Management of COVID-19: Clinical Perspective

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Objectives

• Overview
• Clinical features
• Diagnosis
• Monitoring
• Management
COVID-19 biology

- SARS-CoV-2 is a single stranded RNA enveloped virus
- Spread:
  - Respiratory droplet and fomites
  - Can be transmitted by even asymptomatic individuals
- Binds to the ACE2 receptors on type II pneumocytes
- Incubation time 3-12 days (median 4-5 days; 75% develop symptoms between 2-7 days)
- Predominantly a respiratory disease, with severity ranging from mild illness to fatal outcome
Period of infectivity

• Uncertain

• Viral RNA detection from respiratory specimen, blood and stool

• Viral RNA levels from upper respiratory specimens appear to be higher soon after symptom onset compared with later in the illness

• The duration of viral shedding is also variable; there appears to be a wide range, which may depend on severity of illness
Transmission

• Transmitted person-to-person, predominantly by respiratory droplet spread and contact
  • Larger respiratory droplets (>5 μm) remain in the air for only a short time (<17 minutes) and travel only short distances, generally <1 m
  • Respiratory droplets can probably transmit > 1 meter in certain circumstances, such as being drive by airflow

• Contact transmission
  • Can survive on surfaces (fomites for up to 4 days ).
  • Transmission occurs when contact with virus-laden fomites is followed by contact with mucous membranes (e.g. eye, nose, mouth) from face touching.
Transmission

• Aerosol/airborne transmission does occur
• The SARS-CoV-2 virus is viable for at least 3 hours in aerosolised environments

• Other routes
  • Unconfirmed possibility of fecal-oral transfer
  • Vertical transmission (mother to child) rates appear low
Figure 1. Interaction between SARS-CoV-2 and the Renin–Angiotensin–Aldosterone System.
## Symptoms

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>85%</td>
</tr>
<tr>
<td>Cough</td>
<td>50-80%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>70%</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>20-40%</td>
</tr>
<tr>
<td>URI symptoms</td>
<td>15%</td>
</tr>
<tr>
<td>GI symptoms</td>
<td>10%</td>
</tr>
<tr>
<td>Loss of smell</td>
<td>Variable</td>
</tr>
</tbody>
</table>
Clinical presentation- breathlessness

• Dyspnea onset tends to be around day 6
• Silent hypoxia (severe), especially in elderly- severe hypoxia without breathlessness
Laboratory findings

- Lymphopenia
- Elevated transaminases
- Increased inflammatory markers - CRP, ferritin
- Increased D-dimer, troponin
- Elevated creatinine kinase, IL-6

Diagnosis

- Viral PCR of nasopharyngeal or oropharyngeal samples
### Test results & Clinical Significance

<table>
<thead>
<tr>
<th>PCR</th>
<th>IgM</th>
<th>IgG</th>
<th>Clinical Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>-</td>
<td>-</td>
<td>Patient may be in the window period of infection.</td>
</tr>
<tr>
<td>+</td>
<td>+</td>
<td>-</td>
<td>Patient may be in the early stage of infection.</td>
</tr>
<tr>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Patient is in the active phase of infection.</td>
</tr>
<tr>
<td>+</td>
<td>-</td>
<td>+</td>
<td>Patient may be in the late or recurrent stage of infection.</td>
</tr>
<tr>
<td>-</td>
<td>+</td>
<td>-</td>
<td>Patient may be in the early stage of infection. PCR result may be false-negative.</td>
</tr>
<tr>
<td>-</td>
<td>-</td>
<td>+</td>
<td>Patient may have had a past infection, and has recovered.</td>
</tr>
<tr>
<td>-</td>
<td>+</td>
<td>+</td>
<td>Patient may be in the recovery stage from an infection, or the PCR result may be false-negative.</td>
</tr>
</tbody>
</table>
Chest X-ray

- Bilateral shadowing (72.9%)
- Unilateral disease (25%)
- Local patchy shadowing
- Interstitial abnormalities (5%)
- Pleural effusions - uncommon
CT chest

- Changes seen in 86% of cases
- Involvement of lung proportionate to severity
- Common features include:
  - Ground Glass opacities (98%)
  - Reticular Pattern
  - Consolidation
  - Crazy Paving Pattern
- Role in Diagnosis:
  - Sensitivity 97%,
  - Specificity 25%
Spectrum of severity

- Mild – 81% (mild to moderate URTI symptoms for 7 days followed by recovery)
- Severe – 14%
  - breathlessness
  - RR ≥30,
  - O2 saturation ≤93%,
  - PF ratio <300, and/or lung infiltrates >50%
- Critical – 5%
  - respiratory failure, septic shock and/or multi organ dysfunction

