral antidiabetic drug; FBG, fasting blood glucose.

drink or lozenge or tablet should be kept with the patient in their isolation room or ward. Plenty of fruits and vegetables, at least 2 or 3 servings a day, should be taken. If the patient is unable to eat due to vomiting or cannot remain hydrated, then urgent medical help is needed.<sup>24,25</sup> Enough lean protein such as fish, meat, egg, milk, cheese, seeds or nuts should be consumed. Protein restrictions (0.8 g per kg body weight) may be needed in chronic kidney disease with diabetes.<sup>26</sup> In critical, intubated or ventilated ICU patients with COVID-19, enteral nutrition (EN) should be started through a nasogastric tube. Isocaloric nutrition rather than hypocaloric nutrition can be increasingly implemented after the early stage of acute illness. Blood glucose should be continued at target levels with monitoring of blood triglycerides and electrolytes including phosphate, potassium and magnesium.<sup>26</sup> There are recommendations for the population to take vitamin D supplements during this pandemic.<sup>27</sup> Zinc has been shown to have inhibitory effects on H<sub>1</sub>N<sub>1</sub> viral load, but any effect in COVID-19 is unknown.<sup>28</sup> Vitamin C supplementation has some role in prevention of pneumonia and its effect in COVID-19 needs evaluation.<sup>29</sup> During sick days, vigorous exercise is not advised. If the disease category is mild some home exercises can be done. Breathing exercises and maintaining a prone position is beneficial. The patient should walk for a few steps or move their legs every 2 hours to prevent thromboembolism. Specialist respiratory physiotherapists may be needed in hospitals and ICU setting. Enough sleep is necessary.<sup>30-32</sup>

## Home Management, Indications for Hospital Care and Sick Day Rules Rules for DM Patients with COVID-19 Infection

At home, the patient should remain isolated in a single room, use a single toilet, should practice hand washing with soap-water 20 seconds each time frequently or before/after taking meal or after using washroom, after coughing, sneezing. A 60% alcohol-based sanitizer can be used. Cough/sneezing etiquette can be maintained by using tissue paper, cloth or elbow/hand. Face mask should be used. Care should be given by a single healthy person maintaining protective measures. Home floor, furniture, door knobs, light switch, sink, toilet seat, handles should be cleaned and disinfected after use. Meditation, prayer can help in minimizing stress and anxiety. News that can cause distress or anxiety should be minimized. Regular sleep is essential. Contact with relatives, friends and neighbors via telephone, online communication can be practiced to reduce effects of social isolation. Supply/storage of prescribed anti-diabetic medications/refills at home should be ensured for one to three months.<sup>33-36</sup>

Table 3 shows the proposed indications of hospitalization in diabetic patients with COVID-19.

## Rules for DM Patients to Prevent Exposure to COVID-19

People with DM should stay at home as much as possible to reduce exposure risk. If it is necessary to go out, crowds should be avoided, social distancing should be maintained by 1–2 meters and a face mask should be used. Routine clinic visits can be minimized while telemedicine/video consultations, telephone advice, online drug delivery



**Table 3** Indications of Hospitalization vs Home Management in Diabetic Patients with COVID-19

Diabetes Mellitus with COVID-19 Disease	
Who Can Be Treated at Home <sup>1</sup>	Indication for Hospitalization <sup>33,34</sup>
<ul style="list-style-type: none"> <li>• Mild COVID-19 cases having uncomplicated upper respiratory tract infection with non-specific symptoms (such as fever, fatigue, cough with or without sputum, sore throat, nasal congestion, anorexia, malaise, or headache).</li> </ul>	<ul style="list-style-type: none"> <li>• Blood glucose &gt;15 mmol/l (&gt;270 mg/dL) on repeated measurements.</li> <li>• Ketones in urine.</li> <li>• Excessive thirst.</li> <li>• Vomiting or diarrhea persist for more than 6 hours.</li> <li>• Unable to take food and drinks for 6 hours.</li> <li>• Weight loss of <math>\geq 2.5</math> kg during the illness.</li> <li>• Rapid breathing.</li> <li>• Abdominal pain.</li> <li>• Reduced level of consciousness (drowsiness).</li> <li>• Co-existing serious morbidities.</li> <li>• Clinical feature of moderate, severe and critical Covid-19 cases</li> </ul>

