Management of Diabetes in Critically Ill Patients with COVID-19

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Clinical focus: Diabetes, Endocrine Disease in Pregnancy, General Endocrinology

Research focus: barriers to diabetes care, transition of care, systems improvement and development of innovative models of diabetes care
Disclosures

No conflict of interest or significant financial relationships relevant to this presentation
53-year-old F with HTN, hyperlipidemia, DM2 presenting to ED with SOB

- Symptoms began 12 days prior (fatigue, malaise)
- Tested for COVID-19 due to concern of work-related exposure (negative)
- Subsequent week developed sore throat, diarrhea, fever, progressive dyspnea, repeat SARS-CoV-2 now positive and started on azithromycin and hydroxychloroquine, quarantined at home
- Worsening dyspnea, fever, anorexia and sought acute care. In ED was ill appearing, unable to speak in full sentences, \( O_2 \) saturation 78% RA
53-year-old F with HTN, hyperlipidemia, DM2 presenting to ED with SOB

Biochemical Evaluation:

- normal renal and hepatic function
- BG 151 mg/dL (8.3 mmol/L)
- bicarbonate 20 mmol/L
- lactic acid 1.2 mmol/L
- pH 7.41
- elevated inflammatory markers (ferritin 440 ug/L, ESR 93 mm/hr, CRP 95.4 mg/dL, IL-6 24.4 pg/mL [ref <1.64])
- SARS-CoV-2 positive

Radiologic evaluation:

- bibasilar consolidating concerning for COVID-19 PNA

Admitted to special pathogen unit
53-year-old F with HTN, hyperlipidemia, DM2 presenting to ED with SOB

Shortly after admission increased O₂ requirement (15L) and transferred to ICU for hypoxemic respiratory failure and intubated

Diabetes History:
- Dx >20 years ago, no known complications; HbA1c 7.5%
- Medications:
  - Metformin 1000 mg BID
  - Glimepiride 4 mg daily
  - Empagliflozin 10 mg daily
  - Exenatide 2mg weekly
  - Glargine 22 units daily

Patient endorses compliance with all diabetes medications (last doses day of ED visit). Outpatient regimen discontinued on admission and started on correctional insulin.

Glycemic control at goal with minimal insulin requirements
53-year-old F with HTN, hyperlipidemia, DM2 presenting to ED with SOB

- In next 24 hours developed metabolic acidosis with elevated AG, BG 192 mg/dL (10.6 mmol/L), bicarbonate 15 mmol/L, pH 7.24, lactic acid 1.3 mmol/L, BHB 6.1 mmol/L.

- Started on IV insulin and dextrose support for euDKA

- After resolution of metabolic derangements was treated with IV insulin while in ICU during course of illness had variable insulin requirements 3-28 units/hr
Objectives

• Clinical implications for patients with diabetes during the COVID-19 Pandemic

• Unique considerations and management strategies for hospitalized patients with hyperglycemia and SARS-CoV-2
Hyperglycemia and Diabetes: is there a link to COVID-19 severity?

Several studies have demonstrated patients with diabetes have increased risk of severe complications of infection and life threatening illness from SARS-CoV-2

Singh AK et al. Metab Syndr 2020 Apr 9; 14(4):303-310
Patients with Diabetes Hospitalized for COVID-19: the early data


Single center, retrospective observational study
Tongji hospital, Wuhan, China

Patients with diabetes vs. non-diabetes:

- ICU admission (66.7% vs 41.4%); p 0.002
- Mechanical ventilation (81.3% vs 49.0%); p<0.001
- Mortality (81.3% vs. 47.6%); p<0.001
Patients with Diabetes Hospitalized for COVID-19: similar trends worldwide

Meta-Analysis (n=16,003)
February 7, 2020 - April 17, 2020
33 centers: China, USA, France

Diabetes is associated with 2-fold increase in mortality and severe COVID-19 infection

Similar findings in other studies (Yang et al)

2.12-fold increase in mortality
2.4-fold increase in severe COVID infection
4.6-fold increase in ARDS
3.3 increase in disease progression from mild to severe illness
Inpatient Hyperglycemia