1. Bouadama L. et al. 2020
2. Ruan Q. et al. 2020
Assessment of severity: Clinical

Suspected Patient Arrives → Registration Process → Triage zones → Clinical Assessment of the patient

- **Mild**
  - Fever
  - Cough
  - Malaise
  - Rhinorrhea
  - Sore Throat
  - No SOB
  - CBC/LFT/Sugar
  - Urea/CXR (optional)
  - Respiratory sample for COVID-19
  - Isolation Home/Hospital

- **Moderate**
  - Worsening symptoms SOB
  - High grade Fever
  - Pneumonia on CXR
  - High Risk Patients:
    - Age >60 yrs
    - CVD/HTN
    - Diabetes/other immune-compromised disease
    - Chronic lung/kidney/liver
  - Refer to HDU/ICU

- **Severe**
  - Moderate plus any of the following:
    - RR >24/min
    - SPO2 <94% on room air
    - Confusion
    - Drowsiness
    - SBP <90 mmHg
    - DBP <60 mmHg
  - Refer to HDU/ICU

- **Critical**
  - Severe plus any of the following:
    - Resp Failure
    - Hypotension
    - Worsening Mental Status
    - MODS
  - Refer to HDU/ICU

www.cmc.edu.np
Disease Progression

Brogan G et al. Coronavirus disease 2019 (COVID-19), April 7, 2020
Monitoring of patients

The National Early Warning Score 2
The National Early Warning Score 2

- Six physiological parameters form the basis of the scoring system already recorded in routine practice, when patients present to, or are being monitored in hospital:
  - respiration rate
  - oxygen saturation
  - systolic blood pressure
  - pulse rate
  - level of consciousness or new confusion*
  - temperature.
- *The patient has new-onset confusion, disorientation and/or agitation, where previously their mental state was normal – this may be subtle
- The patient may respond to questions coherently, but there is some confusion, disorientation and/or scores 3 on the NEWS system
Using the NEWS

• To standardize the assessment of acute-illness severity when patients present acutely to hospital and in prehospital assessment
  • to track their clinical condition,
  • alert the clinical team to any clinical deterioration and trigger a timely clinical response

• Should be evaluated with a view to
  • extending its use to primary care,
  • aid triage and communication of acute-illness severity to ambulance and hospital services.
Chart 1: The NEWS scoring system

<table>
<thead>
<tr>
<th>Physiological parameter</th>
<th>3</th>
<th>2</th>
<th>1</th>
<th>Score 0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiration rate (per minute)</td>
<td>≤8</td>
<td>9–11</td>
<td>12–20</td>
<td>21–24</td>
<td>≥25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SpO₂ Scale 1 (%)</td>
<td>≤91</td>
<td>92–93</td>
<td>94–95</td>
<td>≥96</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SpO₂ Scale 2 (%)</td>
<td>≤83</td>
<td>84–85</td>
<td>86–87</td>
<td>88–92</td>
<td>93–94 on air</td>
<td>95–96 on oxygen</td>
<td>≥97 on oxygen</td>
</tr>
<tr>
<td>Air or oxygen?</td>
<td>Oxygen</td>
<td>Air</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>≤90</td>
<td>91–100</td>
<td>101–110</td>
<td>111–219</td>
<td>≥220</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulse (per minute)</td>
<td>≤40</td>
<td>41–50</td>
<td>51–90</td>
<td>91–110</td>
<td>111–130</td>
<td>≥131</td>
<td></td>
</tr>
<tr>
<td>Consciousness</td>
<td>Alert</td>
<td>CVPU</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temperature (°C)</td>
<td>≤35.0</td>
<td>35.1–36.0</td>
<td>36.1–38.0</td>
<td>38.1–39.0</td>
<td>≥39.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NEWS key</td>
<td>FULL NAME</td>
<td>DATE OF BIRTH</td>
<td>DATE OF ADMISSION</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>----------</td>
<td>-----------</td>
<td>---------------</td>
<td>------------------</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A+B</td>
<td>Respiratory Function</td>
<td>2023-01-01</td>
<td>2023-01-02</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A+B</td>
<td>SpO2 Scale 1</td>
<td>94-90</td>
<td>96-95</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A+B</td>
<td>SpO2 Scale 2</td>
<td>88-80</td>
<td>90-95</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Air or oxygen?</td>
<td>Andy</td>
<td>No</td>
<td>Yes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood pressure</td>
<td>120/80</td>
<td>130/90</td>
<td>140/100</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulse</td>
<td>60-70</td>
<td>70-80</td>
<td>80-90</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consciousness</td>
<td>Alert</td>
<td>Confusion</td>
<td>Alert</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temperature</td>
<td>36.5-37°C</td>
<td>37-38°C</td>
<td>38.5-39°C</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**NEWS TOTAL**
- Monitoring
- Evacuation of Care
- Initiate
<table>
<thead>
<tr>
<th>NEWS score</th>
<th>Frequency of monitoring</th>
<th>Clinical response</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Minimum 12 hourly</td>
<td>• Continue routine NEWS monitoring</td>
</tr>
<tr>
<td>Total 1–4</td>
<td>Minimum 4–6 hourly</td>
<td>• Inform nursing in-charge &amp; junior resident to Assess the Patient • Registered nurse decides whether increased frequency of monitoring and/or escalation of care is required</td>
</tr>
<tr>
<td>3 in single parameter</td>
<td>Minimum 1 hourly</td>
<td>• Inform nursing in-charge &amp; junior resident who must assess the patient and inform immediately to the medical team caring for the patient, who will review and decide whether escalation of care is necessary</td>
</tr>
<tr>
<td>Total 5 or more Urgent response threshold</td>
<td>Minimum 1 hourly</td>
<td>• Inform nursing in-charge and junior resident who will inform medical team caring for the patient • Request urgent assessment by a senior resident or team with core competencies in the care of acutely ill patients • Provide clinical care in an environment with monitoring facilities</td>
</tr>
<tr>
<td>Total 7 or more Emergency response threshold</td>
<td>Continuous monitoring of vital signs</td>
<td>• Immediately inform the medical team caring for the patient-this should be at least at specialist registrar level • Emergency assessment by a team with critical care competencies with advanced airway management skills • Consider transfer to HDU or ICU • Clinical care in an environment with monitoring facilities</td>
</tr>
</tbody>
</table>
Management: General