should be considered. Non-emergency routine evaluations should be deferred. Storage of medications and glucose testing kit should be ensured for 1–3 months. With routine SMBG, medication should be adjusted. Home-based exercise like treadmill, stationary cycling, free hand or aerobics, walking in room, roof, parking area or climbing stairs can be done. Diet with plenty of vegetables and citrus foods should be consumed. Hand hygiene should be maintained as mentioned in previous section. When coughing or sneezing, people with DM should cover nose and mouth with a tissue or a flexed elbow. They should avoid touching eyes, mouth or nose and should avoid meeting sick individuals, unprotected contact with wildlife and farm animals, sharing food, tools, glasses, towels. Vaccination to prevent secondary infection (e.g. influenza, streptococcal pneumonia) should be considered.<sup>33–35</sup>

### General Rules During Sickness

Fluid intake should be carefully balanced with vomiting or diarrhea if any. The patient should take plenty of water or calorie-free drinks at 120–180 mL per hour to avoid dehydration and if they cannot take 50 g of carbohydrates through food, it might also be necessary to drink sugary beverages while monitoring SMBG to avoid hyperglycemia. Weight should be measured every day; losing weight can be a sign of high blood glucose. The patient should have daily foot checks to ensure early detection of poor blood supply or infection.<sup>30,34,37</sup>

## Treatment of DM in COVID-19:

### Anti-Diabetic Agents: Oral and Parenteral

Type 2 diabetes treatment in COVID-19 patients with oral or parenteral glucose lowering drugs depends on clinical

severity of illness and associated comorbid situations. Regarding use of antidiabetic agents, there are many controversies and misconceptions during the COVID-19 pandemic. There are also recent recommendations from different authors, experts and organizations. Considering all these, this recommendation is made from the Bangladesh Endocrine Society.

### Considerations to Use Anti-Diabetic Drugs

Metformin is the widely used first-line antidiabetic agent for management of type 2 diabetes mellitus. It is responsible for the activation of the AMP-activated protein kinase (AMPK) in the liver and thereby decreases hepatic glucose output.<sup>38</sup> The activation of AMPK by metformin also leads to phosphorylation of ACE2 which can lead to conformational and functional changes to this receptor.<sup>39</sup> Activation of ACE2 increases its protective anti-inflammatory activity which may prevent hyperinflammation in COVID-19 infection.<sup>40</sup> Metformin also has anticipated antiproliferative and immunomodulatory effects due to activation of AMPK and has shown to have a protective role in pneumonia in mouse model and decreased mortality in sepsis, tuberculosis and COPD in previous human studies.<sup>41</sup> Meanwhile, several studies have reported the outcomes of metformin use in patients with type 2 diabetes with COVID-19. Although one study reported an increase in severity of infection with metformin use, some studies found neither harm nor benefit both in severity and mortality, but the majority reported a significant reduction in mortality.<sup>42</sup> Metformin also has an indirect effect to decrease replication of this virus.<sup>43</sup> Considering all these, although there are no recent good data in COVID-19, metformin may be a real game changer in COVID-19 pandemic.<sup>40</sup> It is evident that lactic acidosis

with metformin use is a rare event and predictable only in severe or critical COVID 19 illness with hypoxia or renal dysfunction.<sup>2,41</sup> Beside a major role in carbohydrate metabolism, DPP4 enzyme also plays an important role in immune regulation, but this is not completely understood. DPP4 activates T cells and upregulates CD86 expression and NF- $\kappa$ B pathway and increases inflammation in type 2 diabetes. So, DPP4 may represent a potential target for preventing and reducing the risk and progression of the acute respiratory complications of COVID-19 infection in type 2 diabetes.<sup>44</sup> A meta-analysis has shown that upper respiratory tract infections do not increase significantly with DPP4 inhibitor treatment.<sup>45</sup> DPP4 inhibitors have shown anti-inflammatory effects.<sup>44</sup> In COVID-19 disease, there can be a cytokine storm and excessive inflammatory response. So exploiting the defending role of DPP-4 inhibitors in decreasing the profound inflammation seems logical. Although available data suggest that DPP4 inhibitors produce no harm, a relatively large study shows that there is emerging evidence that it may lower the risk of severe COVID-19.<sup>46</sup> Recently, it has been hypothesized that SGLT-2i, GLP-1RAs and pioglitazone might induce an over-expression of the ACE2 receptor, which may have more serious consequences if a diabetic patient is infected.<sup>47,48</sup> GLP-1RA has shown over the years a significant anti-inflammatory and anti-adipogenic effect.<sup>49</sup> Similar evidence of anti-inflammatory effect is also seen with SGLT-2i and pioglitazone.<sup>50,51</sup> Although there is increased chance of COVID-19 infection through ACE2 overexpression, pioglitazone also reduces proinflammatory cytokines and inflammatory markers, and cytokine storm and fibrotic lung damage.<sup>41</sup> The usefulness of both GLP-1Ra and SGLT-2i for the prevention of cardiovascular and kidney disease is well known. With COVID-19, people with the presence of a cardiovascular or kidney disease show a worse prognosis.<sup>52,53</sup> Therefore, it seems to be mandatory to preserve the integrity of kidney and of the cardiovascular system in people who could be affected by SARS-CoV-2.<sup>48</sup> Also euglycemic or moderate hyperglycemic DKA with SGLT-2i are rare events and predictable only in severe or critical COVID 19 illness and especially in a background of poor food intake, dehydration and hypovolemia.<sup>2,41</sup> Insulin is the most potent, appropriate and safest antidiabetic agent in any acute infection. Although there are claims and counter claims regarding ACE2 overexpression with insulin in COVID-19, multiple stresses including respiratory failure and sepsis in severe COVID-19 infection lead to defects in insulin secretion and action. So, most patients will require insulin in high dose during this infection.<sup>2</sup>

