COVID-19
MANAGEMENT PROTOCOL
July 21
CME INDIA COVID-19 Management Protocol

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With the rapid rise in Covid-19 cases in INDIA, CME INDIA has now compiled its own guidelines with inputs from key medical experts.

The goal of this document is to help the medical community in managing the current Covid-19 situation. This document will be updated from time to time, so please check www.cmeindia.in and CME INDIA Downloads section regularly.

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3 CME INDIA
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Disclaimer

This is the **first-ever guideline by CME INDIA** on COVID-19 Management. It has been framed and reviewed by experts. As there are lots of guidelines and not all agree on the same protocol, **physicians are advised to apply their own wisdom** especially as recommendations keep changing. This guideline is especially meant to tackle **the ongoing second wave** and the expected third wave. It also contains a section on the management of pediatric cases.

Document Flow

(Best viewed using Google/Drive pdf viewer. Use below links to go to a specific part.)

- **Part 1. Challenges of COVID Management in 2021**
- **Part 2. Time is the Game Changer**
- **Part 3. Initial evaluation of a severe acute respiratory illness (SARI) case**
- **Part 4. High Alert**
- **Part 5. Management of cases**
- **Part 6. Procedure for awake self-proning**
- **Part 7. Patient selection for NIV application**
Part 8. Discharge Policy: Follow state-specific guidelines if any


Part 10. Pearls in pediatric case management

Part 11. Summary Pearls 2021

Part 12. Supplementary materials
- Six patterns of Covid Xray
- HRCT in Covid
- Do’s and Don’ts in Covid
- Diabetes and Covid
- Guideline for tackling Mucormycosis
- Post Discharge
- Treatment of Post Covid Symptoms
- Multisystem Inflammatory Syndrome in Adults

Part 13. CME INDIA Tail Piece

Third Wave Blues

- COVID-19 third wave is inevitable in late 2021, as per factual analytics.
- More youth and children might be affected.
- Severe lung inflammatory disease will be seen.
- Mortality may be more.
- More Admission Beds and ICU care will be needed.
- This updated guideline is in tune to tackle new challenges.


Be Alert for New Pattern of COVID-19

Current strains in India:

Current COVID 19 cases may be a mixture of various strains. Apart from the previously known strains, a new double mutant strain of the SARS CoV2 virus has been detected in India. This is in addition to other UK, South African, and Brazilian variants of the virus already circulating in 18 states of the country.

How variant strain cases differ from first wave:

- The new virus strain having two mutations is highly infectious and has the potential to skip the immunity developed either by natural infection or vaccines.
- That’s why it is not uncommon to see re-infection cases and cases among vaccinated people.
- Newer strains are not only more transmissible, affect the younger population, and can lead to more severe illness.
Salient Observations:

### What is New? More Mortality?

- Severe disease and death may occur even in the absence of comorbidities.
- Deterioration may be fast.
- The strain this time appears to be more virulent. (Observational opinion of few centres)
- The ICU admissions and deaths are a sensitive indicator regarding lethality.
- The worrisome thing is that the % of cases showing CT lesions are far more and the CT lesions appear more diffuse suggestive of ARDS pattern this time than during the first peak. (This is an observational personally communicated data from few centers of Maharashtra and Gujarat and other parts of the country).

1. In 2020 speculations were being made that SARS-CoV has seasonal occurrence spreading more in cold cozy days as in Italy. However, by 2021 the virus proved everyone wrong showing no favorite weather predilection.

2. Surface transmission of virus is unlikely to be a threat now as per new CDC information.

3. Possible air transmission has been proposed strongly.
Is RT PCR not relevant always in such cases?

- Ideally, RT PCR should detect COVID 19 caused by all strains, but still, some newer variants may be missed. According to WHO, some mutations like HV 69/70 have the capability to affect the RT-PCR testing as well and may go undetected in the tests. But the impact of the new mutation on the RT-PCR testing being deployed worldwide is expected to be minimal.
- It is advisable to read the full report of RT-PCR which may still show ORF gene and N gene but the S gene may not be detectable. Some laboratories may interpret these case of S gene drop out as negative.

How to diagnose such cases?

- Clinical Features, Serum Markers, and CT scan of the chest should be used for diagnosis where clinical suspicion is high if RT-PCR is negative.

Part 2. Time is the Game Changer

In the entire management of Covid, it is always important to identify the first day of Illness. It is for all management issues. The day of report of RTPCR must not be taken for all decisions.

1. Disease is most transmissible one day prior and 3 to 4 days after the first symptom.

2. For the initial 2-3 days the patient is likely to have high Fever because of high replication of the Virus but at this time innate immunity by Macrophages, Neutrophils, etc. starts mounting defense against the attack of the virus.

3. The beginning of the second week heralds the worsening of symptoms which is mainly immune-mediated inflammatory process and characterized by high-grade fever and increasing oxygen demand, hypoxia, etc. Unchecked hyper inflammation may lead to covid cytokine storm syndrome and multi-organ damage.

So, it is of utmost importance to act swiftly in the first 7 to 10 days by use of anti-inflammatory medications. And most of the current-day medications like corticosteroids, Tocilizumab, convalescent plasma work best when given in time during this phase.
Incubation Period:

- Symptoms may develop 2 days to 2 weeks following exposure to the virus.
- Current estimates of the incubation period are in the region of 4–5 days.

Timely Actions:

- Corona is not a lung disease, a systemic Thrombo - hyperinflammatory Vasculitis Disease
- The Virus is non – replicating after Day 9
- Fever > 101°F, CRP > 10 mg/L, Rapid rise of CRP, Cough on Day 3 or fall of SpO2 on six minutes walk test by 5% are suggestive of pneumonia.
- Day 5 is the the day in critical phase (Fei Z, et.al. Lancet, 2020;395 (10229):1054-62).
- Day 90 is the day when word COVID ends-Positive RTPCR beyond this period should be considered as reinfection or persistent virus shedders; as updated by CDC.
- Loss of Smell is THE symptom equal to RTPCR test
- 15 minutes the time to get the infection

- Clinical Features, Serum Markers and CT scan of Chest may be used for diagnosis where clinical suspicion is high if RT-PCR is negative.
- If RT-PCR is positive after 3 months or becomes positive after two consecutive negatives, consider possible reinfection.
- The six-minute walk test (6MWT) is useful from Day 3–6. If the patient desaturates by 5% on walking, this is indicative of pneumonia and this is considered as an emergency.
Part 3. Initial evaluation of a severe acute respiratory illness (SARI) case

The Moment You get the Patient

1. Review comorbidities, History of contact/travel/old & recent medical records including recent chest radiology if available (CO RADS 4/5 – the likelihood of COVID 19 High)
2. Assessment of Vital (SpO2, HR, NIBP, RR, etc.)
3. Send ABG if SpO2 < 94% on RA or Respiratory Distress
4. Inform consultant on duty
5. CXR PA View/Screening CT Thorax as advised by Consultant
6. Review History/Vitals/Chest Radiology & Inform Consultant on Duty
7. Shift Patient to Isolation Facility/Holding Area
8. SARS-COV-2 PCR testing for all suspect cases/family members

Recognizing Day 1

Frequently reported signs and symptoms of patients include:
- Fever, usually low grade (77–98%)
- Cough (46%–82%) Dry throat, Dry cough
- Myalgia or fatigue (11–52%)
- Loss of smell – Nose Corona
- Loss of taste – jaggery taste – Throat Corona
- Shortness of breath (3-31%) – Lung Corona
- Happy hypoxia (spo2)
- Low hand grip strength
- 6 minute walk test :Must

Any symptom with close contact
Any 1: symptom: taste, smell loss (partial or total), left red eye
Any 2: Fever, Throat irritation, SOB, Loose Motion
Any 3: Headache, Nausea, Vomiting, Rash, Pain Below Knees, Cystitis, Anorexia, Altered sensorium
Classify COVID Patients Clinically - Table to Access Clinically:

<table>
<thead>
<tr>
<th>Clinical Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MILD</strong></td>
</tr>
<tr>
<td>SpO2</td>
</tr>
<tr>
<td>RR (min)</td>
</tr>
<tr>
<td>Symptoms</td>
</tr>
<tr>
<td>Other symptoms</td>
</tr>
<tr>
<td>Chest Xray (evaluate 3 zones in each lung upper, mid and lower zones)</td>
</tr>
<tr>
<td>CT Severity Score (on a score of 25 or % lung involvement)</td>
</tr>
</tbody>
</table>

| **MODERATE** |
| SpO2          | 90 - 94% on Room Air |
| RR (min)      | 24 - 30             |
| Symptoms      | Fever plus breathing difficulty |
| Other symptoms | |
| Chest Xray (evaluate 3 zones in each lung upper, mid and lower zones) | Pneumonia involving 1 or two zones |
| CT Severity Score (on a score of 25 or % lung involvement) | 8-15/25 or 25-50% |

| **SEVERE** |
| SpO2         | < 90% on Room Air |
| RR (min)     | > 30             |
| Symptoms     | Fever with respiratory distress |
| Other symptoms | |
| Chest Xray (evaluate 3 zones in each lung upper, mid and lower zones) | Pneumonia involving more than 2 zones |
| CT Severity Score (on a score of 25 or % lung involvement) | > 15/25 or > 50% |

Table to Access Risk Factors for Severe Disease:

<table>
<thead>
<tr>
<th>Risk Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>➤ Age &gt; 60 years.</td>
</tr>
<tr>
<td>➤ Presence of any significant comorbidities.</td>
</tr>
<tr>
<td>➤ CAD (MI, PCI, or CABG within previous 6 months).</td>
</tr>
<tr>
<td>➤ CVA within last 6 months.</td>
</tr>
<tr>
<td>➤ Heart Failure (NYHA Class 3 and 4).</td>
</tr>
<tr>
<td>➤ Chronic Respiratory Disease e.g., COPD, BA, ILD, etc.</td>
</tr>
<tr>
<td>➤ Poorly controlled bronchial asthma (daily use of salbutamol inhaler for symptoms, nocturnal symptoms, ED/hospital visit for exacerbation within 1 month).</td>
</tr>
<tr>
<td>➤ Uncontrolled Diabetes Mellitus (HbA1C ≥9% or random glucose &gt;300 mg/dl).</td>
</tr>
<tr>
<td>➤ Systemic hypertension with systolic BP ≥140 mm Hg or diastolic BP ≥90 mm Hg.</td>
</tr>
<tr>
<td>➤ Active cancer.</td>
</tr>
<tr>
<td>➤ Chronic kidney disease.</td>
</tr>
</tbody>
</table>
Decompensated chronic liver disease (Presence of edema, jaundice, ascites, encephalopathy).

Transplantation (SOT or HSCT).

On immunosuppressive treatment currently.

Morbid obesity (BMI ≥40).

Table to access need for critical care intervention any one of the following:

- Respiratory distress with difficult airway
- RR≥30, Unable to speak full sentences
- Cyanosis or SpO2<85% on room air; ABG P/F ratio <250
- Systolic blood pressure <90 despite fluid resuscitation
- Agitated, confused, (or comatose) with respiratory distress
- Early MODS: 2 or more organ failures
- CURB-65 (confusion, urea >40, RR>24, BP<90 and Age >65) score of 3 or more. CURB-65 may serve as a useful prognostic marker in COVID-19 patients, which could be used to quickly triage severe patients in primary care or general practice settings.¹
- Q SOFA score – 2 or more of HAT (Hypotension, Altered mentation, Tachypnoea)

Table to pick up Investigations (in admitted patients):

- PS with CBC. Look at RDW (Red cell distribution width) and NLR (Neutrophil Lymphocyte ratio)
- CRP, LDH
- LFT, KFT, RBS, HbA1c & Urine R/M (HbA1C as a clear predictor of COVID-19 severity shown in few studies)²
- ABG
- Blood culture (Minimum two set of Blood Cultures), S. PCT
- Sputum gram stain and C/S (After RT PCR Report)
- Nasopharyngeal swab for Qualitative PCR for SARS-COV2
- CXR PA view/ Screening CT Thorax if there is a diagnostic dilemma
- ECG
- D-dimer, Ferritin
- CPK-MB, NT Pro BNP, Trop I³
- PT, aPTT, INR (before initiating anticoagulation)
- Echo Doppler of Heart as we get an echo done in all elderly patients (suggested for specific cases)⁴
Haematological
- Lymphocyte count,
- Neutrophil count,
- Neutrophil–lymphocyte ratio (NLR)

Inflammatory
- C-reactive protein (CRP),
- Erythrocyte sedimentation rate (ESR),
- Procalcitonin (PCT)

Immunological
- Interleukin (IL)-6
  - IL-10
  - IL-6/IL-10 Ratio

Biochemical
- D-dimer,
- Troponin,
- Creatine kinase (CK),
- Aspartate aminotransferase (AST)
- Ferritin
- LDH

![Surrogate markers of infection](image)
- Ferritin
- LDH
- C-reactive protein (CRP) correlated to IL-6

Table showing Lab Findings in Mild/Moderate/Severe cases:

<table>
<thead>
<tr>
<th>Laboratory Findings</th>
<th>NLR</th>
<th>CRP</th>
<th>Ferritin</th>
<th>D-dimer</th>
<th>LDH</th>
<th>IL-6</th>
<th>LFT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt; 3.2</td>
<td>3.2 - 5.5</td>
<td>&gt; 5.5</td>
<td></td>
<td>20 - 40</td>
<td>&gt; 40</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt; 20</td>
<td>20 - 40</td>
<td>&gt; 40</td>
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<tr>
<td></td>
<td>&lt; 500</td>
<td>500 -800</td>
<td>&gt; 800</td>
<td>&lt; 0.5</td>
<td>0.5 - 1.0</td>
<td>&gt; 1.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt; 0.5</td>
<td>0.5 - 1.0</td>
<td>&gt; 1.0</td>
<td>&lt; 300</td>
<td>300 - 400</td>
<td>&gt; 400</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt; 5.0</td>
<td>5 - 50</td>
<td>&gt; 50, or rising</td>
<td>&lt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Normal</td>
<td>Slight Derangement</td>
<td>Moderate Derangement</td>
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</tbody>
</table>

Cut-offs for each of these are unclear and changing. The NLR appears less reliable during the second wave. However for all values, the greater the numerical value, the greater the risk for adverse outcomes.
Lab Tests are Torchbearer - Pearls in Important Lab Tests Considerations

- As per some studies, CRP can be a guide for steroid dose. Higher the CRP, use a higher dose of steroid.³ Alert: If CRP rise more than 10-fold.

(Note CRP in some cases can be because of bacterial infection, UTI, line sepsis, etc. In such cases, don't escalate steroids. Taper steroids and cover with the appropriate antibiotic. Use Procalcitonin, WBC, cultures as a guide.)

IL 6 results are very unreliable due to the following reasons:

- Lab methods are not standardized. The same sample can give different readings in different labs.
- Transport delays of the collected blood sample, temperature exposure alters IL 6 values.
- Use the same lab/assay throughout the follow-up for a patient.
- Many stable patients can erroneously have IL 6 values in hundreds or thousands too.

