



DIABETES CARE PECULIARITIES AND MANAGEMENT DURING COVID-19 PANDEMIC: A REVIEW OF CURRENT GUIDELINES

NAVASARDYAN L.V.^{1,2}, MARKOSYAN R.L.^{1,2*}

¹ Department of Endocrinology, Yerevan State Medical University after M. Heratsi, Yerevan, Armenia

² Endocrinology Clinic, "Muratsan" University Hospital, Yerevan, Armenia

Received 27.01.2020; accepted for printing 14.07.2020

ABSTRACT

Severe acute respiratory syndrome coronavirus, the novel coronavirus that causes COVID-19, was first reported in Wuhan, China, in December 2019 and has spread worldwide. The fatality rate for COVID-19 has been estimated to be 0.5-1.0%. The presence of diabetes mellitus and the individual degree of hyperglycaemia seem to be independently associated with COVID-19 severity and increased mortality. Furthermore, the presence of typical complications of diabetes mellitus (heart failure and chronic kidney disease) increases COVID-19 mortality. During a relatively short time of pandemic several guides have been developed concerning diabetic care during COVID-19 pandemic in the world. According to the UK NHS clinical guide, there is a need of virtual clinics and remote consultations, with as many contacts as possible performed via telephone, email, and video conferencing to target the diabetes adequate care. It is mentioned, that, except the urgent situations, the services which should be continued, as long as pragmatic and possible, comprise diabetes patients who are pregnant and those with diabetic foot problem.

KEYWORDS: Diabetes care, COVID-19, pandemic, telemedicine.

Diabetes affects a large part of the worldwide population, and the obstacles and barriers of diabetes care during COVID-19 pandemic are targets to struggle against in the whole world [Kannan S *et al.*, 2020]. The fatality rate for COVID-19 has been estimated to be 0.5-1.0% [Verity R *et al.*, 2020].

During a relatively short time of pandemic several guides have been developed concerning diabetic care during COVID-19 pandemic in the world. Some guides are performed to accelerate innovations in diabetes care, particularly telemedicine. The presence of diabetes mellitus and the individual degree of hyperglycaemia seem to be independently associated with COVID-19 severity and increased mortality [Grasselli G *et al.*, 2020]. Furthermore, the presence of typical complications of diabetes mellitus (heart failure and chronic kidney disease) increases COVID-19 mortality [Barron E *et al.*, 2020; Holman N *et al.*, 2020; Huang I *et al.*, 2020].

According to the UK NHS clinical guide, there is a need of virtual clinics and remote consultations, with as many contacts as possible performed

via telephone, email, and video conferencing to target the diabetes adequate care. It is mentioned, that, except the urgent situations, the services which should be continued, as long as pragmatic and possible, comprise diabetes patients who are pregnant and those with diabetic foot problems.

Reviewing and summarizing the available literature we come to a table of main benefits and challenges of telemedicine in diabetes care (Table).

The current guidelines addressed the management of diabetes during COVID-19 and emphasized some recommendations, which were published online April 23 in The Lancet Diabetes & Endocrinology [Bornstein S *et al.*, 2020; Seewoohary J, Oozageer R.]. The authors noted that insulin resistance among patients with diabetes is more severe with COVID-19 in comparison with other causes of critical illness. It is also given, that patients with COVID-19 also experience a disproportionate burden of diabetic ketoacidosis, which requires its management with insulin therapy.

As it is known, angiotensin-converting enzyme 2 (ACE2) has been revealed as a receptor for the coronavirus spike protein. ACE 2 has anti-inflammatory effects, as well as some effects in glucose metabolism. Nevertheless, how the COVID-19 impacts the ACE 2 and what consequences it results in remains mostly unclear and unknown [Jang J *et al.*, 2020].

ADDRESS FOR CORRESPONDENCE:

Renata L. Markosyan

Department of endocrinology of Yerevan State Medical University after M. Heratsi

2 Koryun Street, Yerevan 0025, Armenia

Tel.: (+374 94) 45-04-69

E-mail: renatamarkosyan@mail.ru

The dipeptidyl peptidase-4 enzyme, which is one of treatment targets in type 2 diabetes, was found to be the receptor for another coronavirus, which promoted Middle East respiratory syndrome (MERS) [Lim S et al., 2020]. It is still unclear if severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) follows this same pattern and how the treatment with the dipeptidyl peptidase-4 inhibitors might impact the infection with SARS-CoV-2 [Lim S et al., 2018; Yang JK et al., 2020].

“The glycemic management of many COVID-19 positive patients with diabetes is proving extremely complex, with huge fluctuations in glucose control and the need for very high doses of insulin” according to a statement from Diabetes UK’s National Diabetes Inpatient COVID Response Team.

As reported by Medscape Medical News, the new inpatient management graphic adds more detail to the previous “front-door” guidance. The new graphic shows extensive details on subcutaneous insulin dosing in place of variable rate of intravenous insulin, when infusion insulin pumps are not available and when the patient has a glucose level >216 mg/dL, but does not have disproportionate burden of diabetic ketoacidosis or hyperosmolar hyperglycemic state. However, the recommendation is not intended for diabetic patients with COVID-19 causing severe insulin resistance in the intensive care unit. [Rayman G, et al., 2020a; Rayman G, et al., 2020b]

A short recently updated page has been developed with an information for diabetic patients, including advice for staying at home, medication use, self-isolating, shielding, hospital and doctor appointments, need for urgent medical guidance, and going to the hospital.

Summarizing the current recommendations in diabetic patients with COVID-19 we would like to highlight some points

Previous outpatient therapy for diabetes should be continued and refined through remote monitoring of plasma glucose levels and telemedicine.