• Ensure safety of the healthcare team in accordance with local hospital protocols
  • All team members MUST don appropriate PPE equipment prior to attending to a patient, regardless of the urgency of the situation
  • Droplet contact precautions are required for most patient care episodes,
  • Airborne/contact precautions are required for aerosol generating procedures
Management: general

• Rapid, coordinated assessment and management with attention to immediate life threats, including:

  • Severe hypoxaemia

    • Treat with oxygen to target SpO2 92-96%

    • Avoid aerosol generating devices if possible, and ensure airborne/contact precautions if they are required

    • Hypoxaemia can occur without significant respiratory distress

    • Intubation is high risk if pre-oxygenation is inadequate

Brogan G et al. Coronavirus disease 2019 (COVID-19), April 7, 2020
Management: General

- Use conservative fluid management when no evidence of shock.
- Antimicrobials to treat likely pathogens preferably within 1 hour of initial patient assessment for patients with sepsis; examples: 3rd generation cephalosporin + azithromycin.
- No Corticosteroids for treatment of viral pneumonia or ARDS unless they are indicated for another reason.
- Monitoring: RR, HR, SpO2, BP, urine output, conscious level, temperature as per Clinical response of NEWS2.

Brogan G et al. Coronavirus disease 2019 (COVID-19), April 7, 2020
Management: General

• COVID-19 has a wide range of clinical presentations: mild URTIs to florid ARDS requiring mechanical ventilation
  • Most of the patients admitted to the hospital will require some form of supplemental oxygen
  • All patients with SpO2 < 92% should be placed on supplemental O2 with nasal cannula
  • Inform ICU team when NEW2 ≥7
  • Change all nebulizations to MDIs when possible (AGPs)
Management of severe COVID-19
Risk factors for severity of disease and fatality

- Age
- High SOFA score
- Co-morbidities
- Laboratory features
  - Lymphocytopenia
  - Myocardial injury- Troponin
  - Elevated end organ damage indices- AST, ALT, BUN, LDH)
  - Elevated inflammatory markers- CRP, ferritin
  - Elevated D-dimer, PT
Age and death in COVID-19

Chinese CDC and South Korea CDC Confirmed Cases and Fatality Rate by Age Group

https://twitter.com/thenntgroup/status/1243193410338476032/photo/2
Comorbidities

• In Italy, of those who died:
  • 0.8% had no disease
  • 25.1% had a single disease
  • 25.6% had two diseases
  • 48.5% had 3 or more diseases
Critical care requirement

• Median duration between symptom onset and ICU admission – 9-10 days
• Primary indication- acute hypoxic respiratory failure
• Other complications
  • Myocarditis, cardiomyopathy, heart failure (33% in critically ill patients)
  • Acute kidney injury
  • DIC (71% in non-survivors)
  • Secondary bacterial or co-infection
Management- Critical Care

• Oxygenation
  • O2 supplementation to correct hypoxia if patient is not distressed
• Supportive care
• Fluid management
• Respiratory support
Management - Critical Care

