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NON-SYSTEMATIC REVIEW

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Narrative review on clinical considerations for patients with diabetes and COVID-19: More questions than answers

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Abstract

Background-Aim: Diabetes, obesity and hypertension are common comorbidities associated with increased severity and mortality rates from Corona Virus Disease (COVID)-19.

Methods: In this narrative review (using the PubMed database), we discuss epidemiological data and pathophysiological links between diabetes and COVID-19. The potential effects of glycaemic control and antidiabetic drugs on the prevalence and outcomes of COVID-19 are also reviewed, as well as the role of telemedicine and diabetes self-management in the post-COVID-19 era.

Results: Diabetes has been linked to COVID-19 morbidity and mortality, although further research is needed to elucidate this association. In the meantime, physicians should be aware of the potential rise in the prevalence of diabetes (due to unhealthy lifestyle changes during the pandemic), its severity and complications and focus on achieving optimal diabetes prevention and management. Telemedicine and diabetes self-management may help towards this direction. Dipeptidyl-peptidase 4 (DPP4) inhibitors, glucagon-like peptide-1 (GLP-1) receptor agonists and sodium-glucose transporter 2 (SGLT2) inhibitors may affect viral entry and infection, and thus COVID-19 outcomes, as shown in observational studies.

Conclusion: Diabetes has been associated with COVID-19 development and progression. Certain antidiabetic drugs may influence COVID-19 prevention and management. The results of ongoing randomized clinical trials will shed more light on this field.

1 | DIABETES AND COMORBIDITIES IN PATIENTS WITH CORONA VIRUS DISEASE (COVID)-19

The COVID-19 pandemic represents a global public health crisis of this generation and, potentially, since the influenza pandemic of 1918. Diabetes and hypertension have been identified as common comorbidities for coronavirus infections. Indeed, Zhou et al showed that among 191 laboratory-confirmed COVID-19 Chinese patients, 48% had at least one comorbidity, with hypertension being the most frequent (30%), followed by diabetes (19%) and coronary heart disease (8%).[1] Similarly, in New York, among 5700 hospitalised patients with COVID-19, 56.6% had hypertension and 33.8% diabetes.[2] In Italy (in the Lombardy region that was mostly affected during the pandemic), among 1591 consecutive patients with laboratory-confirmed COVID-19 that were admitted in an intensive care unit (ICU), the prevalence of hypertension and diabetes was 49% and 17%, respectively.[3] Furthermore, a recent analysis of 909 deceased patients with COVID-19 in Italy showed that diabetes was the second most common comorbidity (31.5%), after hypertension (73.5%).[4] Yang et al in their recent systematic review and meta-analysis on the prevalence of

comorbidities associated with COVID-19 infection in China (eight studies; n = 46 248 infected patients), reported that hypertension and diabetes were prevalent in 17% and 8% of the cases, respectively.[5] Similar results were found in another meta-analysis of six studies (n = 1527 COVID-19 patients); the rates of hypertension and diabetes were 17.1% and 9.7%, respectively.[6]

Diabetes was also related to poorer outcomes in hospitalised patients with COVID-19 (including severity, progression, acute respiratory distress syndrome [ARDS] and mortality), as shown in a recent meta-analysis (30 studies, n = 6452 patients).[7]

Obesity, frequently co-existing with diabetes and characterised by chronic low-grade inflammation and increased vulnerability to infections, was also associated with COVID-19 prevalence and severity.[8,9] In this context, Peng et al[10] in their retrospective analysis of 112 Chinese patients with cardiovascular (CV) disease (CVD) affected by COVID-19 reported that a higher body mass index (BMI), that is, ≥25 kg/m^2, was more frequently seen in critical cases and non-survivors. In another European retrospective cohort study, including 124 patients with COVID-19 positive admitted to an ICU, obesity (defined as BMI ≥30 Kg/m^2) was present in 47.6% of patients; disease severity (defined by the need for invasive mechanical ventilation) increased with BMI.[11] Similarly, 41.7% of 5700 hospitalised patients with COVID-19 in New York were obese (BMI ≥30 Kg/m^2).[2]

