राजस्थान सरकार
चिकित्सा एवं स्वास्थ्य विभाग

क्रमांकः प.1(1)चिस्वा/ग्रुप–2/2020 जयपुर, दिनांक : 17.10.2020

परिपत्र

कोविड–19 के संक्रमण के प्रसार को रोकने तथा इससे होने वाली जनहानि की रोकथाम किये जाने हेतु राज्य सरकार प्रारम्भ से ही कटिबद्व है। तथा इस संबंध में राज्य में निर्धारित **Treatment Protocol** की अन्य राज्यों के साथ–साथ केन्द्र सरकार द्वारा भी सराहना की गई है।

वर्तमान में राजकीय कोविड अस्पतालों के साथ–साथ राज्य के विभिन्न जिलों में स्थित निजी चिकित्सालयों में कोविड–19 मरीजो का उपचार किया जा रहा है। राज्य के समस्त COVID चिकित्सा संस्थानों में चिकित्सा की गुणवत्ता सुनिश्चित करने के लिए, राज्य सरकार की अधिसूचना कमांक प. 1(1)चिस्वा/ग्रुप–2/2020 दिनांक 25.09.2020 के अनुक्रम में COVID मरीजों का हाल ही में चिकित्सा प्रारम्भ करने वाले चिकित्सा संस्थानों में भी पूर्व के संस्थानों के अनुरूप ही निर्धारित Treatment Protocol लागू किया जाना अपेक्षित है।

अतः सभी डेडीकेटेड कोविड अस्पतालों व COVID–19 का उपचार कर रहे राजकीय/निजी चिकित्सालयों के अस्पताल प्रबंधन से यह अपेक्षित है कि पूर्व की भांति COVID–19 के Mild, Moderate व Severe मरीजों का उपचार व चिकित्सकीय प्रबंधन राज्य स्तरीय COVID Technical Core ग्रुप द्वारा निर्धारित संलग्न **COVID–19 Management Standard Protocol** (संलग्न) के अनुसार किया जाए।

Post COVID Management के संबंध में विस्तृत दिशा–निर्देश पृथक से जारी किये जा रहे है।

(अखिल अरोरा)
प्रमुख शासन सचिव

प्रतिलिपि निम्न को सूचनार्थ एवं आवश्यक कार्यवाही हेतु प्रेषित हैः–

1. प्रमुख सचिव, मा. मुख्यमंत्री महोदय।
2. विशिष्ठ सहायक, मा. चिकित्सा मंत्री महोदय
3. विशिष्ठ सहायक, मा. चिकित्सा राज्य मंत्री महोदय
4. वरिष्ठ उप सचिव, मुख्य सचिव महोदय।
5. निजी सचिव, प्रमुख शासन सचिव, चिकित्सा एवं स्वास्थ्य विभाग।
6. निजी सचिव, शासन सचिव, चिकित्सा शिक्षा विभाग।
7. मिशन निदेशक, एनएचएम, राजस्थान, जयपुर।
8. समस्त संभागीय आयुक्त/जिला कलक्टर, राज.।
9. समस्त प्रधानाचार्य एवं नियंत्रक, मेडिकल कॉलेज, राज.।
10. समस्त निदेशक चिकित्सा एवं स्वास्थ्य सेवाये राज. जयपुर।
11. समस्त संयुक्त निदेशक, चिकित्सा एवं स्वास्थ्य सेवाऐं, जोन राज.
12. समस्त प्रमुख चिकित्सा अधिकारी, राज.
13. समस्त मुख्य चिकित्सा एवं स्वास्थ्य अधिकारी, राज.
14. समस्त निजी चिकित्सालय, राजस्थान।
15. जन सम्पर्क अधिकारी, चिकित्सा एवं स्वास्थ्य सेवाये राज. जयपुर।
16. निजी/रक्षित/कम्प्यूटर सैल।
17. प्रभारी सर्वर रूम, मुख्यालय को भेजकर लेख है कि उक्त आदेश आज ही विभाग की वेबसाईट पर अपलोड करे।

(संजय कुमार)
शासन उप सचिव

RAJASTHAN

COVID-19 MANAGEMENT

STANDARD PROTOCOL

(COVID Treatment Protocol Team, SMS Medical College & Hospital, Jaipur)

Index:

Management protocol for adults:

COVID-19 MANAGEMENT

STANDARD PROTOCOL FOR ADULTS

1. Definitions:

ILI / SARI Patient:

An acute respiratory infection with measured fever of ≥ 38 C°(100.5 ^{0}F)and cough; with onset within the last 10 days.

If the condition of the patient requires hospitalization it is known as SARI.

SARI: Summary Points:
Oxygenation (adults):

- Mild ARDS: 200 mmHg < PaO2/FiO2 ≤ 300 mmHg (with PEEP or CPAP ≥5 cm H2O, or n ventilated)
- Moderate ARDS: 100 mmHg < PaO2/FiO2 ≤200 mmHg with PEEP ≥5 cm H2O, or non-ventilated)
- Severe ARDS: PaO2/FiO2 ≤ 100 mmHg with PEEP ≥5 cmH2O, or non- ventilated)
- When PaO2 is not available, SpO2/FiO2 ≤315 suggests ARDS (including in non-ventilated patients)
- Oxygenation (children; note OI = Oxygenation Index and OSI = Oxygenation Index using SpO2)
- Bi-level NIV or CPAP ≥5 cmH2O via full face mask: PaO2/FiO2 ≤ 300 mmHg or SpO2/FiO2 ≤264
- Mild ARDS (invasively ventilated): 4 ≤ OI < 8 or 5 ≤ OSI < 7.5
- Moderate ARDS (invasively ventilated): 8 ≤ OI < 16 or 7.5 ≤ OSI < 12.3
- Severe ARDS (invasively ventilated): OI ≥ 16 or OSI ≥ 12.3

