

Dated 26th August, 2020

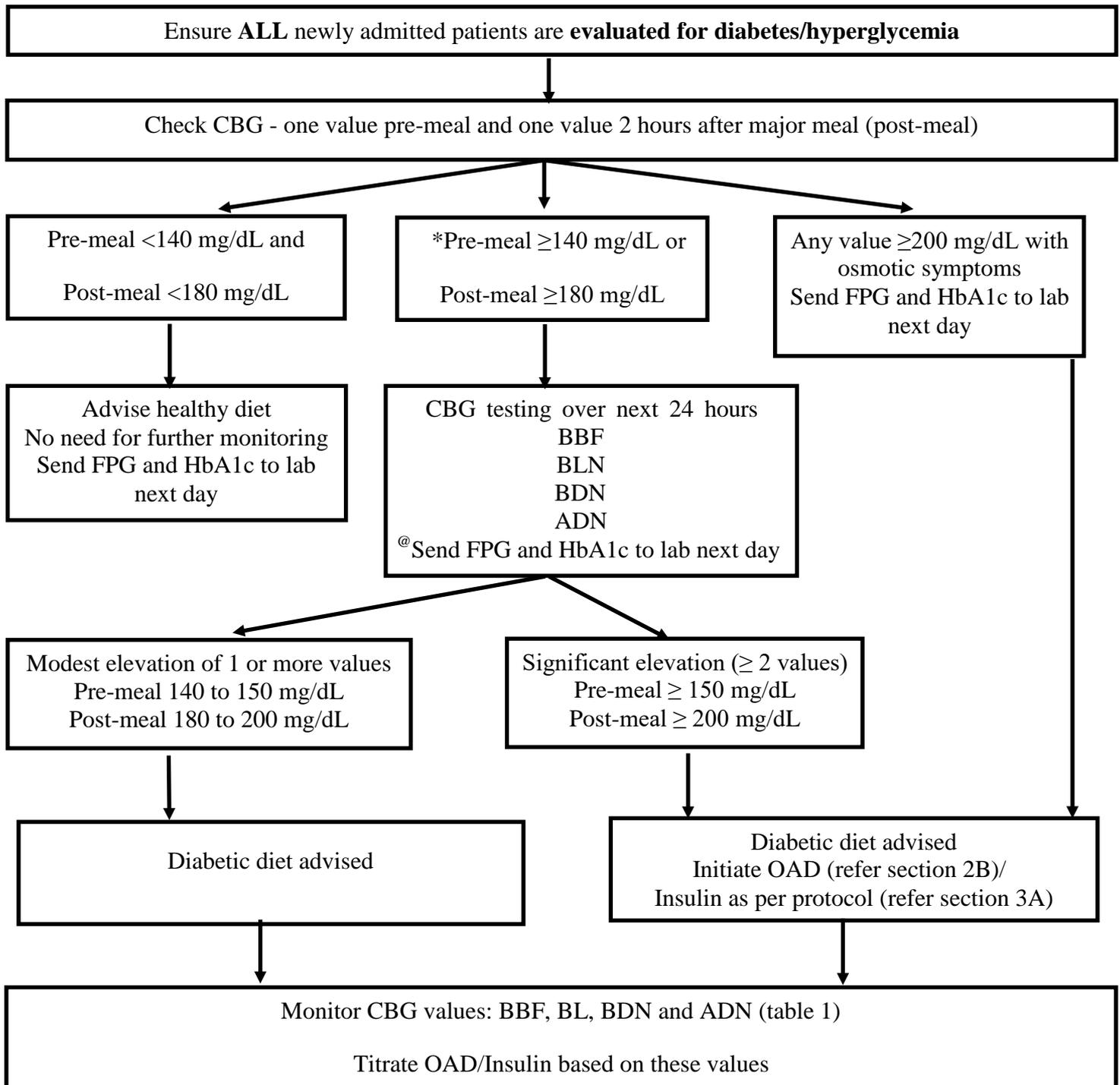
Government of India
Ministry of Health & Family Welfare

**Clinical Guidance on Diabetes Management at COVID-19
Patient Management Facility**

Important points:

- Screen every patient at admission for hyperglycemia with at least two capillary blood glucose values (1 pre-meal and 1 post-meal value) by a glucometer.
- Every patient with diabetes should be started on a diabetic diet. Kindly ensure that the patient strictly adhere to the timing and quantity advised in the diet chart.