The European Society of Cardiology (ESC) recognised hypertension, diabetes and severe obesity (BMI ≥40 Kg/m^2) as "concomitant conditions that may be associated with more severe course of Severe Acute Respiratory Syndrome (SARS)-Corona Virus (CoV)-2 infection" in its recent guidance for the diagnosis and management of CVD during the COVID-19 pandemic.[12] Indeed, there is evidence that older people and those with cardiometabolic diseases, including hypertension, diabetes, severe obesity and CVD, are more likely to be infected with COVID-19 and die from it.[13] Of note, hypertension, obesity and CVD are frequent comorbidities in patients with diabetes[14]; diabetic microvascular complications may also contribute to individual vulnerability to COVID-19 infection.[15] Therefore, such patients, need special attention, especially when infected with COVID-19, since their disease may be associated with increased severity of symptoms and complications.[16]

In this narrative review, we consider the pathophysiological mechanisms linking diabetes and COVID-19, as well as the potential role of glucose control on COVID-19 infection and severity. Furthermore, data on the effects of antidiabetic drugs on COVID-19 incidence are discussed. Finally, we comment on the impact of this pandemic on diabetes prevalence and severity, as well as on the importance of telemedicine and diabetes self-management for daily clinical practice in the COVID-19 era.

2 | METHODS

This is a narrative review. We searched PubMed using the following keywords: diabetes, COVID-19, SARS-CoV-2, hypoglycaemic agents, dipeptidyl-peptidase 4 (DPP4) inhibitors, glucagon-like peptide-1 (GLP-1) receptor agonists, sodium-glucose transporter 2 (SGLT2) inhibitors, glucose control, hydroxychloroquine, antiviral agents, telemedicine and diabetes self-management. As in all narrative reviews, a selection bias cannot be excluded.

Review criteria

- This is a narrative review.
- We searched PubMed using the following keywords: diabetes, COVID-19, SARS-CoV-2, antidiabetic drugs, DPP4 inhibitors, GLP-1 receptor agonists, SGLT2 inhibitors, glucose control, hydroxychloroquine, antiviral drugs, telemedicine, and diabetes self-management.
- As in all narrative reviews, a selection bias cannot be excluded.

Message for the clinic

- There is data linking COVID-19 and diabetes.
- Telemedicine and diabetes self-management may play an important role in the post-COVID-19 era.
- Whether certain antidiabetic drugs may affect the course of COVID-19 remains to be established in future trials.

Highlights

- Diabetes increases the risk of developing COVID-19 and of adverse outcomes.
- Telemedicine and diabetes self-management may play an important role in the post-COVID-19 era.
- Whether certain antidiabetic drugs may affect the course of COVID-19 remains to be established in future trials.

3 | DIABETES AND COVID-19: POTENTIAL PATHOPHYSIOLOGICAL MECHANISMS

There is accumulating evidence that among hospitalised patients with COVID-19, the prevalence of diabetes is high, and mortality is increased.[17] Patients with diabetes are generally more prone to infections, including pneumonia and influenza, and this is why pneumococcal and annual influenza vaccinations are recommended in this patient population.[16] Interestingly, it was previously shown that diabetes was linked to increased mortality in patients infected with SARS-CoV, Influenza A 2009 (H1N1) and Middle East Respiratory Syndrome–related coronavirus (MERS-CoV).[18-21] It follows that people with diabetes are more likely to be infected by other viruses such as the SARS-CoV-2.