Tables 4 and 5 summarize the recommendations for use of anti-diabetic agents and drugs used for other comorbidities in diabetic patients with COVID-19. Table 6 summarizes the recommendations for management of diabetes according to severity.

Follow BES Insulin Guideline for insulin initiation and intensification (section 3).<sup>56</sup>

Regarding use of investigational anti-COVID-19 drugs (e.g., hydroxychloroquine), consider their glycemic effects.<sup>10</sup>

## Diabetes Management in COVID-19 Patients in Hospital Setting

COVID-19 disease is a challenge for diabetic patients. Presence of diabetes increases disease severity and mortality in COVID-19 patients. Glycemic control needs to be optimal during this pandemic situation. Diabetes management in hospital setup both in outpatient department (OPD) and inpatient needs attention. Access of diabetes patients to outpatient clinics is limited during this pandemic and this urges alternative treatment options, particularly the implementation of telemedicine services. In spite of this situation there will be a few required OPD visits and these can be prioritized as follows.

**Table 4** Recommendations for Anti-Diabetic Agents

Therapy	Suggestions for Practice
Metformin	Continue in mild to moderate COVID-19. Stop if severely or critically ill or contraindications like renal failure/hypoxia/acute GI symptoms/dehydration
Sulfonylureas	Continue, adjust dose according to glycemic state, stop if unable to maintain regular oral food intake or at risk of hypoglycemia or if insulin is started or if severely/critically ill
SGLT2 inhibitors	Stop if hospitalized with acute illness/severely or critically ill/acute GI symptoms/dehydration
GLP-1RAs	Continue in mild to moderate COVID-19 but stop if acute GI symptoms/dehydration
DPP4 inhibitors	Continue in mild to moderate COVID-19. Avoid in severe/critical cases
Pioglitazone	Continue in mild to moderate COVID-19. Use cautiously where volume overload. Stop if severely/critically ill with hemodynamic instability, and hepatic and cardiac dysfunction
Insulin	Continue at any stage, adjust dose according to glycemic state, often require high dose

**Note:** Data from Bornstein et al,<sup>2</sup> Singh and Khunti,<sup>41</sup> Singh et al,<sup>42</sup> Ceriello,<sup>51</sup> Royal Australian College of General Practitioners,<sup>54</sup> and Ceriello et al.<sup>55</sup>

**Table 5** Recommendations for Drugs Used for CoMorbid Diseases of Diabetes

Therapy	Considerations for Use During COVID-19	Suggestions for Practice
ACEI/ARBs	<ul style="list-style-type: none"> <li>Uncertain risk/benefit – ACEi and ARB could increase the expression of ACE2, which could accelerate the entry of the virus into the cells, but on the other hand also increase protective anti-inflammatory effect which could protect against severe lung injury</li> </ul>	Continue unless specific contraindications
Statins	<ul style="list-style-type: none"> <li>Restore the reduction of ACE2 induced by high lipids such as LDL or lipoprotein(a)</li> <li>Have anti-inflammatory effects probably due to the upregulation of ACE2</li> <li>Possibility of increased risk of myositis with experimental antiviral agents/macrolides</li> </ul>	Continue but monitor risk