Stress hyperglycemia

Previously undiagnosed diabetes

Established diabetes

Severe Hyperglycemia and DKA in patients with SARS-CoV-2 infection
Dysglycemia with COVID-19: possible mechanisms

Patients with and without prior history of IGT

Metabolic inflammation
• enhanced release of cytokines
• dysregulated immune response

Beta cell dysfunction
• binding of SARS-CoV in pancreatic islets causing direct damage and reduction in insulin release

Müller JA et al Nat Metab. 2021 Feb;3(2):149-165
Hyperglycemia in COVID-19: potential mechanisms

![Diagram showing potential mechanisms of hyperglycemia in COVID-19](Diagram.png)
The *other* Cytokine Storm: Severe Insulin Deficiency

IL-6 has been shown to be elevated in both DKA and COVID-19 and may be an important prognostic factor.

*Palermo NE, Sadhu A, McDonnell, ME et al. J Clin Endocrinol Metab. 2020 Aug 1;105(8)*
Does Glycemic Control Matter?

- Impact of longstanding control (HbA1c)
- Glucose at time of COVID-19 diagnosis
- Glycemic control in patients hospitalized with COVID-19
- Presence of Hyperglycemic Crisis in the setting of COVID-19
Long-term Glycemic Control and COVID-19

Retrospective cohort study, New York City
March 11-May 7 2020 (n=1126)

HbA1c did not predict in hospital mortality

<table>
<thead>
<tr>
<th>Table 2—Mortality odds ratios of preadmission clinical characteristics in hospitalized patients with diabetes and COVID-19 (N = 1,126)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycemic control: HbA1c^†</td>
</tr>
<tr>
<td>------------------------------------------------</td>
</tr>
<tr>
<td>Glycemic control: HbA1c^†</td>
</tr>
<tr>
<td>Treatment regimen (Ref: no treatment)</td>
</tr>
<tr>
<td>Noninsulin only</td>
</tr>
<tr>
<td>Insulin + noninsulin</td>
</tr>
<tr>
<td>Insulin only</td>
</tr>
<tr>
<td>Comorbidity or long-term diabetes complication</td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
</tr>
</tbody>
</table>

Ref, reference. *Adjustment: each variable was adjusted for age, sex, BMI, insurance, and the other variables in the table. †Most recent HbA1c within 3 years prior to or 1 week after hospitalization was used for analyses.

But what about glycemic control during hospitalization?

Glucose on admission is an independent predictor of severe prognosis

**Figure 1**—A: Kaplan-Meier analysis showing survival during hospitalization in COVID-19 patients. B: Kaplan-Meier analysis showing survival during hospitalization in COVID-19 patients stratified by quintiles of at-admission plasma glucose levels.
Benefits of Glycemic Control in Hospitalized Patients with COVID-19

Retrospective Observational Study in patients with COVID-19 with and without DM (n=1122, 88 US hospitals)

Compared those with DM and/or uncontrolled hyperglycemia (n=451) to patients without DM or hyperglycemia (n=671)

- DM HbA1c ≥ 6.5%
- Uncontrolled hyperglycemia ≥ 2 BG > 180 mg/dL within 24h

- Mortality rate 28.8% in DM or uncontrolled hyperglycemia patients vs. 6.2% (p< 0.01)
- Longer LOS (5.7 vs. 4.3 days, p<0.01)

Figure 3. Mortality rates among patients who were discharged or died comparing diabetes and/or uncontrolled hyperglycemia (n = 184) with patients without diabetes or hyperglycemia (n = 386).

In Hospital Glycemic Control Matters

Retrospective, multicenter study
Hubei Province, China (n=7337)
Patients with and without DM
Hospitalized for COVID-19

Lower mortality in well-controlled
(3.9-10 mmol/L; 70-180 mg/dL)

Zhu L et al. Cell Metab. 2020 Jun 2;31(6):1068-1077
Duration of Hyperglycemia Matters

Retrospective (n=230) Patients hospitalized for COVID-19 WITHOUT prior history of DM (SH)

“low stable”
6.63-7.54 mmol/L (119-136 mg/dL)

“high stable”
12.59-14.02 mmol/L (227-252 mg/dL)

“High stable” pattern was an Independent predictor of mortality

Glycemic Control Matters: *window of opportunity*

Patients hospitalized for COVID-19 in critical care and non-critical care units
Glytec Database: 91 hospitals, 12 US states (N=1544)

BG >13.88 mmol/L (250 mg/dL) on days 2-3 was independently associated with mortality [HR] 7.17;95%CI 2.62–19.62) compared with patients with BG<7.77 mmol/L (140 mg/dL).