There are several potential underlying mechanisms linking diabetes with COVID-19 infection. These may include the frequent existence of cardiometabolic comorbidities, a higher affinity for cellular

binding and virus entry, diminished T-cell function, reduced viral clearance and increased susceptibility to inflammation and cytokine storm syndrome.[13] Overall, diabetes is associated with maladaptive inflammatory responses and dysregulated innate immunity, thus increasing susceptibility to and adverse outcomes from viral, bacterial, parasitic and mycotic infections.[22]

There is limited animal data reporting that diabetes may induce the expression of angiotensin-converting enzymes (ACEs) in the pancreas, lung, liver and heart.[23] ACE2 is involved in SARS-CoV-2 (which causes COVID-19) entering cells, thus potentially contributing to the multi-organ failure observed in people with diabetes infected by COVID-19.[23] However, ACE2 overexpression was shown to protect from endothelial dysfunction and microvascular complications in people with diabetes despite longstanding inadequate glycaemic control.[24]

4 | DIABETES AND COVID-19: DOES GLYCAEMIC CONTROL PLAY A ROLE?

It has been suggested that a hyperglycaemic environment may increase the virulence of some pathogens.[25] In this context, whether maintaining good glycaemic control might help in reducing the risk and severity of COVID-19 in people with diabetes remains to be established. A recent retrospective Chinese study (n = 952 patients with COVID-19 with pre-existing type 2 diabetes) evaluated the impact of glycaemic variability (GV) on COVID-19 outcomes.[26] GV was defined as the range between the lowest fasting blood glucose (BG) and 2h postprandial BG (PG) during the study. In-hospital (28-day) all-cause mortality was significantly lower in well-controlled patients (ie, with GV between 0.70 and 1.8 g/L) compared with the poorly controlled ones (ie, with lowest fasting BG ≥0.70 and highest 2hPG >1.8 g/L) [multi-adjusted hazard ratio (HR) 0.13, 95% confidence interval (CI): 0.04-0.44; $P < .001$].[26] Patients in the well-controlled BG group also developed ARDS less frequently (HR 0.41, 95% CI: 0.25-0.66; $P < .001$), acute heart injury (HR 0.21, 95% CI: 0.07-0.59; $P = .003$), acute kidney injury (0.7% vs 3.8%), septic shock (0.0% vs 4.7%) and disseminated intravascular coagulation (0.0% vs 0.6%).[26] Overall, a higher GV in ICU-admitted patients has been associated with increased mortality.[27] Therefore, physicians should focus on BG control and GV monitoring in ICU patients.

In an Italian study (n = 59 hospitalised patients with COVID-19), the presence of hyperglycaemia was linked to disease severity; insulin infusion improved outcomes.[28] Acute hyperglycaemia at hospital admission was also related to COVID-19 infection with or without pre-existing diabetes.[29] In the same study, average BG at day 1 was the strongest independent predictor of SARS-CoV2 radiographic chest imaging, irrespective of the presence or absence of a history of diabetes.[29] Furthermore, among 1122 US hospitalised patients with laboratory-confirmed COVID-19, those with diabetes and/or uncontrolled hyperglycaemia had a higher mortality rate and a longer hospital stay compared with those without diabetes or hyperglycaemia (28.8% vs 6.2%; $P < .001$ and 5.7 vs 4.3 days; $P < .001$, respectively).[30]

The Coronavirus SARS-CoV-2 and Diabetes Outcomes (CORONADO) study is a large nationwide observational study of people with diabetes who were hospitalised for COVID-19 in 68 French hospitals in March 2020.[17] In an intermediate analysis of this study including 1317 participants, previous long-term glucose control (assessed by HbA_{1c} measurement) as well as plasma glucose levels at admission did not independently affect the primary outcome (ie, death and/or tracheal intubation for mechanical ventilation within 7 days of hospital admission).[17]

Acute hyperglycaemic crises [ie, diabetic ketoacidosis (DKA) and/or hyperglycaemic hyperosmolar syndrome (HHS)] can be precipitated by COVID-19 and further worsen clinical outcomes in patients with COVID-19.[31] A recent systematic review reported that among 110 patients with COVID-19 (91 had isolated DKA and 19 had DKA/HHS), in-hospital mortality was higher in the DKA/HHS vs the isolated DKA group (67% vs 29%); the corresponding value for in-hospital death for the total patient population (n = 110) was 45%.[32]

