LITERATURE REVIEW SARS-CoV 2 Clinical Presentation

By: Anisha Guda, Kavina Patel, Aleena Vargas, Tracey Vuong, Caroline Zhu, Taylor McCracken, Salma Yazji, Anusha Sherwani, Cynthia Jiang, Noah Hodson, Keerthana Nimmagadda, and Keerthi Thallapureddy
Peer reviewed by: Dr. Philip Ponce, Dr. Kelly Echevarria

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UT Health San Antonio Long School of Medicine

TYPICAL PRESENTATION

COMMON SYMPTOMS

Fever (70%) **Cough (70%)** **Dyspnea (70%)** **Muscle Aches (36%)** **Headaches (34%)**

Others: fatigue, anorexia, anosmia, dysgeusia, diarrhea, nausea / vomiting, abdominal pain, sputum production, hemoptysis, cutaneous manifestations

LABS

lymphopenia, hypoalbuminemia, elevated CRP, elevated LDH, elevated ESR, normal procalcitonin

IMAGING

Bilateral multi-focal opacities on CXR, bilateral ground glass opacities on CT
Chest ultrasound more useful than CXR in detecting peripheral pulmonary pathologies and interstitial syndromes

INCUBATION PERIOD

14 days from time of exposure, with median incubation period of 4 to 5 days

DURATION OF ILLNESS

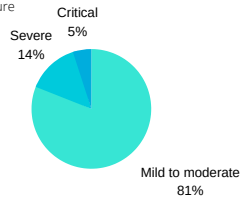
Mild to moderate disease: 2 weeks
Severe disease: 3-6 weeks

ASYMPTOMATIC PRESENTATION

Estimated **18-81%** of infections are **asymptomatic**
May develop symptoms after time of diagnosis - considered *presymptomatic* ← may distinguish with early elevated serum LDH
CT abnormalities: 30% of asymptomatic individuals showed **ground-glass opacities**, and 27% had **diffuse consolidations**

DISEASE SEVERITY

Among 72,314 persons with COVID-19 in China.
Mild: no or mild pneumonia
Severe: dyspnea, respiratory distress
Critical: respiratory failure, septic shock, and/or multi-organ dysfunction or failure



KEY GROUPS FOR ATYPICAL PRESENTATION

IMMUNOCOMPROMISED

- ON LONG TERM GLUCOCORTICOIDS: longer incubation and viral shedding periods
- ORGAN TRANSPLANTS: may present with more severe symptoms of COVID-19 pneumonia, and also have longer incubation and viral shedding periods
- HIV+ PATIENTS: longer course and slower seroconversion, CT with high density patchy shadows and unclear boundaries in peripheral lung involving interlobar fissures

CHILDREN

- Less severe than adults
- Younger age correlates strongly with asymptomatic and mild infections
- If symptoms are present, most common: fever, cough, sore throat
- Young children (infants) more susceptible to severe disease than older children
- Common lab findings: thrombocytosis, lymphopenia, neutropenia, elevated CRP, elevated procalcitonin, elevated CK, elevated ALT
- Imaging: Most common radiologic finding is bilateral ground glass opacities and nonspecific unilateral/bilateral lesions on chest CT
- Multisystem inflammatory syndrome (MIS) is an emerging clinical finding and is discussed on the pediatric infographic

PREGNANT WOMEN

- Most are mild and can be asymptomatic.
- Pregnant women with COVID-19 are more likely to be hospitalized and are at increased risk for ICU admission and receipt of mechanical ventilation than nonpregnant women.

ELDERLY

- Significantly higher rate of severe disease, ICU admission, and mortality than younger patients
- Can be asymptomatic
- Nonspecific signs & symptoms are falls, general health decline, delirium, and GI symptoms

SEVERE DISEASE AND MORTALITY

RISK FACTORS FOR SEVERE DISEASE AND MORTALITY

- **Non-Modifiable**
  - Older age (>65 years)
  - In patients age >60 years: muscle aches, absence of fever
  - Male sex
  - Cancer patients - highest fatality rates seen with hematologic and lung malignancies, and in age groups 45-60 years and >75 years.
  - High SOFA score
  - Down Syndrome
- **Modifiable**
  - Hypertension, cardiovascular disease, cerebrovascular disease
  - Overweight (BMI 25 - <30), obesity (BMI ≥ 30 kg/m^2), diabetes mellitus
  - Smoking history (current>former), COPD
  - High-dose corticosteroid use
  - **Acute kidney injury (AKI) during hospitalization

