Original Articles

Consensus for Management of hyperglycemia for COVID-19 patients

WRITING GROUP:

Dr. Sanjeev Pathak , Dr. Banshi Saboo, Dr. Vidisha Patel, Dr. Urman Dhruv, Dr. Rucha Mehta, Dr. Om Lakhani, Dr Dharmendra Panchal

BACKGROUND

The novel corona virus 2019 has been declared as world pandemic by WHO on 11th March 2020 [2]. Most people with COVID 19, who have associated co-morbidities like diabetes, hypertension and cardiovascular diseases including heart failure, are significantly associated with worse outcomes. There are many uncertainties regarding the management of diabetes or elevated blood sugars in patients presenting with COVID 19.

The objective of this consensus document is to create a unified approach for diabetes management for use in primary and specialist care; as well as in-patient and out-patient treatment of the COVID-19 affected diabetic patient.

Diabetes and COVID 19: the link

Individuals with diabetes are at increased risk of COVID 19 infection; this risk can be reduced, though not completely eliminated, by good glycaemic control. Patients with diabetes have suboptimal innate immunity in general which makes them more susceptible to getting an infection as well as vulnerable to serious manifestation of any infection. Evolving data also suggest that patients of COVID-19 with diabetes are more often associated with severe or critical disease varying from 14 to 32% in different studies [8,9].

The COVID 19 virus gets entry into target cell by binding to angiotensin converting enzyme 2 (ACE 2), that acts as receptor for corona virus spike protein. Corona virus infection reduces the available ACE 2 and propagates inflammation. Acute hyperglycemia is found to upgrade ACE 2 expression which facilitate virus cell entry and chronic hyperglycemia downgrades ACE 2 expression and thereby makes the cell more vulnerable to inflammation. Also expression of ACE 2 on pancreatic beta cells may lead to insulin deficiency and precipitates new onset hyperglycemia as well as complications like diabetes ketoacidosis in people with diabetes[3,4,5]. Dipeptidyl peptidase 4 (DPP 4) enzyme may be a functional receptor for human corona virus and inhibition of DPP 4 may be considered as therapeutic target for COVID 19 infection [6,7].

MANAGEMENT OF HYPERGLYCEMIA IN COVID 19 PATIENTS

GLYCEMIC TARGETS

- Non -hospitalized patients: fasting blood sugar 90-120mg/dl and post prandial blood sugar in the range of 140-160mg/dl and HbA1c< 7% is good control
- Hospitalized patients: Insulin therapy should be initiated for treatment of persistent hyperglycemia starting at a threshold ≥180 mg/dL (10.0 mmol/L). Once insulin therapy is started, a target glucose range of 140–180 mg/dL (7.8–10.0 mmol/L) is recommended for the majority of critically ill patients and noncritically ill patients.

PART 1. Management of hyperglycemia in COVID patient with pre-existing diabetes:

History prior to hospitalization and/or an admission A1C value ≥6.5% (48 mmol/mol) suggests that the onset of diabetes preceded hospitalization.

A. Outpatient management: Asymptomatic or mild symptoms, do not require hospitalization

B. In patient care or Intensive care unit: COVID 19 patients who need hospitalisation

A. OPD treatment:

MANAGEMENT OF TYPE 1 DIABETES IN COVID 19 PATIENT

- Define current glycemic control. Intensify the regimen if patient not in glycemia target.
- Look for clinical signs and symptoms of Diabetes Ketoacidosis
- If DKA is present or severe symptoms of COVID 19 infection hospitalisation and treatment as per standard protocol for DKA with IV insulin infusion and proper rehydration is recommended
- If signs and symptoms of DKA are absent and patient is asymptomatic or mild symptoms of COVID 19,