Specific attention to glycaemic control is also recommended for outpatient COVID-19 positive patients with diabetes.[33] Patients with mild COVID-19 may continue their glucose-lowering agents provided that they are able to drink and eat satisfactorily and that frequent monitoring of capillary glucose levels is performed.[33] Patients who develop severe illness may need treatment modifications and/or hospitalisation; their attending physician will decide the therapeutic strategy taking into consideration several factors such as nutritional and glycaemic status, renal function, haemodynamic stability, risk of hypoglycaemia and drug interactions.[33]

Although more data are needed for COVID-19 patient populations, physicians should consider optimal glycaemic control as an important target of diabetes management, particularly during the COVID-19 pandemic.[34] Insulin remains the preferred agent to control hyperglycaemia in hospitalised patients.[16]

5 | HYPOGLYCAEMIC AGENTS AND COVID-19: ANY INTERACTIONS?

Whether certain hypoglycaemic agents can prevent infection from COVID-19 and/or improve symptoms and prognosis of infected patients remains unknown. It has been suggested that incretin-based therapies may be beneficial in people with diabetes and COVID-19.[32] Such suggestions were based on the fact that DPP4 may affect immune regulation and enhance inflammation via both catalytic and non-catalytic mechanisms.[35-39] In this context, DPP4 inhibitors have been shown to exert anti-inflammatory actions via reduction of pro-inflammatory cytokines.[40] Emerging evidence implicates DPP4 inhibitors as modulators of certain aspects of innate immunity involving monocyte/macrophage, neutrophil and endothelial cells.[41] Furthermore, DPP4 is recognised as a receptor for MERS-CoV.[22] If DPP4 is also proved to be directly involved in SARS-CoV-2 cell

adhesion/virulence, DPP4 inhibitors may represent a therapeutic approach for the treatment of COVID-19 via inhibiting viral entry and infection.[36,42] In this context, DPP4 may facilitate SARS-CoV-2 entry into cells based on its homology with ACE2, thus suggesting that DPP4 inhibitors may decrease SARS-CoV-2 virulence.[43] Indeed, a recent crystallographic study reported that both ACE2 and DPP4 could be involved in the receptor binding domain of SARS-CoV-2.[44] It has also been suggested that DPP4 inhibitors may lead to a conformational change in the DPP4 molecule, thus promoting the interaction between SARS-CoV-2 spike S1 protein and human DPP4.[45,46] Apart from interfering with viral entry, DPP4 inhibitors could possibly limit viral proliferation by raising serum DPP4 levels (as reported in animal studies[47]) that bind SARS-CoV-2.[45] This process can prevent the attachment of SARS-CoV-2 and other coronaviruses to membrane-bound DPP4 in pneumocytes or other cells involved in viral replication and spread.[45] Further research is needed in this field.

The ACE2/Ang-(1-7)/Mas axis has been implicated in inflammation and fibrosis.[48] Drugs that affect this pathway may thus exert anti-inflammatory effects, including statins and renin–angiotensin–aldosterone system inhibitors (and mainly angiotensin II receptor blockers).[49] Furthermore, GLP-1 receptor agonists (GLP-1 RAs) were reported to induce the activity of the protective ACE2 and Mas receptor pathways, thus potentially preventing Co-V from entering the cells via competitive binding to ACE2.[23] For example, liraglutide, a GLP-1 RA, was shown to increase pulmonary ACE2 expression in diabetic rats, leading to improved lung function.[50] Liraglutide was also reported to protect against acute lung injury in rodent models via decreased lung inflammatory chemokine and cytokine gene expression.[51] Overall, GLP-1 RAs have been shown to exhibit anti-inflammatory actions.[52] It should be noted that data from human studies on the effects of DPP4 inhibitors and GLP-1 RAs on the incidence and treatment of COVID-19 is limited to a few observational studies[45,53-55] but there are ongoing randomised clinical trials.[56-58]