Sepsis
Adults: life-threatening organ dysfunction caused by a dysregulated host response to suspected or proven infection, with organ dysfunction. Signs of organ dysfunction include: altered mental status, difficult or fast breathing, low oxygen saturation, reduced urine output, fast heart rate, weak pulse, cold extremities or low blood pressure, skin mottling, or laboratory evidence of coagulopathy, thrombocytopenia, acidosis, high lactate or hyperbilirubinemia.
Children: suspected or proven infection and ≥2 SIRS criteria, of which one must be abnormal temperature or white blood cell
count
Septic shock
Adults: persisting hypotension despite volume resuscitation, requiring vasopressors to maintain MAP ≥65 mmHg and serum lactate level >2 mmol/L

Children: any hypotension (SBP <5th centile or >2 SD below normal for age) or 2-3 of the following: altered mental state; tachycardia or bradycardia (HR <90 bpm or >160 bpm in infants and HR <70 bpm or >150 bpm in children); prolonged capillary refill (>2 sec) or warm vasodilation with bounding pulses; tachypnea; mottled skin or petechial or purpuric rash; increased lactate; oliguria; hyperthermia
or hypothermia

Detailed management of SARI can be accessed at:

https://ncdc.gov.in/WriteReadData/l892s/96997299691580715786.pdf

COVID 19 Case definitions:

Suspect COVID Case:

ILI or SARI or Acute onset of any three or more of the following: fever, cough, fatigue, headache, myalgia, sore throat, coryza, dyspnea, anorexia/nausea/vomiting, diarrhea, altered mental status.

Probable COVID Case:

A suspect COVID case (as above) along with:

a. History of close contact with a confirmed COVID case
b. Radioimaging (X-ray/CT/ USG) findings suggestive of COVID pneumonia

Or a person with recent onset of anosmia (loss of smell) or ageusia (loss of taste) irrespective of any sign or symptoms.

Confirmed COVID Case:

A person with laboratory confirmation of COVID-19 infection, irrespective of clinical signs and symptoms.

2. Clinical Stratification of ILI Patients:

- **Mild:**
  - Fever and/or uncomplicated upper respiratory tract infection without dyspnea or hypoxemia

- **Moderate:**
    - Mild pneumonia with no signs of severe disease
    - RR ≥24/min
    - SpO_2<94% on room air
    - Chest X-RAY:Bilateral lung infiltrates involving<50% of lung fields
    - HRCT Score: <15/25 (should be preferably done between 6-10 days after symptom onset)
- **Severe**
    - RR≥ 30/min
    - SpO_2<90% on room air
    - Severe respiratory distress requiring mechanical ventilation (Invasive or Non-invasive)
    - Chest X-RAY: B/L lung infiltrates involving ≥50% of lung fields
    - HRCT Chest Severity Score >15/25

- **Critically ill:** Onset of new or worsening respiratory symptoms (ARDS) within one week of known clinical insult. ARDS can be mild, moderate and severe.
    - Mild ARDS: 200 mmHg < $PaO_2/FiO_2 \leq$ 300 mmHg(with PEEP ≥5 cm H_2O)
    - Moderate ARDS: 100 mmHg <$PaO_2/FiO_2 \leq$200mmHg (with PEEP≥5 cm H_2O)
    - Severe ARDS: $PaO_2/FiO_2 \leq$ 100 mmHg (with PEEP≥5 cm H2O)
    - When PaO_2 is not available, SPO_2 can be used: SpO2/FiO_2 ≤315
    - Presence of sepsis and septic shock or multi organ dysfunction (MODS)
    - Altered mental status

3. Management of ILI Patients as per clinical stratification:

3.1 Mild Cases:

- Home Isolation/ Covid care center (if home isolation not possible)
- Admit in Covid Hospital if risk factors are present.
- The major risk factors for severe disease are:
    - Age more than 60 years (increasing with age).
    - Underlying non-communicable diseases (NCDs): diabetes, hypertension, cardiac

disease, chronic lung disease, cerebro-vascular disease, chronic kidney disease

- Immune-suppression and cancer

Investigations:

- No investigations are required in completely asymptomatic/ very mild individuals
- In ILI /SARI patients the following may be advised at baseline at the discretion of physician:
  - CBC, ESR
  - Chest Xray
  - ECG (in high risk patients being started on HCQ)
  - Blood sugar
  - Creatinine
  - Liver enzymes
  - Uric Acid
- If there is doubt regarding clinical severity of the disease, HR CT scan of chest and other relevant investigations (e.g. CRP, D-dimer, Interleukin-6 etc.) may be advised.

Treatment:

- Antipyretics (Paracetamol), Antitussives,
- Adequate hydration
- Tab. Hydroxychloroquine (400mg twice a day on first day followed by 200mg twice a day for next four days)
- Antibiotics (Azithromycin / co-Amoxyclav) may be added if clinically indicated.
- Monitor QT interval 2-3 hours after the second dose of HCQ & daily thereafter (If QTc increases by >60ms or is >500ms, reduce the dose or consider discontinuing).
- These patients (particularly those with risk factors) may deteriorate in a course of 7-10 days of symptom onset and therefore, should be taught to actively self-monitor for progression of disease by frequent self-monitoring of respiratory rate, pulse Oximetry.

Referral:

- Refer to a nearest COVID Hospital with oxygen beds linked to concerned Covid Care Centre in case of suspected/acute worsening as manifested by (SPO_2 < 94% on room air), development of new symptoms (i.e. high fever, breathlessness, chest pain, drowsiness etc.)

3.2 Moderate Cases:

The aim is to prevent mortality and progression from moderate to severe category by early identification and aggressive management of these patients.

- Should be admitted in a COVID hospital ward.
- Actively watch for the disease progression.