Hyperglycemic Crisis and COVID-19

19 articles reporting 110 patients

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) [Median (IQR)]</td>
<td>45.5 (36.2–57.7) [7,8,10–16,18–21,23,24,28] b 57.0 (48.0–64.0) [22] b 59.0 (42.3–70.0) [9]</td>
</tr>
<tr>
<td>Sex (N = 102) c</td>
<td>Male (n = 64, 63%)</td>
</tr>
<tr>
<td></td>
<td>Female (n = 38, 37%)</td>
</tr>
<tr>
<td>Ethnicity (N = 84)</td>
<td>Black (n = 30, 36%)</td>
</tr>
<tr>
<td></td>
<td>Hispanic (n = 19, 23%)</td>
</tr>
<tr>
<td></td>
<td>White (Caucasian) (n = 10, 12%)</td>
</tr>
<tr>
<td></td>
<td>Asian (n = 6, 7%)</td>
</tr>
<tr>
<td></td>
<td>Mixed (n = 4, 5%)</td>
</tr>
<tr>
<td></td>
<td>Others (n = 8, 9%)</td>
</tr>
<tr>
<td></td>
<td>Unknown (n = 7, 8%)</td>
</tr>
<tr>
<td>Type of diabetes (N = 97)</td>
<td>Pre-existing T1DM (n = 12, 12%)</td>
</tr>
<tr>
<td></td>
<td>Pre-existing T2DM (n = 74, 77%)</td>
</tr>
<tr>
<td></td>
<td>Newly diagnosed (n = 10, 10%)</td>
</tr>
<tr>
<td></td>
<td>Gestational DM (n = 1, 1%)</td>
</tr>
<tr>
<td>Use of SGLT2 inhibitors</td>
<td>7</td>
</tr>
<tr>
<td>BMI (kg/m²) [Median (IQR)]</td>
<td>26.6 (23.7–32.3) [7,11–13,16,28] b 24.7 (21.3–28.5) [22] b 27.1 (23.2–33.0) [9]</td>
</tr>
</tbody>
</table>

91 (83%) DKA
19 (17%) DKA/HHS

majority were:
male (63%)
Black (77%)
Preexisting DM

~10% newly diagnosed DM

In hospital mortality 45% higher in DKA/HHS group vs. DKA group (67% vs, 29%)
Challenges in Achieving Glycemic Control with COVID-19

• Variability in insulin sensitivity over course of illness (*daily* and in some patients *hourly*)

• Patients with pre-existing CKD or AKI in the setting of SARS-CoV-2 are at increased risk of hypoglycemia

• Significant variability in both SC and IV insulin requirements independent of therapy with glucocorticoids and vasopressors

Korytkowski M et al. J Clin Endocrinol Metab. 2020 Jun 4
Challenges in Achieving Glycemic Control with COVID-19: *it’s a balancing act…*

IV insulin is standard of care in critically ill patients, but this requires frequent monitoring and adjustment.

- Ongoing adjustments to insulin therapy
- Preservation of PPE
- Frequent glucose monitoring
- Reducing time at bedside
Assessment of Patients with Hyperglycemia and COVID-19

- In patients with BG > 180 mg/dL (10 mmol/L) or known DM: HbA1c on admission. Consider fructosamine, glycated albumin, or 5-andyro-glucitol in those HbA1c may not be reliable.

- Glucose monitoring
  POCT AC and q HS (taking po) or q4-6 (NPO)
  q1-2 in patient receiving IV insulin
  q2-4h in patients receiving intensive SC insulin

*CGM

*CGM Devices currently not approved for inpatient use; evidence to date in non-critical care patients notable for decreased frequency of hypoglycemia. April 1, 2020 FDA approved non-invasive remote glucose monitoring devices in hospital setting during pandemic.

