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National Health Mission
SDA Complex, Kasumpti, Shimla-9
Himachal Pradesh
Dated: Shimla-171009, the



Circular

The Ministry of Health and Family Welfare, Govt of India has circulated the pediatric guidelines for COVID 19 (copy Enclosed). This document provides holistic approach for managing the children affected with COVID 19.

Further, the comprehensive guidelines for management of COVID 19 Patients as issued by the ministry Health and Family Welfare, Govt of India are also enclosed. It appries regarding the treatment of COVID 19 Patients, COVID 19 symptoms at glance, self monitoring Performa guide box, 6 minute walk test, rational use of HRCT imaging and management of Mucormycosis.

Also, the revised clinical guidance on diagnosis and management of Diabetes at COVID 19 Patient management facility, Version 2, as issued by GOI is enclosed herewith for further necessary action.

Nep... 3/6/21
Mission Director, NHM
Himachal Pradesh, Shimla – 9

Endst. No. As above

Dated Shimla-9 the

Copy for information and necessary action to:



1. The Secretary Health to the Government of Himachal Pradesh
2. All the Deputy Commissioners, Himachal Pradesh.
3. Director Health Services, Himachal Pradesh.
4. Director Medical Education & Research, Himachal Pradesh.
5. All the Chief Medical Officer, Himachal Pradesh.
6. All the Medical Superintendents, Himachal Pradesh.
7. All Nodal Officers, DCCC/DCHC/DCH in Himachal Pradesh.
8. All the District Surveillance Officers, in Himachal Pradesh.
9. State COVID Clinical Team, Himachal Pradesh.
10. COVID Clinical Committees of all the Medical Colleges of HP.

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MANAGEMENT OF COVID-19 IN **CHILDREN**



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CLINICAL FEATURES



Majority of children with covid infection may be asymptomatic or mildly symptomatic

- Common symptoms include- fever, cough, breathlessness/shortness of breath, fatigue, myalgia, rhinorrhea, sore throat, diarrhea, loss of smell, loss of taste etc



Few children may present with gastrointestinal symptoms and atypical symptoms



A new syndrome named multi system inflammatory syndrome has been described in children. Such cases are characterized by:

- Unremitting fever $> 38^{\circ}\text{C}$
- Epidemiological linkage with SARS CoV – 2
- Clinical features suggestive of Multi System Inflammatory Syndrome

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ASYMPTOMATIC AND MILD CASES



Asymptomatic children are usually identified while screening, if family members are identified

- Require monitoring for development of symptoms & subsequent treatment according to assessed severity



Children with mild disease may present with sore throat, rhinorrhea, cough with no breathing difficulty. Few children may have gastrointestinal symptoms

- They do not need any investigations



These children can be managed at home with home isolation & symptomatic treatment



Children with underlying comorbid conditions including congenital heart disease, chronic lung diseases, chronic organ dysfunction, obesity may also be managed at home

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MILD CASES TREATMENT: HOME ISOLATION

(1/2)



For Fever: Paracetamol 10-15 mg/kg/dose; may repeat every 4-6 hours



For Cough: Throat soothing agents like warm saline gargles in older children & adolescents



Fluids & feeds: Ensure oral fluids to maintain hydration, and nutritious diet



Antibiotics: Not indicated

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MILD CASES TREATMENT: HOME ISOLATION

(2/2)



There is no role of Hydroxychloroquine, Favipiravir, Ivermectin, lopinavir/ritonavir, Remdesivir, Umifenovir, Immunomodulators including Tocilizumab, Interferon B1a, Convalescent plasma infusion or dexamethasone



Maintain monitoring chart including counting of respiratory rates 2-3 times a day, look for chest indrawing, bluish discolouration of body, cold extremities, urine output, oxygen saturation, fluid intake, activity level, especially for young children



Parent/ caregivers to contact the doctor in case of emergency

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MODERATE COVID-19 CASES (1/3)



A child to be categorized as moderate Covid-19 Case if he/she has the following:

- Rapid Respiration (Age based) as follows:
 - Respiratory rate >60 / min for less than 2 months
 - Respiratory rate >50 /min for less 2 to 12 months
 - Respiratory rate >40 /min for 1 to 5 years
 - Respiratory rate >30 /min for more than 5 years
- And oxygen saturations in all these age groups to be above 90%



Child may be suffering from pneumonia which may not be clinically apparent

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MODERATE COVID-19 CASES (2/3)



Investigations: No lab tests required routinely unless indicated by associated comorbid conditions



Treatment: To be admitted in Dedicated Covid Health Centre or Secondary level Healthcare Facility & monitored for clinical progress

- Maintain fluid & electrolyte balance
-

- Encourage oral feeds (breast feeds in infants)
-

- If oral intake is poor, intravenous fluid therapy should be initiated

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MODERATE COVID-19 CASES (3/3)



Child to be administered:

- For fever: Paracetamol 10-15 mg/kg/dose. May be repeated every 4-6 hourly. (temperature > 38°C, i.e. 100.4°F)

- Amoxicillin to be administered, if there is evidence/strong suspicion of bacterial infection

- For SpO₂ below 94%, oxygen supplementation is required

- Corticosteroids may be administered in rapidly progressive disease. Not required in all children with moderate illness, specifically during the first few days of illness

- Supportive care for comorbid conditions, if any

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SEVERE COVID-19 CASES (1/4)



Children with SpO₂ level less than 90% are categorized as having severe Covid-19 infection

- They may have severe pneumonia, Acute Respiratory Distress Syndrome, Septic Shock, Multi-organ dysfunction syndrome, or pneumonia with cyanosis
- Clinically, such children may present with grunting, severe retraction of chest, lethargy, somnolence, seizure
- Such children should be admitted in Dedicated Covid Hospital/ Secondary/ Tertiary level healthcare facility
- Few children may require HDU/ICU care & should be assessed for;
 - thrombosis, hemophagocytic lymphohistiocytosis (HLH) & organ failure

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SEVERE COVID-19 CASES (2/4)



Investigations: Complete blood counts, liver and renal function tests, Chest X-ray



Treatment: Intravenous fluid therapy

- Corticosteroids: Dexamethasone 0.15 mg/kg per dose (max 6 mg) twice a day. Equivalent dose of methylprednisolone may be used for 5-14 days depending on clinical assessment
- Antiviral agents: Remdesivir granted for EUA*, to be used in a restricted manner within three days of onset of symptoms after ascertaining that child's renal & liver functions are normal & to be monitored for side effects
- Suggested doses (body weight based):
 - >40 kg: 200 mg on 1st day then 100 mg once daily for 4 days
 - 3.5 to 4 kgs: 5mg/kg on the 1st day, 2.5 mg/kg once daily for 4 days
 - No role of Hydroxychloroquine, Favipiravir, Ivermectin, lopinavir/ritonavir, Umifenovir

**Emergency Use Authorization*

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SEVERE COVID-19 CASES (3/4)



Children may need organ support in case of organ dysfunction; e.g. Renal Replacement Therapy



Management & Treatment of Acute Respiratory Distress Syndrome (ARDS):

- Mild ARDS: High Flow Nasal Oxygenation, Non-invasive ventilation may be given

- Severe ARDS: Mechanical ventilation may be given with low tidal volume

- If the child does not improve clinically even then, may consider (if available) High Frequency Oscillatory Ventilation, Extracorporeal Membrane Oxygenation

- Awake prone position may be considered in older hypoxemic children if they tolerate.