Hypoglycaemic agents that can cause volume depletion or hypoglycaemia should be avoided and dosage of oral antidiabetic drugs may need to be reduced.[42] Dehydration during acute illness (including COVID-19) can predispose to lactic acidosis and DKA and thus metformin and sodium-glucose-co-transporter 2 (SGLT2) inhibitors should be temporarily discontinued in hospitalised patients.[42] On the other hand, in vitro studies in human renal cells exposed to SLGT2 inhibitors have shown an increment in angiotensin (1-7) due to the independent activation of the non-classical renin–angiotensin system, leading to important anti-inflammatory and antifibrotic effects.[59,60] By analogy, it is reasonable to assume that SGLT2 inhibitors could also beneficially activate the non-classical renin–angiotensin system in the lungs.[61] The recently published dapagliflozin in respiratory failure in patients with COVID-19 (DARE-19) trial evaluated dapagliflozin's efficacy and safety in COVID-19 hospitalised patients with at least one cardiometabolic risk factor (ie, hypertension, type 2 diabetes, CVD or chronic kidney disease).[62] Overall, 1250 patients were randomly (1:1) assigned to receive either dapagliflozin or placebo. Primary outcomes were dual: the outcome of prevention (ie, a composite of time to worsened or new respiratory, CV or kidney organ dysfunction during hospitalisation, or 30-day all-cause death) and the outcome of recovery (ie, change in clinical status by day 30, including death and organ dysfunction during hospitalisation, requirement of oxygen supplementation for those still hospitalised at day 30 without organ dysfunction and hospital discharge before day 30).[62] There was a trend toward improvements in both primary outcomes with dapagliflozin but without reaching statistical significance.[62] Indeed, numerically fewer patients on dapagliflozin had organ failure (64 vs 80 patients [10.2% vs 12.8%], respectively; HR 0.80, 95% CI 0.57-1.11) or died compared with those on placebo (41 vs 54 patients [6.6% vs 8.6%], respectively; HR 0.77, 95% CI 0.52-1.16).[62] The results were similar for the key secondary end-points of all-cause death or worsening renal function. Dapagliflozin was well tolerated; less serious adverse events were observed in the dapagliflozin vs placebo group (10.6% vs 13.3%).[62]

In current clinical practice, antidiabetic drugs and insulin therapy should be used at doses sufficient to achieve glycaemic control (but avoiding hypoglycaemia), taking into consideration the individual's kidney function and other side effects/contraindications, according to guidelines.[63]

Pharmacological interactions between antidiabetic medication and drugs used to treat COVID-19 (eg, chloroquine, hydroxychloroquine, anticytokine or immunomodulatory agents and antivirals, such as lopinavir/ritonavir combination, ribavirin, umifenovir, remdesivir and favipiravir) should also be considered.[64] For example, hydroxychloroquine, currently used in India as an antidiabetic medication, can cause hypoglycaemia.[65] Of note, since there is no definitive evidence for the use of chloroquine and hydroxychloroquine to treat COVID-19, the European Medicines Agency recommends that these drugs should preferably be used in the context of clinical trials or in accordance with national established protocols.[66]

Glucocorticoids, that have been helpful in the treatment of ARDS, are being used as an adjunctive therapy in patients with severe COVID-19, especially in the presence of compelling indications, such as chronic obstructive pulmonary disease exacerbation or refractory shock.[64] However, the severity and the duration of the hyperglycaemia depends on the dose and type of glucocorticoids and needs close monitoring.[67]

Overall, physicians should be aware of such drug side effects.

6 | DIABETES IN THE POST-COVID-19 ERA: ANY IMPACT ON ITS PREVALENCE AND SEVERITY?

