

Evidence-Based Medicine InfoSheet: Clinical Presentation

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Key topic areas / questions identified:

What is the “typical” clinical presentation of COVID-19?

Symptoms:

- Fever, cough, dyspnea

Labs:

- Lymphocytopenia

Imaging

- CT: bilateral ground glass opacities

What are the key groups for whom clinical presentation might be different?









- **Immunocompromised**

| Patient Characteristic | Clinical Features |
|--------------------------------------|---|
| Patient on long term glucocorticoids | Longer incubation and viral shedding periods |
| Organ Transplant | - May present with more severe symptoms of COVID-19 pneumonia - Longer incubation and viral shedding periods |
| HIV + patients | - Longer course and slower generation of specific antibody (for testing) than general population - CT: high-density patchy shadows with unclear boundaries in peripheral lung involving interlobar fissures - ART drug may lead to quicker resolution of lung lesions |

- **Children**
 - Less likely to present with fever, SOB, cough
 - Less severe than adults

- Most common radiologic finding: bilateral ground glass opacity
- **Pregnant Women**
 - Most pregnant patients are asymptomatic or mild.
- **Elderly**
 - Can be asymptomatic
 - ICU patients more likely to be elderly
 - Common symptoms: fever, cough, dyspnea, with lymphocytopenia

What are the common complications of COVID-19?

| | |
|--|--|
| <p>Respiratory</p>  | <ol style="list-style-type: none"> 1. ARDS: 15-33% of cases (8 days after onset of symptoms), increased risk with older age, neutrophilia, increased LDH, increased D-dimer levels, age >65 years, DM, and HTN 2. Acute respiratory failure: 8% of patient cases, leading cause of mortality 3. Pneumonia |
| <p>Cardiovascular</p>  | <ol style="list-style-type: none"> 1. Reported in 7-20% of cases. Prevalence high among patients who are severely ill 2. Vascular inflammation, cardiac arrhythmias, myocarditis, cardiomyopathy, acute onset heart failure, myocardial infarction, cardiac arrest 3. Less common: myopericarditis, cardiac tamponade, fulminant myocarditis |
| <p>Liver</p>  | <ol style="list-style-type: none"> 1. Reported in 14-53% of patients 2. Abnormal aminotransferase levels in patients with severe illness (AST and ALT >40 U/L) 3. Clinically significant liver injury is uncommon |
| <p>Infection</p>  | <ol style="list-style-type: none"> 1. Sepsis and septic shock: Reported in 4-8% of patients 2. Secondary infection: Reported in 6-10% of patients, Staph and Strep are common 3. DIC: Cytokine release syndrome with persistent fevers, increased D dimer and ferritin and proinflammatory cytokines |
| <p>Thrombotic</p>  | <ol style="list-style-type: none"> 1. 31% incidence of thrombotic complications in one study of 184 ICU patients 2. Predisposes to venous and arterial thromboembolic events due to excessive inflammation, hypoxia, immobilization, and DIC 3. PE is most frequent thrombotic complication 4. Age and coagulopathy (PT >3 sec, APTT >5 sec) are independent predictors |
| <p>Kidney</p>  | <ol style="list-style-type: none"> 1. Prevalence is low but is a marker of multi organ dysfunction and severe disease 2. 40% of patients had proteinuria and 26% had hematuria on admission 3. 5% of patients developed an AKI and increased hospital mortality 4. Stage 3 AKI in 1/2 of patients. Rhabdomyolysis, metabolic acidosis, and hyperkalemia 5. Old age, DM, severe illness, and positive fluid balance are associated factors |
| <p>Neurologic</p>  | <ol style="list-style-type: none"> 1. Viral invasion of CNS in patients with severe illness 2. Observed in 36% of 214 patients in one study 3. Acute CVA disease, impairment of consciousness, ataxia, seizures, and encephalopathy. Prognosis is poor for these patients |
| <p>Pregnancy</p>  | <ol style="list-style-type: none"> 1. Fetal distress, premature labor, newborn thrombocytopenia, elevated liver enzymes, respiratory distress 2. Miscarriage, IUGR, and preterm birth 3. 1 case of a still birth |

What are the risk factors for severe disease/morbidity/mortality?

Risk Factors

| Severe Disease | Morbidity | Mortality |
|--|---|---|
| Older age Hypertension High cytokine levels (IL-2R, IL-6, IL-10, and TNF-a) High LDH level Diabetes COPD Cardiovascular disease Cerebrovascular disease | Increased neutrophil count Increased BUN and LDH related to renal failure, heart failure, or multi-organ failure (MOF) Acute cardiac injury 13 times more common in ICU COVID patients than in non-ICU COVID patients | Older age (>65 years) Male sex Cardiovascular disease Diabetes Chronic respiratory disease Dyspnea ARDS Hypertension Cancer Cerebrovascular disease High SOFA score Leukocytosis High LDH level Increased markers for myocardial injury, inflammation, and bacterial infections Cardiac injury Hyperglycemia High-dose corticosteroid use CD3+ CD8+ T cells \leq 75 cell/ μ L Decreased CD4+ count Prolonged PT Cardiac troponin I \geq 0.05 ng/mL D-dimer > 1 μ g/mL High neutrophil-to-lymphocyte ratio (especially in males) Kidney disease AKI during hospitalization |

Seen in Deceased>Recovered

| Symptoms | Lab Value Increases | Complications |
|---|---|---|
| Dyspnea Chest tightness Disorder of consciousness | Alanine aminotransferase Aspartate aminotransferase Creatinine Creatine kinase Lactate dehydrogenase Cardiac troponin I N-terminal pro-brain natriuretic peptide D-dimer | Acute respiratory distress syndrome Type I respiratory failure Sepsis Acute cardiac injury Heart failure Alkalosis Hyperkalaemia Acute kidney injury Hypoxic encephalopathy |