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SEVERE COVID-19 CASES (4/4)



If the child develops septic shock or myocardial dysfunction then he/she may require:

- Crystalloid bolus administration: 10 to 20 ml/kg over 30 to 60 minutes; be cautious if cardiac dysfunction is there

- Early inotrope support with monitoring of fluid overload like any other cause of shock

MANAGEMENT OF MIS* IN CHILDREN & ADOLESCENTS TEMPORALLY RELATED TO COVID-19

*Multisystem Inflammatory Syndrome



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DIAGNOSTIC CRITERIA (1/2)



Children and adolescents, 0–19 years of age with fever ≥ 3 days AND two of these:

- Rash or bilateral non-purulent conjunctivitis or muco-cutaneous inflammation signs

- Hypotension or shock

- Rash or bilateral non-purulent conjunctivitis or muco-cutaneous inflammation signs

- Evidence of coagulopathy (by PT, PTT, elevated d-Dimers)

- Acute gastrointestinal problems (diarrhoea, vomiting, or abdominal pain)

AND _____

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*Multisystem Inflammatory Syndrome



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DIAGNOSTIC CRITERIA (2/2)



Elevated markers of inflammation such as ESR, C-reactive protein, or procalcitonin

AND _____



No other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes

AND _____



Evidence of COVID-19 (RT-PCR, antigen test or serology positive), or likely contact with patients with COVID-19



Investigations: as listed above in criteria and investigations to rule out common differential diagnoses

MANAGEMENT OF MIS*

IN CHILDREN & ADOLESCENTS TEMPORALLY RELATED TO COVID-19

*Multisystem Inflammatory Syndrome



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TREATMENT

(1/3)



Drugs to be used in case the child has cardiac dysfunction, shock, coronary involvement, multi organs dysfunction

- Steroids: Methylprednisolone
1 to 2 mg/kg per day
- Intravenous Immunoglobulin
2 g/kg over 24 to 48 hours
- Antimicrobials



The child needs appropriate supportive care, preferably in ICU. In absence of cardiac dysfunction, shock, coronary involvement, multi organs dysfunction, one may use steroids or IVIG

MANAGEMENT OF MIS*

IN CHILDREN & ADOLESCENTS TEMPORALLY RELATED TO COVID-19

*Multisystem Inflammatory Syndrome



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TREATMENT

(2/3)



If the child does not improve with the above treatment or deteriorates, options include:

- Repeat IVIg
- High dose corticosteroid (Methylprednisolone 10 to 30 mg/kg/day for 3 to 5 days)
- Aspirin: 3 mg/kg/day to 5 mg/kg/day max 81 mg/day (if thrombosis or Coronary Aneurysm Score is >2.5)
- Low Molecular Weight Heparin (Enoxaparin):
 - 1 mg/kg twice daily subcutaneously
 - Clotting Factor Xa should be between 0.5 to 1 (if patient has thrombosis/Coronary aneurysm score > 10 or LVEF < 30%)

MANAGEMENT OF MIS*

IN CHILDREN & ADOLESCENTS TEMPORALLY RELATED TO COVID-19

*Multisystem Inflammatory Syndrome



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TREATMENT

(3/3)

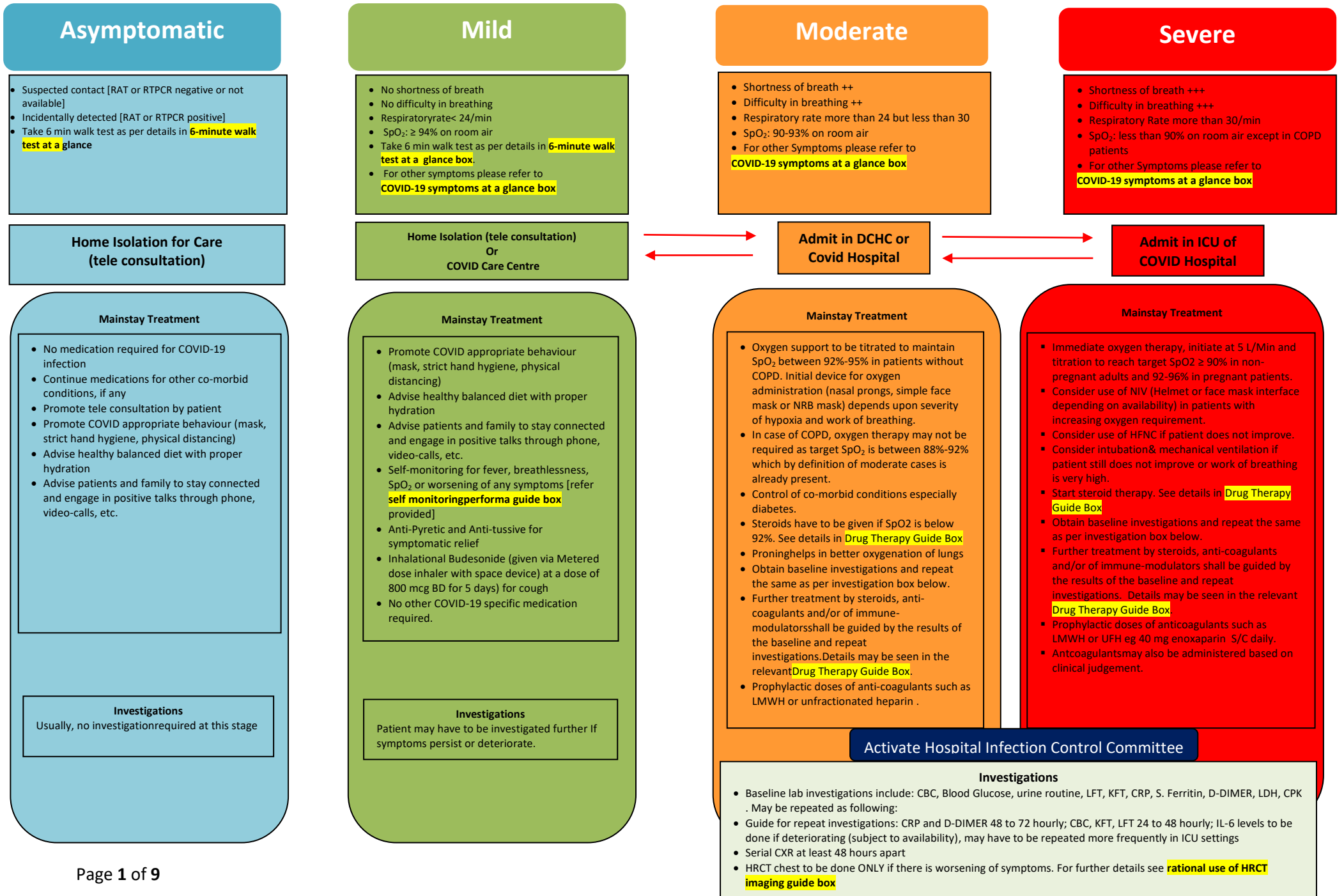


Steroids have to be tapered over 2 to 3 weeks while monitoring inflammatory markers