Quarantine because of the COVID-19 pandemic can lead to psychological disorders, including depression, consequently resulting in unhealthy eating, food addictions and decreased physical exercise.[68,69] Such behaviours are expected to increase to the prevalence of obesity and obesity-related diseases, including diabetes. Furthermore,

it has been suggested that there is a potential direct pancreatic injury by SARS-CoV-2.[70] In this context, it was previously shown that SARS-CoV binding to ACE2 in the pancreas led to acute diabetes development (as a result of islet damage and impaired insulin release) in patients infected with SARS.[71] SARS-CoV-2 infection in people with diabetes may also trigger the release of hyperglycaemic hormones (such as catecholamines and glucocorticoids), leading to hyperglycaemia, abnormal GV and diabetic complications.[72] Indeed, a bi-directional association between diabetes and COVID-19 has recently been suggested.[73] Coronaviruses may exert a diabetogenic effect via stress response and acute hyperglycaemia, but further evidence is needed to support this viral cause of ketosis-prone diabetes.[73] Therefore, the prevalence of new-onset diabetes related to COVID-19 should be recorded.

A recent study assessed the impact of a nationwide lockdown duration on the glycaemic control and diabetes-related complications with a predictive model using multivariate regression analysis.[74] The authors reported predicted increases in HbA_{1c} by 2.26% at the end of a 30 day-lockdown period, as well as annual percentage increments in the complication rates for non-proliferative and proliferative diabetic retinopathy (by 2.8 and 2.9%, respectively), retinal photocoagulation (by 1.5%), microalbuminuria (by 9.3%), proteinuria (by 14.2%), peripheral neuropathy (by 2.9%), lower extremity amputation (by 10.5%), myocardial infarction (by 0.9%), stroke (by 0.5%) and infections (by 0.5%).[74]

More research is needed in this field. Physicians should be aware of the potential rise in the prevalence of diabetes, its severity and complications. Furthermore, diversion of maximum care to COVID-19 patients may lead to neglecting other serious medical conditions. Patients may also not seek medical advice because of their fear of coming into contact with patients with COVID-19.

7 | TELEMEDICINE AND DIABETES SELF-MANAGEMENT IN THE POST-COVID-19 ERA

During the COVID-19 outbreak, the access of people with diabetes to outpatient clinics is limited. Therefore, there is a popularisation of smartphones, internet and fifth-generation networks, to provide remote medical consultation for patients not advised to attend the hospital.[72] Furthermore, educational videos and e-books on diabetes self-management and COVID-19 prevention have been developed.[72] With the use of these electronic sources, patients should be advised, encouraged and educated on how to achieve and maintain healthy lifestyle habits and glycaemic control to prevent diabetes and its complications. Indeed, telemedicine may, at least partly, alleviate the problem of uncontrolled diabetes.[75] Virtual reality technology, through audio-visual-based virtual communication, may also be helpful.[76] Previous meta-analyses have shown that telemedicine strategies, combined with usual care, led to improved glycaemic control in people with diabetes.[77-79]

A recent study reported that transition from inpatient consult services to virtual care models did not affect glycaemic control, thus providing important implications for future diabetes care.[80] The COVID-19 pandemic has forced a system-wide reboot of healthcare delivery models.[81] In addition, a second "wave" of COVID-19 pandemic may occur within the next months; in that case, telemedicine may be more extensively implemented, thus becoming the way routine visits are conducted.[82,83] Therefore, the impact of such online services and resources on diabetes prevention and management should be urgently evaluated.

The COVID-19 pandemic may expand the use of continuous glucose monitoring (CGM) systems both in outpatients setting, as a part of telemedicine programs, and in hospitalised patients. CGM in COVID-19 inpatiens may improve glycaemic control and reduce the biological risk for the healthcare workers associated with point-of-care capillary glucose. Recently, the US Food and Drug Administration (FDA) has allowed the use of CGM in hospital settings during the COVID-19 pandemic.[84]