Investigations:

- Baseline investigations
    - CBC, DLC, ESR, N:L ratio
    - Chest X-ray(every 3^{rd}-4^{th} day)
    - HRCT scan chest (preferable where available)
    - ECG (daily)
    - Blood sugar charting
    - Renal function tests
    - Liver function tests (daily while on Remdesivir)
    - D-dimer assay
    - C-reactive Protein
    - Interleukin – 6

  These tests can be repeated every 72 hours or whenever the clinical condition of the patient warrants.
- Optional : USG, 2-D Echo, Arterial blood gas analysis

  CPK, LDH, Troponins, Ferritin, Procalcitonin, S. cortisol level

Treatment:

- *Oxygen supplementation* should be promptly initiated (preferably in the ambulance/ triage area) to achieve target SPO_2 range: 92% - 96% (in COPD target SPO_2 88- 92%).
  Nasal prongs and simple face masks may be used.
  If target SPO_2 is not achieved then non- rebreathing face masks or high flow nasal cannula (HFNC) may be used.
- *Awake Prone positioning* may be advised to awake and spontaneously breathing patients with oxygen requirement of >4 Lpm, the patients should have a normal mental status and able to change positions spontaneously. The contraindications are Spinal or chest wall instability, hemodynamic instability or raised intracranial pressure. (see section on oxygenation)
- Ensure adequate hydration with cautious conservative fluid therapy with crystalloids guided by hemodynamic parameters.
- *Inj. Dexamethasone*: 6mgIV daily for 10 days (or until discharge) should be started promptly in these patients, especially in those who require supplemental oxygen. Inj. Methylprednisolone (0.5 to 1 mg/kg/day for 10 days) may also be given.
  WHO Warning: Not to use corticosteroids in patients who do not require Oxygen therapy.
- Antivirals: Beneficial in **Early Moderate illness**

- *Inj. Remdesivir*: 200mg IV infusion in normal saline over 90-120minutes on first day (loading dose), followed by 100mg IV infusion daily for4 days (total 5 days).
  The patient should have normal renal and hepatic function. It is contraindicated if hepatic transaminases are raised >5 times the ULN or eGFR is less than 30 ml/min. **HCQ to be stopped prior to starting Remdesivir.** The liver functions should be monitored daily.

- *Convalescent plasma therapy*: if available, convalescent plasma (4-13mL/kg or 200mL) can be infused slowly over 2 hrs. Up to two doses can be given. (Page 18).

- Inj. Tocilizumab: Tocilizumab can be used to combat cytokine storm (CRS) in Covid-19. It can occur within 1-14 days and resolves within a few days to 2-3 weeks. Mild CRS is characterized by high fever, fatigue, headache, rash, diarrhea, arthralgia, and myalgia.
  While Severe CRS can cause hypotension and uncontrolled SIRS with circulatory collapse, vascular leakage, peripheral and/or pulmonary edema, renal failure, cardiac dysfunction, and multi organ system failure.
  The CRS is diagnosed by clinical deterioration and elevated serum markers of CRS (e.g. IL-6, ferritin, CRP etc.). IL-6 levels rise of more than 7 folds of the baseline value can indicate impending CRS (normal value <6pg/mL). The usual dose of Tocilizumab is 12 mg/kg single dose for patients with <30 kg weight and 8 mg/kg single dose for patients >30 kg bodyweight. It can be repeated for 2-3 more doses if desirable clinical response is not achieved. The contraindications to its use are: HIV infection, tuberculosis, active hepatitis, active bacterial and fungal infections, neutropenia (<2000/mm^3) or thrombocytopenia (<100,000/mm^3).
- *Anticoagulation:* Low molecular weight heparins (LMWH) in the dose of 0.5-1 mg/kg daily should be used in all patients if there are no contraindications. inj. Enoxaparin 40mg, SC, once daily can be used. However, in patients with D-dimer>1000ng/mL, 40 mg, SC, twice daily should be used. In patients with ESRD, unfractionated heparin (UFH) instead of LMWH should be used.
- For *bronchodilation*: MDI are preferred over Nebulization.
- *Antibiotics* should be used as per discretion of treating physician.
- Symptomatic treatment: Paracetamol, antiemetics should be continued.
- Associated comorbid conditions esp. diabetes, hypertension should be meticulously monitored and managed. Continue antidiabetics (Preferably use Insulin /DPP4 inhibitors and metformin **whereas Pioglitazone and SGLT2 Inhibitors are contraindicated)** if the patient is already taking.
- Continue ACEI/ARB and Statins if already prescribed.

- Careful monitoring as well as keeping watch for worsening of oxygenation and increase in oxygen requirement in those with high risk factors for severe disease is essential.
- The patients should be immediately shifted/referred to ICU (if not already in an intensive care area) if there are signs of worsening respiratory failure/distress or sepsis.(e.g.: RR ≥30/min; SpO2<90% on room air, confusion, hypotension, anuria etc.)

TABLE-1: RISK FACTORS FOR COVID-19 DISEASE PROGRESSION

Epidemiological- Category 1	Vital Signs- Category 2	Labs- Category 3
Age ≥ 65 years	Respiratory rate > 24 /min	D-dimer > 1000 ng/mL
Pre-existing pulmonary disease	Heart rate > 125 /min	CPK > Twice the upper limit of normal
Chronic kidney disease	SpO_2≤ 94% on room air	CRP > 100
Diabetes with HbA1C > 7.6%	PaO_2/ FiO_2< 300 mmHg	LDH > 245 U/L
History of hypertension		Elevated troponin
History of cardiovascular disease		Admission absolute lymphocyte count < 0.8x 10^9/L
Obesity (BMI ≥ 30 kg/m^2)		Ferritin > 500 µg/L
Use of biologicals		
History of transplant or other immunosuppression		

Referral:

- Refer to a nearest COVID Hospital with ICU facility in case of not able to maintain SPO_2 >92 on oxygen and there is potential need for assisted ventilation or the patient is showing signs of severe major organ dysfunction.
-

Treatment of a Suspect COVID Patient:

If COVID-19 RT-PCR is once or twice negative but HRCT Chest is suggestive of COVID infection (CORADS IV or V) of moderate severity (as per CT Severity Score) the treatment should be started as above according to the clinical judgement of the treating physician.

3.3Severe Cases:

Should be admitted in a COVID ICU under care of multi-specialty ICU team comprising of Anesthetist and/or Intensivists for ventilation management.

Investigations :

- Baseline investigations
  - CBC, ESR

- Chest X-ray
- HRCT scan chest (preferably on 6^{th}-10^{th} day of illness, where available)
- ECG (daily)
- USG
- 2D-ECHO (baseline)
- Blood sugar
- Renal function tests
- Liver function tests
- D-dimer assay
- C-reactive Protein
- Interleukin – 6
- Arterial blood gas analysis
- Procalcitonin

These tests can be repeated every 48-72 hours or whenever the clinical condition of the patient warrants.