For children with cardiac involvement,

- Repeat ECG 48 hourly & repeat ECHO at 7 to 14 days and between 4 to 6 weeks
(and after 1 year if initial ECHO was abnormal)





COVID-19 Symptoms at a glance box

Symptoms*	Asymptomatic	Mild	Moderate	Severe
• Fever	✗	+	++	+++
• Cough	✗	+	+	++
• Sore Throat/Throat irritation	✗	+	+/-	+/-
• Body ache/ Headache	✗	+	+	++
• Malaise/Weakness	✗	+	+	++
• Diarrhoea or gastro-intestinal upset	✗	+	+	+
• Anorexia/ Nausea/ Vomiting	✗	+/-	+/-	+/-
• Loss of Smell and/or Taste	✗	+/-	+/-	+/-
• Shortness of breath/breathlessness	✗	✗	++	+++
• Respiratory rate/min	12-16	May be raised but less than 24	24-30	≥ 30/min
• SpO ₂ on room air	≥95%	≥ 94%	90%-93%	< 90%

* The possible symptoms, signs and findings have been enlisted and patients in each category may have one or many of these.



Self-Monitoring Performa guide box

Monitoring Sheet for Covid-19 Patients at Home

Name: _____ Age: _____ Sex: _____ Date: _____

Co-morbid conditions, if any and drugs being taken: _____ Controlled: (Y/N) _____

1.;

2.;

3.;

4.;

Parameters and record:

Day/time	Malaise*	SOB**	Temp	Pulse	BP	SPO2***	Any other
8:00 AM							
12:00 Noon							
4:00 PM							
8:00 PM							

*Malaise: means feeling of unwellness
 **SOB: Shortness of breath/breathing difficulty/breathlessness (may be recorded as Yes/No)
 ***SPO2: Oxygen levels to be measured by pulse oximeter

Take a 6-minute walk test as given in the 6-minute test at a glance box



6 - Minute walk test at a glance box

How to conduct a 6-minute walk test?

- ❖ A 6-minute walk test is an established simple clinical test to assess cardio-pulmonary exercise tolerance. This test is used to unmask hypoxia.
- ❖ Patient with pulse oximeter attached to his finger is asked to walk in the confines of his room for 6 minutes continuously.
- ❖ Any drop in saturation below 94%, or an absolute drop of more than 3% to 5% or feeling unwell (lightheaded, short of breath) while performing the test or at end of 6 minutes are significant findings. Such patients are labelled as positive for 6-min walk test.
- ❖ Patients with positive 6-minute walk test may progress to become hypoxic and hence early admission to hospital [for observation and oxygen supplementation] is recommended.
- ❖ The test can be repeated every 6 to 8 hours of monitoring in home setting.
- ❖ It should not be done in patients older than 70 years, those with uncontrolled asthma, pregnant patients.



COVID-19 Treatment/What-to-do at a glance box

Do's/Treatment	Asymptomatic	Mild	Moderate	Severe
Wearing Mask	✓	✓	✓	✓
Physical distancing	✓	✓	✓	✓
Hand hygiene	✓	✓	✓	✓
Cough etiquettes	✓	✓	✓	✓
Anti-pyretic (PCM)	✗	✓	✓	✓
Anti-tussive SOS	✗	✓	✓	✓
Inhalational Budesonide	✗	✓	✗	✗
Oxygen Support#	✗	✓	✓	✓
Anti-inflammatory/ Immunomodulatory therapy#	✗	✗	✓	✓
Anticoagulation#	✗	✗	✓	✓
Monitoring (CXR/ HRCT/ Lab investigations)*#	✗	✗	✓	✓

*Please see detailed guidelines for HRCT

To be done in hospital setting as per the guidance of treating physician.



COVID-19 Management: EUA/Off Label Drugs use at a glance box

Emergency Use Authorisation (EUA)/ Off label use (based on limited available evidence and only in specific circumstances)

Guidelines for use of Remdesivir

1. Remdesivir is reserved drug approved by DCG (I) under Emergency Use Authorization only based on limited scientific evidence globally. It is to be used only in select moderate/ severe hospitalised COVID-19 patients on supplemental oxygen within 10 days of onset of disease.
2. It is not indicated in mild COVID-19 patients who are in home care/ COVID Care Centres.
3. Physicians are advised to exercise extreme caution in using remdesivir as this is only an experimental drug with potential to harm.

Further, the following additional steps are recommended to stop misuse of Remdesivir:

- ❖ It must be advised by senior faculty members/ specialists directly involved in patient's care.
- ❖ If it has to be advised/ ordered during odd hours, it should be done by the duty doctor after telephonic consultation with a senior faculty member/ specialist/ unit in - charge.
- ❖ Advise/ order for Remdesivir must be written and bear the name, signature and stamp of the concerned doctor.
- ❖ Every hospital needs to set up Special Drug Committee (SDC) which must review use of Remdesivir in their hospital periodically. It would be preferable to have a Pharmacology Professor/ faculty as a member of the SDC wherever available.
- ❖ The Special Drug Committee should share their findings with the clinicians periodically to ensure rational and judicious use of Remdesivir.
- ❖ It should be procured and provided by the hospitals only; the patient's attendants/ relatives should not be asked to procure Remdesivir from retail market.

Guidelines for use of Tocilizumab

- ❖ Tocilizumab is an immunosuppressant drug and it has been approved by DCG (I) for use as an off-label drug***ONLY** in severe and critically ill patients of COVID-19 meeting following conditions:
 - If the patient shows no signs of improvement in terms of oxygen requirement even after 24-48 hours of administration of steroids, and
 - Has significantly raised inflammatory markers (C-Reactive Protein ≥ 75 mg/L)
- ❖ However, it must be ensured that the patient is free of any bacterial/ fungal/ tuberculous infection at the time of administration of Tocilizumab.
- ❖ Dosage: single dose of 8 mg/kg body weight (not more than 800 mg) in 100 ml normal saline over one hour.

* Off-label use is the use of pharmaceutical drugs for an indication, age group, dosage, or route of administration that is not approved by the regulatory agencies and is not mentioned in the prescribing information for the drug.