PROGNOSTIC MARKERS OF SEVERE DISEASE

- **Hematologic**
  - Thrombocytopenia, lymphopenia
  - Elevated RDW (>14.5%) at admission and increasing RDW during hospitalization
  - High neutrophil:lymphocyte ratio (especially in males)
  - Significantly elevated WBC count (WMD: 4.15×10^9/L), CD8+ T cells ≤ 75 cell/microliter, decreased CD4+ count
- **Coagulation Parameters**
  - Prolonged PT
  - Increased fibrin degradation products; D-dimer > 1microgram/mL
  - Fibrinolysis shutdown (elevated D-Dimer and complete failure of clot lysis at 30 minutes on TEG) predicts thromboembolic events and need for hemodialysis
- **Liver/Kidney Biomarkers and Enzymes**
  - High LDH levels
  - Significant elevations in ALT, AST, total bilirubin
  - Significant elevations in BUN and creatinine
  - Elevated C-reactive protein (CRP)
  - Elevated procalcitonin associated with a nearly 5-fold higher risk of severe disease
- **Others**
  - Cardiac troponin significantly elevated (WMD: 32.7 ng/L)
  - Acute cardiac injury 13 times more common in ICU-COVID patients than in non-ICU COVID patients
  - Cancer patients - advanced tumor stage, elevated TNF-α and NT-proBNP, and decreased CD4+ T cells and albumin–globulin ratio
  - Chills, body temperature > 37.5 °C, findings of pneumonia on chest X-ray

POTENTIAL COMPLICATIONS

LUNGS	• ARDS: 15-33% of cases (8 days after sx onset); increased risk in older age, neutrophilia, increased LDH, increased D-Dimer, age >65yrs, DM, HTN • Acute respiratory failure: 8% of cases; leading cause of mortality • Pneumonia	**THROMBOTIC**	• 31% incidence of thrombotic complications in one study of 184 pts • Predisposes to venous and arterial thromboembolic events due to excessive inflammation, hypoxia, immobilization and DIC • PE is most frequent thrombotic complication • Age and coagulopathy (PT>3s, APTT>5s) are independent predictors
CARDIO-VASCULAR	• Reported in 7-20% of cases. Prevalence high among patients who are severely ill • Vascular inflammation cardiac arrhythmias, myocarditis, cardiomyopathy, acute onset heart failure, MI, cardiac arrest • Less common: myocarditis, cardiac tamponade, fulminant myocarditis • 1 case of ITP	**KIDNEY**	• Low prevalence, but is a marker of multi organ failure and severe disease • 40% pts with proteinuria and 26% with hematuria on admission • 5% pts developed AKI and increased hospital mortality • Stage 3 AKI in 50% of pts; rhabdomyolysis, metabolic acidosis, and hyperkalemia • Old age, DM, severe illness, and positive fluid balance are associated factors
LIVER	• Reported in 14-53% of cases • Abnormal aminotransferase levels in patients with severe illness (AST and ALT >40) • Clinically significant liver injury is uncommon	**NEUROLOGIC**	• Viral invasion of CNS in patients with severe illness • Observed in 36% of 214 patients in one study • Acute CVA disease, impairment of consciousness, ataxia, seizures, and encephalopathy; prognosis is poor for these patients • Guillain-Barre syndrome seen in 4 cases
INFECTION	• Sepsis and septic shock reported in 4-8% of cases • Secondary infection reported in 6-10% of cases; staph and strep are common • DIC: cytokine release syndrome with persistent fevers, increased ferritin, D-dimer, and proinflammatory cytokines • Conjunctivitis seen in several cases	**PREGNANCY**	• Incidence of preterm birth, low birth weight, C-section, NICU admission are higher than the general population • Maternal death, pregnancy loss, and laboratory evidence of vertical transmission are infrequently reported • Most common symptoms are fever (62.9%) and cough (36.8%)
CUTANEOUS	• Exanthematous rash in several cases at disease onset or after recovery • "COVID toes" - pernio acral lesions reported across age spectrum • Retiform purpura and necrotic vascular lesions with severe cases • Vesicular varicella-like eruptions in several reports • Multisystem inflammatory syndrome in children (Kawasaki-like)	**LINGERING SYMPTOMS**	• Reported cases of persistent loss of smell despite clinical resolution • Long-term impaired respiratory functions in some patients who had developed ARDS • Potentially increased likelihood for developing cognitive decline after infection

For details and references please visit **https://oume.uthscsa.edu/longco/**