- Optional: blood/urine cultures for bacteria/fungi (especially after using Tocilizumab),coagulation studies etc.

Treatment:

- *Oxygen supplementation*: Oxygenation with appropriate device (nasal prongs, high flow masks or HFNC) aiming for a target $SpO_2$92% -96% (in COPD target SpO2 88-92%).At this stage Non-invasive ventilation (NIPPV) should be instituted as soon as possible if the patient is not maintaining sufficient oxygenation. If he is still not responding then consider intubation with invasive mechanical ventilation (IPPV) with lung protective ventilation strategy. (Section-5)
- Cautious conservative fluid therapy with crystalloids guided by hemodynamic parameters
- Empirical antibiotics (Ceftriaxone/ Piperacillin-Tazobactum) if bacterial pneumonia is suspected. The antibiotic choice is mainly dependent on local bacterial flora and their sensitivity.
- *Vasopressors:* In presence of shock: noradrenaline infusion is the drug of choice. Vasopressin can be used subsequently with the aim to maintain MAP ≥65mmHg.
- *Corticosteroids:* Hydrocortisone 50mg IV QID can be used to combat refractory septic shock. In case of Cytokine Storm, high dose Dexamethasone (10 mg every 6hours) can be used.
- *Anticoagulation:* Low molecular weight heparins (LMWH) should be used in all these patients if there are no contraindications. Full therapeutic dose (enoxaparin 40mg SC BD) should be used for all these patients in ICU. In patients with ESRD, unfractionated heparin (UFH) may be used.
- Antivirals and convalescent plasma therapy as per moderate cases

- Inj.Tocilizumab: to combat CRS if IL-6 values are above 7 times baseline values along with appropriate clinical setting.
- Care should be taken to minimize the risks of nosocomial infections incl. VAP, pressure sores (frequent turning), stress ulcers and GI bleeds (by use of PPI), venous thromboembolism (by using LMWH).
- Appropriate chest and limb physiotherapy and enteral and parenteral nutrition should be ensured.

Referral:

- Refer to a nearest tertiary care COVID Hospital with multispecialty ICU facility (level 3) in case of acute worsening in form of unresponsive major organ dysfunction or respiratory failure.

Treatment of a Suspect COVID Patient:

If COVID-19 RT-PCR is once or twice negative but HRCT Chest is suggestive of COVID infection (CORADS IV or V) of moderate severity (as per CT Severity Score) the treatment should be started as above according to the clinical judgement of the treating physician.

3.4 Critically Ill Cases:

- Should be admitted in a COVID ICU under care of multi-specialty ICU team of Anesthetist/Intensivist for active ventilation management.

Treatment:

- Oxygenation: NIV by CPAP or BiPAP or Invasive Mechanical ventilation by Lung protective strategy
- Cautious conservative fluid therapy with crystalloids guided by hemodynamic parameters
- Empirical antibiotics (Ceftriaxone/ Piperacillin-Tazobactum) if bacterial pneumonia is suspected. The antibiotic choice is mainly dependent on local bacterial flora and their sensitivity.
- *Vasopressors:* In presence of shock: noradrenaline/ Vasopressin infusion with the aim to maintain MAP ≥65mmHg.
- *Corticosteroids:* Dexamethasone 6mg-10mg IV OD or Hydrocortisone 50mg IV QID can be used to combat refractory septic shock.
- *Anticoagulation:* Low molecular weight heparins (LMWH) should be used in all these patients if there are no contraindications. Full therapeutic dose (enoxaparin 0.4 mg SC BD) should be used for those in ICU. In patients with ESRD, unfractionated heparin (UFH) may be used.
- Nutrition and sedation as per guidelines

- Antivirals as per moderate cases
- Convalescent plasma therapy
- Inj.Tocilizumab (only if clinically indicated)
- Hemodynamic Monitoring

3.5 Discharge Policy:

The discharge policy as laid down by the ministry of health and family welfare, Government of India to be followed in above cases. The document can be accessed at : https://www.mohfw.gov.in/pdf/ReviseddischargePolicyforCOVID19.pdf .

4 Airway Management and Oxygen therapy:

Causes of acute hypoxemia in Covid:

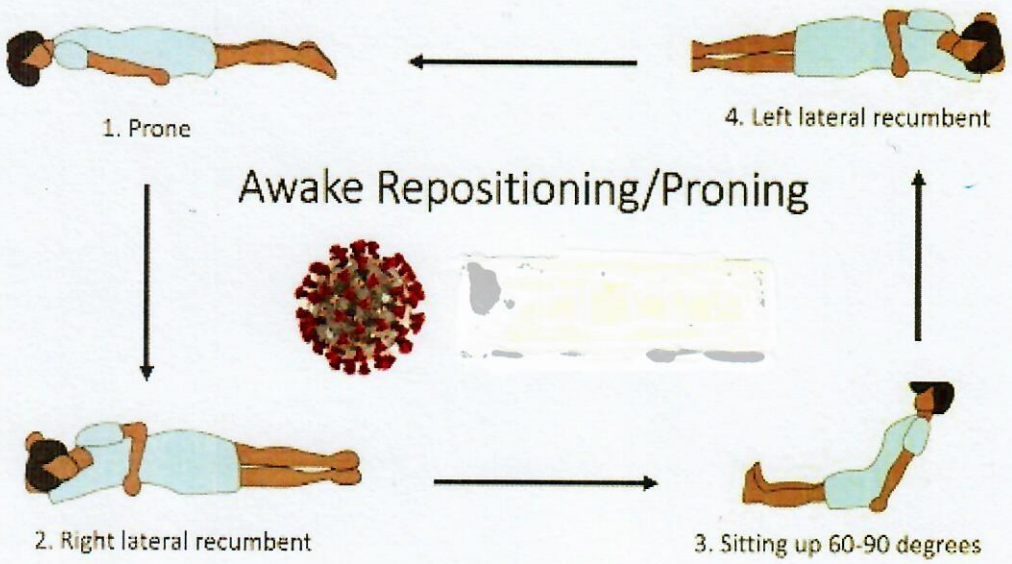
- Bilateral Viral Pneumonia
- Bacterial Pneumonia
- Cardiogenic pulmonary edema
- Coexisting COPD with AE
- Pulmonary Embolism
- Pneumothorax
- Aspiration Pneumonia

4.1 Awake Prone Positioning:

Awake prone positioning with oxygenation should be considered in mild respiratory distress in awake non-intubated patients. Any COVID-19 patient with respiratory embarrassment severe enough to be admitted to the hospital may be considered for rotation and early self-proning. Care must be taken to not disrupt the flow of oxygen during patient rotation. 50% may again become hypoxic on re-supination.