COVID-19 Management: Use of steroids and anti-coagulants guide box

Guidelines for use of Steroids

- **Steroids are not indicated and are harmful in asymptomatic and mild cases of COVID-19.**
- Steroids are indicated in only hospitalized moderately severe and critically ill COVID-19 cases.
- Steroids should be used at the **Right Time, in Right dose and for Right duration**
- Self-medication of steroids must be avoided.
- **Recommended dose:**
 - Dexamethasone 6mg IV once daily or per oral for initially for 10 days or till the time of discharge whichever is earlier, based on clinical judgement on daily basis.
 - Equivalent glucocorticoid dose may be substituted (if dexamethasone is unavailable) by methylprednisolone 32 mg orally or 40 mg I/V or 50 mg hydrocortisone intravenously every 8 hours or Prednisone 40 mg (per oral).
- Monitoring of blood glucose is mandatory in all patients put on steroids as it may precipitate hyperglycaemia. In any case, COVID-19 infection and its treatment are likely to precipitate diabetes in previously normal individuals or worsen diabetes in known cases
- It must be also remembered that steroids may prolong viral shedding, and hencecaution is required.

Guidelines for use of Anti-coagulants

- **Moderate cases:**
 - Prophylactic doses to be used in moderate cases of COVID-19 with un-fractionated heparin or low molecular weight heparin (weight based e.g., Enoxaparin 0.5 mg/kg per day SC OD).
 - There should be no contraindication or high risk of bleeding.
- **Severe cases:**
 - Prophylactic doses to be used in severe cases of COVID-19 with un-fractionated heparin or low molecular weight heparin (weight based e.g., Enoxaparin 0.5 mg/kg per day SC OD), therapeutic dose to be used only if there is evidence of thromboembolism.
 - There should be no contraindication or high risk of bleeding.



COVID-19 Management: Rational use of HRCT imaging guide box

High-resolution CT (HRCT) scan of chest provides better visualization of the extent and nature of lung involvement in patients with COVID-19. However, any such additional information gained from HRCT scan of chest often has little impact on treatment decisions. At present, treatment decisions are based almost entirely on clinical severity and physiological impairment. Therefore, treating physicians should be highly selective in ordering HRCT imaging of Chest in patients of COVID-19.

Why routine HRCT imaging of chest in COVID-19 patients is NOT recommended?

- Nearly two-thirds of persons with asymptomatic COVID-19 have abnormalities on HRCT chest imaging which are nonspecific. Most of them do not progress clinically.
- HRCT imaging of chest done in the first week of illness might often underestimate the extent of lung involvement, giving a false sense of security.
- Correlation between extent of lung involvement by HRCT imaging of chest and hypoxia is imperfect. Often, young individuals with extensive lung involvement will not develop hypoxia, while elderly individuals with minimal/ less extensive lung involvement are likely to develop hypoxia.
- Radiation exposure due to repeated HRCT imaging may be associated with risk of cancer later in life.

Situations when HRCT imaging of Chest should not be done:

- HRCT scan chest should not be done for the purpose of diagnosing/ screening Covid-19 infection. Diagnosis of Covid-19 should be done only by using approved laboratory tests as recommended by the ICMR.
- It is not indicated in asymptomatic and mild cases of COVID-19.
- It is not required to initiate treatment in COVID-19 patients with hypoxia and an abnormal chest radiograph.
- It is not required to assess response to treatment. More often, the lung lesions show radiological progression despite clinical improvement.

Appropriate indications for HRCT imaging of chest in COVID-19 patients:

- Suspected and confirmed cases of moderate COVID-19 who continue to deteriorate clinically even after initiation of appropriate therapy especially when there is high risk of invasive fungal infection.
- Treating Physician/ Intensivist may consider HRCT chest depending on clinical assessment of the patient.

In view of the above, treating physicians should exercise caution while advising HRCT imaging of chest.



COVID-19 Management: Managing Mucormycosis guide box

What is Mucormycosis?

Mucormycosis is a fungal disease which occurs in patients with the underlying conditions and predisposing factor such as diabetes mellitus, rampant misuse/overuse of steroids, malignancies, organ transplantation etc. Mode of infection is through inhalation of fungal spores from air. It is not contagious.

Time of presentation: variable but usually around 3rd week of onset of symptoms of COVID-19.

Reasons for increase in Mucormycosis in COVID-19 patients

1. Uncontrolled hyperglycemia due to any reason
2. Misuse, overuse and irrational use of steroids.
3. Prolonged ICU stay, unhygienic humidifiers and irrational use of broad spectrum antibiotics may also be associated with mucormycosis
4. Pre-existing co-morbidities such as haematological malignancies, use of immunosuppressants, solid organ transplant etc.

Signs and symptoms:

1. Facial pain, pain over sinuses, pain in teeth and gums
2. Paraesthesia / decreased sensation over half of face.
3. Blackish discolouration of skin over nasolabial groove/ alae nasii.
4. Nasal crusting and nasal discharge which could be blackish or blood tinged.
5. Conjunctival injection or chemosis.
6. Periorbital swelling.
7. Blurring of vision/ diplopia.
8. Loosening of teeth
9. Discoloration (pale) of palate/ turbinates insensitive to touch, eschar over palate
10. Worsening of respiratory symptoms, haemoptysis, and chest pain; headache, alteration of consciousness and seizures etc

Diagnosis:

- KOH mount and microscopy, histopathology of debrided tissue (presence of Ribbon like aseptate hyphae 5-15 μ thick that branch at right angles). Culture (don't wait for results to initiate therapy as mucormycosis is an emergency).
- Relevant radiological Investigations such as CT of sinuses, CT chest for suspected pulmonary involvement (presence of more than 10 nodules, reverse halo sign, CT bronchus sign, pleural effusion-highly suggestive of mucor), MRI brain etc to see the extent of systemic involvement

Management:

- One should have a high index of suspicion of invasive fungal infection such as Mucormycosis in the presence of predisposing conditions as mentioned above. Timely initiation of treatment reduces mortality. Multidisciplinary Team approach is required. Treatment of Mucormycosis involves combination of surgical debridement and antifungal therapy.
- **Liposomal Amphotericin B** in initial dose of 5mg/kg body weight (10 mg/kg body wt in case of CNS involvement) is the treatment of choice. It should be diluted in 5% dextrose, it is **incompatible** with normal saline/ Ringer Lactate. It should be given over 2-3 hours and should be started with full dose from day 1. Monitoring for kidney function tests and serum electrolytes is recommended. It has to be continued till a favourable response is achieved and disease is stabilized which may take 3-6 weeks following which step down to oral Posaconazole (300 mg delayed release tablets twice a day for 1 day followed by 300 mg daily) or Isavuconazole (200 mg 1 tablet 3 times daily for 2 days followed by 200 mg daily) shall have to be taken for prolonged period as per advice of the physician..
- The therapy has to be continued until clinical resolution of signs and symptoms of infection as well as resolution of radiological signs of active disease and elimination of predisposing risk factors such as hyperglycemia, immunosuppression etc., It may have to be given for quite long periods of time.
- Conventional Amphotericin B (deoxy cholate) in the dose 1-1.5mg/kg may be used if liposomal form is not available.
- Kidney Functions must be monitored during the entire management period.