Section 1: Screening of hyperglycemia in every patient hospitalized with COVID-19 (at admission and on starting steroids[#])



[#] Even if initial blood glucose monitoring was normal, repeat monitoring should be considered if: a) steroids or drugs with a potential to affect glycemic status are initiated, and b) there is an increase in severity of COVID-19 (to account for stress hyperglycemia)

*If BG level is ≥ 250 mg/dl, check urine/blood ketone levels →if positive, immediately consult endocrinologist/physician

*If Pre-meal BG level ≥ 300 mg/dl and/or post-meal BG level ≥ 400 mg/dl →immediately consult endocrinologist/physician irrespective of ketone levels (to start insulin infusion – section 4)

[@] FPG ≥ 126 mg/dl and/or HbA1c $\geq 6.5\%$ (lab values) are diagnostic of Diabetes Mellitus

Abbreviations: ADN: After dinner; BBF: Before breakfast, BDN: Before dinner, BL: Before lunch, CBG: Capillary blood glucose; FPG: Fasting plasma glucose, HbA1c: Hemoglobin A1c; OAD: Oral antihyperglycemic drug

Section 2: Oral antihyperglycemic drugs (OAD)

2A: Treatment of patients with known diabetes who are on OAD at admission

- A. To continue existing OAD if all of the below mentioned criteria are fulfilled:
 - i. BG levels are controlled (Pre-meal <140 mg/dl and post-meal <180 mg/dl)
 - ii. Patient is conscious, oriented and has good oral acceptance
 - iii. COVID symptoms are mild
 - iv. KFT and LFT are normal
- B. If patient *does not fulfil all of the above criteria*, consult endocrinologist/physician [to start on basal-bolus insulin regimen (also called as multiple subcutaneous insulin injections or MSII regimen) or intravenous (IV) insulin infusion, depending on BG levels [section 3B]

2B: To initiate OAD in patients newly detected to have diabetes at admission

(At admission: pre-meal BG: 150 to 180 mg/dl and/or post-meal BG 200 to 250 mg/dl)

- A. Consult Endocrinologist/physician at earliest to initiate or optimize OAD
- B. If there is an anticipated delay in consulting endocrinologist/physician, initiate on Tab Metformin (either immediate or sustained release) 500 mg BD and a Gliptin (Tab Vildagliptin 50 mg BD or Tab Sitagliptin 100 mg OD or Tab Linagliptin 5 mg OD or Tab Teneagliptin 20 mg OD), provided patient meets all the following criteria:
 - i. Pre-meal blood glucose is between 150 and 180 mg/dl **and/or** post-meal blood glucose is between 200 and 250 mg/dl.
 - ii. Other criteria as mentioned in Section 2A are fulfilled.
- C. If BG levels at admission are above the range mentioned (pre-meal ≥ 180 mg/dl or post-meal blood glucose ≥ 250 mg/dl) → start on insulin (Preferably consult endocrinologist or physician/ refer section 3A)

***Capillary BG monitoring in both section 2A and 2B: BBF, ABF, BL, AL, BDN and ADN (refer to table 1)**

Section 3: Basal-bolus insulin regimen

3A: To initiate insulin for patients newly detected with diabetes

Indication: At admission: pre-meal BG: ≥ 180 mg/dl or post-meal BG ≥ 250 mg/dl

- A. **Total daily dose (TDD) = 0.4 units/kg/day** (age > 65 yr, nephropathy or liver disease, use 0.2 units/kg/day)
- B. Total daily dose is divided equally into 4 doses (25% each): 3 doses are for bolus insulin (Regular insulin 30 min before breakfast, before lunch and before dinner) and 1 dose for basal insulin (Inj. NPH insulin at bed time/ 2 hours after dinner)