Typical protocols include 30–120 minutes in prone position, followed by 30–120 minutes in left lateral decubitus, right lateral decubitus, and upright sitting position:

- 30-120 minutes in prone position
  ⬇
- 30-120 minutes in right lateral decubitus position
  ⬇
- 30 -120 minutes in sitting position 60-90 degrees
  ⬇
- 30-120 minutes in the left lateral decubitus position



4.2 Oxygen supplementation

- *Oxygen supplementation* should be promptly initiated whenever SPO_2 falls below 94% (preferably in the ambulance/ triage area) to target SpO_2 range: 92% - 96% (in COPD target SpO_2 88- 92%).
- Nasal prongs and simple face masks may be used.
- Initiate oxygen therapy with nasal prongs (2-5 L/min)/ simple face mask (5-10 L/min) and titrate flow rates as per oxygen saturation. Patients on supplementary oxygen via nasal cannula should wear a surgical mask.
- If not maintaining saturation then deliver oxygen via face mask with reservoir bag (flow rates of 10–15 L/min).
- ABG should be done if patient's general condition is deteriorating and is not maintaining oxygen saturation in target range.
- If patient is not maintaining oxygen saturation>92% and PaO_2>60 mm Hg, consider Non-invasive ventilation / high flow nasal cannula (HFNC).

4.3 High Flow Nasal Cannula (HFNC):

- When the oxygen saturation is not maintained with 10-15 liters of oxygen, the HFNC may be used with flow rates up to 60 liters per minute.
- HFNC provides a PEEP up to 5-6 cm H2O.
- HFNC flow rates to be set from 30-60 L/min to achieve and maintain SPO2 >92% .
- If not maintaining oxygen saturation and PaO2 with NIV / HFNC consider invasive ventilation

4.4 Non-Invasive Ventilation (NIPPV):

- Trial of NIPPV for 1-2 hours is suggested with close monitoring to avoid unrecognized severe respiratory decompensation.
- NIV may be started with IPAP of 10 cm of H2O , EPAP of 6 cm of H2O and FiO2 60% to 100%.
- NIV should be preferably delivered with properly fitted non-vented mask through ICU ventilator to minimize aerosol generation.
- If patient is conscious and tolerates NIV and maintains saturation>92% and PaO2 >60 mm Hg: continue with NIV.
- If the patient requires high PEEP or FiO2 >80% on NIV, the patient may be considered for invasive mechanical ventilation.
- During oral feedings or when NIV mask is being removed patient should receive oxygen via nasal prongs with a flow of 5 to 6 lit/min.
- If not maintaining oxygen saturation and PaO2 with NIV consider invasive ventilation.

4.5 Invasive Mechanical Ventilation (IPPV)

Indications of intubation

- SpO2 below 90% or PaO2 ≤ 60 mm of Hg inspite of standard oxygen therapy
- Clinical features (sweating, restlessness, agitation, shallow rapid breathing, drowsy/Unresponsiveness) should also be considered.

Preparing the ventilator

- Connect oxygen, compressed air and AC mains supply.
- Use disposable ventilator tubings &connect closed suction assembly.
- Connect one HMEF/HEPA filter at patient end to Y connector and mention date and time on it & one HMEF/HEPA filter at ventilator end of expiratory limb.
- Oral endotracheal intubation
- Pre-oxygenate with 100% oxygen for at least 3-5 minutes.
- Rapid Sequence Induction with no or minimal positive pressure ventilation
- Ensure tight seal of mask (hold mask with two hand technique)
- Clamp the patient end of the tube before intubating and declamp it after connecting with circuit.
- Inflate the cuff immediately after intubation of the trachea
- Start mechanical ventilation
- Mode :- Control mode
- Tidal volume:- 4–8 mL/kg predicted body weight.

- FiO2:- 100% (To be tapered down later to keep SpO2 above 90%),
- Maintain plateau pressure < 30 cmH2O
- Neuromuscular blockade: - Paralyze patient with Atracurium infusion for 24 to 48 hours.
- Sedation:- Consider infusion of fentanyl or midazolam.
- Recruitment maneuvers:- If required
- Fluid:- Conservative fluid management strategy for patients without tissue hypoperfusion.
- Vasopressors: Norepinephrine is the first-line vasoactive agent.
- Suction:- In-line catheters (closed suction catheter).

5 Convalescent Plasma therapy in COVID-19:

Convalescent plasma therapy may be considered in Covid-19 patients with moderate disease who are not improving (oxygen requirement is progressively increasing) despite use of steroids. Plasma for therapy must have been obtained from a healthy donor who has recovered from mild to moderate COVID-19 and has a negative RT-PCR test not less than 14 days before the date of donation of plasma.

Special prerequisites while considering convalescent plasma include:

- ABO compatibility and cross matching of the donor plasma
- Neutralizing titer of donor plasma should be above the specific threshold or if the latter is not available, plasma IgG titer (against S-protein RBD) above 1:640 should be used.
- Recipient should be closely monitored for several hours post transfusion for any transfusion related adverse events e.g. transfusion reactions, TACO, TRALI etc.
- Use should be avoided in nulliparous females, patients with IgA deficiency or immunoglobulin allergy

Dose: Dose is variable ranging from 4 to 13 ml/kg but usually a 200 ml single dose is given slowly over not less than 2 hours under observation. (ICMR guidelines should be followed)

6 Other therapeutic agents in Covid-19

Favipiravir

May be beneficial in mild cases. However, has a low-quality evidence in Covid-19. Currently not recommended by this treatment group or by national treatment guidelines group.