**Note:**Data from Ceriello et al<sup>48</sup> and Royal Australian College of General Practitioners.<sup>54</sup>

**Table 6** Recommendations for Management of Diabetes According to Severity

Severity of COVID-19	Treatment Regimen
Mild	Continue current treatment of oral antidiabetic agents (OAD) and/or insulin/GLPI-agonists. Monitor BG frequently and adjust regimen accordingly
Moderate	(a) Continue current treatment regimen if appetite is normal, patient can take food regularly and blood glucose is controlled (b) If patient cannot eat regularly or blood glucose is high -If on OAD/Premixed insulin/GLPI-agonists → switch to Basal- bolus/Split-mix SC insulin or IV insulin and adjust dose according to blood glucose profile. TDD premixed insulin is converted to same TDD of Split-mix/Basal-bolus insulin
Severe and Critical	IV insulin should be the 1st line treatment, but SC insulin may be used in severe case, especially if insulin pump is not available
On steroid	Long acting insulin/NPH - 10-20 U once/two divided doses daily and add rapid/short acting insulin subsequently depending on blood glucose.

**Note:**Data from Alshaikh et al.<sup>10</sup>

### Outpatient Appointment Prioritization for Specialist Diabetes Departments During the Coronavirus Pandemic

Urgent face to face appointment is needed in cases of newly diagnosed type 1 diabetes,<sup>2,57,58</sup> severe hyperglycemia requiring insulin initiation, teaching blood glucose monitoring in an urgent situation such as pregnancy or education about CGM, when blood test monitoring is needed (as in declining renal function or electrolyte imbalance), and if urgent physical examination is required (such as in pregnancy emergencies and severe foot infection). Virtual consultations i.e. telephone, video, email are recommended for follow up of newly diagnosed type 1 DM, vulnerable patients for example with history of recent hospital admission, recurrent severe hypoglycemia, HbA<sub>1c</sub>>11% and for diabetes follow up and insulin dose adjustment in pregnancy. Appointment should be deferred in stable and well managed DM, if risk of attending OPD is greater than benefit, and for health education sessions.

### Patients Requiring Hospital Admission

Intravenous insulin is rational for most general surgical and medical patients outside the ICU. Insulin analogues usually produce a lower incidence of hypoglycaemia than do regular human or Neutral Protamine Hagedorn (NPH) insulin. This is preferred treatment for non-critically ill hospitalized patients' basal insulin and a basal plus bolus correction insulin regimen is the preferred treatment with poor oral intake or those who are taking nothing by mouth. An insulin regimen with basal, prandial, and correction components is the preferred treatment for non-critically ill hospitalized patients with good nutritional intake and also for patients requiring glucocorticoid. Only gliding scale insulin use regimen in the inpatient hospital setting is strongly discouraged. If analogue insulin is unaffordable, conventional insulin can be continued being careful about more hypoglycemia while frequent monitoring is necessary. For management of diabetes in hospital setting, DKA and HHS, please refer to BES Insulin Guideline, Sections



4 and 5.<sup>56</sup> After the patient improves from the critical illness, when discontinuing intravenous insulin, a transition protocol is recommended. A patient transitioned to an intravenous regimen should receive a dose of subcutaneous basal insulin 2–4 h before the intravenous infusion is discontinued. For more details, please follow BES Insulin Guideline Section 4.<sup>56</sup>

## Diabetes Management After Recovery from COVID-19

### Advice at Discharge from Hospital

During home isolation for diabetes management the patient should start the drugs according to the advice<sup>33</sup> of the discharge certificate. They should do SMBG 4 times per day in initial days and contact endocrinologist/diabetologist as soon possible. The endocrinologist/diabetologist will modify, if needed, the management plan gradually to achieve usual glycemic target of the patient. Insulin may be continued, if started during hospital. For the patients who were on insulin prior to hospital stay, they will continue it. When they feel well, they should start physical exercise. The patients should stop smoking, try to reduce body weight, if overweight or obese, check BP at home and be vaccinated for influenza and pneumonia, if not done as per schedule. After discharge from hospital, COVID-19 patients with diabetes should maintain home isolation for at least 3 weeks.