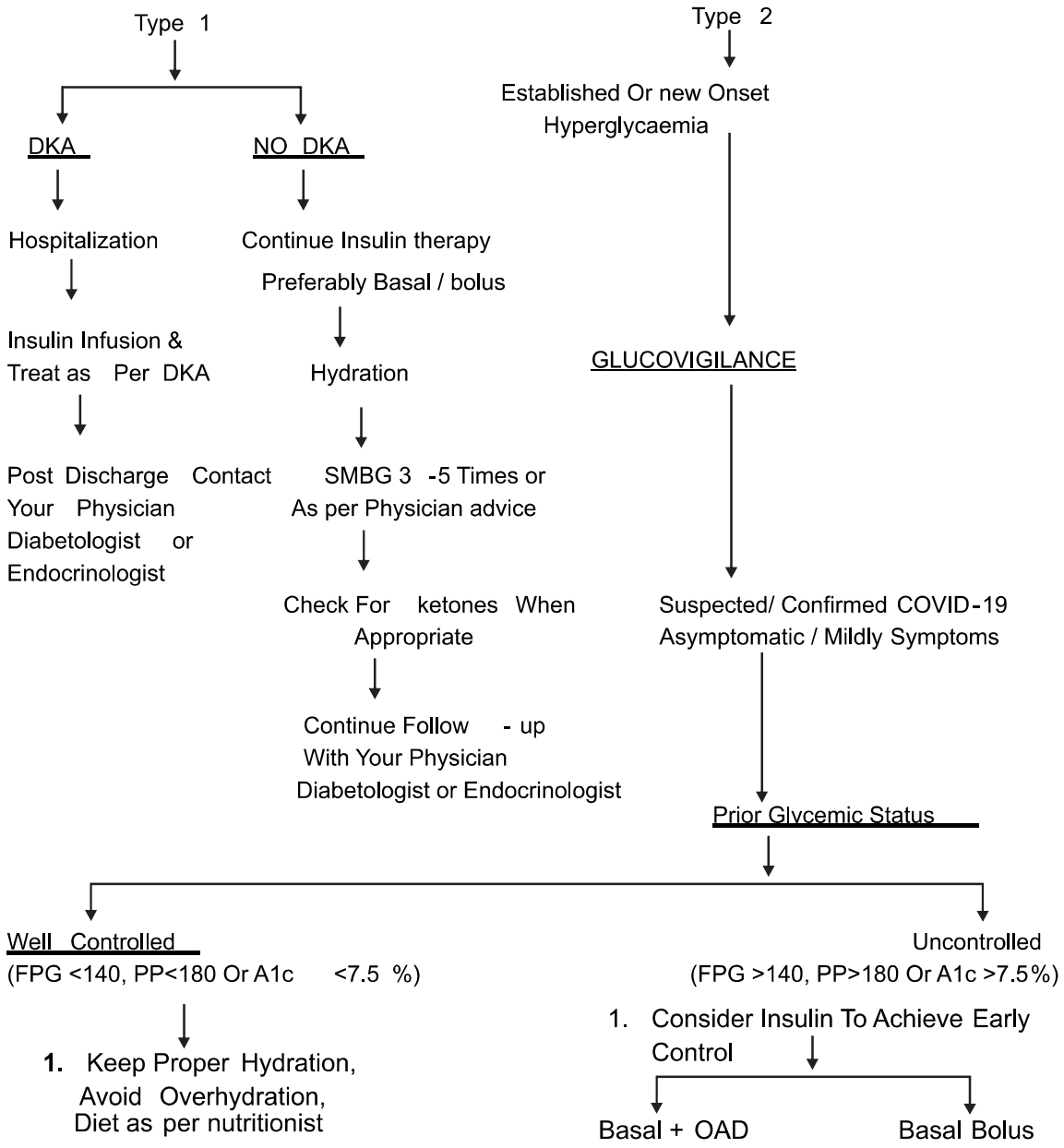
Correspondence Address : **Dr. Sanjiv Phatak** (Diabetes Care and hormone Clinic)
101, Trade Square, Opp. Torrent Power, Sabarmati, Ahmedabad.
sanjeevphatak@hotmail.com

continue insulin preferably basal bolus regimen, ensure proper hydration, increase frequency of sugar monitoring by at least four times a day and keep check on ketones.