1st June, 2021

**Government of India
Ministry of Health & Family Welfare**

Clinical Guidance on Diagnosis and Management of Diabetes at COVID-19

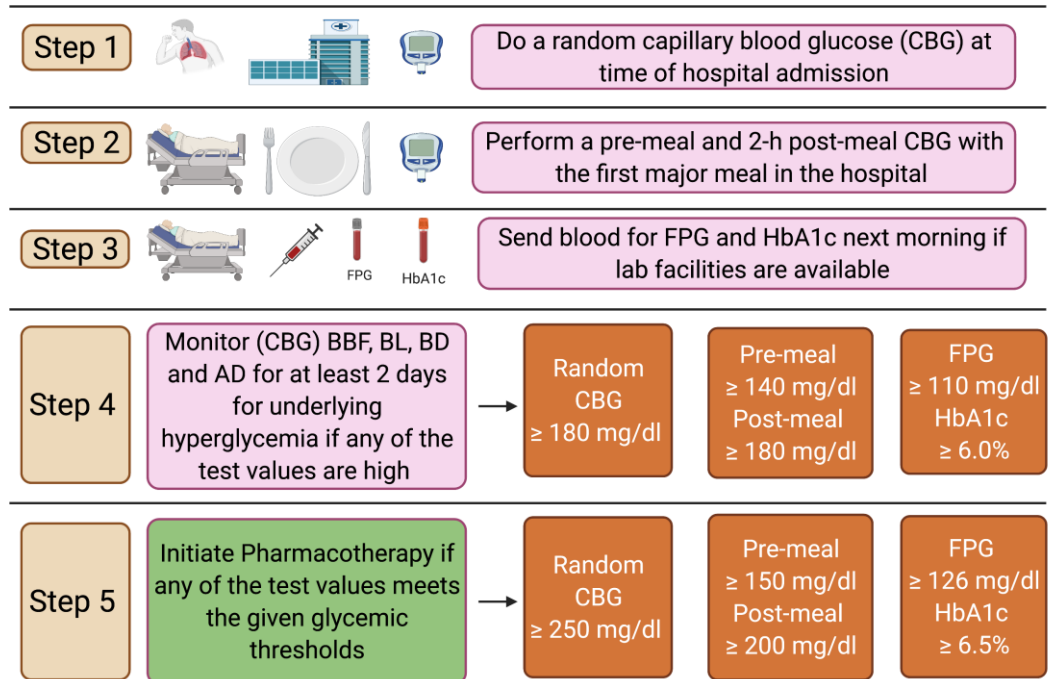
Patient Management facility.

Version 2.0.

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.**

A suggested algorithm for screening of hyperglycemia in patients admitted to a COVID care facility

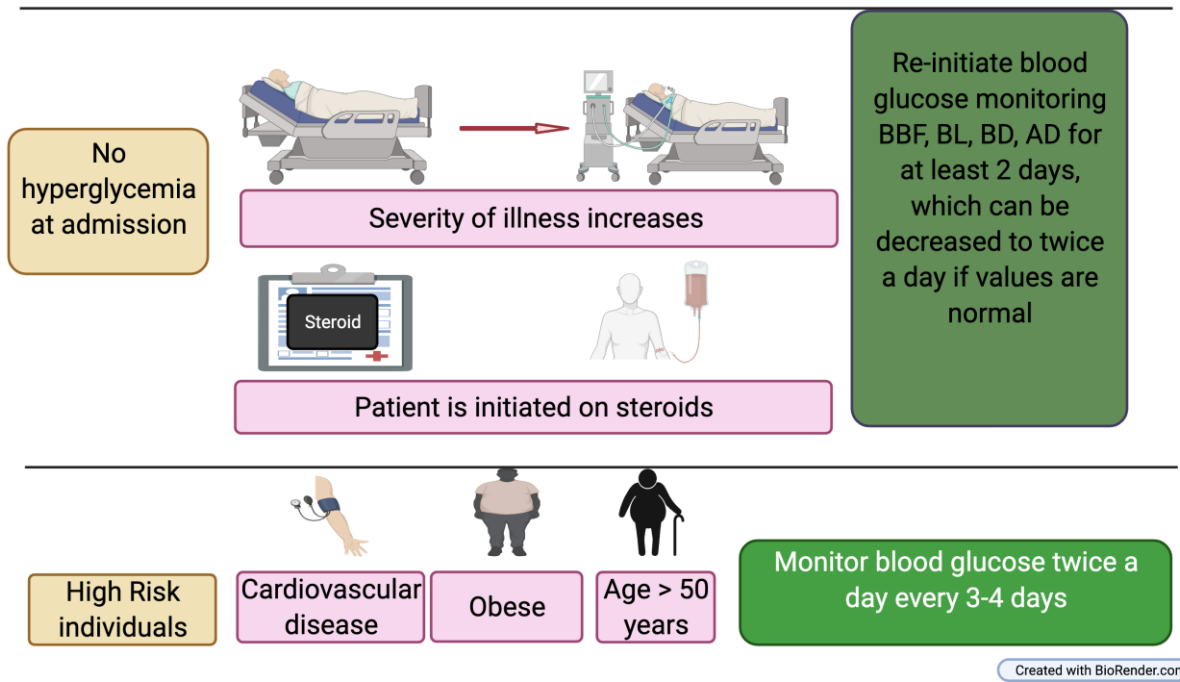


Created with BioRender.com

Abbreviations: BBF: Before breakfast, BL: Before lunch, BDN: Before dinner, ADN: After dinner

- We have suggested three steps (Step 3 if lab facilities are available) for screening of undiagnosed hyperglycemia in initial 24 hours of admission.
- If BG level is ≥ 250 mg/dl, check urine/blood ketone levels →if positive, immediately consult endocrinologist/physician.
- Start “**Diabetic Diet**” if the values are higher than the cut-offs given in Step 4
- Start “**Pharmacotherapy**” if the values are higher than the cut-offs given in Step 5.
- FPG ≥ 126 mg/dl and/or HbA1c $\geq 6.5\%$ (lab values) are diagnostic of Diabetes Mellitus
- 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) [see figure given below]
- **High RBG at admission and outcomes in COVID-19:** Coppelli et al explored its association with mortality in patients hospitalized for coronavirus disease 2019 (COVID-19). They found that RBG ≥ 140 mg/dl was found in 24.3% of patients. Mortality was greater in patients with RBG ≥ 140 mg/dl (39.4% vs. 16.8%; unadjusted hazard ratio [HR] 2.20, 95% CI 1.27-3.81, $P = 0.005$) than in patients with RBG < 140 mg/dl (16.8%) and even higher than seen in patients with known diabetes (28.6%; 1.73, 0.92-3.25, $P = 0.086$). The study was published in Diabetes Care “Hyperglycemia at hospital admission is associated with severity of the prognosis in patients hospitalized for COVID-19: The Pisa COVID-19 Study”