**Table 7** Precautions to Prevent COVID-19 in People with Diabetes

<p><b>General Precautions for COVID Prevention:</b></p> <ul style="list-style-type: none"> <li>● Hand hygiene</li> <li>● Respiratory hygiene</li> <li>● Social and physical distancing</li> <li>● Avoid non-essential travels</li> </ul>
<p><b>Specific Precautions for Diabetic Patients During COVID Pandemic:</b></p> <ul style="list-style-type: none"> <li>● Frequent BG monitoring</li> <li>● Good glycemic control</li> <li>● Stabilize cardiac &amp; renal status (control BP and lipid, stop smoking)</li> <li>● Proper nutrition</li> <li>● Regular exercise</li> <li>● Vaccinate if not taken previously* (e.g., influenza, pneumococcus)</li> </ul>

**Note:** \*Patients with diabetes should be vaccinated against COVID-19 complying with national policies.

## Prevention of COVID-19 in People with Diabetes

General precautions are mandatory for patients and caregivers, to prevent contracting COVID-19<sup>59</sup> (Table 7).

### Pregnancy and Diabetes

Pregnant women experience immunological and physiological changes according to the CDC which might make them more susceptible to viral respiratory infections, including COVID-19.

### Pre-Existing Diabetes

Women with pre-existing diabetes have been identified as being more vulnerable to the severe<sup>60</sup> effects of COVID-19. Additional tests at antenatal visit should include HbA<sub>1c</sub>, renal and thyroid function, and urinary albumin-creatinine ratio (ACR) and fundoscopy where possible. Face-to-face review is needed if early, this should coincide with the 11–14-week scan. All women with pre-existing diabetes should be educated about SMBG, diet chart and sick day rules, information on hypoglycemia avoidance, prescription for folic acid and aspirin. Close and regular phone or email communication between obstetric and diabetic teams is essential to plan care and follow up. Women affected by COVID-19 should be advised to more frequent review of SMBG report.

### Gestational Diabetes

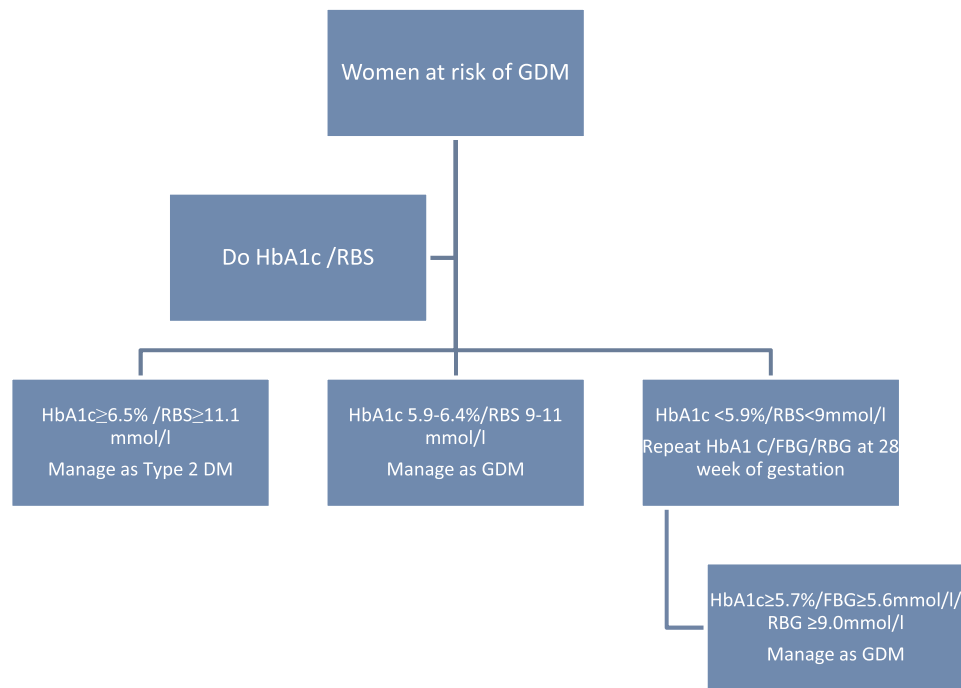
#### Screening

In view of the prolonged waiting period in hospital,<sup>61</sup> 2-hour oral glucose tolerance test (OGTT) may be postponed in this COVID 19 situation. For women having high risk of GDM the following modifications (as per Figure 2) could be used.