Korytkowski M et al. J Clin Endocrinol Metab. 2020 Jun 4
Insulin Pumps and Closed Loop Systems in COVID-19

- If patient safely able to self manage may continue CSII
- Hybrid Closed Loop Insulin Systems (Medtronic 670G, Tandem Control IQ) rely on CGM data for algorithm and with variability noted in COVID generally not recommended to continue “auto” mode and instead use “manual mode”
Strategies for Acute Diabetes Care in COVID-19

Noninsulin agents:

• Discontinue metformin (MALA), sulfonylureas (hypoglycemia), TZDs (fluid retention), GLP1α (nausea and variable po intake)

• DPP4 inhibitors increasing use in inpatient environment, but all published trials using in acute care setting were conducted in combination with insulin. Note: DPP4 enzyme has been identified as co-receptor for MERS-CoV; at this time no data demonstrating either harmful or beneficial impact in patients with COVID-19. Consensus given unstable nature of COVID is to use insulin therapy.

Insulin:

• IV insulin infusion vs. SC insulin

Korytkowski M et al. J Clin Endocrinol Metab. 2020 Jun 4
Good evidence for subcutaneous insulin for the treatment of mild to moderate uncomplicated DKA.

Table 2. Summary of subcutaneous insulin RCTs in DKA and potential strategies in COVID-19

<table>
<thead>
<tr>
<th>Population</th>
<th>Intervention vs conventional IVI protocol</th>
<th>Outcomes measured</th>
<th>Key findings</th>
<th>Notes for use in COVID-19</th>
</tr>
</thead>
<tbody>
<tr>
<td>Della Manna, et al. (2005)</td>
<td>Pediatric and adolescent patients with DKA (n = 60) SC lispro 0.15 units/kg every 2 hours until BG &lt; 13.8 mmol/L (250 mg/dL) then interval increased to every 4 hours until resolution of DKA</td>
<td>Time to resolution of DKA</td>
<td>Both groups reached BG &lt; 13.8 mmol/L (&lt;250 mg/dL) within 6 hours</td>
<td>every 2-4 hours insulin dosing outside of ICU was effective but slightly slower to resolution</td>
</tr>
<tr>
<td>Esöz, et al. (2006)</td>
<td>Patients with mild/moderate DKA (n = 20) IV regular insulin then 0.075 units/kg every 1 hour until resolution of DKA</td>
<td>Time to resolution of DKA, amount of insulin used, mortality, hypoglycemia rate</td>
<td>No differences between groups with respect to time of resolution of DKA, amount of insulin use rate of DKA</td>
<td>every 1 hour monitoring used in both groups</td>
</tr>
<tr>
<td>Hsia, et al. (2012)</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Karolli, et al. (2011)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Umpierrez, et al. (2004)</td>
<td>Patients with uncomplicated DKA (n = 40) SC lispro, managed on ward (n = 10) or an intermediate care unit (n = 10) initial dose of 0.3 units/kg followed by 0.1 units/kg every 2 hours until BG &lt; 250 mg/dL, dose reduced to 0.05 units/kg</td>
<td>Duration of treatment and resolution of hyperglycemia and ketoacidosis. Other endpoints: total length of hospitalization, amount of insulin administration, hypoglycemia rate</td>
<td>No difference in mean duration of treatment until resolution of hyperglycemia or ketoacidosis or rate of hypoglycemia between group</td>
<td>Medical ward can be a safe environment for intensive SC protocol though every 1 hour monitoring used in all groups</td>
</tr>
<tr>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: IVI, intravenous insulin; DM1, diabetes mellitus type 1; DM2, diabetes mellitus type 2; SC, subcutaneous; IV, intravenous; DKA, diabetic ketoacidosis; LOS, length of stay.