MANAGEMENT OF TYPE 2 DIABETES IN COVID 19 PATIENT

- Define current glycemic control, patient with FPG < 140mg/dl, PPG < 180mg/dl and HbA1c < 7.5% are considered as good glycemia control
- Asymptomatic or mild symptom COVID 19 Patients with good glycemia control are treated as OPD.
- Ensure proper hydration.
- Encourage SMBG practise and good nutrition. Continue OHA as before. If hypoxia or acute kidney injury or volume depletion or DKA develops; stop metformin and SGLT2i, replace GLP1RA with DPP4i. and if hospitalisation is needed switch to insulin.
- Asymptomatic or mild symptom COVID 19 patient with poor glycemia control, consider insulin therapy, preferably basal insulin or basal bolus regimen to achieve good glycemia target.

ALGORITHM FOR MANAGEMENT



2. Continue Previous Therapy
Stop Metformin and SGLT2i if Hypoxia / AKI Develop.
recommended.
Hospitalization recommended.

Stop SGLT– 2i*, If s/s Of Volume depletion/DKA.
depletion/DKA
Withhold GLP-1a# & Replace with DPP-4i^
DPP-4i^
If GI s/s Or Low appetite.

3. Consider Insulin if Control Deteriorates

4. Monitor Blood sugar at least twice a day (Fasting and Post meal)

2. Stop Metformin and SGLT2i If Hypoxia/ AKI Develop. Hospitalization

Stop SGLT -2i*, if s/s of volume

Withhold GLP -1a# & Replace with

if GI s/s Or Low appetite.

3. Monitor Sugar at least 4 times a day. (Fasting, prelaunch, predinner and bed time)

4. Check Acetone.

Be in Contact with your physician, diabetologist or Endocrinologist.

B. In patient care or Intensive care unit

B1. In patient with no hypoxia and no signs of acute crisis

- In patients with good glycemia control, keep monitoring blood sugar. Ensure good hydration and avoid over hydration. Give diet as per the advise from dietitian. If hypoxia or acute kidney injury or volume depletion or DKA develops stop metformin and SGLT2i, replace GLP1RA with DPP4i Consider basal insulin if needed.
- In patients with uncontrolled Diabetes, stop all OHA and consider basal bolus insulin regimen. Monitor blood sugar and titrate insulin dosage. Avoid sliding scale. If patient develops hypoxia or severe symptoms switch IV insulin infusion.

B2. In patient with hypoxia

- In patients with good oral intake and can be managed by inhalational O2 therapy who do not require intubation, initiate basal bolus regimen. Stop all OHA. Keep aggressive watch on blood sugar preferable 7 times a day and ketones.
- In patients who need intubation and ventilator support IV insulin infusion is mandatory. Target blood sugar 140-180mg/dl. If blood sugar is > 300mg/dl check every hourly and if blood sugar is < 300mg/dl check every two hourly. One may consider CGM when appropriate.

INSULIN THERAPY IN HOSPITALIZED PATIENTS

- Insulin therapy should be initiated for treatment of persistent hyperglycemia starting at a threshold ≥180 mg/dL (10.0 mmol/L). Once insulin therapy is started, a target glucose range of 140–180 mg/dL (7.8–10.0 mmol/L) is recommended for the majority of critically ill patients and noncritically ill patients.

SQ Insulin and Starting dose for Sq Insulin

Basal insulin : Use Insulin glargine (Lantus, Basalog, Basaglar)as the preferred basal insulin to be given once a day generally after checking bedtime blood sugar and calling physician on call with same

Recommended Initial Basal Insulin dosing for patients with diabetes prior to admission:

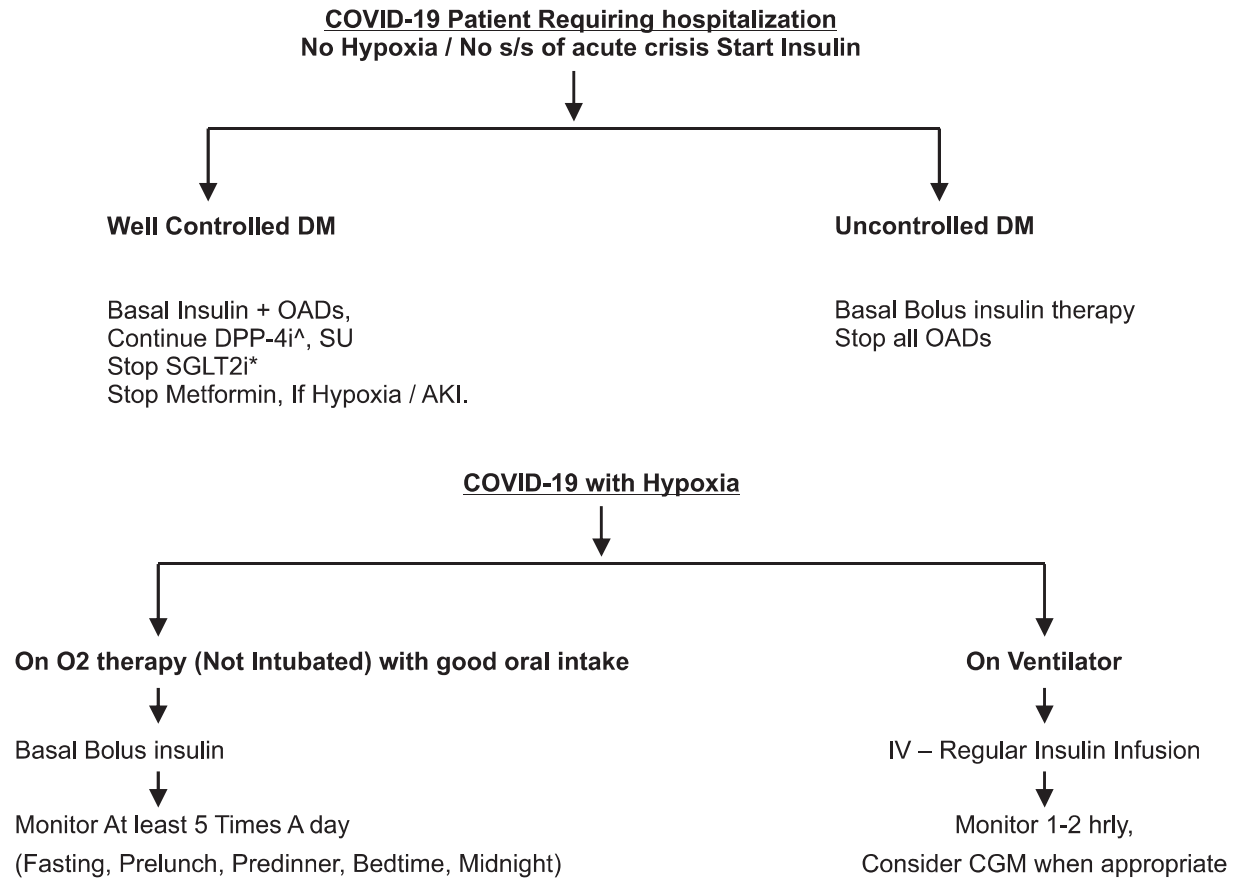
Diabetic	10 units Glargine	dose to be adjusted by physician / diabetologist daily
Covid-19 with hyperglycemia	Usually will not require	Based on sugar readings and physician/ diabetologist decision

Bolus Insulin : means insulin that is given before meals in patients who are eating or tolerating feeds.

Preferred is insulin lispro or aspart or glulisine (eg., Humalog or Novarapid or Apidra), can also use Regular Insulin (eg., Human Actrapid)

Check sugars at least 4 times (Fasting, Prelunch, Predinner and Bedtime)

Each sugar should be informed to medical officer for approval of insulin dosage.



SGLT-2i*- Canaglifozin, Dapaglifozin, Empaglifozin , Remoglifozin.

GLP-1a# - Dulaglutide, Liraglutide, Lixisenatide,

DPP-4i^ - Vildagliptin, Sitagliptin, saxagliptin, linagliptin, Teneligliptin, Alogliptin, Evogliptin.

Dosage of Bolus Insulin:

BLOOD SUGAR	Diabetes A1c >/=7.5	Diabetes A1c<7.5	Covid Hyperglycemia
141 - 180	2	2	0
181 - 220	5	4	2
221 - 260	6	5	3
161 - 300	8	6	4
301 - 340	10	7	5
341 - 380	12	8	6
381 - 400	14	9	8

Caveats:

If AKI or GFR is < 45, reduce dose by 2 units from each column

If patient is receiving corticosteroids may need to add plus 2 units to each column.