References:

Typical

- <https://www.theijoem.com/ijoem/index.php/ijoem/article/view/1921/1195>
- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7102608/>
- <https://www.ncbi.nlm.nih.gov/pubmed/32109013>
- <https://www.ncbi.nlm.nih.gov/pubmed?term=32091533>
- <https://www.ncbi.nlm.nih.gov/pubmed?term=32031570>
- <https://www.ncbi.nlm.nih.gov/pubmed?term=32215618>
- <https://www.ncbi.nlm.nih.gov/pubmed?term=32251668>

Key Groups

- **Immunocompromised**

<https://www.sciencedirect.com/science/article/pii/S1521661620302059?via=ihub>

<https://www.ncbi.nlm.nih.gov/pubmed/32251539>

[https://www.jhltonline.org/article/S1053-2498\(20\)31467-4/fulltext](https://www.jhltonline.org/article/S1053-2498(20)31467-4/fulltext)

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7166037/>

<https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.120.047549>

<https://www.ncbi.nlm.nih.gov/pubmed/32335339>

<https://www.ncbi.nlm.nih.gov/pubmed/32285949>

- **Children (<=18)**

https://www.cdc.gov/mmwr/volumes/69/wr/mm6914e4.htm?s_cid=mm6914e4_w

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7090728/>

<http://pediatrics.aappublications.org/lookup/doi/10.1542/peds.2020-0702>

<https://www.nejm.org/doi/10.1056/NEJMc2005073>

- **Pregnant women**

<https://onlinelibrary.wiley.com/doi/full/10.1002/jmv.25789>

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7156118/>

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)30360-3/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30360-3/fulltext)

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7144599/>

- **Elderly**

<https://www.cdc.gov/mmwr/volumes/69/wr/mm6914e2.htm>

<https://jamanetwork.com/journals/jama/fullarticle/2761044>

<https://www.ncbi.nlm.nih.gov/pubmed/32242738>

<https://www.ncbi.nlm.nih.gov/pubmed/32240670>

Complications:

1. ARDS:
<https://www.ncbi.nlm.nih.gov/pubmed/?term=Clinical+Characteristics+of+138+Hospitalized+Patients+With+2019+Novel+Coronavirus+Infected+Pneumonia+in+Wuhan%2C+China>
2. Acute Respiratory Failure:
<https://www.ncbi.nlm.nih.gov/pubmed/?term=Epidemiological+and+clinical+characteristics+of+99+cases+of+2019+novel+coronavirus+pneumonia+in+Wuhan%2C+China%3A+a+descriptive+study>
3. Cardiovascular:
<https://www.ncbi.nlm.nih.gov/pubmed/32219363>
4. Acute Liver Injury:
<https://www.ncbi.nlm.nih.gov/pubmed/?term=Liver+injury+during+highly+pathogenic+human+coronavirus+infections>
5. Sepsis and Septic Shock:
<https://www.ncbi.nlm.nih.gov/pubmed/31986264>
6. DIC:
<https://www.ncbi.nlm.nih.gov/pubmed/32234718>
7. Thrombotic:
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7146714/>
8. Secondary Infection:
<https://www.ncbi.nlm.nih.gov/pubmed/?term=Clinical%2Claboratory+and+imaging+features+of+COVID-19%3A+A+systematic+review+and+meta-analysis>
9. Acute Kidney Injury:
<https://www.ncbi.nlm.nih.gov/pubmed/?term=Epidemiological+and+clinical+characteristics+of+99+cases+of+2019+novel+coronavirus+pneumonia+in+Wuhan%2C+China%3A+a+descriptive+study>

10. Neurologic:

<https://www.ncbi.nlm.nih.gov/pubmed/?term=Neurologic+manifestations+of+hospitalized+patients+with+coronavirus+disease+2019+in+Wuhan%2C+China.+JAMA+Neuro>

11. Pregnancy:

[https://www.ncbi.nlm.nih.gov/pubmed/?term=Dashraath+P%2C+Jing+Lin+Jeslyn+W%2C+Mei+Xian+Karen+L%2C+et+al.+Coronavirus+disease+2019+\(COVID-19\)+pandemic+and+pregnancy](https://www.ncbi.nlm.nih.gov/pubmed/?term=Dashraath+P%2C+Jing+Lin+Jeslyn+W%2C+Mei+Xian+Karen+L%2C+et+al.+Coronavirus+disease+2019+(COVID-19)+pandemic+and+pregnancy)

Risk Factors

- Severe disease

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7099829/pdf/12931_2020_Article_1338.pdf

<https://www.aging-us.com/article/103000/text>

[https://www.jacionline.org/article/S0091-6749\(20\)30495-4/pdf](https://www.jacionline.org/article/S0091-6749(20)30495-4/pdf)

- Morbidity

[https://www.journalofinfection.com/article/S0163-4453\(20\)30153-5/pdf](https://www.journalofinfection.com/article/S0163-4453(20)30153-5/pdf)

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7087935/pdf/392_2020_Article_1626.pdf

- Mortality

<https://www.thelancet.com/action/showPdf?pii=S0140-6736%2820%2930566-3>

<https://www.bmj.com/content/bmj/368/bmj.m1091.full.pdf>

[https://www.journalofinfection.com/article/S0163-4453\(20\)30208-5/pdf](https://www.journalofinfection.com/article/S0163-4453(20)30208-5/pdf)

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7110296/>

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7144257/pdf/ERJ-00524-2020.pdf>

<https://jamanetwork.com/journals/jama/fullarticle/2762130>

<https://www.ncbi.nlm.nih.gov/pubmed/32240670>