Blood glucose monitoring strategy for individuals with no evidence of stress hyperglycemia or undiagnosed diabetes at the initial screen



- A patient with normal initial glycaemic profile may develop stress hyperglycemia during the course of illness, especially if COVID severity increases. Besides, institution of glucocorticoids for treatment of primary disease may also contribute to hyperglycemia in such an individual. Thus, glycaemic assessment should be an ongoing dynamic process and not a one-time event

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]

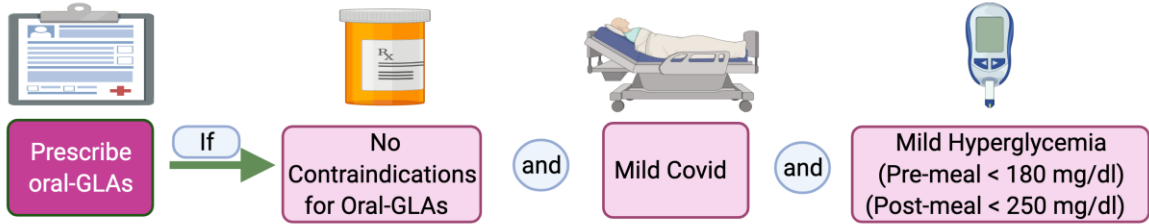
2B: To initiate OAD in patients newly detected to have diabetes at admission

(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 Teneligliptin 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)
- D. Do not initiate drugs like pioglitazone and SGLT2 inhibitors in patients with COVID.
- E. In moderate to severe COVID, stop pioglitazone and SGLT2 inhibitors if patient is already taking them. (See figure given below)

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

Guidance on the use of oral glucose lowering agents (Oral-GLAs)



Relatively Safe	Caution	Stop if disease severity increases Do not initiate if patient is not on these drugs
<p style="text-align: center;">DPP-4 inhibitors</p> <p>Vildagliptin/ Teneligliptin Sitagliptin/ Linagliptin</p>	<p style="text-align: center;">Metformin</p> <p>Risk of lactic acidosis if moderately to severely ill with hemodynamic instability or hypoxia</p> <p style="text-align: center;">Sulfonylureas</p> <p>Risk of hypoglycemia if oral intake is poor or with concomitant use of insulin therapy</p>	<p style="text-align: center;">SGLT-2 Inhibitors</p> <p>Increase risk of dehydration and euglycemic ketoacidosis</p> <p style="text-align: center;">Pioglitazone</p> <p>Risk of fluid retention and edema; contraindicated in cardiac or hepatic dysfunction</p>

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 30 min before breakfast, 6 units SC 30min before lunch and 6 units SC 30 min 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 → 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 → 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 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

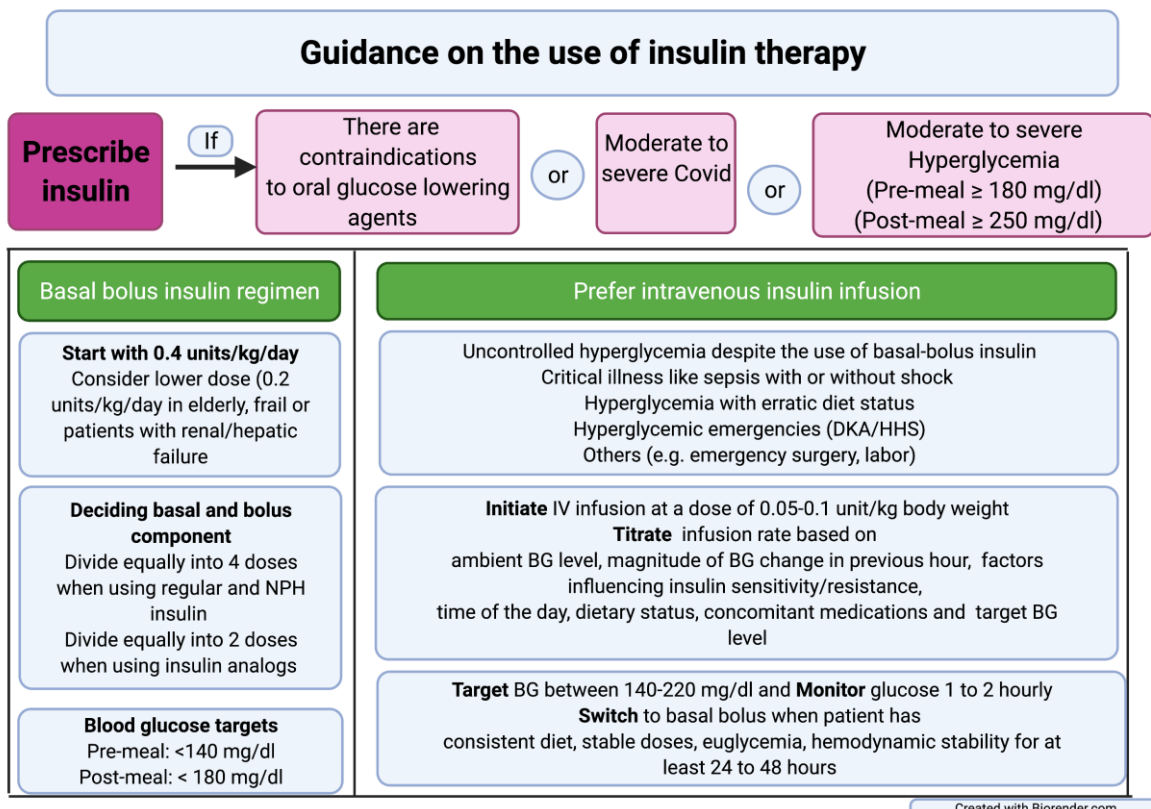
A. Like standard meals, RT feeds should be divided into 3 major and 3 minor feeds. Major and minor feeds are defined by calories/quantity of feeds. (Example: major feed: 300ml each and minor feed: 150 ml each)

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 (See figure given below).



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.