D DIMER is an important marker

- D DIMER is also an important marker for treatment decisions after CRP.
- All hospitalized patients should receive LMWH (e.g., Enoxaparin 40 mg daily. Start prophylactic dose LMWH (e.g., enoxaparin or equivalent) for all admitted patients.
- Start therapeutic anticoagulation (Enoxaparin 60 mg BD) for proven or strongly suspected DVT or PE till excluded on venous doppler/CTPA.
- Monitor d-dimer every 2-3 days. Patients on 60 BD, daily Hb, h/o Melena, etc. should be observed.
- At discharge, consider starting oral anticoagulant (e.g., Apixaban 2.5 mg BD or Rivaroxaban 10 mg OD for 4 weeks high-risk patients (modified IMPROVE-VTE score>4 or score>2 with d-dimer >2 times the upper limit, advanced age, underlying malignancy).

LDH - the increase in LDH is a sign of cell death

- LDH is an enzyme implicated in the conversion of lactate to pyruvate in the cells of most body tissues and increased following tissue breakdown.
- Elevated serum LDH is present in numerous clinical conditions, such as hemolysis, cancer, severe infections and sepsis, liver diseases, hematologic malignancies, and many others.
Nowadays, there was much evidence suggesting that the serum LDH levels serve as a non-specific indicator of cellular death in many diseases. An increase in LDH by 62.5 U/L has an acceptable sensitivity and high specificity for a significantly higher probability of disease progression. LDH is a potentially useful follow-up parameter in COVID-19 pneumonia, which might assist in the recognition of disease progression and thus help in risk stratification and early intervention.

Procalcitonin is a mediator of inflammation

Procalcitonin is the pro-peptide of calcitonin devoid of hormonal activity. Under normal circumstances, it is produced in the C-cells of the thyroid gland. In healthy humans, PCT levels are undetectable (<0.1 ng/mL). During severe infection (bacterial, parasitic, and fungal) with systemic manifestations PCT levels may rise to over 100 ng/mL, produced mostly by extra-thyroid tissue. PCT is a mediator of inflammation. PCT value remains within reference ranges in patients with non-complicated SARS-CoV-2 infection; any substantial increase reflects bacterial co-infection and the development of a severe form of the disease and a more complicated clinical picture. PCT in the initial days is to rule out a secondary co-infection and not to assess the severity of covid19 disease. PCT values may be influenced by pre-existing comorbid conditions, such as CKD and congestive heart failure, baseline values may be high.

Table - Practical widely available GAME CHANGER clinical/biochemical pearls

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Identification of 'day one of the symptoms' is vital in the clinical guidance of different treatment initiation in COVID-19.</td>
</tr>
<tr>
<td>2.</td>
<td>Treat the viral stage with an antiviral (like Remdesivir) in the symptomatic phase of the first nine days of symptoms.</td>
</tr>
<tr>
<td>3.</td>
<td>Treat the immune system with anti-inflammatory steroids early in the pulmonary phase or inflammatory phase to counter the immune dysregulation. The pulmonary phase appears after the viral replicable period.</td>
</tr>
<tr>
<td>4.</td>
<td>Lymphopenia is found in 80% of critically ill adult COVID-19 patients, and only 25% of patients with mild COVID-19 infection(observational) It suggests that lymphopenia may correlate with infection severity (Changes in lymphocyte populations in patients severely affected by COVID-19 indicate a low T cells count, an increase in naïve helper T cells and a decrease in memory helper T cell)</td>
</tr>
<tr>
<td>5.</td>
<td>Eosinopenia may be associated with unfavorable progression of COVID-19</td>
</tr>
</tbody>
</table>

15 CME INDIA
6. NLR has been identified as a prognostic biomarker for patients with sepsis. NLR has been shown to be an independent risk factor for severe disease. NLR ≥ 3.5 may indicate COVID-19 infection severity. NLR elevation may be due to dysregulated expression of inflammatory cytokines, an aberrant increase of pathological low-density neutrophil, and the upregulation of genes involved in the lymphocyte cell death pathway.

7. Red blood cell distribution width (RDW) of more than 14.5 is a simple marker for progression.

Part 4. High Alert

Be vigilant

- Fever > 101°F with drugs or > 103°F without anti-pyretics.
- Persistent cough starting after day 3.
- Sudden onset of shortness of breath (or exertional SOB).
- Rapid rise in CRP (>10 mg/L).
- More than 50% lung involvement on CT (13/25 score).
- Altered sensorium.

Think again

- Clinicians should be aware of the potential for some patients to rapidly deteriorate 1 week after illness onset.
- The median time to Covid-19 associated acute respiratory distress syndrome (CARDS) ranges from 8 to 12 days.
- Lymphopenia, neutrophilia, elevated serum alanine aminotransferase and aspartate aminotransferase levels, elevated lactate dehydrogenase, high CRP, and high ferritin levels may be associated with greater illness severity.
Table - Monitoring of Mild, Moderate and Severe Cases

<table>
<thead>
<tr>
<th>COMORBIDITIES AND COMPLICATIONS</th>
<th>Treat Appropriately; seek expert opinion where needed</th>
</tr>
</thead>
</table>

| MONITORING (Decide based on clinical status; stated timings are for guidance) |
|---------------------------------|-----------------------------------------------------|
| BP / HR                         | Daily                                               |
|                                 | 6th Hourly                                          |
|                                 | 4th Hourly                                          |
| RR / WOB /spO₂                  | 6th Hourly                                          |
|                                 | 2nd Hourly                                          |
|                                 | Continuously                                         |
| CBC/RFT /LFT                    | Baseline                                            |
|                                 | Every 2 Days                                         |
|                                 | Daily                                               |
| D Dimer                         | Repeat every 4 days                                  |
|                                 | Once every 4 days                                    |
|                                 | Once every 2 days                                    |
| Troponin/CK-MB                  | Repeat after 24 hours & 36 hours                     |
|                                 | Once every 2 days                                    |
|                                 | Once everyday                                        |
| ECG                             | Baseline                                            |
|                                 | Once every 2 days                                    |
|                                 | Daily                                               |
| ABG                             | Guided by clinical status                           |
| X Ray                           | Guided by clinical status                           |

Part 5. Management of cases

Mild Disease: Home Isolation

Identify

i. Symptomatic patients meeting the case definition for COVID-19

New Alert:

17 CME INDIA
- Extra-pulmonary symptoms such as vomiting and diarrhea
- Conjunctivitis
- Neurological symptoms
- Loss of smell/taste
- A fairly constant feature is disproportionate fatigue

ii. No evidence of viral pneumonia or hypoxia/SpO2 > 94% on Room Air (Many guidelines now consider mild disease if SpO2 >90%).

iii. Respiratory rate < 24/min.

iv. No need of doing CT Scan, do only if strong clinical suspicion, CT of Corads 5, in the absence of a positive RT-PCR (Covid syndrome).
CT Severity Score (On a score of 25 or % lung involvement) < 8/25 < 25%.

v. Must have an identified care giver during this period communicating with a health provider as required.

**Manage:**

i. Isolation and all COVID appropriate behaviour

ii. Monitoring
   - Check SpO2 three to four times, NIBP, HR, Temperature
   - The 6MWT will ascertain evidence of hypoxia identified by SpO2 less than 94% or an absolute drop in SpO2 by more than 3% from base line during or at end of the test. Patients over 60 years of age may have a shorter 3-minute walk test (3MWT) if they are unable to perform a 6-minute test.

iii. What to inform patients

<table>
<thead>
<tr>
<th>Monitor following things:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1)</strong>* Temperature with a clinical thermometer every 3 to 4 hours. Maintain a chart. Temperature more than 100°F for more than 5 days, in spite of tablet Paracetamol, should be informed to the doctor.</td>
</tr>
<tr>
<td><strong>2)</strong>* Look for Pulse rate, if possible, by putting fingers in the wrist below the thumb. Count the numbers for 1 minute. Check for every 3 to 4 hours. Maintain</td>
</tr>
</tbody>
</table>
a chart. More than 100 per minute for more than 5 days, in spite of Tablet Paracetamol, should be informed to the doctor.

3) Look for Respiratory rate, if possible, by putting palm on abdomen while lying straight. Check for every 3 to 4 hours. Maintain chart. More than 20 per minute for more than 5 days, should be informed to the doctor.

4) Check oxygen saturation by Pulse oximeter, every 5 to 6 hours. Ensure that oximeter fluctuations have stopped before you take the reading. Maintain chart. Less than 94% in the last three readings is an emergency.

5) Six Minute Walking Test (SMWT) is very important and you do it two times daily during regular oxygen saturation measurement. Check oxygen saturation and start walking for six minutes in a normal way, maybe inside the room, now check oxygen saturation again, If the oxygen saturation has dropped below 93% or if there is an absolute drop of more than 3% to 5%, patient is at risk and may need hospital care.

Other important advices:

- Patients may perform warm water gargles and take steam inhalation twice a day.
- Sequential change of position every 1-2 hours; supine, prone, sitting up, right lateral and left lateral.
- Continue taking medicines that you were already on for any pre-existing comorbidity - diabetes, hypertension, asthma, cancer etc. and consult a health care provider
- Support own mental wellbeing:
  - Do not watch negative news and social media posts excessively.
  - Meditate and talk with family and friends.
  - Read books.
  - Do walking and light exercises within the room
  - Have proper sleep.
- Nutritional support—high protein diet

Red flag signs (If developed likely to deteriorate):

- High-grade fever/ severe cough
- Shortness of breath (while walking, talking, sitting), tightness in chest
- Feeling of disorientation
- Slurred speech/seizures
- Unable to wake up or stay awake
- respiratory rate ≥ 24/ min
• Oxygen saturation < 94% on room air
• A low threshold should be kept for patients with high-risk factor/co morbidities
• PF ratio < 300
• Focus on 3 Lab tests
  1. Neutrophil Lymphocyte Ratio >3.2; or RDW above 14.5; or Eosinopenia (Zero eosinophilic syndrome)
  2. Raised CRP
  3. Raised D-Dimer

Note: D-dimer has been shown to increase with age, which can cause a lower specificity (i.e., more false positive tests) in older patients. So, age adjusted D dimer may be useful which can be calculated by: The formula is: Age (years) x 10 ug/L for patients > 50 years of age. Example: Patient age 88 = age adjusted d-dimer of 880 ug/L would be normal for 88 years.

Raised CRP- 5 times of ULN limit, rising CRP from baseline 3 times and D dimer - 2 times above normal limit-Need to act fast

iv. Treatment

• Rehydration.
• Antipyretic (Paracetamol) Take paracetamol tablet 650 mg every 4-6 hours if you have fever - not more than four times in 24 hours. If fever is more than 101 degrees F, do tepid sponging using tap water (not cold water or ice) or take a shower. Mefenamic acid 500mg tablet can be added if fever not subsiding. Mefenamic acid should not be used in renal compromised cases.
• Nutritional support.
• No role of Azithromycin/ Doxycycline. Note: Most of centers/experts use these drugs on personal experiences and have found them useful.
• Supportive: Anti-tussive SOS /Vitamin C 500 mg OD or 2 weeks /T. Zinc 50 mg BD for 2 weeks Vit D 2000 units once daily or 60000 IU once weekly for 4-8 weeks
• Tab Melatonin or Clonazepam if needed to allay anxiety.
• Say No to HCQs.
• No solid evidence with Ivermectin - has weak antiviral properties in high concentrations, difficult to achieve with therapeutic current doses in Pulmonary endothelium, still few state guidelines recommend. Tab Ivermectin (200 mcg/kg once a day for 3 to 5 days) may be considered in patients with high-risk features. (Avoid in pregnant/ lactating and very elderly beyond 80 years) Category: Optional.
Favipiravir is an antiviral drug with limited value, may clear the virus, but most may not need it especially those with mild disease. May be useful only in first 48 hours to 72 hours, not later. We do not recommend its use.

Category: Optional. Dose - The recommended dosage of favipiravir for adults is 1800 mg orally twice daily on 1st day followed by 800 mg orally twice daily, up to maximum of 14 days. It may ay cause elevation of liver enzymes and uric acid. Avoid around conception and in Gout.

Note: Molniperavir (800 mg twice a day for 5 day) may be available in near future which also needs early use in first week of viral replication but better data is needed.

Steroids MUST NOT be used in patients with only mild disease. Concept of starting steroid on day is detrimental and must be abandoned.

Recently Budesonide Inhalation (given via DPI/MDI with Spacer at a dose of 800 mcg BD for 5 to 7 days) to be given if fever and respiratory symptoms are persistent beyond 5 days of disease onset or even early if in High-Risk Group (PRINCIPLE Trial).

Prophylactic dose of LMWH if risk factor for thrombotic disease - Enoxaparin dose is 1mg/ kg OD not 40mg od for all or Inj Fondaparinux 2.5mg s/c OD. For Home, we prefer Apixaban 2.5 mg BD Alternatively: Tab Aspirin 75 mg (or clopidogrel 75/ mg) in high risk groups.

Anti-SARS-CoV-2 Monoclonal Antibodies\textsuperscript{23,24}

1. Casirivimab,600 mg plus Imdevimab 600 mg: Antibody cocktail- now available in India.
2. Bamlanivimab 700 mg plus etesevimab 1,400 mg: Now not recommended as use of bamlanivimab plus etesevimab has been found to increase in the proportion of the variants of concern (VOC) Gamma (P.1) and Beta (B.1.351). These VOCs have reduced susceptibility to both bamlanivimab and etesevimab.
3. Single monoclonal antibody (sotrovimab). (Casirivimab plus imdevimab and sotrovimab remain active against these variants).

We suggest the use of casirivimab/imdevimab in patients with mild to moderate COVID-19 who are at high risk for progression to severe disease.

Among hospitalized patients with severe COVID-19, we do not recommend this therapy.

But patients who are admitted to the hospital for reasons other than COVID-19, and who have mild-moderate COVID-19, may also receive this therapy. The NIH and CDC suggest that treatment decisions (including use of monoclonal antibody therapy) be made regardless of COVID-19 vaccination status.
This therapy must be initiated in highly selective high-risk patients only as per following table:

- FDA's EUA defines high-risk patients as meeting at least one of the following criteria:
  - Have a body mass index ≥35;
  - Have chronic kidney disease;
  - Have diabetes;
  - Have immunosuppressive disease;
  - Are currently receiving immunosuppressive treatment;
  - Are ≥65 years of age;
  - Are ≥55 years of age AND have cardiovascular disease, OR hypertension OR chronic obstructive pulmonary disease/other chronic respiratory disease;
  - Are 12–17 years of age AND have BMI ≥85th percentile for their age and gender based on CDC growth charts, OR sickle cell disease, OR congenital or acquired heart disease, OR neurodevelopmental disorders, for example, cerebral palsy, OR a medical-related technological dependence, for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19), OR asthma, reactive airway or other chronic respiratory disease that requires daily medication for control.

- **When to start:** Treatment should be started as soon as possible after the patient receives a positive result on a SARS-CoV-2 antigen test or a nucleic acid amplification test and within 10 days of symptom onset.

- **How to give:** The intravenous administration takes about 20 to 30 minutes. For the subcutaneous route, four syringes of 2.5 ml (2 each of Casirivimab & Imdevimab) need to be administered concurrently at four different sites on the abdomen or thigh. Patients should be monitored during the infusion and observed at least one hour after the completion of the infusion and 15-30 minutes after the subcutaneous injection.

