

COVID-19: Clinical Presentation & Management

Pathogen: SARS-CoV-2

Disease: Coronavirus disease 2019 (COVID-19)

Basic Biology:

- (+) ssRNA, large, enveloped beta-coronavirus
- Zoonotic origin with mammalian sources including the bat, pangolin, or snake
- SARS-CoV-2 spike (S) protein binds the ACE2 receptor and requires TMPRSS2 and furin proteases to facilitate host cell entry

Transmission: viral particle entry via respiratory droplets

Pathogenesis:

1. Infection of type II pneumocytes in the lung by SARS-CoV-2 particles
2. Impaired interferon response and cytolysis results in increased levels of inflammatory cytokines and chemokines in the circulation (IL-6, IL-8, TNF)
3. Vasodilation and increased vascular permeability
4. Edema and compression of alveoli
5. Decreased production of lung surfactant, reduced gas exchange → ARDS

Epidemiology:

- R_0 (no. of infections from 1 case) = 2.5-2.9
- Attack rate = 0.25%
- CFR = 1.3% (influenza CFR = 0.1%)
- Incubation time = 5.2 days (-14 days)

Affected populations:

- > **Pediatric patients** (multisystem inflammatory syndrome in children [**MIS-C**): Kawasaki-like syndrome with fever, hypotension, GI symptoms, rash, *myocarditis*; respiratory symptoms may be absent
- > **Pregnant women:** complications of the maternal/placental vasculature (e.g., microthrombi formation), preeclampsia
- > **Elderly patients:** mortality in pts > 75 is 75x rate among 18-44-year-olds

Control Strategies (WHO):

- Social distancing / quarantine
- Use of face masks
- Contact tracing and screening

Recommended Precautions:

- Hand hygiene: soap/water for 20 sec when visibly soiled, before eating, and after restroom use; otherwise, alcohol-based hand rub and gloves
- Airborne precautions for aerosolizing procedures (intubation, suction, NIPPV)
- Droplet precautions (all else)

Symptoms: Cough (76%), fever (98%), dyspnea (50%), myalgias or fatigue (44%), GI (10%)

- Asymptomatic (1.2%)
- Mild to medium (80.9%)
- Severe (13.8%)
- Critical (4.7%) -- death (2.3%)

Laboratory Assessment:

- ↑ CRP, ferritin, D-dimer, PCT, LDH
- ↑ IL-6, IL-10, TNF-α

Liver function tests (LFTs)

- ↑ AST/ALT
- ↑ Total bilirubin

Basic metabolic panel (BMP)

- ↑ BUN / Cr

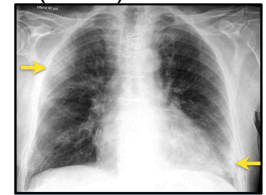
Complete blood count (CBC)

- ↓ lympho-/leukocytes
- ↑ neutrophil count & neutrophil-to-lymphocyte ratio

Imaging:

CXR/CT

- Bilateral, multilobar involvement
- GGO and consolidation (below)



POCUS (Point-of-care ultrasound)

- B-lines, pleural lines, air bronchograms

Prognosis:

Risk factors

- Age; cardiovascular, endocrine, liver and pulmonary disease; CKD, obesity, cancer, residence in nursing homes/long-term care facilities

Independent Predictors of Clinical Severity

- ↑ CRP, LDH, lymphocyte count, IL-6, TNF-α, D-dimer
- ↑ Neutrophil: lymphocyte ratio

Complications

- ARDS
- Sepsis
- AKI
- Transaminitis
- Venous thromboembolic events
- Cardiac (cardiomyopathy, HF, MI, arrhythmias)
- Empyema

COVID calculators: <https://www.mdcalc.com/covid-19>

Management Strategy:

Testing

- RT-PCR (order early - can take days; see testing criteria)
 - 66-80% sensitive; i.e. 20-34% false negative rate

Basic care

- Lung protective ventilation, proning, restrictive fluid management and management of organ failures
- SpO₂ target ≥ 93%
- Oxygenation – HFNC, face mask, or non-invasive ventilation
- Systemic anticoagulation (see pathway)

Mechanical ventilation

- Indicated by SaO₂ < 93-96% + acute lung injury
- 7 P's: PEEP, Paralysis, Prone positioning, Prostacyclins, Pleural evacuation, Peeing (diuresis), Peripheral oxygenation (ECMO)

Drugs / vaccines

- **Remdesivir** is the only FDA-approved drug (nucleotide analog, inhibits RNA-dependent RNA polymerase)

Therapeutic Options Available for COVID-19

| | FDA-approved | In clinical trial | Compassionate use |
|---------------------|------------------------|---|-------------------|
| Class | Drug | Mechanism of Action | |
| Antivirals | Remdesivir | (broad-spectrum): nucleotide analog | |
| | Lopinavir | (broad-spectrum): protease inhibitor | |
| | Ritonavir | (broad-spectrum): protease inhibitor | |
| Immuno-modulators | HCQ | No longer a treatment for COVID-19 | |
| | Tocilizumab | (monoclonal Ab) inhibits IL-6 receptor | |
| | Sarilumab | (monoclonal Ab) inhibits IL-6 receptor | |
| | Siltuximab | (monoclonal Ab) inhibits IL-6 | |
| | Gimsilumab | (monoclonal Ab) inhibits GM-CSF | |
| | Eculizumab | inhibitor of C5a complement protein | |
| | Genivriroc | inhibition of CCR2 and CCR5 | |
| | IFN-α | exogenous interferon therapy | |
| | Remestemcel-L | mesenchymal stem cell transfer | |
| Convalescent Plasma | (hyperimmune globulin) | | |