Example: 58 yr old male with body weight of 60 kg presented with pre-meal BG of 184 mg/dl and post-meal BG of 302 mg/dl

Total daily dose = **0.4 units/kg/day** = $0.4 \times 60 = 24$ units per day

Initial insulin regimen to be prescribed for him:

- Inj. Regular insulin 6 units SC 30min before breakfast, 6 units SC 30min before lunch and 6 units SC 30min before dinner
- Inj. NPH insulin 6 units SC at bed time/ 2 hours after dinner

3B: If patient is on OAD and blood glucose levels are uncontrolled (Pre-meal BG ≥ 140 mg/dl or post-meal BG ≥ 180 mg/dl)

- A. If pre-meal BG value is 140 to 180 mg/dl and/or post-meal BG value is 180 to 250 mg/dl \rightarrow consult endocrinologist/physician for OAD optimization
- B. If pre-meal BG value ≥ 180 mg/dl and/or post-meal BG value ≥ 250 mg/dl despite being on OAD \rightarrow start basal-bolus insulin regimen using calculation mentioned in section 3A (Kindly note that in this particular scenario, OADs apart from Metformin and Gliptins need to be stopped). Consult endocrinologist/physician for optimization.

Caveat: Bolus insulin (Inj. Regular insulin) may not always be needed for all the three meals and can only be added to individual meals requiring prandial coverage (i.e., for meals with pre-meal to post-meal BG increment of >40 mg/dl on a given day, regular insulin should be added before these meals on the next day). For example, on a given day BG levels increased from 112 mg/dl (BL) to 204 mg/dl (2h AL). Since increment is >40 mg/dl (92 mg/dl), Inj. Regular insulin should be added before lunch on the next day.

- C. If FPG is ≥ 140 mg/dl and post-meal increment in BG level is normal (< 40 mg/dl), then one can just add basal insulin (Inj. NPH insulin bedtime/ 2 hours after dinner)

3C: Patient is already on basal-bolus insulin regimen at admission

Continue existing regimen. Monitor blood glucose levels and review with BG log to an endocrinologist/ physician.

3D: To switch to basal-bolus insulin regimen from insulin infusion

- A. Consult endocrinologist/ physician to switch to basal-bolus insulin regimen
- B. If there is an anticipated delay in consulting the endocrinologist/physician, follow the steps mentioned below to switch to basal bolus regimen:
- i. Calculate the total daily dose (TDD) based on insulin infusion requirements for the last 24 hours: **TDD** = 80% of the total daily insulin requirement on IV infusion in the last 24 hours.
 - ii. Once you have the TDD, calculate the doses of bolus insulin (Inj. Regular insulin) and basal insulin (Inj. NPH insulin) as described in section 3A (refer step B and example)
 - iii. Important pointers:
 - a. Do not switch from insulin infusion to basal bolus regimen until BG levels are controlled on insulin infusion, patient is orally accepting or on RT feeds and is hemodynamically stable
 - b. Insulin infusion has to be overlapped with basal-bolus insulin regimen for 60-120 minutes before stopping. Do not stop insulin infusion abruptly.

Example: A 54-year-old male patient is on IV insulin infusion and his BG levels are adequately controlled for the last 24 hours. His oral acceptance is good and vitals are stable. At **11 am his BG level is 132 mg/dl and we decide to switch to basal-bolus insulin regimen**. We calculate the dose and plan to start Inj. Regular insulin 6 units SC BBF, 6 units SC BL and 6 units SC BDN and Inj. NPH insulin 6 units SC at bed time/ 2 hours after dinner. **We should not stop insulin infusion at 11 am, rather continue it till lunch. At 12.30 pm we give Inj. Regular insulin 6U SC (as calculated), patient takes lunch at 1:00 pm, insulin infusion is continued as per scale and finally stopped 1 hour later at 1.30 pm (after the overlap).**

3E: Patient is on Ryles Tube (RT) feeds

A. Like standard meals, RT feeds should be divided into 3 major and 3 minor feeds. Major and minor feeds are defined by calories/quantity of feeds. (Example: major feed: 300ml each and minor feed: 150 ml each)

Timings of major feed: 9 am, 1.30 pm, 7 pm.