- **How supplied:** Each pack of Antibody Cocktail (Casirivimab and Imdevimab) contains one vial of Casirivimab and one vial of Imdevimab totaling 2400 mg of the antibody cocktail (one vial of Casirivimab (1200 mg) and one vial of Imdevimab (1200 mg)). Each pack can treat two patients as the dosage per patient is a combined dose of 1200 mg (600 mg of Casirivimab and 600 mg of Imdevimab) administered by intravenous infusion or subcutaneous route. The vials need to be stored at 2°C to 8°C. If opened for the first patients’ dose, a vial can be used for the second patients’ dose within 48 hours if stored at 2°C to 8°C.
• **How much priced:** The price for each patient dose [a combined dose of 1200 mg (600 mg of Casirivimab and 600 mg of Imdevimab)] will be INR 59,750 inclusive of all taxes. The maximum retail price for the multi-dose pack (each pack can treat two patients) is INR 119,500 inclusive of all taxes.

• **Alert:** Receipt of a COVID-19 vaccine should be deferred for at least 90 days in those who have received anti-SARS-CoV-2 monoclonal antibodies.

**Moderate Disease**

**Identify**

i. **Respiratory rate > 24/min.**

ii. **SpO2 90-94% on room air (Many guidelines now consider SpO2 84-90%).**

iii. **CT Severity Score (on a score of 25 or % lung involvement) 8-15/25 or 25-50%**

**Manage:**

i. **Admit in ward**

ii. **Oxygen Support:**
   - Target SpO2: 92-96% (88-92% in patients with COPD).
   - Preferred devices for oxygenation: O2 face mask in most as it can deliver around 40 to 60 % oxygen at 6 to 10 L/min.
   - Awake proning may be used in those with persistent hypoxia despite use of high flow oxygen (sequential position changes every 1-2 hours).
iii. Laboratory and Clinical Monitoring

- Clinical Monitoring: Work of breathing, hemodynamic instability and change in oxygen requirement.
- Serial CXR and HRCT Chest (if worsening).
- Lab monitoring:
  - CRP
  - D-dimer & Ferritin 48-72 hourly
  - CBC, LFT, KFT 24-48 hourly
  - IL-6 levels to be done if deteriorating (subject to availability)

(Note: Close monitoring of SpO2 either by themselves or in a hospital/isolation centre is needed for starting Steroids rather than CRP/D-dimer/NLR monitoring).

iv. Drugs

A. Antiviral therapy

- Remdesivir (Most of the guidelines do not recommend it).
- Dose: Inj Remdesivir 200 mg IV on day 1.
- Then, 100 mg IV daily for 4 days (can be extended up to 10 days in case of progressive disease)
(Use based on limited available evidence and case to case basis only).

- **Explain** - Only reduces days of hospitalization without significant improvement in mortality rates.
- **Start Early** - Using this agent after 10 days of symptom onset has no benefits.
- **Reserve** - Best reserved for moderate disease (respiratory rate > 24 < 30 and Fever & oxygen saturation below 92) within first 5 to 7 days of symptom onset.
- **Safety** - One should remember that drug is not a safe drug especially in presence of moderate to severe liver or renal disease.
- **Hospitalize** - Strictly not to be given at HOME.

**B. Convalescent plasma (CP)**

- It may be considered in carefully selected patients, but all standard guidelines do not recommend it.

**C. Anti-inflammatory or immunomodulatory therapy**

- Inj. Dexamethasone 6 mg IV OD or Oral dexamethasone 6 mg OD for 5-10 days or inj. Methyl Prednisolone 0.5 -1 mg/kg ≈ 60mg OD x 5 -10 Days Stop or taper if significantly better.
- **Dexamethasone 1.5 mg = Methylprednisolone 8mg = Prednisolone 10 mg**. So, taking 12 mg Dexamethasone daily is equal to 64 mg methylprednisolone.
- Good to keep this in mind when prescribing steroids.
- **Anticoagulation**: Low dose prophylactic UFH or LMWH (weight based e.g., enoxaparin 0.5mg/kg per day SC). Enoxaparin dose is 1mg/ kg OD not 40 mg OD for all or Inj Fondaparinux 2.5mg s/c OD in High-Risk Group. In ESRD, Unfractionated Heparin – 5000U SC BD

**D. Consider about Antibody Cocktail (Casirivimab and Imdevimab) (Details given above).**

**E. Stay ALERT for Cytokine Storm** (on Day 7/8 of disease). During Moderate illness keep watch for:

- Unremitting fever.
- Cytopenia, Hyper ferritinemia.
- If the patient in the second week having SOB (even with previous normal CT), rising CRP above 50, CT worsening, fever onset in the second week, etc. points towards impending cytokine storm.
- Daily CRP monitoring and steroid dose adjustments are crucial here.
Remdesivir

• Consider Remdesivir in Patients who are RT-PCR positive for SARS-CoV-2, >18 yrs. Old, Pneumonia confirmed by chest imaging, Oxygen saturation of 94% or lower on room air, or a ratio of arterial oxygen partial pressure to fractional inspired oxygen (PF Ratio) of 300 mm Hg or less and were within 10 days of symptom onset.

• Remdesivir's role is in the first 10 days. Reduces symptoms duration, but no mortality benefit. CT severity score more than 8 (out of 25). Can use in patients with CT severity score less than 8 with dense consolidation (rather than GGO), high fever without raised CRP (viremia phase) especially in the elderly, and with co-morbidities even with normal CT too.

• Hospitalization is important for all age groups to initiate Remdesivir.

• Remdesivir is available through an FDA EUA for the treatment of COVID-19 in hospitalized pediatric patients weighing 3.5 kg to less than 40 kg or hospitalized pediatric patients less than 12 years of age weighing at least 3.5 kg.

Caution while using Remdesivir.

• No data exists about safety in pregnancy or during breastfeeding.

• Avoid if hepatic cirrhosis; alanine aminotransferase or aspartate aminotransferase more than five times the upper limit of normal; known severe renal impairment (estimated glomerular filtration rate <30 mL/min per 1.73 m2) or receipt of continuous renal replacement therapy, hemodialysis, or peritoneal dialysis).

• However, many centers are using Remdesivir if clearly indicated, in compensated cirrhosis patients, renally compromised patients and patients on hemodialysis with careful monitoring without any major issues.
Controversies with Early Steroid

It is **totally unscientific to start steroids** in viral replication phase. It has become a common practice in India that primary care physicians start on Day 1. This harms immensely the patient’s immune system as
viral replication is accelerated due to immune suppression. We recommend to completely avoid steroid within 7 days of illness. (Unless indicated for a specific condition).

**Steroids should be strictly avoided in:**

1. **Asymptomatic**
2. **Mild symptoms less than 7 days**
3. **CT score less than 8 with disease duration less than 5 to 7 days**
4. **Viremia phase (high fever with normal CRP and CT)**

Steroids should be used in all moderate and severe cases i.e., all patients with SPO2 less than 94 irrespective of the day of onset of symptoms. All these patients should receive 40 to 120 mg Methylprednisolone/day or dexamethasone 6mg/day.

**Role of steroid in mild Covid 19 disease:** Mild cases second week with fever, malaise, myalgia, headache, fatigue (suggestive of hyper inflammation) can use low dose such as methylprednisolone 4 to 16 mg per day (or equivalent another steroid for 5 to 7 days). This statement is based on expert opinion only.

The anti-inflammatory steroid should be initiated early in the pulmonary phase to counter the immune dysregulation. Ideal time for steroid initiation is after eighth day of symptoms, when virus has very low tendency to replicate and inflammatory response is persistent.

**Steroids Consideration: Revisited**

- The anti-inflammatory steroid should be initiated early in the pulmonary phase to counter the immune dysregulation. Ideal time for steroid initiation is after eighth day of symptoms, when virus has very low tendency to replicate and inflammatory response is persistent.
- *However, it must be emphasized that corticosteroids should not be used in mild disease, early on in the course of COVID19 illness if not indicated.*
- The overall pooled estimate (observational studies and RCTs) has shown significantly reduced mortality in the corticosteroid group.\(^{13}\)
- For patients who have significant lung involvement defined as resting SpO2 < 94 percent or a 6-minute walk test showing a drop in O2 saturation by 4% or more, patients may be initiated on Inj Methylprednisolone 0.5-1 mg per kg per day preferably in two divided dosages (or equivalent dosages of dexamethasone).
- The patient on corticosteroids can be followed up. If their oxygen requirements, inflammatory markers such as CRP are going up, the dose can be escalated to 2mg per kg
per day of Inj Methylprednisolone (or equivalent dosages of inj. dexamethasone) for a brief period till the patient stabilizes (3-5 days) and then we can taper down the dose to 1 mg per day and then to 0.5 mg per day.

- Some centers use pulse therapy with higher dosages of methylprednisolone with doses approaching 500mg-1gm methylprednisolone per day although this approach is not substantiated with multiple or large multiple trials and RCTs.
- Higher dosages of steroids are used after a meticulous exclusion of bacterial coinfection and tapered off at the earliest.
- At dosages of 0.5-1 mg per kg, methylprednisolone can be used for an extended period of 10 days or more.

**Steroid treatment right time, right drug, right dose and right duration is very important.**

- **Methylprednisolone is better than Dexamethasone and Dexamethasone is better than Prednisolone.**
- **Methylprednisolone penetrates much better into the lungs and binds much better into the glucocorticoid receptors among all steroids, so it gives best anti-inflammatory response.**
  (EVMS updated)

**Severe illness**

**Identify**

Any one of:

i. Respiratory rate > 30 /min
ii. SpO2 < 90% on room air
(Many guidelines follow <85% now)

Manage

i. **Respiratory support** Oxygen delivery by *nasal cannula*, face mask, Venturi mask, or mask with reservoir bag ± NIV*

![Maintain Target SPo2 > 90 % NRM (10 -15 lit / min)](image)

- HFNC (30 - 60 lit / min)
- NIV
- MV (ARDS Protocol)

ii. **Consider broad spectrum empirical antibiotic treatment** for possible superadded bacterial pneumonia/infection (↑S.PCT/Significant Leucocytosis/Leukopenia).

iii. **Inj Dexamethasone** 6mg iv OD or Inj Methylprednisolone 1 to 2mg/kg in 2 divided doses for 5 to 10 days in appropriate indication (Clinical worsening, Age<60, no diabetes), Dexamethasone dose could be - 0.2 – 0.4 mg/kg/day (12 – 24 mg /day).

iv. **Anticoagulation:**
- Unless contraindicated, FULL anticoagulation (on admission to the ICU) with enoxaparin, i.e., 1 mg kg s/c q 12 hourly (dose adjust with Cr Cl < 30mls/min) in those patients with a D-dimer > 3-5 X ULN and those with a rising D-dimer can be administered. Heparin is suggested with CrCl < 15 ml/min.
- In all other ICU patients medium dose anticoagulation; enoxaparin should be given as 0.5 mg/kg q 12 hourly.

v. **Inj Remdesivir** 200mg iv Day 1 Followed by 100mg IV OD (Day 2-5)
(Antivirals may be considered if duration of illness < 10-14 days)

vi. **Tocilizumab** may be considered on a case-to-case basis preferably within 24 to 48 hours of progression to severe disease. Tocilizumab (Off-label) may be considered when all of the below criteria are met:

- Severe disease.
- Significantly raised inflammatory markers (CRP &/or IL-6) are seen and not improving despite use of steroids.
- No active bacterial/ fungal infections.
- The recommended dose is 4 to 8mg/kg (with a maximum dose of 800 mg at one time) in 100 ml NS over 1 hour (dose can be repeated once after 12 to 24 hours depending on clinical response).
- IDSA conditionally suggests the use of tocilizumab among hospitalized patients with progressive severe or critical covid-19 and with elevated inflammatory markers. NIH recommends it in combination of dexamethasone if patient is experiencing a rapid respiratory decline with following criteria:
  1. Hospitalized within the last 3 days, admitted to an intensive care unit in the last 24 hours, and require either invasive mechanical ventilation, noninvasive ventilation, or high flow nasal cannula OR
  2. Hospitalized within the last 3 days, not admitted to the intensive care unit, have rapidly increasing oxygen requirements requiring either noninvasive ventilation or high flow nasal cannula, and who have increased markers of systemic inflammation.¹⁹

**If not available**

Itolizumab

Very small study - By Biocon company-30 patient study. Dose-1.6 mg/kg in 250 mL NS over 6 hours. (- 25 mg in the first hour and the remaining dose over 5 hours).

If well tolerated and improvement in patient observed, clinician has the discretion to repeat a dose (after 1 week for itolizumab or after 12 hours for tocilizumab only after expert opinion) Informed consent is mandatory.

Bevacizumab and Sarlijumab are other options.

vii. **JAK Inhibitors**: Among hospitalized adults with severe COVID-19 having elevated inflammatory markers but not on invasive mechanical ventilation, the IDSA panel suggests baricitinib rather than no baricitinib. (Conditional recommendation, Moderate certainty of evidence). Baricitinib appears to
demonstrate the most benefit in those with severe COVID-19 on high-flow oxygen/non-invasive ventilation at baseline.

Among hospitalized patients with severe COVID-19 who cannot receive a corticosteroid (which is standard of care) because of a contraindication, the IDSA guideline panel suggests use of baricitinib with remdesivir rather than remdesivir alone (Conditional recommendation, Low certainty of evidence).

Tab Baricitinib 4 mg once daily for 10 days (*Renal modification - 2mg once daily if GFR is between 30 to 60ml/ml/min, avoid if GFR < 30 ml/min) Cost: 4mg tab, 30Rs /tab.

We do recommend it.

viii. Supportive measures

- Maintain euvoelement
- If sepsis/septic shock: manage as per existing protocol and local antibiogram

ix. Monitoring

- Serial CXR, HRCT Chest (if worsening)
- Lab monitoring: CRP, D-dimer & Ferritin 24-48 hrly; CBC, LFT, KFT daily; IL-6 levels to be done if deteriorating (subject to availability)
- Clue for cytokine storm:

  Yes. We can predict. If the patient in the second week having SOB (even with previous normal CT), rising CRP above 50, CT worsening, fever onset in the second week, etc. points towards impending cytokine storm. Daily CRP monitoring and steroid dose adjustments are crucial here.

x. Critical Illness recommendations by NIH(UK)

- Hospitalized and requires oxygen delivery through High-flow Device of NIV.
- Use one of the following:
  1. Dexamethasone.
  2. Dexamethasone plus Remdesivir.
- For patients having rapidly increasing oxygen needs and systemic inflammation: Add either Baricitinib or Tocilizumab to one of the two above options.
- Hospitalized and requires IMV or EMCO.
  1. For most patients -Dexamethasone.
  2. For patients who are within 24 hours of admission-Dexamethasone plus Tocilizumab.
xi. EMCO (Extracorporeal Membrane Oxygenation)

At present there are insufficient data to recommend either for or against the use of extracorporeal membrane oxygenation in patients with COVID-19 and refractory hypoxemia.

xii. Lung Transplantation

When to consider lung transplantation for COVID-19 patients?