Other Considerations: Subcutaneous Rapid Acting Insulin

SC-1h
Initial 0.3 units/kg followed by 0.1 unit/kg q1h

SC-2h
Initial 0.3 units/kg followed by 0.2 unit/kg q2h

Table 3—Response to medical treatment

<table>
<thead>
<tr>
<th></th>
<th>SC-1h</th>
<th>SC-2h</th>
<th>Regular IV insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>15</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>Length of hospital stay (days)</td>
<td>3.4 ± 3</td>
<td>3.9 ± 3</td>
<td>4.5 ± 3</td>
</tr>
<tr>
<td>Duration of therapy until glucose &lt;13.8 mmol/l (h)</td>
<td>6.9 ± 4</td>
<td>6.1 ± 4</td>
<td>7.1 ± 5</td>
</tr>
<tr>
<td>Duration of therapy until resolution of DKA (h)</td>
<td>10 ± 3</td>
<td>10.7 ± 3</td>
<td>11 ± 3</td>
</tr>
<tr>
<td>Amount of insulin until glucose &lt;13.8 mmol/l (units)</td>
<td>67 ± 37</td>
<td>65 ± 26</td>
<td>62 ± 28</td>
</tr>
<tr>
<td>Amount of insulin until resolution of DKA (units)</td>
<td>89 ± 33</td>
<td>94 ± 32</td>
<td>82 ± 28</td>
</tr>
<tr>
<td>Episodes of hypoglycemia</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

are means ± SD.

Our practice:
SC-2h for mild uncomplicated DKA

Other Considerations: Early Basal

Initiation of long-acting insulin (0.25 units/kg) within 12h of insulin infusion decreased rate of rebound hyperglycemia (n=61, p<0.001)

Our practice

If eGFR >45: 0.25 unit/kg
If eGFR <45: 0.15 unit/kg

Example Subcutaneous Insulin Algorithm for Critically Ill Patients with COVID-19

<table>
<thead>
<tr>
<th>Patient characteristic</th>
<th>Glargine (Lantus)</th>
<th>NPH</th>
<th>Aspart fixed dose</th>
<th>Aspart scale q 4h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior Diabetes</td>
<td>0.25 units/kg/dose q 24h</td>
<td>0.12 units/kg/dose q 12h</td>
<td>Low</td>
<td></td>
</tr>
<tr>
<td>No known Diabetes</td>
<td>0.2 units/kg/dose q 24h</td>
<td>0.1 units/kg/dose q 12h</td>
<td>Low</td>
<td></td>
</tr>
<tr>
<td>High dose steroids or continuous nutrition support</td>
<td>0.15 units/kg/dose q 12h</td>
<td>0.05 units/kg/dose scheduled q 4h</td>
<td>Low</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient characteristic</th>
<th>Glargine (Lantus)</th>
<th>NPH</th>
<th>Aspart fixed dose</th>
<th>Aspart scale q 4h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior Diabetes</td>
<td>0.3 units/kg/dose q 24h</td>
<td>0.15 units/kg/dose q 12h</td>
<td>Moderate</td>
<td></td>
</tr>
<tr>
<td>No known diabetes</td>
<td>0.25 units/kg/dose q 24h</td>
<td>0.1 units/kg/dose q 12h</td>
<td>Moderate</td>
<td></td>
</tr>
<tr>
<td>High dose steroids or Continuous nutrition support</td>
<td>0.25 units/kg/dose q 12h</td>
<td>0.15 units/kg/dose scheduled q 4h</td>
<td>Moderate</td>
<td></td>
</tr>
</tbody>
</table>

Recommend start at Low dose strategy for all patients EXCEPT patient on > 0.5 unit/kg/day TDD start Medium dose strategy

SC approach gives ability to delivery high dose insulin therapy distributed across multiple doses throughout the day to allow for frequent adjustments and address unique considerations during pandemic.
### High dose strategy A

Starts at total daily insulin dose = 1.5 to 1.95 units/kg/day. **NOTE:** Before moving to High Dose, INJECT INTO NEW subcutaneous injection site. Abdomen (anterior or side) and upper buttock are preferred for best subcutaneous absorption.

