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PRESENTATION

INCUBATION PERIOD

- Most cases occur about 4-5 days after exposure¹⁹
- 97.5% of patients will develop symptoms by day 12

SYMPTOMS, IN ORDER OF DECREASING FREQUENCY

SYMPTOM	FREQUENCY
Fever	83-99% during disease course ¹⁻⁷ 44-52% at presentation ^{5,8}
Cough	59-83% ¹⁻⁹ Productive in 23-41% ^{1,3,5-7}
Fatigue	23-70% ^{1,4-7}
Myalgia	10-35% ¹⁻⁶
Dyspnea	May be as low as 19% in a mix of inpatients/outpatients ⁵ On presentation to the hospital ranges 31-76% ^{1,3,4,7,8}
Sore throat	5-17%, ^{1,2,5} although one case series reported rates up to 61% ⁹
Headache	6-14% ¹⁻⁵
Diarrhea	2-15% ^{1-3,5,9}
Nausea	1-10% ^{1,2,5,6}
Rhinorrhea	4-6% ^{2,4,5,9}
Chest pain	2% ^{2,4}

SEVERITY

REQUIRING ICU	PERCENTAGE
Inpatients/outpatients	5% ^{5,10}
Hospitalized patients	23-32% ^{1-3,6}

TIME TO PRESENTATION

	NUMBER OF DAYS
Days to hospital admission	7-11 ^{1,3,6}
Days from illness onset to ICU admission	9-12 ^{4,6}

PRESENTATION

(CONTINUED)

LABORATORY DATA

LABS	ABNORMAL LABORATORY FINDINGS
Complete Blood Cell Count	Lymphocytopenia (~70%) ^{1-5,11}
	Normal WBC count or leukopenia ¹⁻⁵ - Elevated WBC can be seen in severe disease and is associated with nonsurvivors ¹¹
	Elevated neutrophils ¹⁻⁵
	Mild Thrombocytopenia ¹¹
Biochemistry ^{1-5,11}	↑ BUN and creatinine
	↑ AST, ALT, total bilirubin
	↓ albumin
	↑ LDH (~40%), D-dimer, CRP, ESR, troponin
Coagulation Function	Prolonged prothrombin time ^{3,11,12}
Biomarkers	Procalcitonin not elevated in the majority of cases and if elevated may be associated with secondary infection ^{1-5,12}
	↑ IL-6 and IL-10 ^{6,12}
	↑ ferritin ^{6,12}

Laboratory abnormalities associated with increased severity^{3,6,11,12}

- Higher white blood cell and neutrophil counts
- Higher ESR, D-dimer, lactate dehydrogenase, creatinine kinase, troponin, and creatinine levels

IMAGING

Chest CT

- Up to 50% of COVID-19 positive patients may have a normal CT scan 0-2 days after onset of symptoms¹³
- Early Lung Abnormalities^{1-5,12-15}
 - ◆ Multifocal or peripheral focal ground-opacities bilaterally in ~ 50-75% of patients
- Progressive/Severe Disease Abnormalities^{6,7}
 - ◆ Consolidation with air bronchograms, crazy paving, bronchial wall thickening
- Atypical Findings^{14,15}
 - ◆ Reverse Halo sign
 - ◆ Discreet pulmonary nodules with halo sign
 - ◆ Pleural Effusion
 - ◆ Mediastinal Lymphadenopathy

Point of Care Lung Ultrasound^{16,17,18}

- Presence of B-lines
- Irregular, thickened pleural line with scattered discontinuities
- Subpleural consolidations
- Alveolar consolidation with air bronchograms associated with severe disease