1. Candidates should be younger than 65 years of age. Existing experience from ECMO bridge to lung transplantation shows poor outcomes in older patients.

2. Candidates eligible for transplantation should have only single organ dysfunction.

3. Sufficient time should be allowed for lung recovery. It is in the best interest of the patient to be able to survive without a transplant given the suboptimal long-term survival rates of lung transplantation (about 60% at 5 years).

4. There should be radiological evidence of irreversible lung disease, such as severe bullous destruction or evidence of established fibrosis.

5. The patient should be awake and, in a position, to discuss and consent to his transplantation.

6. Patients should be able to participate in physical rehabilitation while on the transplantation waiting list.

7. Patients should fulfil the remaining typical criteria for transplantation. For example, adequate body-mass index and absence of other notable comorbidities, such as severe coronary artery disease etc.

8. The patient should have a recent negative SARS-CoV-2 PCR test result, or infectivity assays using deep respiratory tract samples showing the absence of viable virus.

9. The transplantation centre should have substantial experience with cases involving high-risk transplantation.

10. The centre should have access to a broad donor pool and low waiting-list mortality.
Goals of oxygen therapy:

- **Improve oxygenation:** target saturation >96% in those without Type 2 respiratory failure and 88-92% in those with hypercapnic respiratory failure
- **Decrease the work of breathing:** respiratory rate <35 breaths/min and with no use of accessory muscles of respiration

Experimental /Emerging therapies:

CONSIDERATION for following drugs - Colchicine, piroxicam, itolizumab, bevacizumab is also relevant as tocilizumab has scarce availability
• **Piroxicam use:** Some physicians have used in those cases where oxygen was needed but beds were not available in moderate cases in dose of 20mg SL dispersible tablet and observed improvement in oxygen saturation. We do not recommend it in absence of any case-controlled study.

• **Colchicine use:** Except few studies, most of studies did not found any significant improvement. It is now being used in mild, moderate and severe cases despite any recommendations by standard guidelines. • It is considered if fever persists despite paracetamol • Loading dose: 1.5 mg followed by 0.5 mg of colchicine 60 minutes later if no adverse gastrointestinal effects • Maintenance dosage: 0.5 mg BD until discharge or a maximum of 21 days (reduce to OD if body weight <60 kg) Contraindicated if eGFR<30mL/min/1.73m². We do not recommend either for or against the use of colchicine for the treatment of non-hospitalized patients. Do not use it in hospitalized patients.

• **Tofacitinib/baricitinab:**
  - Two drugs are available, any one of them can be used:
    - **Tab Baricitinib** 4 mg once daily for 10 days (*Renal modification - 2mg once daily if GFR is between 30 to 60ml/ml/min, avoid if GFR < 30 ml/min) Cost: 4mg tab, 30Rs /tab.
    - **Tablet Tofacitinib** 10 mg twice daily for 10 days (* avoid if GFR <30ml/min).
    - Two drugs are available, but we recommend to use only Baricitinib as there is no sufficient clinical data on the use of tofacitinib to treat COVID-19.

• For the Initial Viral Replicative Phase of Illness (First 5 days of illness) we recommend AGAINST the use of steroids or any other immunomodulatory medicines during this period.

• For the Inflammatory Phase of Illness (From Day 6 of onset of symptoms) Immunomodulatory Treatment is recommended for the covid-19 positive patients with any of the following signs of deterioration (after exclusion of alternative causes like secondary infections etc.):
  - SpO2 below 94% at rest on room air.
  - SpO2 falling by > 4% from baseline after 6-minute walk at normal pace.
  - CRP > 30 mg/l; or Doubling of CRP from baseline in second week of illness (if baseline values available).
  - HRCT Severity score >9 score.

• It has been recommended to start anticoagulation treatment for all patients on JAK inhibitors who have intermediate or high-risk factors for thrombosis. Drug and duration should be decided on Individual basis, based on age, risk factors and D-Dimer levels. (Risk Factors: reduced mobility, active cancer, prior history of DVT, prior h/o anti-phospholipid antibody syndrome, elevated D-dimer levels (>2 times the upper limit of normal).
- **Methylene Blue:**
  - As there are only anecdotal reports, it is not indicated.
- **Bevacizumab - (Avastin 400mg single dose vial):**
  - It is an anti VEGF recombinant humanized monoclonal antibody
  - It is being tried with severe Covid-19, with respiratory rate ≥30 times/min, oxygen saturation ≤93% with ambient air, or partial arterial oxygen pressure to fraction of inspiration O₂ ratio (PaO₂/FiO₂) >100 mmHg and ≤300 mmHg, and diffuse pneumonia confirmed by chest imaging
  - It is priced between Rs37,500 to Rs39,000
  - Bevacizumab 7.5mg/kg body weight + 0.9% NaCl 100ml, intravenous drip
- **2-Deoxy-D-Glucose by DRDO:**
  - A total of 110 patients were part of the Phase-II clinical trials of DRDO's 2-DG drug. The results showed that in terms of improvement of vital signs of COVID-19 symptomatic patients there was a difference of 2.5 days compared to Standard of Care (SoC). (INDE-GENIUS study)
  - The 2 DG drug, like glucose, spreads through the body, reaches the virus-infected cells and prevents virus growth by stopping viral synthesis and destroys the protein's energy production. The drug also works on virus infection spread into lungs which help us to decrease patient’s dependability on oxygen."
  - The anti-COVID drug 2-DG has been developed in powder form and is ingested orally by dissolving it in water.
  - Phase III trial on (40 patients) report led to DCGI approval - 8th May 2021
  - Dose and Regimen: 2-DG: 45 mg/kg body weight AM + 45 mg/kg body weight PM, twice daily for not more than 10 days. Instructions for preparation of one dose (morning or evening) of 2-DG (Dose level - 90 mg/kg body weight/day, administered in two equally divided doses approximately 12 hours apart) DO NOT USE the reconstituted dose solution for further dosing of the patient. Each dose of 2-DG should be prepared using a fresh 5.85 g sachet.
  - At present, we do not recommend for or against its use.
- **Virafin:**
  - On April 23, 2021, Virafin had received restricted, emergency use approval from the Drug Controller General of India (DCGI).
  - ‘Virafin’ is pegylated interferon alpha-2b. Interferons are signalling proteins that help the body’s immune system defend against viral infections. Pegylated interferon alpha 2b have been used to help treat Hepatitis C.
  - Its phase 2 trial results were published in the *International Journal of Infectious Diseases*, in its April 2021 issue.
  - It was conducted with 40 patients who had moderate COVID-19 – 20 of them were assigned to the control arm and 20 to the treatment arm.
  - It was used in RT-PCR confirmed SARS-CoV-2 infection, pneumonia with no signs of severe disease, respiratory rate 15-30 breaths/min, oxygen saturation 90%—
94%.

- Each dose of Virafin costs Rs 9,000 per injection.
- Due the many flaws in the study, we do not recommend its use at present

- **Fluvoxamine:** It is a selective serotonin reuptake inhibitor (SSRI) which is not FDA-approved for the treatment of any infection. There is insufficient evidence either for or against the use of fluvoxamine for the treatment of COVID-19.

- **Drugs not to be used:**
  - Baricitinib with tocilizumab.
  - Interferons (alpha or beta) for the treatment of severely or critically ill patients with COVID-19.
  - Kinase inhibitors:
    - Bruton's tyrosine kinase inhibitors (e.g., acalabrutinib, ibrutinib, zanubrutinib).
    - Janus kinase inhibitors other than baricitinib (e.g., ruxolitinib, tofacitinib).
  - Non-SARS-CoV-2-specific intravenous immunoglobulin (IVIG). But it should not preclude the use of IVIG when it is otherwise indicated for the treatment of complications that arise during the course of COVID-19.
  - Sarilumab for patients who do not require ICU-level care or who are admitted to the ICU for >24 hours but do not require invasive mechanical ventilation, noninvasive ventilation, or high-flow oxygen.
  - The anti-IL-6 monoclonal antibody, siltuximab.

**Part 6. Procedure for awake self-proning**

**Monitoring**

- Continuous O2 monitoring is required. ECG leads to be connected to the posterior chest wall for continuous monitoring.
Before Proning

- Make plans for toileting, Feeding, Oral Medications, etc.
- If possible, place the bed in reverse Trendelenburg (head above feet, 10 degrees) to help reduce intraocular pressure.
- Have patient empty bladder
- Educate the patient. Explain the procedure and rationale of the intervention to the patient.
- Arrange tubing to travel towards the top of the bed, not across the patient, to minimize the risk of dislodging. Ensure support devices are well-secured to the patient. (Ex. Sleeve over IV access site, position urinary catheter)
- Assess pressure areas to avoid skin breakdown- avoid pressure with proning with the use of pillows/gel pads

Prone positioning - the procedure

1. The patient should lay on their abdomen (arms at sides or in “swimmer” position).
2. If a patient is unable to tolerate, they may rotate to lateral decubitus or partially prop to the side (in between proning and lateral decubitus) using pillows or waffle cushioning as needed. Ideally, the patient should be fully proned rather than on the side as there is currently no data about whether side positioning is beneficial.
3. 15 Minutes after each position change, check to make sure that oxygen saturation has not decreased. If it has, try another position.
4. If the patient has a significant drop in Oxygen saturation, follow these steps:
   - Ensure the source of the patient’s Oxygen is still hooked up to the wall and is properly placed on the patient (this is a common cause of desaturation).
   - Ask the patient to move to a different position as above.
   - If after 10 minutes, the patient’s saturations have not improved to prior levels, consider escalation of oxygen therapy via the same/different modality vs. trial of additional position.
Time spent proning

- The patient should try proning every 4 hrs. and stay prone as long as tolerated. Proning is often limited by patient discomfort, but they should be encouraged to reach achievable goals, like 1-2 hours (or more if possible).
- The ideal duration is 16 hrs. per 24 hours (e.g., 4 times for 4 hours each session).
When to stop awake proning?

- A patient can choose to stop awake proning at any time.
- In case of hemodynamic instability or if impending respiratory failure, it is recommended that the clinician stops proning and considers intubation.

Contraindications of awake self-proning

- Hemodynamic instability (on vasoactive medications): preferable to prone these patients in a monitored environment; if severe/refractory hemodynamic instability, proning is not advised.
- Increased intracranial pressure.
- Increased abdominal pressure.
- Abdominal, Chest, and facial wounds.
- Cervical spine precautions.
- Extreme obesity.
- GCS <8.
- Pregnancy 2nd or 3rd trimester.

Part 7. Patient selection for NIV application

<table>
<thead>
<tr>
<th>Step 1</th>
<th>An etiology of respiratory failure likely to respond favorably to NIV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Step 2</td>
<td>Identify patients in need of ventilatory assistance by using clinical and blood gas criteria. Moderate to severe dyspnea, tachypnea, and impending respiratory muscle fatigue.</td>
</tr>
<tr>
<td>Step 3</td>
<td>Exclude patients for whom NIV would be unsafe.</td>
</tr>
</tbody>
</table>

Predictors of NIV success in acute respiratory failure

- Lower acuity of illness (APACHE score).
- Ability to cooperate; better neurologic score (GCS≥10).
- Ability to coordinate breathing with a ventilator.
- Hypercarbia, but not too severe (PaCO2 b/w 45- and 92-mm Hg).
- Acidemia, but not too severe (pH b/w 7.1 and 7.35).
- Improvement in gas exchange, HR & RR within first 2 hours.
Contraindications for NIV application

- Cardiac/Resp arrest or need for immediate intubation.
- Severe encephalopathy (e.g., GCS <10).
- Severe UGI bleeding.
- Hemodynamic instability or unstable cardiac arrhythmia.
- Facial or neurological surgery, trauma, or deformity.
- Upper airway obstruction.
- Inability to cooperate/protect the airway.
- Inability to clear secretions/ High risk for aspiration.
- Untreated pneumothorax.

Part 8. Discharge Policy: Follow state-specific guidelines if any


Management of SARS-CoV-2 in Pregnancy

- Compared to non-pregnant women with COVID-19, pregnant women with COVID-19 have higher rates of intensive care unit (ICU) admission; this may reflect a lower threshold for admission to ICU, rather than more severe disease.
• Pregnant women are not at increased risk of death from COVID-19, according to the largest systematic review.
• Compared to pregnant women without COVID-19, pregnant women with symptomatic COVID-19 requiring hospitalization have overall worse maternal outcomes, including an increased risk of death, although that risk remains very low (the UK maternal mortality rate from COVID-19 is 2.2 per 100 000 maternities).

Risk factors for hospital admission with Covid-19 infection in pregnancy

Risk factors that appear to be associated both with being infected and being admitted to hospital with COVID-19 include:

• Black, Asian and minority ethnic (BAME) background
• Having a BMI of 25 kg/m2 or more
• Pre-pregnancy co-morbidity, such as pre-existing diabetes and chronic hypertension
• Maternal age 35 years or older.13,23
• Living in areas or households of increased socioeconomic deprivation (data not specific to pregnancy).

Effect of Covid-19 on the fetus Key findings

• Symptomatic maternal COVID-19 is associated with an increased likelihood of iatrogenic preterm birth.
• Aside from preterm birth, there is no evidence that COVID-19 infection has an adverse effect on the fetus or on neonatal outcomes.

Key considerations when caring for symptomatic women with suspected or confirmed Covid-19

Consideration:

Setting for birth: If homebirth or birth in a midwifery-led unit is planned, a discussion should be initiated with the woman regarding the potentially increased risk of fetal compromise in active phase of labour if symptomatic with SARS-CoV-2.97

Attending an obstetric unit, where the baby can be monitored using continuous electronic fetal monitoring (CEFM), should be recommended for birth.
Timing for birth: A positive COVID-19 result in an otherwise well woman, when there is also no evidence of fetal compromise, is not an indication to expedite birth.

Induction of labour (IOL) is associated with longer periods of inpatient stay than for spontaneous onset of labour. Review the indication for IOL and consider whether the likely benefits outweigh possible risks. Where possible, review the provision and possibility of outpatient IOL.

Mode of birth: There is currently no evidence to favour one mode of birth over another in women who are SARS-CoV-2 positive, so mode of birth should be discussed with the woman, taking into consideration her preferences and any obstetric indications for intervention. Mode of birth should not be influenced by the presence of COVID-19, unless the woman’s respiratory condition demands urgent intervention for birth.

Respect and consent: Women must still be able to make decisions about the care they receive in line with the principles of informed consent.

Fetal surveillance: Discuss with women the options for fetal surveillance in labour in accordance with existing NICE guidelines. Recommend CEFM for women who are symptomatic of COVID-19. Current infection with SARS-CoV-2 is not a contraindication for application of a fetal scalp electrode or for fetal blood sampling.

Pain relief: There is no evidence that epidural or spinal analgesia or anaesthesia is contraindicated in the presence of coronaviruses. Epidural analgesia should therefore be recommended in labour to women with suspected or confirmed COVID-19 to minimize the need for general anaesthesia.

Intrapartum care: When a woman with confirmed or suspected COVID-19 is admitted to the maternity suite, the following members of the multidisciplinary team should be informed: consultant obstetrician, consultant anaesthetist, midwife-in-charge, consultant neonatologist, neonatal nurse-in-charge, and the infection control team.