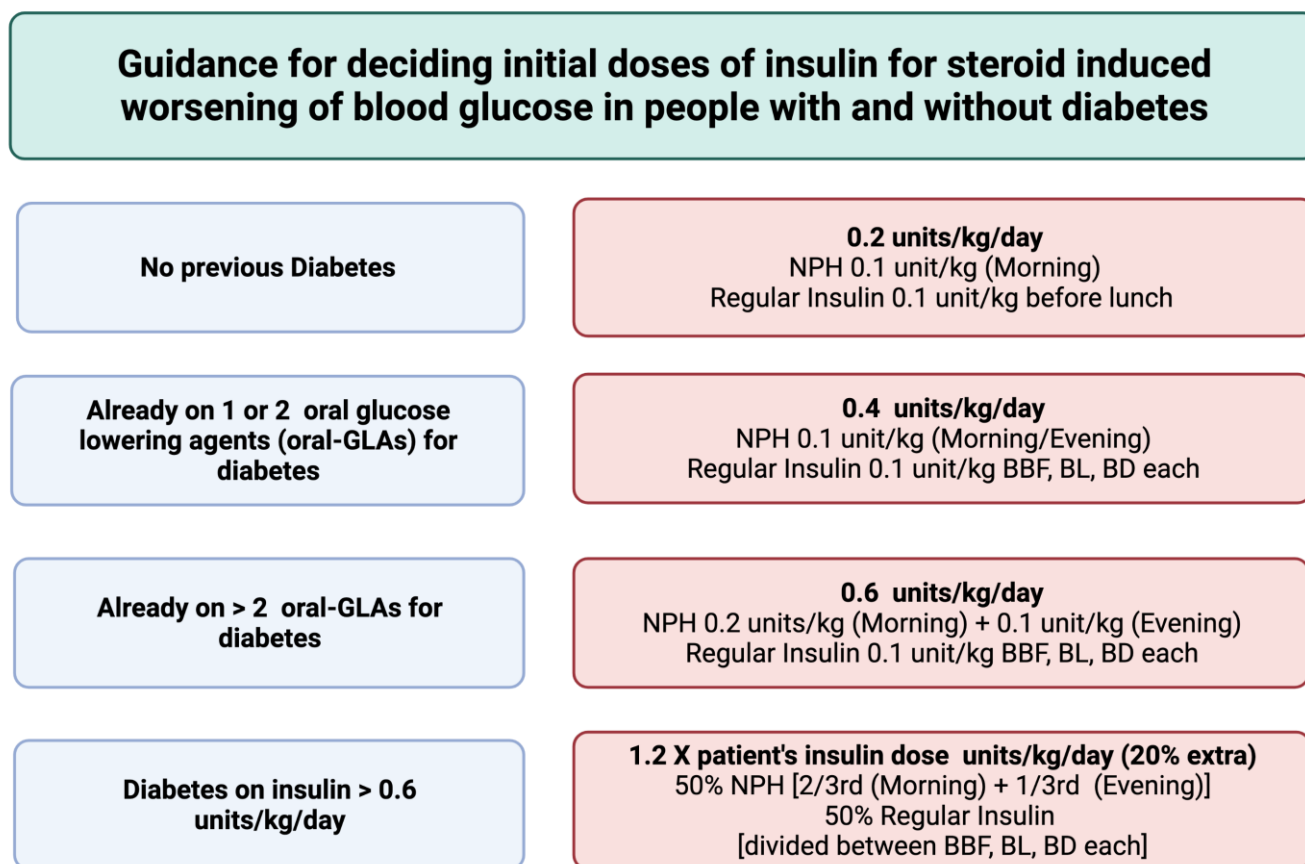
Example: At lunch (or major feed # 2), if at a dose of 6 units (Inj. Regular insulin), pre-meal to post-meal BG increment was 80 mg/dL (refer to table 1, date: 22/6/2020 and 23/6/2020), the insulin dose can be increased to 8 units (Inj. Regular insulin) from the next day provided the insulin injection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

Guidance on approximate doses required in different scenarios when steroids are used is provided in the figure given below. The doses of insulin will vary depending upon steroid type, dose and frequency of administration.



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: Blood glucose log

Blood glucose Log

Date		BBF	ABF	BL	AL	BD	AD	3am
	Glucose							
	Insulin							
	Steroid							
	Glucose							
	Insulin							
	Steroid							
	Glucose							
	Insulin							
	Steroid							
	Glucose							
	Insulin							
	Steroid							
	Glucose							
	Insulin							
	Steroid							

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)- despite use of subcutaneous insulin. 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: Infusion rate (units/hr) = 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. A guidance on use of insulin regimens in different scenarios is provided in figure given below.
4. Gliptins: Sitagliptin, Teneligliptin, Vildagliptin, Linagliptin
5. 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

Suitable Insulin regimens for various situations

Insulin regimens	Situations
Basal Bolus	3 doses of prandial regular insulin + 1 or 2 doses of NPH insulin. Suited for patients with moderate-severe hyperglycemia who have a regular diet pattern and experience prandial excursion with each meal
Basal plus	1 or 2 doses of prandial regular insulin + 1 or 2 doses of NPH insulin Suited for patients with moderate-severe hyperglycemia who have a regular diet pattern and experience prandial excursion with 1 or 2 meals (like patients initiated on steroids in morning only)
Basal insulin with or without oral glucose lowering drugs	Suited for patients who have normal prandial excursions (< 50 mg/dl), but require insulin therapy for control of basal hyperglycemia
Correctional insulin with or without basal insulin	Not recommended for routine use. Should only be used in patients with erratic diet patterns, preferably with a basal insulin
Monitoring	Monitor capillary blood glucose BBF, 2 hours ABF, BL, 2 hours AL, BD and 2 hours AD for patients on Basal Bolus Monitor patients on other insulin regimens with BBF, BL, BD, and AD if 6 point monitoring is not feasible

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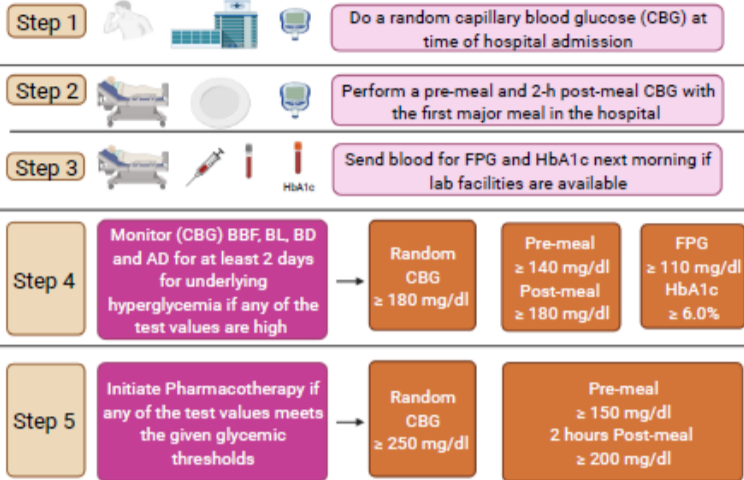
Suggested Readings

- 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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- Kelly JL. Continuous Insulin Infusion: When, Where, and How?. *Diabetes Spectr.* 2014;27(3):218-223.
- Gupta Y, Goyal A, Kubihal S, Golla KK, Tandon N. A guidance on diagnosis and management of hyperglycemia at COVID care facilities in India. *Diabetes Metab Syndr.* 2021 Jan-Feb;15(1):407-413.