Timings of minor feed: 11 am, 4.30 pm, 10 pm.

B. Basal-bolus insulin regimen would be preferred in such patients. Bolus insulin (Inj. Regular insulin) should be given 30 min before each major feed and basal insulin (Inj. NPH insulin) should be given at 10 pm. along with the last minor feed. Capillary blood glucose monitoring should be performed before and 2 h after each major feed.

C. Dose calculation for basal-bolus insulin regimen (section 3A) and indications for insulin infusion (section 4) discussed elsewhere in the document would similarly apply for such patients.

3F. Titration of insulin doses and glycemic targets

A. The most important point to remember while titrating insulin doses is that we titrate proactively and not reactively, i.e., insulin doses are adjusted based on the previous day's BG log (taking into account action of bolus and basal insulin on the previous day) and not the current BG value.

B. The dose of bolus insulin for each major meal (or major feed) is titrated such that pre-meal to post-meal BG increment remains around 30 to 50 mg/dl. If postprandial excursion is above this range, one should check whether the insulin injection technique is correct, there is an adequate time gap between the injection of prandial insulin and the meal (30 minutes for regular insulin) and that the quality and quantity of carbohydrate in the meal is appropriate and relatively fixed. If these factors do not contribute to the postprandial excursion or the excursion persists despite addressing these factors, the dose of prandial insulin (regular insulin) should be increased on a subsequent day.

Example: At lunch (or major feed # 2), if at a dose of 6 units (Inj. Regular insulin), pre-meal to post-meal BG increment was 80 mg/dL (refer to table 1, date: 22/6/2020 and 23/6/2020), the insulin dose can be increased to 8 units (Inj. Regular insulin) from the next day provided the insulin injection technique is correct, the time gap between regular insulin and meal was appropriate and quantity and quality of carbohydrate in lunch was appropriate and consistent.

C. Basal dose is adjusted based on FPG. If FPG is ≥ 140 mg/dl, the basal dose (Inj. NPH insulin) administered at bed time should be increased (usually by 2 units, but may be higher) to target the FPG to < 140 mg/dl on the next day. (Refer to table 1, date 25/6/2020 and 26/6/2020). Increment in the dose of basal insulin should be done after excluding nocturnal (especially 3 am) hypoglycemia.

D. Titration of insulin doses in patients prescribed glucocorticoids: Glucocorticoids are known to worsen hyperglycemia and may necessitate adjustment in insulin doses. The adjustment will depend upon the type of glucocorticoid used: short acting (hydrocortisone, duration of action: 8-12 hours), intermediate acting (prednisolone, duration of action: 12-36 hours) and long acting (dexamethasone, duration of action: 36 hours) and frequency of its administration. Methylprednisolone and dexamethasone are the commonly used glucocorticoids in patients with COVID-19. If patient receives a long acting glucocorticoid (say 8 mg dexamethasone) as a single daily dose or twice daily methylprednisolone, the hyperglycemic effect is likely to persist throughout the day and so the titration of insulin doses would be same as mentioned above (point A to C) with the exception that higher insulin doses/increments would be required in case of steroids.

If patient is on high-dose intermediate acting steroid (say prednisolone or methylprednisolone 60 mg) administered as a single dose at 9 am, the peak hyperglycemic effect is expected in the afternoon and evening hours (between 12pm to 8pm). Accordingly, the patient would require a higher dose before lunch. Alternatively, Inj. NPH insulin may be useful since pharmacokinetics of NPH closely mimics the effect of steroid (prednisone/methylprednisolone) on blood glucose level; NPH insulin can be administered at before breakfast or at 9 am in such a scenario.