Maternal observations and assessment: Should be continued as per standard practice, with the addition of hourly oxygen saturations.

Aim to keep oxygen saturation above 94%, titrating oxygen therapy accordingly. If the woman develops a fever, investigate and treat as per RCOG guidance on sepsis in pregnancy.
Flowchart for Management in Pregnant Women (Adapted from Lancet)
Example of a maternity escalation plan for women with suspected or confirmed Covid-19 (adapted from buy's and St Thomas’ NHS Foundation Trust)

<table>
<thead>
<tr>
<th>Category</th>
<th>Clinical criteria for oxygenation</th>
<th>Suggested actions</th>
<th>Other considerations for viable fetus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Green</td>
<td>SpO₂ 94%–98% in room air and RR ≥ 20</td>
<td>Ensure no obstetric or medical concerns</td>
<td>Assess fetal wellbeing</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Discharge for self-isolation in line with national guidance</td>
<td>Consider fetal monitoring</td>
</tr>
<tr>
<td></td>
<td>Target SpO₂ 94%–98% on ≥ FiO₂ 28% and/or RR ≥ 21</td>
<td>Increase oxygen flow rate to maintain SaO₂ 94%–98%</td>
<td>Discuss timing of birth</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Assessment by obstetric registrar</td>
<td>Depending on the gestational age:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>In-patient care</td>
<td>• Consider steroids for fetal lungs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Inform maternity escalation team:</td>
<td>• Consider magnesium sulfate for neuroprotection if considering birth of the baby</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Obstetric consultant</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Obstetric anaesthetist</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• On-call medical team</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Give oral prednisolone 40 mg for treatment of COVID-19</td>
<td></td>
</tr>
<tr>
<td>Amber</td>
<td>Target SpO₂ 94%–98% on ≥ FiO₂ 35% and/or RR ≥ 25</td>
<td>Increase oxygen flow rate to maintain SaO₂ 94%–98%</td>
<td>Discuss the risks and benefits of emergency caesarean birth</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Consider 15l/min O₂ via non-rebreather mask</td>
<td>Depending on the gestational age:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Refer to ITU team</td>
<td>• Consider steroids for fetal lungs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Urgent review by the maternity escalation team</td>
<td>• Consider magnesium sulfate for neuroprotection if considering birth</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Consider awake proning position</td>
<td></td>
</tr>
<tr>
<td>Red</td>
<td>SpO₂ &lt; 94% on 15l/min O₂ via non-rebreather mask</td>
<td>Urgent review by ITU team</td>
<td>Discuss the risks and benefits of emergency caesarean birth</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Urgent attendance by the maternity escalation team</td>
<td>Depending on the gestational age:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Consider awake proning position when feasible/high flow oxygen in critical care setting only</td>
<td>• Consider steroids for fetal lungs</td>
</tr>
<tr>
<td>Peri-arrest</td>
<td>Call 2222 – adult cardiac arrest team, obstetric crash team and neonatal crash team</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


EMORY INTERNAL MEDICINE RESIDENCY: COVID-19 VISUAL SERIES

COVID-19: Breastfeeding in COVID-19 (+) mothers

4/15/20

Maternal recommendations

IF AFTER BIRTH:  THEN:

COVID-19 +

Mother is asymptomatic or displays few symptoms

Roaming-in + Direct breastfeeding

Mother has cough, fever, dyspnea

Mother/infant separation + Infant given pumped milk from mother

OR

Newborn needs ICU care

Still recommended:

🔹 Handwashing prior to handling infant
🔹 Mask during breastfeeding/contact
🔹 6-foot distance when not feeding
🔹 Suspend visitors

LIMITATIONS:

🔹 Experts in China advise separation and use of formula or donor milk
However:

→ No justification given
→ Benefits of breast milk not addressed

Case study recommended

There is no evidence of transmission of SARS-CoV2 through breast milk reported to date and expressed breast milk should be given as mother can pass antibodies via breast milk.


Based on recommendations by WHO, UNICEF, ISS, IJOG, RCOG, and ABM

* If hospital census at capacity, may require earlier discharge with close follow up with PCP

Keep up to date with CME India on social media. Please follow us on Twitter, Facebook, Instagram, and LinkedIn.
Part 10. Pearls in pediatric case management

Community transmission of SARS-CoV-2 is happening in my city. How should I approach a sick child?⁸,⁹

Children with fever, respiratory tract symptoms, loss of taste or smell, or multiple infectious symptoms should undergo testing for covid-19 or be considered to have the disease until proved otherwise.

Clinicians should consider a range of other diagnoses, including other pulmonary infections and systemic illnesses with respiratory manifestations, including non-infectious diagnoses such as diabetic ketoacidosis and watch for labored breathing, dehydration, persistent fever, severe abdominal pain, or altered mental status.

Children with fever and gastrointestinal symptoms (abdominal pain, vomiting, or diarrhea) or any child with other features consistent with Kawasaki disease (e.g., persistent fever plus lymphadenopathy, mucocutaneous changes, conjunctivitis, or swelling of extremities) could have MIS-C.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Range123*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
<td>16-19%</td>
</tr>
<tr>
<td>Fever</td>
<td>48-59%</td>
</tr>
<tr>
<td>Cough</td>
<td>39-56%</td>
</tr>
<tr>
<td>Rhinorrhea, nasal congestion</td>
<td>7-20%</td>
</tr>
<tr>
<td>Myalgia</td>
<td>14-19%</td>
</tr>
<tr>
<td>Sore throat</td>
<td>14-18%</td>
</tr>
<tr>
<td>Headache</td>
<td>3-13%</td>
</tr>
<tr>
<td>Tachypnoea, dyspnea</td>
<td>8-12%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>7-10%</td>
</tr>
<tr>
<td>Nausea, vomiting</td>
<td>2-9%</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>6-7%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>5-8%</td>
</tr>
<tr>
<td>Rash</td>
<td>&lt;1%</td>
</tr>
</tbody>
</table>
- MIS-C defined as the Presence of fever for ≥24 hours, Elevated inflammatory markers, Multi-organ dysfunction (≥2 systems: cardiac, dermatological, gastrointestinal, renal, respiratory, hematological, and/or neurological), No plausible alternative diagnosis, Positive viral or serological testing for SARS-CoV-2 or close contact with a person with covid-19 within four weeks of symptom onset.
- MIS-C is typically a progressive illness, and patients who initially had mild symptoms can develop a severe illness with multi-organ dysfunction within a few days of symptom onset, Critical signs should be evaluated for hemodynamic instability, tachycardia, left ventricular dysfunction, and respiratory distress, which could be primary or caused by cardiac dysfunction. Laboratory abnormalities often include lymphopenia, anemia, and thrombocytopenia, in addition to elevations in liver enzymes, creatinine, pro-brain natriuretic protein, troponin, and coagulation studies.
- All patients in whom there is a strong suspicion for MIS-C should have an echocardiogram to evaluate cardiac function and to look for evidence of coronary artery dilatation.
- Children with mild acute covid-19 benefit from usual supportive care measures, including rest, hydration, and antipyretics.
- Dexamethasone was shown to decrease mortality in adults with moderate to severe respiratory distress and may be considered in children with significant respiratory illness, though pediatric data are still forthcoming.
- Similarly, Remdesivir may be prescribed for children with respiratory deterioration (DATA UNDER EVALUATION). Other treatments, such as convalescent plasma or monoclonal antibodies, might be considered in high-risk patients, but these therapeutics require further study in adults and children. Children with MIS-C most commonly are treated with intravenous immunoglobulin and often steroids.
- Primary measures to prevent infection and transmission of SARS-CoV-2 remain important for children and their families and include basic steps such as face masks for children aged 2 years and older, social distancing, and hand hygiene for both children and adults around them. Young children or those with developmental delays may not tolerate or wear masks properly; however, there is value in practicing.
- Given that the risks associated with SARS-CoV-2 are much lower in children than in adults, initial studies and vaccine distribution did not prioritize children. Patients should maintain routine preventive care and vaccination schedules, including seasonal influenza vaccine, as a critical strategy to stay healthy during and beyond the pandemic.
Operational flow chart

To be managed in usual care areas for neonates (not applicable if it is an exclusive COVID hospital)

Neither suspect not positive

COVID status

Suspect

Positive

Sick or gestation <34 weeks

No

Yes

A. COVID suspect stable neonate

B. COVID positive stable neonate

C. COVID suspect neonate with Gestation <34 weeks or sick

D. COVID positive neonate with Gestation >34 weeks or sick

Classify at admission and periodic assessment during course of illness

Mother sick

No

Yes

Room-in with mother in "COVID postnatal ward" Allow breastfeeding with droplet and contact precautions.

Shift to "Well-baby COVID ward" Give EBM if it can be given safely. Else give formula feed.

Shift to "COVID suspect area" in SNCU/NICU

Shift to "COVID positive area" in SNCUNICU

Keep suspect and positive neonates/mothers in separate areas/rooms

If not possible in same ward. May create a temporary physical barrier to ensure separation.

Area characteristics

Healthcare provider

Equipment needed

PPE

Mother should wear mask perform hand hygiene before breastfeeding

Suspect include

- Mother COVID-19 positive within 2 weeks prior to delivery
- Neonate born to a mother with suspected infection or to a mother from a containment area
- Postnatal exposure to infected mother or another person including a healthcare worker
- Presenting with respiratory distress with or without fever and cough, chest X-ray beyond 48-72 h of age and no other alternative explanation for the illness

Positive means RT-PCR is positive for COVID-19

H

Needs air isolation. If not possible install exhaust fans to create negative pressure.

Entry and exit separate from usual neonatal care areas. Coning and dropping areas to be warmed

Doctors, nurses, and other support staff.

If possible, a separate set of staff for exposed and infected neonates.

COVID-19 positive mother or family member not allowed to visit if declared to be cured as per national guidelines.

All equipment as per standard of care in SNCU or NICU

All equipment as per standard of care in SNCU or NICU

Nurse to assist in initiation of breastfeeding. Consider allowing a family member to stay with mother to provide support to mother

Nurse for feeding and other care of well baby

Crash-cart and resuscitation station, equipment for usual neonatal monitoring and care should be available

Crash-cart and resuscitation station, equipment for usual neonatal monitoring and care should be available

Crash-cart and resuscitation station, equipment for usual neonatal monitoring and care should be available

D"COVID positive area" in SNCUNICU

If neonate in suspect area tests positive, shift to COVID positive ward/NICU.

If neonate in neonatal ward becomes sick shift to SNCUNICU.

Keep suspect and positive neonates in separate areas/rooms

If not possible refer to a nearby hospital with such facility (e.g. COVID hospital)
Part 11. Summary Pearls 2021

- Older age, male sex, and comorbidities increase the risk for severe disease.
- For people hospitalized with Covid-19, 15-30% will go on to develop covid-19 associated acute respiratory distress syndrome (ARDS).
- When used appropriately, high flow nasal cannula (HFNC) may allow CARDS patients to avoid intubation and does not increase the risk for disease transmission.
- Remdesivir may have modest benefit in time to recovery in patients with severe disease but shows no statistically significant benefit in mortality or other clinical outcomes.
- Active symptomatic support remains the key treatment for mildly to moderately ill patients, such as maintaining hydration, nutrition, and controlling fever and cough.
- Hospitalized for mild to moderate Covid-19 (not hypoxemic) Supportive care:
  - No clear benefit for Remdesivir or Convalescent plasma.
  - Steroids have no demonstrated benefit and may cause harm.
- Hospitalized for severe covid-19, but not critical (hypoxemic needing low flow supplemental oxygen):
  - Corticosteroids (dexamethasone 6 mg/day × 10 days or until discharge or an equivalent dose of hydrocortisone or methylprednisolone).
  - May consider Remdesivir.
  - May benefit from use of tocilizumab.
- Hospitalized for covid-19 and critically ill (needing HFNC, NIV, IMV, or ECMO) Supportive care:
  - Corticosteroids (dexamethasone 6 mg/day × 10 days or until discharge or an equivalent dose of hydrocortisone or methylprednisolone).
  - May consider Remdesivir.
  - May benefit from use of tocilizumab.
- Timely and accurate diagnostic SARS-CoV-2 testing is a crucial step in managing the patient.
- Avoid Fancy anti-virals and HCQS. At present Ivermectin is also not scientifically supported.
- Low molecular weight heparin, Aspirin, NOACs, (novel oral anticoagulants: dabigatran, rivaroxaban, apixaban, and edoxaban) to be used as it was earlier.
- Colchicine might help.
- Tocilizumab: More sepsis-related complications, can be used in selected cases with cytokine storm.
- Anticoagulants may need to be given for 3 weeks or more (2-4 weeks).
- People are developing Myocardial infarctions, Stroke, etc. few weeks after Corona infection - the Thromboembolic phenomenon.
- Oxygen is the superhero.
• New addition is use of neutralizing antibodies. The ability to standardize the amount of neutralizing activity and the possibility of conferring protection more rapidly than with vaccine-induced immune responses led to emergency use authorization after results of 5 RCTs. Indication: Patients with mild to moderate COVID-19 who are at high risk of progression to severe disease may receive bamlanivimab/etesevimab, casirivimab/imdevimab, or sotrovimab. Local variant susceptibility should be considered in the choice of the most appropriate neutralizing antibody therapy. There are limited data on efficacy in high-risk patients under 18 years of age.

• Angiotensin-converting enzyme inhibitors, statin therapy, nonsteroidal anti-inflammatory drugs, and oral, inhaled, and intranasal corticosteroids that are prescribed for comorbid conditions should be continued as directed.

• To be sensible, clinicians must recognize that highly selective, fully effective treatments are uncommon in acute care. Focus on High-Quality Evidence Some clinical research is biased.

• Even the best research methods, such as randomized trials, can be unreliable. This has been amplified by the rapid pace of research undertaken during the COVID-19.

• It follows that treatment guidelines, national mandates, and bedside care adapt to new data only when the evidence is rigorous, reproducible, and sufficiently strong.

Part 12. Supplementary materials

1. Six patterns of Covid Xray
2. HRCT in Covid
3. Do’s and Don’ts in Covid
4. Diabetes and Covid
5. Guideline for tackling Mucormycosis
6. Post Discharge
7. Treatment of Post Covid Symptoms
8. Multisystem Inflammatory Syndrome in Adults
1. Six patterns of Covid Xray:

X-Ray Chest

6 patterns of COVID on chest x-ray

Pattern 1 - Reverse Batwing
Pattern 2 - Multifocal lower lobe predominant consolidation
Pattern 3 - Peribronchial rounded consolidations
Pattern 4 - Multifocal bilateral consolidations
Pattern 5 - Ball pattern or round pneumonia
Pattern 6 - Bilateral symmetrical diffuse lung involvement

2. HRCT in Covid - Indications and importance of HRCT Thorax:

All Covid patients do not need to undergo HRCT Thorax examination.14

Indications:

- In patients having co-morbidity above the age of 40 and minimal respiratory symptoms (mild disease: RR < 20, SpO2>94), HRCT may be delayed till the end of first week of symptom onset.
- In patients presenting with moderate disease (RR 24-30 and/or SpO2 90-94) or severe disease (RR> 30 and/or SpO2 <90), HRCT may be done at the earliest possible opportunity. If HRCT facilities are not available, X-ray chest must be performed in these cases.
- In patients with high suspicion of Covid (Symptoms, contact, travel, markers), HRCT may be done if 2 consecutive RT PCR tests are negative. However, presence of typical radiological picture is not conclusive of active disease and must be correlated with clinical picture.
- In centers where RT PCR reports are delayed due to scanty resources, HRCT may be used for probable diagnosis as a remote tool.
- Patients coming to the emergency center with atypical signs of COVID 19 should be considered for the possibility of chest CT15.
(The last three indications must be used very judiciously because most of the viral disease may possibly present with similar radiological picture.)