All women diagnosed with GDM should have an appointment with the diabetes team who will provide glucometer training and diet advice. Where feasible, this should be done via video call. Further diabetes follow up should be done remotely. For GDM women having target glycemic control on diet only, no further hospital visits for diabetes test are needed. They will contact with diabetes team if they have >3 abnormal blood glucose levels/week or >10–15% of all readings. Postpartum screening for maternal dysglycemia should be deferred until after the COVID-19 pandemic is over.

## Health Care Professional (HCP) and Diabetes

Health-care professionals with diabetes and those with age >60 years should be deployed away from front-line clinical duties



**Figure 2** Screening for women with risk factors for GDM. **Note:**Data from Ceriello et al.<sup>55</sup>

where possible.<sup>2</sup> For cases in which this is not possible or desirable, high-grade protection or increased protection should be used.<sup>2</sup> All healthcare personnel should adhere to standard precautions when caring for patients with SARS-CoV-2 infection, using respirator face mask, isolation gown, face shield or goggles, and performing hand hygiene before putting on gloves.<sup>62</sup> SARS-CoV-2 infection patients whether confirmed or possible should wear a facemask when being evaluated medically.<sup>62</sup> Any HCP who develops fever or symptoms consistent with COVID 19 should immediately self-isolate and contact to arrange for medical evaluation and testing.<sup>62</sup>

## Management of Endocrine Diseases During COVID-19 Pandemic

### Adrenal Insufficiency

Individuals with adrenal insufficiency have an increased rate of respiratory infection-related deaths, possibly due to impaired immune function reported in studies.<sup>63</sup> After diagnosis of COVID-19, a prompt modification of the replacement dose as indicated for the “Sick days” should be established when minor symptoms appear. In general, patients should double their usual glucocorticoid dose to avoid adrenal crisis. Additionally, patients are also recommended to have sufficient stock at home of steroid pills and injections, ideally a 90-day preparation.<sup>63</sup> In case of

inability to take oral glucocorticoids due to vomiting/diarrhea, injectable steroids should be initiated and hospital admission should be advised.<sup>64</sup> If adrenal crisis is suspected (fever, hypotension), 100–200 mg hydrocortisone IV 4–6 hourly should be initiated.

### Cushing's Syndrome

Individuals with uncontrolled Cushing's syndrome of any origin are at higher risk of infection in general.<sup>63</sup> If experiencing fever or cough supportive treatment should be initiated. In case of shortness of breath, hospital admission should be advised.

### Thyroid Disease

In COVID-19 patients admitted in hospital, routine thyroid function tests are not recommended. There is no benefit of levothyroxine treatment in patients with euthyroid syndrome.<sup>65</sup> Patients with thyrotoxicosis should continue taking medications as prescribed as those with uncontrolled thyrotoxicosis may be at higher risk of complications (such as thyroid storm) from any infection. Patients on corticosteroids or immunosuppressive agents for thyroid eye disease are more susceptible and are at high risk of severe illness from COVID-19 and such patients need to take more precautions.<sup>66</sup> Carbimazole induced agranulocytosis and subacute thyroiditis should be kept in mind as

differentials in patients presenting with sore throat. According to recent case reports, COVID-19 infection may cause subacute thyroiditis. Hypothyroidism patients should continue taking levothyroxine treatment as suggested.<sup>66</sup>

## Bone and Mineral Metabolism (Osteoporosis)

While there is no evidence of increased risk of COVID-19 to patients with bone and mineral metabolism disorders, the unprecedented global lockdowns have significantly affected their care. It is advisable for those on medications such as denosumab and romosozumab to receive timely infusions, however, infusions of bisphosphonates such as Zoledronic acid may be deferred due to their long half-life.<sup>67</sup>

## Sodium Metabolism (Diabetes Insipidus)

Central and nephrogenic diabetes insipidus (DI) pose a particular challenge due to reduced availability of laboratory (electrolyte) testing. An opinion piece recently highlighted this challenge, encouraging the practice of once a week aquaresis by omitting one dose of vasopressin in individuals with existing DI.<sup>68</sup>

## Conclusion

The fight against COVID-19 has been proven to be a challenging one. As in every war, it's the duty of the frontline fighters to protect the vulnerable group with utmost preference – the elderly and those with comorbid conditions. Therefore, all healthcare personnel should make the best use of updated knowledge and skills to ensure adequate protective measures and timely treatment for COVID-19 patients having diabetes, other endocrine diseases or any other comorbidities.

## Disclosure

The authors report no conflicts of interest in this work.

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