E. Glycemic targets: For most patients on basal-bolus insulin regimen (or for in-patient hyperglycemia management, in general), pre-meal BG level of < 140 mg/dl and post-meal BG level of < 180 mg/dl can be targeted. In selected individuals, target levels of < 120 mg/dl (pre-meal) and < 160 mg/dl (post-meal) can be considered, provided these can be achieved without causing undue hypoglycemia.

***Capillary BG monitoring in section 3A to D: BBF, ABF, BL, AL, BDN and ADN
(refer to table 1)**

Table 1: Capillary BG monitoring chart

(Kindly try to maintain exact similar format of BG charting for every patient)

Date	BBF	ABF	BL	AL	BDN	ADN	#3am	Remarks
22/6/2020	224 (R8)	256	212 (R6)	292	198 (R8)	302 (N14)	192	
23/6/2020	172 (R8)	216	180 (R8)	211	368* (R10)	392 (N16)	164	*Had heavy snack at 6pm
24/6/2020	142 (R8)	179	132 (R8)	60*	154 (R10)	186 (N10)	158	*Didn't take lunch properly
25/6/2020	162 (R8)	149	150 (R8)	182	138 (R10)	174 (N 12)	102	
26/6/2020	114 (R8)							

Abbreviations: BBF: Before breakfast, ABF: After breakfast, BL: Before lunch, AL: After lunch, BDN: Before dinner, ADN: After dinner, R: Regular insulin, N: NPH insulin

Monitor 3 am blood glucose when fasting blood glucose is persistently out of target

Section 4: Intravenous insulin infusion

A. Indications for the use of intravenous insulin infusion

Advised when blood glucose is persistently above 180 mg/dl (two or more values) under following situations:

1. Patients with nothing by mouth (NPO) status or those having erratic diet pattern (in time and content)
2. Diabetic Ketoacidosis (DKA)
3. Uncontrolled hyperglycemia despite MSII use
4. Severe hyperglycemia at onset (Pre-meal BG level ≥ 300 mg/dl and post-meal BG level ≥ 400 mg/dl)- ketone status should be checked before starting infusion
5. Critically ill like in sepsis and septic shock

B. Initiation of insulin infusion:

Insulin can be initiated at dose of 0.05-0.1 units/kg body weight/hour.

C. Infusion preparation: 50 units of regular insulin in 50 ml NS (1unit/ml). A full label should be placed on the 50 ml syringe barrel which should not obscure the numerical scale. Priming should be done before starting the infusion by flushing 20 ml of prepared solution through intravenous tubing. Any unused insulin solution should be discarded after 24 hours. If syringe pumps are not available, gravity-assisted pediatric infusion sets could be used for IV insulin delivery.

D. Frequency of blood glucose monitoring: 2 hourly. Can be extended to 4 hourly, where requirement is low, glucose values are stable and in target.

E. Glycemic targets: To achieve and maintain blood glucose of 140 to 180 mg/dl for most individuals. BG target can be tightened to 110-180 mg/dl in a scenario where this target can be achieved without causing significant hypoglycemia and relaxed to 200-220 mg/dl where even a target of 140-180 mg/dl is unsafe and associated with increased risk of hypoglycemia.

F. Further titration of insulin infusion rate: Further titration of insulin infusion rates should be done based upon ambient blood glucose level, target blood glucose level and magnitude of blood glucose change in the previous hour. Other factors that should be accounted for are timing and content of meals, insulin sensitivity, and previous day's glycemic response.

A simple and popular formula: $\text{Infusion rate (units/hr)} = \text{BG level (mg/dl)}/100$ is good to calculate initial infusion rate. However, it should not be relied upon for titration because it does not account rate of BG change in the preceding hours.