**CT severity Score:**
- There are different ways to calculate CT severity score which determines number of lobes of lungs involved and gives a concise picture of pulmonary inflammation. Common score pattern is given out of 25.
- A score of 12/25 should alert the treating physician to possibility of development of Covid Associated Respiratory Distress and should be an indication to start steroids and also for hospitalization and intensive monitoring of oxygen saturation and inflammatory markers.
- A score of 8/25 in a patient having co-morbidity should be a warning symptom for accurate vigilance and more frequent monitoring.

**Other usefulness of HRCT Thorax**
- CT severity score has been correlated well with severity of disease and also with outcome in Covid patients. However, one should remember that density of ground glass opacities also has equal importance and therefore, radiologist’s opinion should not only mention the distribution of these opacities but also the density.
- HRCT in a Covid patient having sudden onset of breathlessness may point to the need of Pulmonary angiography especially when correlated with ECG, 2D echo (for RV events) and venous Doppler.
- HRCT also points to clinical outcome and possibilities of Covid associated pulmonary fibrosis and help in deciding “Long Covid Symptoms” and need for anti-fibrotic agents.

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**HRCT SEVERITY (TOTAL SCORE 25)**

<table>
<thead>
<tr>
<th>INFECTION CRITERIA (SINGLE LOBE)</th>
<th>CT FINDINGS</th>
<th>SEVERITY</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 % INFECTED</td>
<td>Intermediate</td>
<td>Score 1</td>
</tr>
<tr>
<td>5-25 % INFECTED</td>
<td>Abnormalities</td>
<td>Score 2</td>
</tr>
<tr>
<td>25-50 % INFECTED</td>
<td>Abnormalities</td>
<td>Score 3</td>
</tr>
<tr>
<td>50-75 % INFECTED</td>
<td>Abnormalities</td>
<td>Score 4</td>
</tr>
<tr>
<td>&gt; 75 % INFECTED</td>
<td>Abnormalities</td>
<td>Score 5</td>
</tr>
</tbody>
</table>

Score calculation is done based on each lobe involvement. Each lobe has maximum score 5.
And so 5 lobes has maximum score of 25.
For example, score 5 means that lobe is > 75% involved or affected by COVID-19.

**CT Useless for COVID-19 Diagnosis, Study Affirms.** — Even AI couldn't tell flu pneumonia from COVID in chest scans

CT Manifestations of Coronavirus Disease (COVID-19) Pneumonia and Influenza Virus Pneumonia: A Comparative Study, Liaoyi Lin, MD¹, Gangze Fu, MD¹, Shuangli Chen, MD¹, Jiejie Tao, MD — American Journal of Roentgenology
3. Do’s and Don’ts in Covid

1. **Documenting the day of symptom onset very precisely** is of the prime importance as it decides line of investigations, Modes of treatment and need to hospitalize and duration of isolation.

2. **A positive Rapid Antigen Test** is highly specific and does not require corroboration with RT PCR test. However, a negative RAT in a symptomatic patient needs to go for RT PCR test.

3. **Immediate isolation** (even when test results are awaited) is of paramount importance and needs to be stressed emphatically to patient. Ignoring the disease, delaying the RT PCR test (or Rapid Antigen Test) by certain group of family physicians (in however good faith) is not justified.

4. It is equally important to explain the patient about **duration of isolation, precautions to be taken during isolation and diet and exercise** that he needs to manage while being isolated. It is extremely important to address his anxiety and also to see that he has a **direct communicating link to an experienced health care worker**. All efforts must be taken to avoid unnecessary outings of patients who are being managed at home.
5. **Assessment of comorbid conditions** at the time of diagnosis and measures to control those comorbidities which can be corrected (Hypertension, Diabetes) should be always be kept in mind at the time of initiating treatment.

6. **Battery of investigations for Covid** (so called Covid Package) may not be needed for all the patients at the time of diagnosis. They may be best reserved for patients coming late after symptom onset or those who are at high risk due to multiple comorbidities. Basic investigations must include vital data, CBC with N/L ratio, CRP and sugar levels. Investigations like IL-6 at the time of diagnosis have no role to play and may be misleading.

7. **HRCT of thorax may not be advocated** early in the course of disease in mild disease. It may be ordered on day 5 unless patient has definite signs and symptoms of lung involvement with comorbidities. A normal 6-minute walk test may alleviate the need for HRCT scan.

8. **Time to say bye-bye to Azithromycin, HCQS** as they are likely to produce more harms and have no benefits. Role of Favipiravir in mild disease should be restricted to those having multiple comorbidities and having age above 45 or 50 especially when reaching to a doctor very early in the course of disease. Remdesivir may be reserved for moderate disease having comorbidity and coming early in the course of disease. (5 to 7 days)

9. **Many trials have now signified** the role of Vitamin D in management of Covid. One may use it judiciously. However, zinc that is being used extensively is not safe drug above 50 microgram doses and restrain must be used in its use.

10. **Steroids prescribed on day 1 or early in the course of disease** (unless documented hypoxia) may cause harm or may not be beneficial.

11. **Injectable LMWH and/or newer oral anticoagulants** should be used in patients having rapidly rising D Dimer values or history of thrombo embolic risk.

12. **Role of aspirin has been established** in multiple trials and may be used as 75 mg single dose medication for those above 40 years of age.

13. Role of statin in Covid is quite debated. No harm has been recorded in any trials.

14. **Role of repeat RT PCR is limited** only to those patients who do not improve from their critical condition despite all possible interventions.

15. Monitoring the patients is the most important factor in management of disease. Regular measurement of **temperature** by properly calibrated thermometer, **measurement of sPO2** by a properly used pulse oximeter and **measurement of blood pressure and glucose** levels at home in addition to a regular eye on inflammatory markers will screen the moderate and severe disease from mild disease.

### 4. Diabetes and Covid

During the COVID-19 pandemic, tight control of glucose levels and **prevention of diabetes complications** might be crucial in patients with diabetes mellitus to keep susceptibility low and to prevent severe courses of COVID-19.
In Type 2 diabetes:
For Asymptomatic or mild cases, any diabetic therapy which has kept the glycemia under control should be continued. Monitoring of blood glucose should be more frequent and extra vigilance should be the motto.

Considerations regarding the use of anti-hyperglycemic agents:
Evidence suggests that insulin and dipeptidyl peptidase 4 inhibitors can be used safely in patients with diabetes mellitus and COVID-19; metformin and sodium–glucose cotransporter 2 inhibitors might need to be withdrawn in patients at high risk of severe disease.

i. Metformin:
- Metformin, a first line antidiabetic drug in the treatment of type 2 diabetes, has anticipated antiproliferative and immunomodulatory effects but has risks of dehydration and lactic acidosis. Those who have the potential to progress to severe COVID-19 (e.g., who have greater dehydration) should stop taking this drug.
- Most of the patients can continue with metformin as evidence shows that it could be of benefit and inhospital mortality was lower in patients on metformin.

ii. Dipeptidyl peptidase (DPP)-4 inhibitors:
- They (alogliptin, linagliptin, saxagliptin, sitagliptin, and others) are generally well tolerated and can be continued in these patients.

iii. Sodium-glucose co-transport-2 inhibitors (canagliflozin, dapagliflozin, and empagliflozin):
- These are associated with risks of dehydration and diabetic ketoacidosis, and hence, patients who are prone to infections or have higher chances of severe COVID-19 should stop taking this drug.

iv. Glucagon-like peptide -1 receptor agonists:
- These (dulaglutide, exenatide-extended release, liraglutide, and semaglutide) also have a risk of dehydration, so close monitoring needed.

v. Alpha glucosidase inhibitors:
- Can be continued if gastrointestinal side effects are not a hindrance.
vi. Pioglitazone:
- It has anti-inflammatory and antifibrotic properties but it is known the therapy was associated with weight gain and oedema and more importantly was associated with aggravation of heart failure, which did not support the use of pioglitazone in patients with COVID-19 particularly with moderate disease.
- Though pioglitazone has been shown to decrease the secretion of various proinflammatory cytokines in the monocytes and macrophages and have the potential of blunting the cytokine storm by blocking caspase recruitment domain-containing protein 9 (CARD9) at the center of the immune activation mechanism in macrophages. More clinical trials are needed to optimize the risk-benefit ratio of using pioglitazone in patients with COVID-19.

Choosing Anti-hyperglycemic medications:

Choosing Anti-hyperglycemic medications:

<table>
<thead>
<tr>
<th>Uninfected but living in environment with prevalent COVID-19</th>
<th>Ambulatory mild disease</th>
<th>Hospitalized: moderate disease</th>
<th>Hospitalized: severe disease (admitted to ICU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin, DPP4 inhibitors, Metformin, GLP1 analogues, TZD</td>
<td>Insulin, DPP4 inhibitors, Metformin, GLP1 analogues</td>
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<td>Insulin, DPP4 inhibitors, Metformin, GLP1 analogues</td>
</tr>
</tbody>
</table>

- Recommended to use
- Can be used with caution
- Not recommended

vii. Insulin:

- Importantly, if any anti-hyperglycemic drugs are discontinued, the alternative treatment of choice is usually insulin. Further, if insulin therapy is already ongoing in a patient, it should be continued and not stopped.

- Insulin is always a preferred modality in any emergent situation irrespective of the degree of renal and hepatic dysfunction and thus it can be used at any stage of COVID-19.

- Subcutaneous (SC) insulin in patients with diabetes and mild to moderate COVID-19, in those taking food orally, is not a challenging issue.

- However, most hospitalized COVID-19 patient with diabetes with poor oral intake or on mechanical ventilator will eventually need intravenous insulin infusion with hourly or 2-hourly monitoring and frequent adjustment of infusion rates.

- This would increase the chance of exposure of health care providers (HCP). To minimize frequent exposure, use of SC short acting insulin analogues can be one approach, however, its role in critically ill patients is not fully known.

- Alternatively, to minimize the exposure, even a single per day SC dose of long-acting basal insulin could be an attractive option.

- Models of Insulin pump or continuous subcutaneous insulin infusion (CSII), where insulin rates can be remotely adjusted via a Bluetooth can be useful to minimize exposure of HCP.

- **For type 1 diabetes and COVID-19**, there is clear need more frequent and close blood glucose monitoring and adjustments of insulin dose based on blood glucose values.

- Overall, the patient and treating physician together should individualize the management of diabetes by assessing and carefully adjusting regular therapy to reach individualized therapeutic goals according to diabetes type, comorbidities, and health status.
Steroid induced hyperglycemia in Covid patients (ward patients):

Methylprednisolone is a short/intermediate acting glucocorticoid of 4–6 h duration, while dexamethasone is a long-acting steroid with steroid induced hyperglycemia lasting for more than 24 h after the last dose, with a minimal fall after an overnight fast.

Recent data suggests that the impact is maximum when steroid is administered acutely, but a spontaneous remission usually happens With a short course of steroids in most of the COVID-19 trials (10-days of dexamethasone in RECOVERY, 3–7 days by other trials with methylprednisolone), it is less likely that steroid induced hyperglycemia or worsening of glycemic control in pre-existing diabetes contributed in any significant way given the fact that in RECOVERY trial both dexamethasone and usual care arm had equal percentage (nearly 25%) of patients with diabetes.

- In combination, high-dose glucocorticoid-therapy-induced impaired glucose metabolism, COVID-19 induced insulin resistance and COVID-19 related impaired insulin production could result in significant hyperglycemia, HHS and DKA in people with and without diabetes, increasing both morbidity and mortality.
- Sulphonylureas are NOT recommended in this context as beta cell function may be impaired and insulin resistance is likely to be severe.
- It is recommended to use larger insulin doses to overcome the greater insulin resistance which may be encountered in many patients treated with high doses of glucocorticoids and should ONLY be used in this context.
• If Diabetic Ketoacidosis and Hyperglycemia Hyperosmolar Syndrome have been ruled out, use a subcutaneous rapid acting insulin analogue for correcting initial hyperglycemia [glucose above 216mg(12mmol/L)].

• For maintaining glycemic control, for people NOT already on an intermediate acting (NPH) or long acting insulin, where glucose has risen above 216mg (12.0 mmol/l) due to dexamethasone, start NPH insulin which has an intermediate duration of action 0.3 units/kg/day is conservative, but experience suggests that a dose of 0.5 units/kg/day or more may be required depending on severity of illness, BMI and pre-existing diabetes control as indicated by HbA1c. Give two-thirds of the total daily dose in the morning and the remaining one-third in the early evening. If older (>70 yrs.), frail, or serum creatinine >175 umol/l (eGFR <30 ml/min), use a reduced NPH insulin dose of 0.15 units/kg. There should be a low threshold for dose escalation and referral to the diabetes team. (This is as per NHS-UK guidelines).

• 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 (Ministry of health, India, guideline).

• For people already using once or twice daily long-acting insulin or twice daily NPH including those on basal-bolus regimens, increase the long acting basal or NPH insulin by 20% but this may need rapid escalation by as much as 40% depending on response.

• For people on twice-daily pre-mix insulin, continue mixed insulin and adjust dose. Consider increasing the morning dose by 20% but this may need rapid escalation by as much as 40% each day depending on the response. There should be a low threshold for referral to the diabetes team.

• After glucocorticoid therapy is stopped insulin resistance and requirements usually fall gradually requiring a gradual reduction in insulin requirements, however in COVID-19 patients a faster and more aggressive reduction in insulin may be necessary. From day one, the total insulin dose may need to be reduced by as much as 50% guided by ‘pre-steroid’ insulin requirements.

• Note: 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.

• 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. (Ref: Dated 26th August, 2020 Government of India Ministry of Health & Family Welfare Clinical Guidance on Diabetes Management at COVID-19 Patient Management Facility).
Corticosteroid therapy in COVID 19- its sequelae

- Increased lipolysis, increased hepatic glucose output and can increase the insulin resistance by up to 60–80% by directly interfering with the signaling cascade of the GLUT-4 receptors.

- This leads to a 30–50% reduction of insulin stimulated glucose uptake of the skeletal muscle cells, contributing to a postprandial hyperglycemia, as well as a 50–70% reduction of hepatic glycogenesis.

- Corticosteroids also produce breakdown of proteins and the resultant surge in amino acids also interferes with the insulin signaling of the muscle cells.
- Corticosteroids also have a direct inhibitory action on β cells. Lipotoxicity from the lipolysis can also have a similar effect on the β cells.
- The effects of steroids are usually transient and reversible with the stoppage of the steroids.