Doxycycline-Ivermectin

Can be used along with ivermectin in mild cases **where hydroxychloroquine is contraindicated or not tolerated**. The doses are Tab. Ivermectin 12 mg daily for 3 days along with Tab. Doxycycline 100 mg

twice a day for 10 days.

Ulinastatin, Mycobacterium w (sepsivac),Nitazoxanide,Niklosamide,Umifenovir, currently do not have strong evidence and are not recommended.

7 Post-COVID Care

- COVID appropriate behaviour (use of mask, hand & respiratory hygiene, physical distancing) should be advised.
- Post Covid fatigue can be tackled with 1-2 week vitamin and mineral supplements.
- Maintain adequate hydration.
- Steroid, if used for long term (>14 days), can be gradually tapered.
- Mucolytics (N-acetyl cysteine) and bronchodilators may be prescribed.
- Anticoagulants (rivaroxaban/ apixaban) may be prescribed for 2 weeks post discharge if there is history of pulmonary thromboembolism.
  Prolonged anticoagulation use should depend on:

  IMPROVE-VTE score of > 4

  D-dimer values >2 times normal

- Chest and limb physiotherapy, breathing exercises should be taught and advised.
- May take AYUSH medicines as prescribed by a qualified practitioner to boost health.
- In case of severe infection, *wait for at least 4-6 weeks for a follow up imaging to demonstrate radiologic resolution.*

Post Covid fibrosis

- Patients with a severe illness are more likely to develop pulmonary fibrosis later.
- The risk factors for post Covid fibrosis are: age > 65, prolonged ICU stay, and a history of smoking and chronic alcoholism.
- May be reduced with the use of lung protective ventilation (low tidal volume / low inspiratory pressure)
- Usually require long term oxygen therapy (Adequate oxygen beds /NIV beds be made available)
- Long term low dose steroids may be considered in selective individuals with above risk factors.

8. COVID-19 MANAGEMENT

STANDARD PROTOCOL for Children

Department of Pediatric Medicine, SMS Medical College, Jaipur

COVID 19 in children

Clinical Features: Fever, Cough, Fatigue, Shortness of breath, Other features: Expectoration, Myalgia, Rhinorrhea, Sore throat, Diarrhea, Loss of smell (anosmia) or loss of taste (ageusia) preceding the onset of respiratory symptoms.

Clinical syndromes associated with COVID - 19 infection and suggested management protocol

Asymptomatic Children	No symptoms/ signs. Diagnosed by contact tracing.	No treatment needed
Uncomplicated Illness/ Mild disease	Children with uncomplicated upper respiratory tract viral infection, may have fever, cough, sore throat, nasal congestion, malaise, headache.	Symptomatic: Paracetamol for fever. Adequate Hydration and nutrition HCQS (Chloroquine if HCQS not available) – specially in children with high risk features for severe disease*
Moderate disease	Patient with pneumonia, with cough or fast breathing: (fast breathing - in breaths/min): <2 months, ≥60; 2–11 months, ≥50; 1– 5 years, ≥40 And no signs of severe pneumonia SpO2 90-94% in room air.	Symptomatic: PCM for fever Adequate Hydration and nutrition O2 support: Nasal prong/ Mask Empirical Antibiotics- specially in <5yrs preferably IV Ceftriaxone LMWH- 0.5-0.8 mg/kg SC OD (max 40 mg) HCQS (Chloroquine if HCQS not available) IV Methylprednisolone 1mg/kg OD / Dexamethasone 0.2 mg/kg/day OD for 3 days May consider Remdesivir- on case to case basis (Avoid use with HCQS)
Severe pneumonia	Child with cough or difficulty in breathing, plus at least one of the following: central cyanosis or SpO2 <90%; severe respiratory distress (e.g. grunting, chest indrawing); Signs of pneumonia with any of the following danger signs: inability to breastfeed or drink, lethargy or unconsciousness, or convulsions. Other signs of pneumonia may be present.	Symptomatic and supportive treatment Conservative fluid management if there is no evidence of shock O2 support Antibiotic preferably IV Ceftriaxone LMWH- 0.5-0.8 mg/kg SC BD (Max 40 mg BD) IV MPS 2 mg/kg OD / Dexamethasone 0.2-0.4 mg/kg OD for 5-7 days Should consider Remdesivir- on case to case basis

***High risk conditions like**: Diabetes, hypertension, cardiac disease, chronic lung disease, chronic liver disease, cerebro-vascular disease, chronic kidney disease, immune-suppression, cancer and obesity.

Complications: ARDS, Sepsis, Septic Shock, MIS-C (Multisystem Inflammatory Syndrome in children)

Laboratory Investigations

1. Throat swab/ nasal swab for RT PCR for Covid 19 (and H1N1 preferably)
2. CBC with DLC, Lymphocyte count
3. Chest x-ray PA view
4. Other: LFT, RFT, ESR, LDH, PT, PTTK
5. D-dimer, CRP, Ferritin, S Electrolytes, ABG and HRCT Chest in moderate and severe disease
6. Cytokine levels (specially IL6), in severe disease or rapidly progressive disease

Medications

Hydroxychloroquine sulfate (HCQS)

Dose: 7- 8 mg/kg/dose BD for Day 1 and then 7- 8 mg/kg once a day from D2- D5;

An ECG should ideally be done before prescribing the drug to measure QTc interval. Avoid HCQ in patients with underlying cardiac disease, history of unexplained syncope or QTc prolongation (>480 ms). HCQS should be avoided in patients with severe disease. Avoid giving HCQS with Azithromycin as it may lead to arrhythmia.

Remdesivir: It may be considered in patients with moderate to severe disease (those on oxygen), preferably early disease, with none of the following contraindications:

1. AST/ALT > 5 times Upper limit of normal (ULN)
2. Severe renal impairment (i.e., eGFR < 30ml/min/m2 or need for hemodialysis)
3. Children (< 12 years of age). However, may be used under emergency use authorization on case to case basis with informed written consent from parents explaining possible risks and benefits.