Examples:

1. At an ongoing rate of 3 units/hr, BG decreased from 280 mg/dl 2-hour before to a current level of 250 mg/dl (drop of 15 mg/dl/hour). We expect the level to be 220 mg/dl (above target) after 2 hours at the current rate. So, the infusion rate should be increased.
2. At an ongoing rate of 1.8 units/hr, BG decreased from 185 mg/dl 2-hour before to a current level of 170 mg/dl (drop of 7.5 mg/dl/hour) and we expect the level to be 155 mg/dl (in target) after 2 hours at the current rate. So, we can continue the same infusion rate.
3. At an ongoing rate of 1.2 units/hr, blood glucose decreased from 144 mg/dl 2-hour before to a current level of 100 mg/dl (drop of 22 mg/dl/hour), and we expect the level to be 56 mg/dl after 2 hours at the current rate. So, the infusion rate should be decreased (say by 50% to 0.6 units/hr).
4. At an ongoing rate of 1.2 units/hr, BG decreased in the middle of night from 108 mg/dl 2-hour before to a current level of 60 mg/dl. In such a scenario, infusion should be discontinued, correction should be provided (50 ml of 50% dextrose in a sedated/unconscious patient, and 15-20 grams of oral glucose solution in a conscious patient) and blood glucose checked every 15-20 minutes till 2 or more values are >100 mg/dl, when the infusion can be restarted at 0.6 units/hr with close monitoring every 30-60 minutes for next 2 hours.

G. Target rate of BG change: Initially, it should be between 50-100 mg/dl/hour (50-75 mg/dl/hour may also be appropriate), target BG levels are reached and steady state is maintained. If the rate of blood glucose change is <50 mg/dl or >100 mg/dl, consider increasing and decreasing the infusion rates, respectively.

H. Coverage for meals: For prandial coverage, increase the infusion rate by 2-4 units/hour over and above the basal rate just before taking the major meal and continue the increased rate for next 2 hours. It is important to remember that IV insulin infusion has two components: a) basal coverage provided by the maintenance rate of IV insulin, and b) prandial coverage provided by an increment in the maintenance rate for 2 hours around a meal.

Example: A 54-year-old male patient is on IV insulin for hyperglycemia management. He has good oral acceptance and is planning to take lunch at 1 pm. At 1 pm, his BG level is 202 mg/dl and according to scale, infusion rate is 2 U/hr, but we increase the infusion rate to 5 U/hr (2+3 U/hr) from 1pm to 3pm to provide prandial coverage. From 3pm onwards, the basal infusion rate (or maintenance rate) is continued till the time of next meal. Increment in rate for meal coverage is subjected to change on the next day based on pre-meal to post-meal change in BG level on the previous day.

I. Monitoring of serum potassium: Intravenous insulin is associated with potassium shifts inside the cell. Therefore, serum potassium should be monitored every 6 hours in patients with NPO status and every 12 hours in those who are accepting orally.

General Comments

1. The discontinuation of insulin infusion (where necessary) should be for a minimum period of time to ensure better glycemic control. For example, if insulin infusion is discontinued for the patient's bath, it should be restarted as soon as patient comes back with total interruption time of less than 10 to 15 minutes.
2. The timings and doses of insulin described in this document are with regard to use of Inj. Regular insulin as a bolus (or prandial) insulin and Inj. NPH insulin as a basal insulin. However, in a scenario where insulin analogs are used (rapid-acting analogs such as insulin aspart, insulin lispro, and insulin glulisine, and long-acting basal analogs such as insulin glargine, and insulin degludec) these specifications would change accordingly. For instance, a) the onset of action is faster with rapid-acting insulin analogs and a gap of 5-15 minutes before the meal is adequate, b) long acting basal insulin analogs have a prolonged duration of action lasting 24 hours or more, and can be administered at any relatively fixed time of the day, c) when using insulin analogs for basal-bolus insulin regimen, basal insulin constitutes 50% of TDD, while bolus insulin account for the rest 50% (further divided into three equal portions for each meal)
3. Gliptins: Sitagliptin, Teneligliptin, Vildagliptin, Linagliptin
4. Abbreviations: ADN: After dinner; BBF: Before breakfast, BDN: Before dinner, BL: Before lunch, BG: Blood glucose; CBG: Capillary blood glucose; COVID-19: Coronavirus disease 2019; DKA: Diabetic ketoacidosis; FPG: Fasting plasma glucose;