Covid-19 and newly diagnosed Diabetes:

- There is increasing evidence that coronavirus disease 2019 (COVID-19) may lead to new-onset diabetes mellitus (DM). This may occur even in patients without predisposing factors for impaired glucose metabolism.
- Both impaired pancreatic insulin secretion and insulin resistance have been implicated as underlying mechanisms. Importantly, new-onset hyperglycemia is associated with worse prognosis in patients with COVID-19. Indeed, its prognosis may be even more sinister than in patients with pre-existing DM.
- Controversies remain about whether these cases which are reported are truly newly onset or unmasking of previously undiagnosed diabetes.

Tips:

- If blood sugar is satisfactory, running treatment should not be interfered much.
- Dpp4i and Metformin showed beneficial outcomes.
- If patient is moderate symptomatic and condition is stable, if on SGLT2i alongside other anti-diabetics, we may continue SGLT2i, but if patient’s condition is compromised SGLT2i should be withdrawn with adjustments of other molecules.
- If patient’s condition is severe to critical, insulin is the best way to manage diabetes.
- If patient is on steroid, best is to add basal bolus regimen to have better glycemic control, alongside OHAs if continued from before.
• While the role of admission HbA1c as a marker of COVID-19 severity is yet to be fully established, HbA1c assists in identifying patients with newly diagnosed diabetes.

5. Guideline for tackling Mucormycosis

Prevention and treatment

ALERT

• **Rhino-Orbito-Cerebral Mucormycosis (ROCM)** being a rapidly progressive disease, even a slight delay in the diagnosis or appropriate management can have devastating implications
• Outcome can be optimized by early diagnosis prompted by awareness of warning signs and symptoms and high index of clinical suspicion, confirmation of diagnosis by appropriate modalities, and initiation of aggressive medical and surgical treatment by a multidisciplinary team

(Adapted from Mucormycosis Study Group Sir Ganga Ram Hospital, New Delhi and IJO-2021)

Suspected OR confirmed Mucormycosis

Look for

• Covid history.
• History of steroid therapy, other medication, hospital stay.
• Known medical history: DM, renal failure, immunocompromised pt, malignancy.
• Findings: Facial Swelling, Periorbital Swelling, Severe Headache, Nasal Blockage.
• Intraoral Pus Discharge, Gingival Abscess, Teeth Mobility.

Do Investigation

• Blood investigation: CBC, CRP, HbA1c, Renal profile
• Radiological: CT PNS or 3D CT Face, MRI Findings- • Early stage: sinusitis • Intermediate stage: Bony erosion in maxilla • Aggressive stage: involvement of orbit and brain
• Diagnostic Nasal Endoscopy (DNE) + Otoscopy + Palatal Examination.
Deep Nasal Swab for KOH smear & Fungal Culture.
- Biopsy (in Sterile Saline for Mycology & Formol Saline for Histopathology)
  [At any point, in very high clinical suspicion - Day 1 till whenever and start liposomal amphotericin B (in very high clinical suspicion) without waiting for the Microbiology Reports]

Treatment

Antifungal medication
- Inj Amphotericin B (1.0-1.5 mg/kg/day)
- Inj Liposomal Amphotericin B (5-10 mg/kg/day)
- For 14 to 21 days

Note: Liposomal Amphotericin is preferred as it has relatively lesser nephrotoxic. The duration of therapy is highly individualised and should encompass the resolution of associated symptoms and findings normalization of radiologic findings, negative cultures from affected site, and resolution of immunosuppression
- Tab Posaconazole GR 100 mg (step down or adjutant therapy) First day -300 mg BD Other days- 300 mg OD for 45 days

Alternate day perform • S. Creatinine • S. Electrolyte to avoid Nephrotoxicity and hypokalaemia
Regular follow-up (CT PNS every 15 days to 1 month)

Amphotericin B administration protocol

Pre-hydration:
- 500ml Normal saline 2 hr before infusion Amphotericin B
- To reduces the risk of renal toxicity and hypokalaemia: - 500ml Normal Saline + 1 Amp (20mmol) KCL

Hydration:
- Dilution: 1mg in 10 ml
- Always use 5% or 10% dextrose
• Avoid Normal saline
• 500 mL NS IV given pre-infusion
• If fluid overloaded, use 250 mL pre/post or skip post-hydration
• If hyperchloremic, may use normosol instead of NS
• Protect from light during administration Drugs

Recommended Dose Duration
Amphotericin B 1.0-1.5 mg/kg/day 14 to 21 days depending on severity

Surgical

Early stage (only sinus is involved no bony change)
• Excisional biopsy (deep bone) + sinus lining
• FESS (Functional Endoscopic Sinus Surgery)

Confirmed or late stage (bony erosion)
• Debridement and curettage till healthy bone,
• Orbital exenteration if indicated after ophthalmologist opinion
• FESS

Test sampling:
• Bacterial or fungal cultural and sensitivity
• Histopathological investigation

<table>
<thead>
<tr>
<th>New Mantra in COVID cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Baseline HbA1c on Admission.</td>
</tr>
<tr>
<td>2. The strict control of blood sugar levels (110-180 mg/dl) and</td>
</tr>
<tr>
<td>3. Proper management of Diabetic Ketoacidosis (DKA)</td>
</tr>
<tr>
<td>4. Rational use of steroids in the high-risk group.</td>
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<tr>
<td>5. Adequate humidification with distilled water used in the humidifiers of the Conventional / Low Flow / High Flow Oxygen delivery systems.</td>
</tr>
<tr>
<td>6. Isotonic-Saline Nasal Douche / Spray x 2 Times a day.</td>
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<tr>
<td>8. Complete ENT Evaluation</td>
</tr>
</tbody>
</table>
### New Sutra to Educate patients about the early signs and symptoms of Mucor

<p>| | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>1.</td>
<td>Nasal Blockage</td>
</tr>
<tr>
<td>2.</td>
<td>Blood-tinged nasal discharge</td>
</tr>
<tr>
<td>3.</td>
<td>Headache</td>
</tr>
<tr>
<td>4.</td>
<td>Pain in the Eye</td>
</tr>
<tr>
<td>5.</td>
<td>One sided Facial Pain &amp; Swelling or Numbness</td>
</tr>
<tr>
<td>6.</td>
<td>Toothache, Loosening teeth, discomfort during chewing</td>
</tr>
<tr>
<td>7.</td>
<td>Swelling of the Eye &amp; Adnexa</td>
</tr>
<tr>
<td>8.</td>
<td>Double Vision</td>
</tr>
</tbody>
</table>

### Warning signs and symptoms of Rhino-Orbito-Cerebral Mucormycosis (ROCM)

- Nasal stuffiness
- Foul smell
- Epistaxis
- Nasal discharge - mucoid, purulent, blood-tinged or black
- Nasal mucosal erythema, inflammation, purple or blue discoloration, white ulcer, ischemia, or eschar
- Eyelid, periocular or facial edema
- Eyelid, periocular, facial discoloration
- Regional pain – orbit, paranasal sinus or dental pain
- Facial pain
- Worsening headache
- Proptosis
- Sudden loss of vision
- Facial paresthesia, anesthesia
- Sudden ptosis
- Ocular motility restriction, diplopia
- Facial palsy
- Fever, altered sensorium, paralysis, focal seizures

6. Post Discharge

i. Anti-coagulation

- We do not recommend anticoagulants and antiplatelet therapy for non-hospitalized patients with COVID-19. It should not be initiated for the prevention of venous thromboembolism (VTE) or arterial thrombosis unless the patient has other indications for the therapy.
- All admitted patients should, if there are no contraindications, receive anticoagulants in a prophylactic dose. Some guidelines do not recommend it but others do. So, aspirin and statin are not recommended for everyone on discharge.
- The decision on use of anticoagulants needs to take into account the risk of thrombosis and of bleeding on anticoagulants.
- The National Institutes of Health (NIH) does not recommend routine post discharge VTE prophylaxis for patients with COVID-19.
- The signal for increased thrombotic risk is sufficient to recommend pharmacologic venous thromboembolism (VTE) prophylaxis in all hospitalized COVID-19 patients as long as there is no contraindication.
- Extended post-hospital VTE prophylaxis should be considered in patients with COVID-19 (up to 45 days- MAGELLAN, APEX and MARINER studies).
- It is reasonable to employ individualized risk stratification of thrombotic and bleeding risk, to consider patients with elevated risk of VTE [e.g. Reduced mobility, active cancer, prior DVT, elevated D-dimer (>2 ULN)]. VTE options include Apixaban 2.5 bid, rivaroxaban 10 mg daily or Enoxaparin SQ daily (prevention dose adjusted for weight).
- When the risk of thrombosis is high, (as assessed by the ISTH SIC score) and a high bleeding risk has been ruled out (using the HAS-BLED score), we would recommend therapeutic anticoagulation.
A high HAS-BLED score (≥3) is indicative of the need for regular clinical review and follow-up, but should not be used per se as a reason for stopping oral anticoagulation. All scores are available through online calculators.

At hospital discharge, patients must be educated on the signs and symptoms of VTE and advised to seek urgent medical attention should these develop.

Postdischarge VTE prophylaxis decisions should be individualized, taking into consideration the patient’s risk factors, including reduced mobility, bleeding risks, and feasibility.

Pregnancy Issues: If antithrombotic therapy is prescribed during pregnancy prior to a diagnosis of COVID-19, continue it. If hospitalized for severe COVID-19, prophylactic dose of anticoagulants is recommended. After hospital discharge is not recommended for pregnant patients. Decisions to continue VTE prophylaxis in the pregnant or postpartum patient after discharge needs individualization and consideration of concomitant VTE risk factors. Anticoagulation therapy use during labor should be managed in pregnant patients with COVID-19 in a similar way as in pregnant patients with other conditions that require anticoagulation in pregnancy.

Lactation Issues: Unfractionated heparin, low molecular weight heparin, and warfarin do not accumulate in breast milk and do not induce an anticoagulant effect in the newborn. These can be used by breastfeeding individuals with or without COVID-19 who require VTE prophylaxis or treatment.

Note: Use of direct-acting oral anticoagulants during pregnancy is not routinely recommended due to lack of safety data.

ii. Corticosteroid therapy

Based on data from the Randomized Evaluation of COVID-19 Therapy (RECOVERY) trial, NIH guidelines recommend using dexamethasone 6 mg per day for up to 10 days for the treatment of COVID-19 in patients who are mechanically ventilated (level of evidence: AI—strong, based on ≥1 randomized trial) and in patients who require supplemental oxygen but who are not mechanically ventilated (level of evidence: BI—moderate, based on ≥1 randomized trial).

It is advised to continue a course of dexamethasone for 10 days even after discharge in recovered COVID-19 patients who required oxygen during hospital admission.

NIH guidelines do not recommend the use of dexamethasone for COVID-19 cases not requiring supplemental oxygen due to lack of survival benefits and potential harmful effects (AI).
iii. Oxygen therapy

- Although there is no evidence about the beneficial use of oxygen therapy at home in discharged COVID-19 patients, short-term home oxygen therapy may be considered in hypoxemic patients at rest (oxygen saturation <88% on room air). Risks and benefits should be weighed before discharging patients on home oxygen.

iv. Adjuvant therapies

- Some vitamins and minerals such as vitamin C, vitamin D, and zinc have been proposed for use in COVID-19 due to their beneficial antioxidant immunomodulatory effect, but NIH does not recommend using them due to lack of adequate safety and efficacy data in COVID-19 patients.
- We opine to use these on case-to-case basis.

7. Treatment of Post Covid Symptoms

Investigate it

Not all patients will need all

- CBC: Anaemia, Lymphopenia
- CRP persistent inflammation or super aided infection
- LFT, KFT, Blood Sugar,
- ECG- Bradycardia Cardiac involvement
- Ferritin (inflammation and continuing prothrombotic state),
- D-dimer (thromboembolic disease).
- Troponin and D-dimer tests may be falsely positive, but a negative result can reduce clinical uncertainty.
- Troponin (acute coronary syndrome or myocarditis)
- Chest x-ray for all patients continued respiratory symptoms >12 weeks. --Lung Fibrosis, Residual Pneumonitis, associated Fungal infections.
Issues and Management

Fever

- After recovery from Covid it is not uncommon to see resurgence of episodes of fever lasting few hours to days, especially after heavy physical activity. Such patients usually don't land up into serious complications.
- Rest, paracetamol and short 3-to-5-day course of Non-steroidal anti-inflammatory drugs like Mefenamic acid and Naproxen may be helpful.
- Some patients may require low dose of Non-steroidal Anti-inflammatory drugs for long duration. However, it may be important to monitor Kidney function in such cases.

Cough

- Rule out super-infection
- Rule out other complications as pleuritis (painful)
- Graded physical activity in case cough/fever/fatigue/breathlessness is precipitated by walking or talking
- Medication where indicated
- Antihistaminic
- Nebulization with Budesonide, Bronchodilators
- Proton pump inhibitors (if reflux is suspected)
- Cough Lozenges
- Respiratory Exercises: Helpful in Chronic cough aimed at normalising breathing patterns and increasing the efficiency of the respiratory muscles (including the diaphragm)

Technique:

- The patient should sit in a supported position and breathe in and out slowly, preferably in through the nose and out through the mouth, while relaxing the chest and shoulders and allowing the tummy to rise.
- They should aim for an inspiration to expiration ratio of 1:2. This technique can be used frequently throughout the day, in 5–10-minute bursts (or longer if helpful). Other breathing techniques—such as diaphragmatic breathing, slow deep breathing, pursed lip breathing, yoga techniques Pranayama are immensely helpful.

Breathlessness

- Some breathlessness is common after covid-19. It tends to improve with breathing exercises
- Treatment remains the same as for cough.
• But it is important to monitor oxygen by pulse oximeter. Oxygen level of 96% or above and the absence of desaturation on exertional tests like six-minute walk test is reassuring.
• Oxygen therapy should not be delayed at a level of 92% or below. Amount of supplemental oxygen should be titrated to target a range 94-98%.
• Survivors of covid-19 ARDS are at risk of long-term impairment of lung function and may require long-term home-based oxygen therapy.

**Lung Fibrosis**

• Pirfenidone 200mg BD/TDS is being tried but most of the pulmonologist do not advocate. It appears that majority of post Covid patients recover with time with insignificant/zero lung fibrosis over 3 to 4 months. The key is oxygenation, preventing secondary complications & nursing care.
• Ninteddenib 150mg OD/BD is also being used as anti-fibrotic drugs. It needs to be used with LFT monitoring and only if HRCT shows Fibrosis.
• We recommend starting these drugs only after consultation of a Pulmonologist.

**Silver Lining**

• Serious interstitial lung disease is rare in patients who are not hypoxic.
• Lung changes are largely reversible in most of the patients despite high CT severity score.

**8. Multisystem Inflammatory Syndrome in Adults**

**Diagnosis Clues**

• Evidence of acute or recent SARS-CoV-2 infection (documented by a nucleic acid amplification test [NAAT] or antigen or antibody testing) with minimal respiratory symptoms.
• With laboratory markers of severe inflammation (e.g., elevated C-reactive protein [CRP], ferritin, D-dimer, cardiac enzymes, liver enzymes, and creatinine).
• With various other symptoms, including fever and shock; and signs of cardiovascular, gastrointestinal, dermatologic, and neurologic disease.