<table>
<thead>
<tr>
<th>Patient characteristic</th>
<th>Glargine (Lantus)</th>
<th>NPH</th>
<th>Aspart fixed dose</th>
<th>Aspart Scale q 4h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior Diabetes</td>
<td>0.5 units/kg/dose q 24h OR 0.25 units/kg/dose q 12h</td>
<td>0.15 units/kg/dose scheduled q 4h</td>
<td><strong>Custom</strong></td>
<td></td>
</tr>
<tr>
<td>No known diabetes</td>
<td>0.3 units/kg/dose q 24h OR 0.15 units/kg/dose q 12h</td>
<td>0.1 units/kg/dose scheduled q 4h</td>
<td><strong>Custom</strong></td>
<td></td>
</tr>
<tr>
<td>High dose steroids or Continuous nutrition support</td>
<td>0.25 units/kg/dose q 8h</td>
<td>0.2 units/kg/dose scheduled q 4h</td>
<td><strong>Custom</strong></td>
<td></td>
</tr>
</tbody>
</table>

**High dose strategy B.** Starts at total daily Insulin dose = 2.1-3 units/kg/day **NOTE:** This requires inpatient diabetes consultation. Please page Unit based Pharmacist, Endocrinology (11519) or DMS (34444) for starting IV hourly dose. If target glucose not achieved after 36 hours on step 2, consider continuous IV insulin protocol provider adjusted with modified targets and frequency of glucose monitoring.

<table>
<thead>
<tr>
<th>Patient characteristic</th>
<th>Glargine (Lantus)</th>
<th>NPH</th>
<th>Aspart fixed dose</th>
<th>Aspart Scale q 4h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior Diabetes</td>
<td>0.3 units/kg/dose q 8h</td>
<td>0.2 units/kg/dose scheduled q 4h</td>
<td><strong>Custom</strong></td>
<td></td>
</tr>
<tr>
<td>No known diabetes</td>
<td>0.3 units/kg/dose q 8h</td>
<td>0.2 units/kg/dose scheduled q 4h</td>
<td><strong>Custom</strong></td>
<td></td>
</tr>
<tr>
<td>High dose steroids or Continuous nutrition support</td>
<td>0.4 units/kg/dose q 8h</td>
<td>0.3 units/kg/dose scheduled q 4h</td>
<td><strong>Custom</strong></td>
<td></td>
</tr>
</tbody>
</table>

*Glargine is preferred for patients at higher risk of hypoglycemia: GFR <30, Age >75, advanced cirrhosis*

*High dose steroids: equivalent of >40 mg prednisone, >100 mg hydrocortisone or >6 mg dexamethasone per day*
COVID-19 Subcutaneous DKA Protocol

Insulin Therapy:
Administer both long acting insulin (glargine) dosed every 24 hours and rapid acting insulin (aspart), which should be dosed q4 hours

<table>
<thead>
<tr>
<th></th>
<th>Subcutaneous rapid acting insulin (aspart) q4 hours</th>
<th>Subcutaneous long acting insulin (glargine) q24 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial dose</td>
<td>0.3 units/kg/dose</td>
<td>If eGFR &gt;40: 0.25 units/kg/dose</td>
</tr>
<tr>
<td></td>
<td>Maximum of 20 units</td>
<td>If eGFR &lt;40: 0.15 units/kg/dose</td>
</tr>
<tr>
<td>Subsequent dose</td>
<td>0.2 units/kg every 4 h</td>
<td>Re-dose glargine in 24 h based on response to initial dose</td>
</tr>
<tr>
<td></td>
<td>Maximum of 20 units</td>
<td></td>
</tr>
<tr>
<td>Blood glucose &lt; 250 mg/dL</td>
<td>0.05-0.1 units/kg every 4 h and start IV Dextrose containing fluid</td>
<td>Re-dose glargine q 24h based on response to subsequent dose</td>
</tr>
</tbody>
</table>

DKA Monitoring and Transition Recommendations:
Patients will need q4-6h chemistry monitoring (BMP) and electrolyte repletion as above. When AG < 12 and bicarbonate > 18 mEq/L, transition to non-DKA subcutaneous regimen. Dextrose may be tapered to off. Please see NON-DKA HYPERGLYCEMIA guide above or pocket card reference guide. For patients who are not critically ill and/or eating meals: Please refer to the BWH Management of Diabetes and Hyperglycemia in non-ICU patients guideline.