HbA1c: Hemoglobin A1c; IV: Intravenous; MSII: Multiple subcutaneous insulin injections; N: NPH insulin; NPH: Neutral Protamine Hagedorn; NPO: Nothing by mouth; NS: Normal saline; OAD: Oral antihyperglycemic drug; R: Regular insulin; RT: Ryles tube; TDD: Total daily dose

Section 5: Clinical Guidance on Anti-hyperglycemic Treatment Initiation and Titration in Patients with COVID-19 and Diabetes

Scenario	BG level	Action*
1. Detected to have hyperglycemia at admission or on starting steroids	Pre-meal <140 mg/dL and post-meal <180 mg/dL	Healthy diet. No further monitoring
	Pre-meal \geq 140 mg/dL and/or post-meal \geq 180 mg/dL	Monitor BG levels and diabetic diet
	Pre-meal between 150 and 180 mg/dl and/or post-meal between 200 and 250 mg/dl	Start Tab Metformin 500 mg twice daily and a Gliptin [@]
	Pre-meal: \geq 180 mg/dl and/or post-meal \geq 250 mg/dl	Start on basal-bolus insulin
	Pre-meal: \geq 300 mg/dl and/or post-meal: \geq 400 mg/dl	Start on IV insulin infusion
	DKA	Start on IV insulin infusion (DKA protocol)
2. Patient on OAD at admission/during follow-up	Pre-meal <140 mg/dL and post-meal <180 mg/dL	Continue existing OAD [@]
	Pre-meal: \geq 140 mg/dl and/or post-meal: \geq 180 mg/dl	Uptitrate OAD
	Pre-meal: \geq 180 mg/dl and/or post-meal: \geq 250 mg/dl	Start on basal-bolus insulin
	Just FPG is \geq 140mg/dl	Add basal insulin at bed time
	Pre-meal: \geq 300 mg/dl and/or post-meal: \geq 400 mg/dl	Start on IV insulin infusion
	DKA	Start on IV insulin infusion (DKA protocol)
3. On basal-bolus regimen at admission/during follow-up	Pre-meal <140 mg/dL and post-meal <180 mg/dL	Continue basal-bolus regimen [§]
	Pre-meal: \geq 140 mg/dl and/or post-meal: \geq 180 mg/dl	Optimise insulin doses
	Pre-meal: \geq 300 mg/dl and/or post-meal: \geq 400 mg/dl	Start on IV insulin infusion
	DKA	Start on IV insulin infusion (DKA protocol)
4. Patient is NPO	BG level (2 hrly): If \geq 2 values \geq 180 mg/dl	Start IV insulin infusion

*Refer to the main document for details of starting/ titrating various regimens.

[@] OAD to be initiated/continued only in stable, orally accepting mild COVID-19 cases without any contraindications for their use. Gliptin could be Vildagliptin 50 mg BD, Sitagliptin 100 mg OD, Linagliptin 5 mg OD or Teneligliptin 20 mg OD.

[§]Continue existing basal-bolus regimen if there are no episodes of hypoglycemia.

Abbreviations: BG: Blood glucose; DKA: Diabetic ketoacidosis; IV: Intravenous; NPO: Nothing by mouth; OAD: Oral antihyperglycemic drug

Suggested Readings

1. Goyal A, Gupta S, Gupta Y, Tandon N. Proposed guidelines for screening of hyperglycemia in patients hospitalized with COVID-19 in low resource settings [published online ahead of print, 2020 May 29]. *Diabetes Metab Syndr.* 2020;14(5):753-756.
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6. Rayman G, Lumb A, Kennon B, et al. New Guidance on Managing Inpatient Hyperglycaemia during the COVID-19 Pandemic. *Diabet Med.* 2020;37(7):1210-1213. doi:10.1111/dme.14327
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