- **Indications of Intubation:**
  - Deteriorating patients should be considered for *early* endotracheal intubation.
  - Considerations for invasive mechanical ventilation
    - Worsening hypercapnia/acidemia
    - Respiratory fatigue
    - Hemodynamic instability
    - Altered mental status
Management: Critical

• **Tips for Intubation:**
  • Aim for early intubation as opposed to use of BIPAP or HFNC. (Adequate NMB is preferred to prevent coughing, gagging, and aerosolization of particles.)
  • Intubation should be done using video bronchoscope/laryngoscope
  • Don enhanced **respiratory PPE with N95** and use double-glove technique.
  • Limit to a **3-person intubation team, if possible,** with all necessary equipment at bedside, including video bronchoscope
ARDS diagnostic criteria (Berlin 2012)

- Acute onset (<7 days) from known cause e.g., COVID-19
- Bilateral opacities on chest radiograph
- Not entirely due to pleural effusions, volume overload or cardiogenic edema
- $\text{PaO}_2/\text{FiO}_2$ (P/F ratio) < 300 on PEEP of $\geq 5$ cm of H2O or $\text{SpO}_2/\text{FiO}_2 < 315$

**Classification of Severity:**
- Mild: $200 \leq \text{PaO}_2 / \text{FiO}_2 < 300$
- Moderate: $100 \leq \text{PaO}_2 / \text{FiO}_2 < 200$
- Severe: $\text{PaO}_2 / \text{FiO}_2 < 100$
Protective ventilator strategies

- Tidal volume: 6mL/kg PBW (4-8)
- P plateau: \( \leq 30 \text{ cmH}_2\text{O} \)
- Driving pressure: \( <15 \text{ cmH}_2\text{O} \)
Desaturation

Set FiO₂ = 1.0

Yes

Chest moving?

Examine patient
look for:
- Endobronchial intubation
- Pneumothorax
- Collapse
- Pulmonary oedema
- Bronchospasm

No

Manually ventilate

Yes

Easy to ventilate?

Yes

Ventilator problem

No

ETT/patient problem

High resistance or low compliance

Treat cause
± adjust ventilator settings

Check settings & function
Myocardial injury in COVID-19

A Time from symptom onset

Survival rate, %

Days

<table>
<thead>
<tr>
<th>No. at risk</th>
<th>With cardiac injury</th>
<th>Without cardiac injury</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>82</td>
<td>334</td>
</tr>
<tr>
<td>68</td>
<td>329</td>
<td>320</td>
</tr>
<tr>
<td>46</td>
<td>323</td>
<td>319</td>
</tr>
<tr>
<td>40</td>
<td>40</td>
<td>40</td>
</tr>
</tbody>
</table>

With cardiac injury: 51% mortality rate
Without cardiac injury: 5% mortality rate

Shi, et al. JAMA Cardiol 2020; published online March 25, 2020
Acute Kidney Injury

- Occurs in about 5% of patients, late in the course 1-2 weeks
- Acute tubular necrosis
- Supportive
- Outcome with RRT is extremely poor
Hypotension

Vasodilation

- Septic (most likely)
- Meds/sedation
- Neurogenic
- Anaphylactic
- Adrenal insufficiency

Distributive

Warm skin
Wide pulse pressure
Low diastolic pressure

Cool skin
Narrow pulse pressure
Low $S_{cv}O_2$

Low Cardiac Output

Large IVC or neck veins
Ultrasound, EKG, CXR

Cardiogenic
- Cardiomyopathy
- ACS
- Arrhythmia
- Valvular

Obstructive
- PE
- Tension
- Tamponade

Hypovolemic
- Hemorrhage
- Third spacing
- Fluid losses

Flat IVC or neck veins
Nursing care

• All team members MUST don appropriate PPE equipment prior to attending to a patient, regardless of the urgency of the situation

• General care

• Monitoring as per NEWS 2

• Prevention of VAPs and other complications

• Fluid and nutrition
Medications

• Antimalarials
• Antivirals
• Monoclonal antibodies, Interferon
• Convalescent serum
Controversies

• Potential for airborne transmission
• Thresholds and timing of interventions, including different oxygenation strategies and intubation
• How to maintain oxygenation during intubation
• Appropriate PEEP settings in mechanical ventilation
• Utility of specific therapies (e.g. antivirals, steroids, immunotherapy)
• Care of isolated patients and families
• Long term outcomes and recovery of COVID-19 survivors
• Staff wellbeing and moral distress
Summary

- Single stranded RNA virus transmitted by droplets and fomites
- Mild respiratory illness to fatal
  - Severe: 14%
  - Critical: 5%
- Monitoring is the most important
  - Sudden deterioration
  - Silent severe hypoxia
- Mainly supportive treatment with proper PPE
Thank You