BWH COVID-19 Protocol 2020
https://covidprotocols.org/protocols/endocrine/
53-year-old F with HTN, hyperlipidemia, DM2 presenting to ED with SOB

Treated for euDKA, variable insulin requirements 3-28 units/hr- transitioned to SC regimen with q4h insulin dosing and glucose monitoring.
Resources for COVID-19 and Diabetes

https://covidprotocols.org/

https://covidindiabetes.org

ICU Management of Hyperglycemia and Diabetic Ketoacidosis

1. Hyperglycemia, DKA with concomitant increased insulin requirements are common in critically ill patients with COVID-19.

2. In an effort to minimize the number of patients on insulin infusions, the Diabetes Subcommittee has developed a guideline for COVID-19 patients who are critically ill and/or in mild-moderate DKA to allow for q 4h monitoring and SC insulin dosing.

   a. This strategy will minimize exposure with RN time at bedside and conserve PPE while maintaining the ability to deliver high dose insulin therapy distributed across multiple adjustable doses per day.

   b. The major difference to highlight is the change to a q 4h interval (as compared to the q 1h monitoring and insulin dosing with BHP and q 2h with the SC DKA protocol). This guideline also expands the use of a SC DKA protocol to include both mild and moderate DKA and with this in place only severe DKA/HHS will require an insulin infusion.

3. Guidelines on COVID-specific DKA and Hyperglycemia Insulin treatment are available here [Link].
Which of the following has been shown to influence mortality in patients with Diabetes and COVID-19?

A. Glycemic control during hospitalization
B. Glucose level on admission
C. Glucose level on day 3
D. Glycemic variability during hospitalization
E. All of the above
Which of the following has been shown to influence mortality in patients with Diabetes and COVID-19?

A. Glycemic control during hospitalization
B. Glucose level on admission
C. Glucose level on day 3
D. Glycemic variability during hospitalization
E. All of the above
87-year-old female with longstanding DM type 2 is admitted for COVID-19 pneumonia. HbA1c 8.5% and home regimen for diabetes includes metformin 500 mg BID, glipizide 5mg daily, linagliptin 5 mg daily and insulin degludec 12 units nightly. Labs on presentation are notable for BG 450 mg/dL, bicarbonate 16 mg/dL, BHB 3.5, pH 7.27, lactic acid 0.8 mmol/L, creatinine 1.7 mg/dL (baseline 1.0). Which of the following may be a strategy to consider for insulin therapy?

A. Correctional insulin only  
B. Restart home medications  
C. IV insulin  
D. Subcutaneous insulin q2-4h  
E. C and D  
F. A and B
87-year-old female with longstanding DM type 2 is admitted for COVID-19 pneumonia. HbA1c 8.5% and home regimen for diabetes includes metformin 500 mg BID, glipizide 5mg daily, linagliptin 5 mg daily and insulin degludec 12 units nightly. Labs on presentation are notable for BG 450 mg/dL, bicarbonate 16 mg/dL, BHB 3.5, pH 7.27, lactic acid 0.8 mmol/L, creatinine 1.7 mg/dL (baseline 1.0). Which of the following may be a strategy to consider for insulin therapy?

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F. A and B
Hyperglycemia in COVID-19

1. In Hospital glycemic control and timing is extremely important!

2. Alternative strategies with SC insulin in critical illness and mild/moderate uncomplicated DKA should be considered to address unique concerns during the COVID-19 pandemic.

3. Further research is needed to explore the incidence and pathogenesis of NEW diabetes, DKA or acute worsening of pre-existing diabetes with SARS-CoV-2 infection and the glycemic targets necessary to improve morbidity and mortality in DM patients.
References


Bornstein SR et al. Nat Rev Endocrinol. 2020 Apr 2

Cariou et al. Diabetologia 2020 Aug;63(8):1500-1515


Coppelli A et al. Diabetes Care 2020;43:2345–2348

Hsia E et al. J Clin Endocrinol Metab. 2012 Sep;97(9):3132-7


Korytkowski M et al. J Clin Endocrinol Metab. 2020 Jun 4

Muller JA et al. Nat Metab. 2021 Feb;3(2):149-165

Palermo NE et al. J Clin Endocrinol Metab. 2020 Aug 1;105(8)


Zhu L et al. Cell Metab. 2020 Jun 2;31(6):1068-1077
Questions
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