Most adults in whom MIS-A has been described have survived.

<table>
<thead>
<tr>
<th>MIS-A is defined by the following criteria:</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ A severe illness requiring hospitalization in an individual aged ≥21 years;</td>
</tr>
<tr>
<td>▪ Current or past infection with SARS-CoV-2;</td>
</tr>
<tr>
<td>▪ Severe dysfunction in one or more extrapulmonary organ systems;</td>
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</tbody>
</table>

**70 CME INDIA**
Laboratory evidence of elevated inflammatory markers (e.g., CRP, ferritin, D-dimer, interleukin [IL]-6);

- Absence of severe respiratory illness; and
- Absence of an alternative unifying diagnosis.

Management

There are currently no controlled clinical trial data in patients with MIS-A to guide treatment of the syndrome.

Most of the cases have been managed by use of intravenous immunoglobulin, corticosteroids, or anti-IL-6 therapy.

Part 13. CME INDIA Tail Piece

Rapid antigen testing (RAT):

- Results available in an hour or less, tests for SARS-CoV-2
- RAT is most often antibody-based to capture SARS-CoV-2 antigens (typically N protein). They offer the potential to improve access to testing through point-of-care assays.
- In certain scenarios where rapid isolation is desired, it can be used as an initial screening test.
- While the rapid test can get results very quickly, the results may not always be accurate.
- Interpretation:

Positive test: The patient test is positive and the patient actually has the disease.

False-negative test: It means that the test is negative but the patient actually has the disease.

Disadvantages of rapid test: The chances of the false-negative rate can be as high as 50%.

Advantages: The chances of the false positive rate are quite low. So, if a patient tests positive from a rapid test it is more likely that he actually has the disease. In symptomatic patients If RAT is negative, we need to confirm his condition with an RT PCR test

RT-PCR

RT-PCR is considered Gold standard test as of now for the detection of SARSnCOV-2 virus.
This is a real-time Polymerase Chain Reaction (PCR) assay that involves sample purification, nucleic acid amplification, detection of the target sequence in the sample.

- Common gene targets include envelope (E gene), nucleocapsid (N gene), Structural (S gene), RNA-dependent RNA polymerase (RdRP gene) ORF1ab.
- E gene is intended for screening of Sarbecovirus while RdRP gene / N gene / ORF1ab gene / S gene are used for confirmation SARS-CoV-2.
- CT value is inversely proportional to the amount of genetic material present in the sample, although ICMR doesn’t correlate CT values with severity of the disease, it merely indicates amount of viral load.
- Sample - As only nasopharyngeal or oropharyngeal sample has low sensitivity, it is recommended that combination of both advocates high sensitivity.
- Multiple factors can affect the test result like stage of disease, quantity of virus present during sampling, sampling methods, transport, storage, extraction systems, detection kits used etc. There can also be variation in results between two different samples collected. A fresh sample is advised if results don’t correlate clinically.

### New COVID 19 Definitions

- **COVID-19**: Disease caused by SARS CoV-2 (or its mutant variants) in unvaccinated people for the first time.
- **Recurrent COVID**: Disease caused by SARS CoV-2 (or its mutant variants) in people who have already had COVID-19 and recovered from it.
- **Post-Vaccine COVID**: Disease caused by SARS CoV-2 (or its mutant variants) in people who have had full COVID vaccination.
Timely Prediction is vital

**Timely Prediction**

- In severe disease, WBCs show lymphocytopenia, affecting both CD4+ and CD8+ cells, as well as a decrease in monocytes and eosinophils, and a clear increase in neutrophils and NLR. These simple parameters can be used for early diagnosis and identification of critically ill patients

- Markedly higher concentrations of ALT, AST, creatinine, CK, LDH, cardiac troponin I, N-terminal pro-brain natriuretic peptide, and D-dimer are clearly good severity predictor

- Current clinical practice suggests that the determination of IL-6, D-dimer, LDH, and transaminases in addition to routine laboratory tests, is useful for the stratification of high-risk patients

- Coagulation abnormalities in PT, aPTT, FDP, and D-dimer, along with severe thrombocytopenia, are associated with life-threatening DIC, which necessitates continuous vigilance and prompt intervention

- These are in fact not only predictive of disease severity, but are also helpful for the therapeutic management, based on drugs preventing the activation of coagulation processes.

- A laboratory score, taking into account haematological, inflammatory, biochemical and immunological parameters, would help to stratify COVID-19 positive patients into risk categories, which would be of utmost importance in the clinical setting and therapeutic management.

Keep updated for ever changing COVID related recommendations

**What is working & not working in COVID 19 in 2021**

**Low or Very Low certainty of Interventions against COVID 19 in 2021**

1. Angiotensin-converting enzyme inhibitors
2. Azithromycin, Anakinra
3. Full dose anticoagulation, HCQ
4. Ivermectin, ivermectin plus doxycycline
5. Ilopinav-ritonavir plus interferon-beta, peginterferon lambda, proxalutamide, sulodexide
6. Vitamin C & Vitamin D

**New evidence showing drugs with benefit**

- IL-6 inhibitors probably reduce mechanical ventilation (moderate certainty) and may reduce duration of hospitalisation (low certainty)
- JAK inhibitors probably reduce duration of mechanical ventilation (moderate certainty) and may reduce mortality (low certainty), & duration of hospitalisation (low certainty)
- Colchicine may reduce mortality (low certainty) and mechanical ventilation (low certainty) in outpatients with non-severe disease

**Drug treatments for covid-19: living systematic review and network meta-analysis**
Prophylaxis against covid-19: living systematic review and network meta-analysis

<table>
<thead>
<tr>
<th></th>
<th>Laboratory confirmed SARS-CoV-2 infection</th>
<th>Suspected, probable, or laboratory confirmed SARS-CoV-2 infection</th>
<th>Admission to hospital</th>
<th>Mortality</th>
<th>Adverse effects leading to drug discontinuation</th>
<th>Time to symptom resolution or clinical improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard care*</td>
<td>65 per 1000</td>
<td>167 per 1000</td>
<td>5 per 1000</td>
<td>3 per 1000</td>
<td>15 per 1000</td>
<td></td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>2.1 (1.8 to 2.9)</td>
<td>-15 (-4.4 to 4.1)</td>
<td>-1 (3 to 4)</td>
<td>-1 (2 to 3)</td>
<td>19 (-1 to 2)</td>
<td></td>
</tr>
<tr>
<td>Ivermectin, Iota-cartagenan</td>
<td>-52 (-58 to -37)</td>
<td>-159 (-165 to -144)</td>
<td>-1 (3 to 6)</td>
<td>-1 (3 to 6)</td>
<td>-1 (3 to 6)</td>
<td></td>
</tr>
<tr>
<td>Ivermectin</td>
<td>-50 (-59 to -16)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

High or moderate certainty
Low certainty
Very low certainty

No currently available drug in India is protecting you against COVID 19

Mild disease: No role for Vitamin C & Zinc

RCT: Effect of High-Dose Zinc and Ascorbic Acid Supplementation on Symptom Length Among Ambulatory Patients with SARS-CoV-2 Infection

**POPULATION**
82 Men, 132 Women

**INTERVENTION**
214 Patients randomized and analyzed

| 50 Standard of care
| Standard outpatient prescription for usual items
| 48 Ascorbic acid
| 8000 mg Ascorbic acid
| 58 Zinc gluconate
| 50 mg Zinc
| 58 Zinc and ascorbic acid
| 50 mg Zinc and 8000 mg of ascorbic acid

**FINDINGS**
The study was stopped for a lack of evidence for benefit with no significant difference among the 4 groups for the primary end point, a 50% reduction in symptoms

**TIME TO 50% SYMPTOM REDUCTION**
Usual care: Mean (SD): 6.7 (4.4) days
Ascorbic acid: Mean (SD): 5.6 (3.3) days
Zinc gluconate: Mean (SD): 5.9 (4.2) days
Zinc and ascorbic acid: Mean (SD): 5.5 (3.4) days

74 CME INDIA
Standard dose Ivermectin failed to show benefit..

**QUESTION** What is the effect of ivermectin on duration of symptoms in adults with mild COVID-19?

**CONCLUSION** This randomized trial found that the duration of symptoms was not significantly different for patients who received a 5-day course of ivermectin compared with placebo, findings that do not support the use of ivermectin for treating mild COVID-19.

**POPULATION**
231 Women 167 Men
Adult patients with mild COVID-19 and symptoms for 7 days or fewer
Median age: 37 years

**INTERVENTION**
- 200 Patients randomized
- 398 patients analyzed
- 400 Patients randomized
- 398 Patients analyzed

- **Ivermectin**
  - Oral ivermectin in solution, 300 μg per kg of body weight per day for 5 days

- **Placebo**
  - Placebo daily for 5 days

**FINDINGS**

<table>
<thead>
<tr>
<th>FINDINGS</th>
<th>Median time to symptom resolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ivermectin</td>
<td>Day 0 10 days (IQR, 9–13)</td>
</tr>
<tr>
<td>Placebo</td>
<td>Day 12 days (IQR, 9–13)</td>
</tr>
</tbody>
</table>

Absolute difference: −2 days (95% CI, −4 to 2)
Hazard ratio for resolution of symptoms: 1.07 (95% CI, 0.87 to 1.32)

Inhaled Budesonide

- Inhaled budesonide is a simple, safe, well studied, inexpensive, and widely available treatment.
- In-vitro studies have shown that inhaled glucocorticoids
  - reduce the replication of SARS-CoV-2 in airway epithelial cells
  - downregulate expression of ACE2 and TMPRSS2 genes, which are critical for viral cell entry.

Budesonide as it was widely used

Budesonide for which patients?

- Inhaled budesonide can reduce symptom duration by 3 days.
- Start early within 3-6 days
- Useful for mildly ill patients with comorbid illness
- Above 50 years, 2 or more comorbid, Plus high CRP, not vaccinated
Role of Colchicine

- 10 days course would accelerate recovery faster
- 0.5 mg BD for 3 days then OD
- NNT to treat 70
- NNT cause harm 11
- Selected patients, male, with 2 co-morbid conditions minimal role.

Corticosteroids for COVID-19

Recommendation 1:
We recommend systemic corticosteroids rather than no systemic corticosteroids for the treatment of patients with severe and critical COVID-19 (strong recommendation, based on moderate certainty evidence).

Recommendation 2:
We suggest not to use corticosteroids in the treatment of patients with non-severe COVID-19 (conditional recommendation, based on low certainty evidence).
Second Wave New Insights

Act Before This Stage to Save Life

- Inflammation Markers ➔ Rising Lung Damage ➔ Decreasing PaO2 ➔ Decreasing SpO2

- Virus does not kill directly, it kills by immune Inflammation.
- Monitor Clinical and Biochemical Inflammatory Parameters.
- Fight Inflammation at Right time.
- Don’t Give Steroid in Early Viral Replicative Phase.
- “Cat Like Observation” and “Timely Step Up.”
- Timely Escalation and De-escalation.
- SAVE LIFE with Right Knowledge, Right Practice, and Courage.
- Decreased SpO2 is a very Late Finding.
- If CRP > 5 x ULN, D-Dimer > 2 x ULN, NLR > 3.2, Dexamethasone is the Game Changer.
- If Started in RIGHT Time, in HOME ISOLATION phase We can AVOID HOSPITALISATION, OXYGEN REQUIREMENT and DEATH.
- It is critical to pick up this time as Dexamethasone could be detrimental in viral replication phase and delay in initiation at right time could lead to poor outcome.

Courtesy: Dr. Prof. Soumitra Ghosh, HOD, Medicine, IPGMER and SSKM Hospital, Kolkata.
Comprehensive Guidelines for Management of COVID-19 patients

Asymptomatic
- Sustained cough
- Fever
- Sore throat
- Runny nose
- Headache
- Malaise
- Muscle pain
- New loss of taste or smell

Mild
- No dyspnea
- No diffuse interstitial pattern
- Oxygen saturation > 94%
- Tachycardia
- Tachypnea
- May require oxygen therapy

Moderate
- Shortness of breath
- Difficulty breathing
- Respiratory rate more than 30
- Temperature > 100.4°F
- SPO2: 90-94%

Severe
- Shortness of breath
- Difficulty breathing
- Temperature > 103°F
- Oxygen saturation < 90%
- SPO2: < 90%

COVID-19 Symptoms at a glance box

<table>
<thead>
<tr>
<th>Symptoms*</th>
<th>Asymptomatic</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>X</td>
<td>+</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Cough</td>
<td>X</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Sore Throat</td>
<td>X</td>
<td>+</td>
<td>+/-</td>
<td>+/-</td>
</tr>
<tr>
<td>Headache</td>
<td>X</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Malaise</td>
<td>X</td>
<td>+</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>X</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Anorexia</td>
<td>X</td>
<td>+/–</td>
<td>+/-</td>
<td>+/-</td>
</tr>
<tr>
<td>Vomiting</td>
<td>X</td>
<td>+/–</td>
<td>+/-</td>
<td>-</td>
</tr>
<tr>
<td>Loss of Taste</td>
<td>X</td>
<td>+/–</td>
<td>+/-</td>
<td>+</td>
</tr>
<tr>
<td>Respiratory rate/min</td>
<td>12-16</td>
<td>May be raised but less than 24</td>
<td>24-30</td>
<td>≥ 30/min</td>
</tr>
<tr>
<td>SPO2 on room air</td>
<td>≥95%</td>
<td>≥94%</td>
<td>90-93%</td>
<td>&lt; 90%</td>
</tr>
</tbody>
</table>

* The possible symptoms, signs and findings have been enlisted and patients in each category may have one or many of these.
Directorate General of Health Services, MoHFW, GOI
Comprehensive Guidelines for Management of COVID-19 patients

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

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

---

**Monitoring Sheet for Covid-19 Patients at Home**

Name: ____________________________  Age: ________  Sex: ________  Date: ________

Co-morbid conditions, if any and drugs being taken:
1. ________________________________
2. ________________________________
3. ________________________________
4. ________________________________

Controlled: (Y/N)

Parameters and record:

<table>
<thead>
<tr>
<th>Day/Time</th>
<th>Malaise*</th>
<th>SOB**</th>
<th>Temp</th>
<th>Pulse</th>
<th>BP</th>
<th>SPO2***</th>
<th>Any other</th>
</tr>
</thead>
<tbody>
<tr>
<td>8:00 AM</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12:00 Noon</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4:00 PM</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8:00 PM</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*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
Read all updates and apply your own wisdom

To be clear, sensible medicine does not mean clinicians should not intervene.

- Rather, it proposes a gentler, moderate, and humble view of available treatment options and their effectiveness in patients with COVID-19.
- In the middle is a sensible approach, which acknowledges that some interventions are effective but, perhaps, confidence should be tempered.
- With sensible medicine, the translation of knowledge to the bedside is appropriately calibrated to the rigor and reasoning of the available evidence and the severity of the outcome to be avoided.

- Christopher W. Seymour, MD, MSc, Associate Editor, JAMA/ Erin K. McCreary


Read the concise version of the CME INDIA Covid-19 Management Protocol 2021

81 CME INDIA
Suggested Reading:

Read CME INDIA Covid-19 Vaccination Protocol 2021

References:


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