To overcome it is possible, due to the uniting the knowledge and will of all doctors in the world



TABLE

The main benefits and challenges of telemedicine in diabetes care during COVID-19 pandemic

Benefits	Challenges and barriers
Limits face-to-face exposure	Obtaining current objective data is not always possible
Provides more frequent personal connection with patients	Primary care clinicians are responsible for more, than before
Allows for data monitoring and review during personal connection	Patients may struggle with technology
Allows for treatment adjustment	Patients are responsible for reporting weight and BP
Gives an opportunity for more patients education simultaneously	No possibility to conduct physical exam
Gives patients more control over their disease	It is not easy to integrate supporting staff into care

Outpatients with diabetes should continue to try to optimize glycaemic control, with a target plasma glucose concentration of 72 to 144 mg/dL. In general, the target glycated hemoglobin (HbA_{1c}) level for outpatients is $<7\%$.

Tighter glycaemic control may improve patients’ risk of acquiring COVID-19. The recommendations also state that blood pressure and lipid control can reduce the impact of COVID-19.

Although modulation of ACE2 is thought to influence infection rates and the severity of COVID-19, patients should generally continue treatment with ACE inhibitors and angiotensin receptor blockers.

Metformin and sodium-glucose cotransporter 2 (SGLT2) inhibitors may be continued among patients with mild COVID-19, but they should be held among patients with severe and critical illness and dehydration because of the risks for lactic acidosis with metformin and DKA with SGLT2 inhibitors.

Dipeptidyl peptidase-4 inhibitors may be continued among patients with COVID-19.

Insulin therapy may be continued among outpatients with less severe cases of COVID-19. Insulin needs may increase during COVID-19, so monitoring of blood glucose levels every 2 to 4 hours, or with a continuous glucose monitor, is recommended.

Patients with diabetes and concomitant fatty liver disease may be at particularly high risk for a

cytokine storm and having COVID-19 they should be closely monitored.

Obesity is a risk factor for ventilatory failure, and patients with diabetes and obesity may have a higher

risk and need for intubation and ventilatory support.

Health caregivers with diabetes should stay away from frontline clinical duties upon possibility because of their increased health risks with COVID-19.

REFERENCES

1. Barron E, Bakhai C, Kar P, Weaver A, Bradley D., et al. Associations of type 1 and type 2 diabetes with COVID-19-related mortality in England: a whole-population study. *Lancet Diabetes Endocrinol.* 2020; 8: 813-822
2. Bornstein SR, Rubino F, Khunti K, Mingrone G, Hopkins D., et al. Practical recommendations for the management of diabetes in patients with COVID-19. *Lancet Diabetes Endocrinol.* 2020; 8(6): 546-550
3. Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L., et al. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy region, Italy. *JAMA.* 2020; 323: 1574-1581
4. Holman N, Knighton P, Kar P, O'Keefe J, Curley., et al. Risk factors for COVID-19-related mortality in people with type 1 and type 2 diabetes in England: a population-based cohort study. *Lancet Diabetes Endocrinol.* 2020; 8(10): 823-833
5. Huang I, Lim MA, Pranata R. Diabetes mellitus is associated with increased mortality and severity of disease in COVID-19 pneumonia – A systematic review, meta-analysis, and meta-regression. *Diabetes Metab Syndr.* 2020; 14(4): 395-403
6. Jang H-W; Ko Y.; Kim D.H.; Kwon H.; Lim S.J.; Jung, J.H. et al., Beneficial effects of post-transplant dipeptidyl peptidase administration early after pancreas transplantation to improve β cell function, *Transplantation*: September 2020 - Volume 104 - Issue S3 - p S572
7. Kannan S, Shaik Syed Ali P, Sheeza A, Hemalatha K. COVID-19 (Novel Coronavirus 2019) - recent trends. *Eur Rev Med Pharmacol Sci.* 2020; 24(4): 2006-2011
8. Lim S, Kim KM, Nauck MA. Glucagon-like Peptide-1 Receptor Agonists and Cardiovascular Events: Class Effects versus Individual Patterns. *Trends Endocrinol Metab.* 2018; 29(4): 238-248
9. Lim S, Oh TJ, Dawson J, Sattar N. Diabetes drugs and stroke risk: Intensive versus conventional glucose-lowering strategies, and implications of recent cardiovascular outcome trials. *Diabetes Obes Metab.* 2020; 22(1): 6-15
10. Rayman G, Lumb A, Kennon B, Cottrel C, Nagi D., et al. Guidance on the management of Diabetic Ketoacidosis in the exceptional circumstances of the COVID-19 pandemic FRONT DOOR GUIDANCE. National Inpatient Diabetes COVID-19 Response Team. Concise advice on Inpatient Diabetes (COVID: Diabetes): London, England, United Kingdom: Diabetes UK; April 20, 2020a. https://www.diabetes.org.uk/resources-s3/public/2020-04/COVID_Front_Door_v2.0_0.pdf. Accessed May 20, 2020
11. Rayman G, Lumb A, Kennon B, Cottrel C, Nagi D., et al. New Guidance on Managing Inpatient Hyperglycaemia during the COVID-19 Pandemic. *Diabet Med.* 2020b; 37: 1210-1213
12. Seewoodhary J, Oozageer R. Coronavirus and diabetes: an update. *Practical Diabetes.* 2020; 37(2): 41-42
13. Verity R, Okell LC, Dorigatti I, Winskill P, Whittaker C., et al. Estimates of the severity of coronavirus disease 2019: a model-based analysis. *Lancet Infect Dis.* 2020; 20: 669-677
14. Yang JK, Lin SS, Ji XJ, Guo LM. Binding of SARS coronavirus to its receptor damages islets and causes acute diabetes. *Acta Diabetol.* 2010; 47(3): 193-199