Dose: >40 Kg: 200 mg IV on day 1 followed by 100 mg IV daily for 4 days (total 5 days)

3.5- <40 kg: 5mg/kg od kg IV over 30–120 minutes, on day 1, followed by 2.5 mg/kg od.

Concomitant use of Remdesivir and HCQS is not recommended, as HCQS exhibits antagonistic effect in

vitro as well HCQS as may increase hepatotoxicity of Remdesivir. If patient require invasive mechanical ventilation, treatment duration of remdesivir can be extended to 10 days on case to case basis.

Tocilizumab: It may be used, in cases with progressive disease with high levels of inflammatory markers as IL6, Ferritin and CRP. It should be used only under emergency use authorization on case to case basis with prior informed consent from parents explaining possible risks and benefits.

Tocilizumab is contraindicated in patients with active bacterial or fungal infection, TB, HIV, neutropenia (< 2000/ mm3) and thrombocytopenia (<1,00,000/ mm3)

Dose: 8mg/kg (adult dose 400mg) single dose in 100 ml NS over 1 hour; may be repeated once after 12- 24 hours if no improvement after 1st dose.

Convalescent Plasma (off label use): It may be considered in patients with moderate disease who are not improving despite use of steroids (O2 requirement is progressively increasing). It should be ABO compatible and cross matched. Recipient should be closely monitored for several hours post transfusion for any transfusion related adverse events.

Dose: 4-13 ml/kg IV slow over >2 hours.

Vitamins and Minerals: Oral ascorbic acid (100-500 mg/d), zinc (2 mg/kg/d max 50 mg/day) and vitamin D (60,000U single dose) may also be given as immune boosters and micronutrients.

Note: These recommendations are mainly based on recent guidance issued by MOHFW for adults. As enough studies in children are not yet available, the doses mentioned above have been extrapolated from the doses recommended for adults.

ARDS, Sepsis, Septic Shock should be treated as per standard protocols. Details about MIS-C are attached.

MIS-C (Multisystem Inflammatory Syndrome (MIS) in Children)

Case definition (CDC):

1. A child presenting with fever*, laboratory evidence of inflammation**, and evidence of clinically severe illness requiring hospitalization, with multisystem (>2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological); AND

2. No alternative plausible diagnoses; AND

3. Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or exposure to a suspected or confirmed COVID-19 case within the 4 weeks prior to the onset of symptoms.

*Fever >38.0°C for ≥24 hours, or report of subjective fever lasting ≥24 hours

**Including, but not limited to, one or more of the following: an elevated C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), fibrinogen, procalcitonin, d-dimer, ferritin, lactic acid dehydrogenase (LDH), or interleukin 6 (IL-6), elevated neutrophils, reduced lymphocytes and low albumin

Additional comments:

a. Some individuals may fulfill full or partial criteria for Kawasaki disease but should be reported if they meet the case definition for MIS-C.

b. Consider MIS-C in any pediatric death with evidence of SARS-CoV-2 infection.

Investigations:

in addition to investigations done in moderate to severe Covid 19, additionally ECG, echocardiogram, cardiac enzyme or troponin testing, and B-type natriuretic peptide (BNP) or NT-proBNP should be done if possible.

Treatment

IVIG 1-2 gm/kg single dose

IV Methyl Prednisolone 2mg/kg OD till inflammatory markers are high followed by oral MPS/ Prednisolone in tapering doses.

High dose IV pulse MPS (30 mg/kg/day) may be considered to treat patients with life-threatening complications, such as shock, and specifically, if a patient requires high dose or multiple inotropes and/or vasopressors.

Low dose aspirin (3-5 mg/kg/day; max 81 mg/day) should be used in patients with MIS-C and thrombocytosis (platelet count ≥450,000/μL) and continued until normalization of platelet count and confirmed normal coronary arteries at ≥4 weeks after diagnosis.

9. COVID-19 MANAGEMENT

STANDARD PROTOCOL FOR CHEMOPROPHYLAXIS

Chemoprophylaxis

- The National Task force for COVID-19 constituted by ICMR recommends the use of hydroxychloroquine for prophylaxis of SARS-CoV -2 infection for high risk population.
- Asymptomatic healthcare workers involved in the care of suspected or confirmed cases of COVID-19.
- Asymptomatic household contacts of laboratory confirmed cases

DOSE

- Asymptomatic healthcare workers involved in the care of suspected or confirmed cases of COVID-19:
- 400 mg twice a day on Day 1, followed by 400 mg once weekly for next 7 weeks : to be taken with meals.
- Asymptomatic household contacts of laboratory confirmed cases: 400 mg twice day on Day 1, followed by 400 mg once weekly for next 3 weeks, to be taken with meals.

Exclusion/contraindication

- Drug is not recommended for prophylaxis in children under 15 years of age.
- Drug is contraindicated in persons with retinopathy, hypersensitivity to HCQS or 4-aminoquinoline compounds
- Hydroxychloroquine prophylaxis is to be taken ONLY as per the prescription of a physician and baseline
- QTc interval should be calculated for all persons prior to administering the drug