A guidance on diagnosis and management of hyperglycemia at COVID care facilities in India.

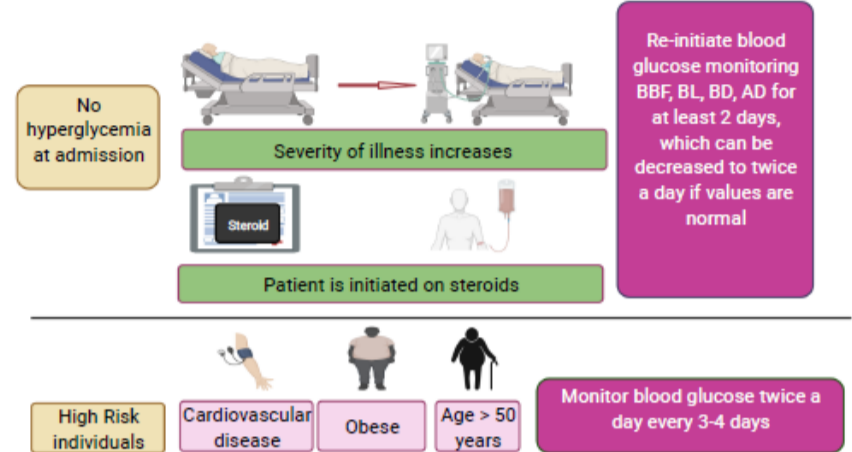
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A suggested algorithm for screening of hyperglycemia in patients admitted to a COVID care facility



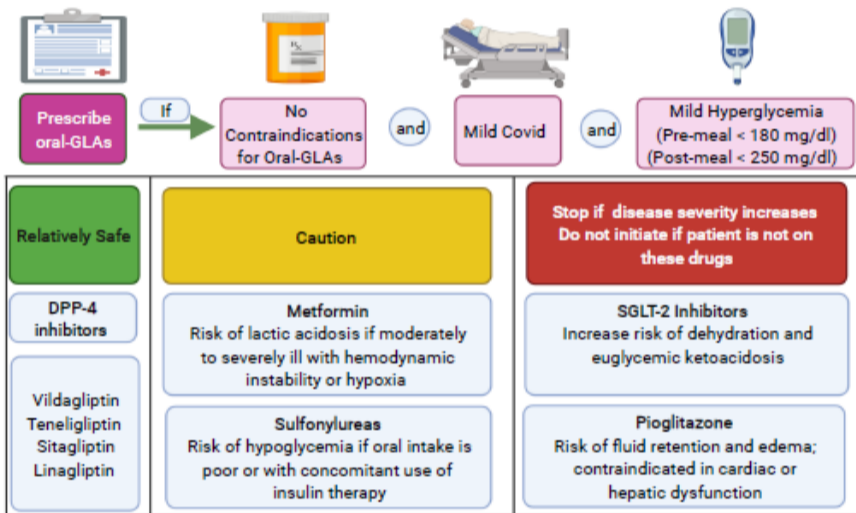
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Blood glucose monitoring strategy for individuals with no evidence of stress hyperglycemia or undiagnosed diabetes at the initial screen



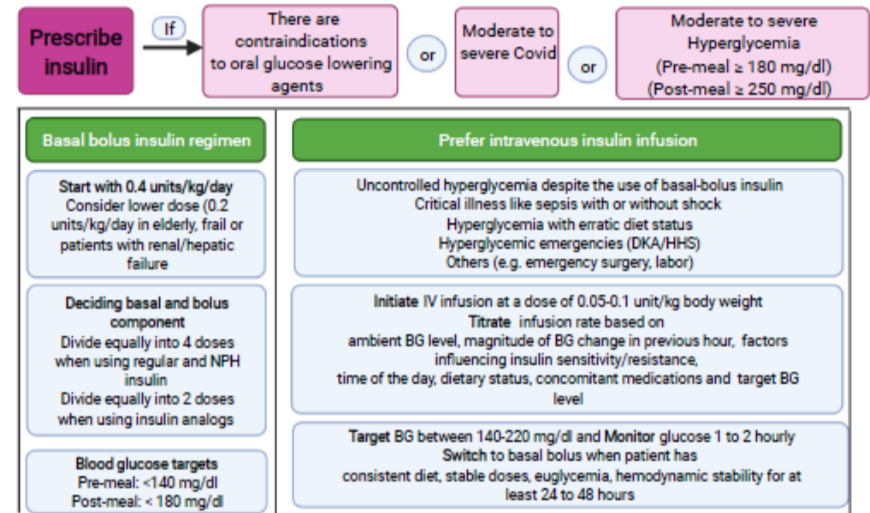
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Guidance on the use of oral glucose lowering agents (Oral-GLAs)



4

Guidance on the use of insulin therapy



5

Guidance for deciding initial doses of insulin for steroid induced worsening of blood glucose in people with and without diabetes

No previous Diabetes	0.2 units/kg/day NPH 0.1 unit/kg (Morning) Regular Insulin 0.1 unit/kg before lunch
Already on 1 or 2 oral glucose lowering agents (oral-GLAs) for diabetes	0.4 units/kg/day NPH 0.1 unit/kg (Morning/Evening) Regular Insulin 0.1 unit/kg BBF, BL, BD each
Already on > 2 oral-GLAs for diabetes	0.6 units/kg/day NPH 0.2 units/kg (Morning) + 0.1 unit/kg (Evening) Regular Insulin 0.1 unit/kg BBF, BL, BD each
Diabetes on insulin > 0.6 units/kg/day	1.2 X patient's insulin dose units/kg/day (20% extra) 50% NPH [2/3rd (Morning) + 1/3rd (Evening)] 50% Regular Insulin [divided between BBF, BL, BD each]

6

Suitable Insulin regimens for various situations

Insulin regimens	Situations
Basal Bolus	3 doses of prandial regular insulin + 1 or 2 doses of NPH insulin. Suited for patients with moderate-severe hyperglycemia who have a regular diet pattern and experience prandial excursion with each meal
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Basal insulin with or without oral glucose lowering drugs	Suited for patients who have normal prandial excursions (< 50 mg/dl), but require insulin therapy for control of basal hyperglycemia
Correctional insulin with or without basal insulin	Not recommended for routine use. Should only be used in patients with erratic diet patterns, preferably with a basal insulin
Monitoring	Monitor capillary blood glucose BBF, 2 hours ABF, BL, 2 hours AL, BD and 2 hours AD for patients on Basal Bolus Monitor patients on other insulin regimens with BBF, BL, BD, and AD if 6 point monitoring is not feasible