If not eating or feeds not tolerated give insulin post meal as per the sugar level.

If sugars remain persistently above 300 mg/dl then IV insulin infusion is recommended

HYPOGLYCEMIA:

Definitions and management:

- Hypoglycemia: Blood glucose < 70 mg /dl but > 54 mg /dl- hold insulin or medication, and give 15-30 grams of carbohydrates such as 200 ml milk with sugar one spoon, or glucon d in water if patient is awake. Check sugar every 15 minutes till sugar is 100mg/dl or more
- Severe Hypoglycemia: Blood glucose < 54 mg per dl or any blood glucose with symptoms such as confusion, blurry vision, sweating or in severe cases loss of consciousness requiring medical intervention.

Management with **D25 Protocol: TARGET BLOOD SUGAR > 100mg/dl**

1. Hold insulin drip/insulin dose/medication
2. Give D25 IV Dose in ml = [(100-SUGAR) × 0.8], to simplify
    1. BG 60-70: Give 30ml D25 IV
    2. BG 50-60: Give 40ml D25 IV
    3. BG 40-50: Give 50ml D25 IV
    4. BG 30-40: Give 60ml D25 IV
    5. BG 20-30: Give 80ml D25 IV
    6. BG < 20: Give 100ml D25 IV
3. Repeat BG q15m until BG >70 mg/dL, then Check q30 until BG >100 mg/dL
4. Once BG >100 mg/dL, check BG hourly and restart infusion at 1/2 of the prior rate once BG >140 mg/dL

PART 2 COVID HYPERGLYCEMIA

COVID Hyperglycaemia is defined as plasma blood glucose in hospitalized patient is >140 mg/dL (7.8 mmol/L) and HbA1c is < 6.5%. Treatment is initiated if plasma blood glucose remains ≥180 mg/dL persistently on 2 separate occasions.

Blood glucose levels persistently above this level should prompt conservative interventions, such as alterations in diet or changes to medications and or/initiation of insulin and frequent blood sugar monitoring.

If HbA1c is ≥6.5%,. then the patient is having pre – existing diabetes. Management as per pre-existing diabetes.

DOs In COVID-19

1. Proper Hydration.
2. Diet
3. Glucose Monitoring

DON'Ts in COVID-19

1. Avoid Religious fasting.
2. Avoid NSAIDS.
3. Avoid Fluroquinolones.

Diet

1. At least 3 serving of vegetables and 2 serving of fruits, Include pulses in each meal OR as per Dietitian Advise
2. Hospitalized patients-High protein Diet+ More citrus Fruits.
3. Parenteral Feeding (Intubated Patient)

SOURCE

1. Research Society for the Study of Diabetes in India (RSSDI) Guidance for People with Diabetes on COVID - 19 for Healthcare Professionals
2. https://www.who.int/emergencies/diseases/novel-coronavirus-2019
3. Bindom SM, Lazartigues E. The sweeter side of ACE2: physiological evidence for a role in diabetes. Mol Cell Endocrinol 2009; 302: 193–202.
4. Roca-Ho H, Riera M, Palau V, Pascual J, Soler MJ. Characterization of ACE and ACE2 expression within different organs of the NOD mouse. Int J Mol Sci 2017; 18: e563.
5. 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: 193–99.
6. Raj VS, Mou H, Smits SL, et al. Dipeptidyl peptidase 4 is a functional receptor for the emerging human coronavirus-EMC. Nature 2013; 495: 251–54.
7. Iacobellis G. COVID-19 and diabetes: can DPP4 inhibition play a role? Diabetes Res Clin Pract 2020; 162: 108125.
8. Awadhesh Kumar Singh, Ritesh Gupta, Amerta Ghosh, Anoop Misra Diabetes in COVID-19: Prevalence, pathophysiology, prognosis and practical considerations Diabetes Metab Syndr. 2020 July-August; 14(4): 303–310.
9. Hussain A, Bhowmik B, do Vale Moreira NC. COVID-19 and diabetes: Knowledge in progress. Diabetes Res Clin Pract. 2020;162:108142.