Annexure -1

MANAGEMENT PROTOCOL TEAM OF DEPARTMENT OF MEDICINE, SMS MEDICAL COLLEGE, JAIPUR

STRATIFICATION OF PATIENTS ACCORDING TO SEVERITY OF ILLNESS OF COVID-19

MILD	MODERATE	SEVERE	CRITICALLY ILL
• Fever and/or uncomplicated upper respiratory tract infection without dyspnea or hypoxemia	• Pneumonia with no signs of severe disease • CHEST X-RA: Bilateral lung infiltrates involving <50% of lung fields • RR ≥24/MIN • SpO2 <94% on room air	• Severe respiratory distress requiring Mechanical ventilation (Invasive or Non-invasive) • CHEST X-RAY: Bilateral lung infiltrates involving ≥50% of lung fields • RR≥ 30/min SpO2 <90% on room air	• Rapidly progressive Type 1 respiratory failure • Sepsis and septic shock • Multi organ dysfunction (MODS) Altered mental status
HOME ISOLATION/ **ADMIT IF RISK FACTORS**	ADMIT IN WARD	ADMIT IN ICU	ADMIT IN ICU
⊙ Antipyretics (Paracetamol), Antitussive ⊙ Adequate hydration ⊙ Tab. HCQ (400mg BD× 1 day, f/b 200mg BD× 4 days) ⊙ Monitor for progression by RR ≥24/min , SpO2<94% on room air ⊙ Refer to COVID Hospital	• **Oxygen supplementation** initiated to target SpO2 >92% - 96% (in COPD target SpO2 88- 92% ; use Non-rebreathing face mask preferably or HFNC • **Prone positioning** for awake spontaneously breathing patients, if no contraindication[e] • **Dexamethasone[d]*** 6mg IV OD for 10 days • **Antivirals[#]:** **Inj. Remdesivir:** 200 mg iv over 30-120 min on day 1 f/b 100 mg iv OD days 2-5. Stop HCQ prior to starting. • **Convalescent plasma therapy[f]*#** (4-13mL/kg or 200ml slowly over 2 hrs). Second dose of 200mL if required. **PaO2/FiO2: 200-300** • **Inj.Tocilizumab[g]*#** 8mg/kg IV once (Max. dose 800mg, usual dose 400mg). **Raised IL-6 plus clinical picture suggestive of Cytokine Storm.** • **Anticoagulation[c#]:** Prophylactic dose: once daily, LMWH/UFH, if no contraindications (especially in patients with D-dimer >1000ng/mL) • **Cautious** conservative fluid therapy with crystalloids guided by dynamic parameters[c] • **MDI preferred** over Nebulization • **Continue ACEI/ARB and Statins** if already prescribed • **Monitor* plus** watch for worsening in those with high **risk factors[a]** for severe disease • **Refer to ICU** if: RR ≥30/min; SpO2<90% on room air	**Oxygen supplementation:** target SpO2 >92% -96% (in COPD target SpO2 88-92%); use HFNC or NIV such as CPAP or BiPAP. If not responding then consider Intubation with *Lung protective ventilation strategy*. **Empirical antibiotics** if bacterial pneumonia is suspected (MRSA/MDRO) ⊙ **Septic shock:** Vasopressor Nor adrenaline drug of choice f/b Vasopressin; maintain MAP ≥65mmhg; Use High dose corticosteroids if sepsis is present. ⊙ **Corticosteroids[d#]:** Dexamethasone 6mg IV OD for 10 Days ⊙ **Antivirals[#]** as per moderate **cases** ⊙ **Convalescent plasma therapy[f]*#** **Inj.Tocilizumab[g]*#** ⊙ **Anticoagulation[c#]:** Full therapeutic dose (0.5mg/kg BW SC BD) for those in ICU ⊙ watch for signs of rapidly progressive respiratory failure, sepsis and refractory septic shock, MODS and altered mental status	**Oxygenation:** NIV by CPAP or BiPAP or Invasive Mechanical ventilation by Lung protective strategy **Empirical antibiotics** if bacterial pneumonia is suspected (MRSA/MDRO) **Septic shock:** Vasopressor Nor adrenaline drug of choice f/b Vasopressin; maintain MAP ≥65mmhg; Use High dose corticosteroids. **Corticosteroids #:** As in severe cases. •**Antivirals#** as per moderate cases **Convalescent plasma therapy** •**Inj.Tocilizumab #** **Anticoagulation #:** As in severe cases •**Cautious** conservative fluid therapy with crystalloids guided by dynamic parameters[c] Nutrition and sedation as per guidelines •**Monitor***

a. Monitor QT interval 2-3 hours after second dose of HCQ & twice daily thereafter (If QTc increases by >60ms or is >500ms, reduce the dose or consider discontinuing)

b. Contraindications to prone positioning in awake spontaneously breathing patient: Spinal or chest wall instability, facial or pelvic fracture, uncontrolled intracranial pressure
c. Dynamic parameters include capillary refill time, serum lactate levels, pulse pressure variation, stroke volume variation
d. To be initiated early (within 48 hours) in those on supplementary oxygen
e. Inj. Enoxaparin 40mg SC OD (Prophylactic dose), modify as per creatinine clearance, Obese dose is 40mg SC BD,assess risk of bleeding
f. Use according to discretion of treatment protocol team (Institutional Protocol to be followed)
g. Monitor Transaminases and eGFR (Discontinue if ALT ≥ 5 times the ULN, or eGFR <30ml/min)
h. Plasma for therapy must have plasma IgG titer (against S -protein RBD) above 1:640
i. Contraindicated in Tuberculosis, active bacterial or fungal infections, active hepatitis & PLHIV; Used in Cytokine storm syndrome with increased levels ofIL-6. Used once, dose repeated after 12-24 hours, if improvement seen with first dose
j. Low Tidal volume (4-8 ml/kg bw); low Inspiratory pressures (<30 cm h2o); high peep referred; individualize peep by monitoring of plateau pressures and benefit

* Monitor CBC with differential counts, LFT, RFT, ECG at baseline and daily; PT, INR & D-dimer baseline and EOD; LDH, CRP, Ferritin, Troponin, IL-6 for risk stratification. Procalcitonin baseline, repeat on day 3 and 7

Use of these medicines to be modified or avoided if the underlying co- morbidity is of significance

** All doses to be modified according to liver and renal functions.

$ RISK FACTORS FOR COVID-19 DISEASE PROGRESSION		
EPIDEMIOLOGICAL-CATEGORY 1	VITAL SIGNS-CATEGORY 2	LABS- CATEGORY 3
Age ≥ 65 years	Respiratory rate > 24 /min	D-dimer > 1000 ng/mL
Pre-existing pulmonary disease	Heart rate > 125 /min	CPK > Twice the upper limit of normal
Chronic kidney disease	SpO2 ≤ 94% on room air	CRP > 100
Diabetes with HbA1C > 7.6%	PaO2/ FiO2 < 300 mmHg	LDH > 245 U/L
History of hypertension		Elevated troponin
History of cardiovascular disease		Admission absolute lymphocyte count < 0.8x 109/L
Obesity (BMI ≥ 30 kg/m^2)		Ferritin > 500 µg/L
Use of biologicals		
History of transplant or other immunosuppression		
Uncontrolled HIV (Viremic or CD4 < 200)		