8 | VACCINATION FOR COVID-19 AND DIABETES

As diabetes increases the risk and severity of COVID-19 infection, prioritising the vaccination against SARS-CoV-2 in patients with diabetes has been claimed.[85] However, because glycaemic control may affect the immune response, it seems reasonable to wonder whether euglycaemia should be attained or not before administering the vaccine to optimise its efficacy.[86] Humoral immune response against SARS-CoV-2 has been observed in patients with diabetes, being even greater for timing and antibody titres compared with that of nondiabetic patients and not being influenced by glucose levels.[87] However, data with regard to response to COVID-19 vaccination in patients with diabetes are lacking and several unresolved issues remain, including the preferred vaccine type, vaccine durability and efficacy, frequency of administration, vaccination in children/adolescents and pregnant/lactating women with diabetes.[88]

In terms of safety, there have been a few reports on acute hyperglycaemic crisis following vaccination against COVID-19 in patients with type 2 diabetes.[89] In the majority of the cases, a mild and transient increase of BG occurred that was self-limiting and did not required major changes in treatment.[90] It has been suggested that this side effect may be attributed to immediate vaccine induced inflammation and consequent immune response.[90] However, COVID-19 vaccine was also reported to cause new-onset type 2 diabetes in a patient presenting as hyperosmolar hyperglycaemic state.[91] Further research is needed in the field.

In addition, systemic and local side effects have been reported after COVID-19 vaccination.[92-94] Whether patients with diabetes are more prone to such vaccine-related complications remain to be elucidated. Of note, COVID-19 vaccine hesitancy has been reported in patients with type 2 diabetes, especially in those that experienced side effects following past vaccinations.[95]

TABLE 1 Diabetes in the COVID-19 era: unanswered questions

- Is more frequent self-monitoring of blood glucose levels required during the COVID-19 pandemic?
- How can previous glycaemic control influence disease severity?
- Should glycaemic goals be stricter during the COVID-19 pandemic?
- Are there any specific antidiabetic drugs helpful to prevent COVID-19 prevalence or severity?
- Do hospitalised patients with severe COVID-19 need more frequent blood glucose monitoring?
- How important is the control of hyper- or hypoglycemia in isolated hospitalised patients?
- How can telemedicine and continuous glucose monitoring assist in the management of diabetes during the COVID-19 pandemic?
- How will the prevalence of diabetes be affected by the COVID-19 pandemic?
- How will glycaemic control be affected by the COVID-19 pandemic?
- How will diabetic complications be affected by the COVID-19 pandemic?

9 | CONCLUSIONS

Although the link between diabetes and COVID-19 morbidity and mortality has been recognised,[96] several issues remain unanswered and should be addressed in future, large, multicentre, randomised clinical trials with long-term follow-up (Table 1). Meanwhile, physicians should focus on optimal diabetes prevention and management according to current guidelines.[63] Certain hypoglycaemic agents (ie, DPP4 inhibitors, GLP-1 RAs and SGLT2 inhibitors) may affect viral entry and infection, and thus COVID-19 outcomes. However, only observational data are currently available, and we need to wait for the results of ongoing randomised clinical trials to elucidate the role of antidiabetic drug therapy on COVID-19 development and progression.

DISCLOSURES

NK has given talks, attended conferences and participated in trials sponsored by Angelini, Astra Zeneca, Bausch Health, Boehringer Ingelheim, Elpen, Mylan, Novo Nordisk, Sanofi and Servier. RG-H has given talks and participated in trials sponsored by Astra Zeneca, Boehringer-Lilly, Janssen-Cilag, Merck Sharp & Dohme, Novo Nordisk, Novartis and Sanofi. DPM has given talks, acted as a consultant or attended conferences sponsored by Amgen, Novo Nordisk and Libytec. PP-M has given talks and participated in trials sponsored by Boehringer Ingelheim, Merck Sharp & Dohme, Novartis, Ferrer, Esteve, Novo Nordisk, GlaxoSmithKline, Janssen-Cilag, Amgen and Sanofi.

DATA AVAILABILITY STATEMENT

This is a review and thus no original data were used.

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