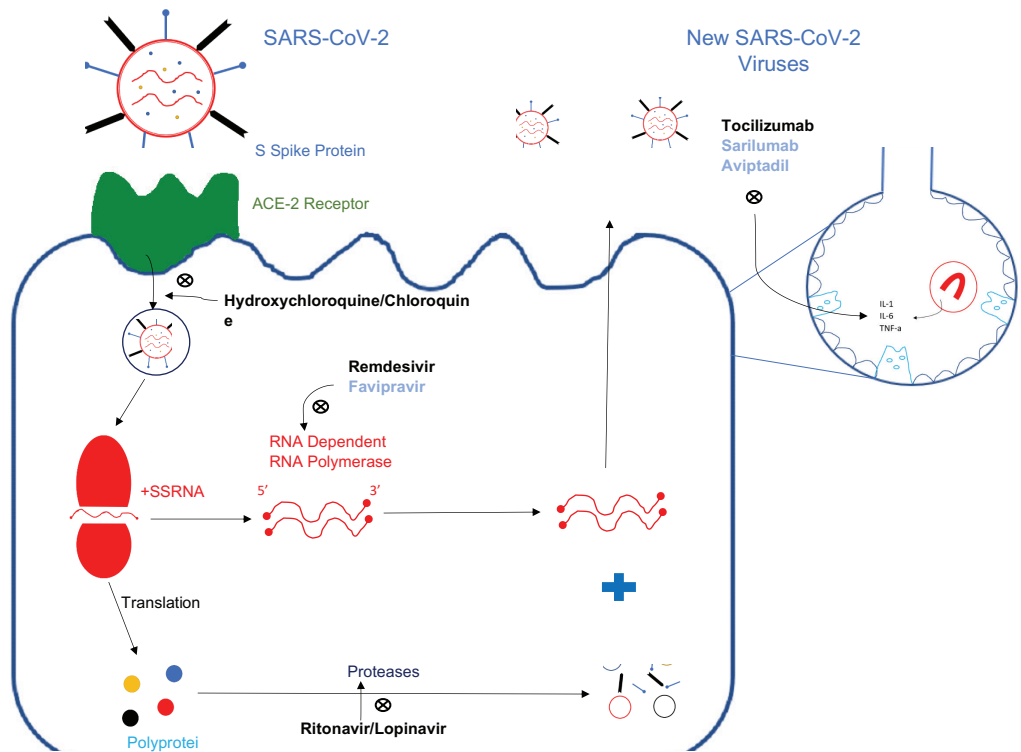
PRESENTATION

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CRITERIA FOR TESTING

- COVID should be considered in patients with new onset fever and/or respiratory symptoms (shortness of breath, cough).
- Given the large degree of community transmission, patients with an acute lower respiratory process that is severe with no apparent cause should also be considered for testing.

TREATMENT



Chloroquine/ Hydroxychloroquine	Remdesivir	Ritonavir/Lopinavir	Tocilizumab
Mech: Interferes with virus entry into the cell at ACE-2 receptor	Mech: Nucleotide analogue that inhibits RNA-Dependent RNA Polymerase preventing viral replication	Mech: Reverse transcriptase inhibitor, blocks viral replication by inhibiting proteinases	Mech: Binds to the IL-6 receptor and inhibits its function. Decreases inflammatory response to the virus.
In vitro data shows promise: - 2020 Wang et al - 2020 Yao et al		Clinical data with negative efficacy - 2020 Cao NEJM - 2020 Young JAMA	In vitro data suggests benefit - 2005 Vincent et al
In vivo data encouraging: - 2020 Gautret et al			Retrospective data in 21 patients - 2020 Xu et al
Active Trials: - NCT04303507	Active trials: - NCT04280705 , NCT04292899 , NCT04292730	Active Trials: - NCT04307693 , NCT04255017	Active Trials: - NCT04317092 , NCT04320615 , NCT04322773

Other Drugs Under Investigation

- RNA polymerase inhibition: Favipravir - [NCT04310228](#), [NCT04303299](#)
- Membrane fusion inhibitor: Umifenovir - [NCT04260594](#)
- Interleukin 6 inhibition: Sarilumab - [NCT04315298](#)
- Vasoactive intestinal peptide analog: Aviptadil - [NCT04311697](#)

RISK FACTORS

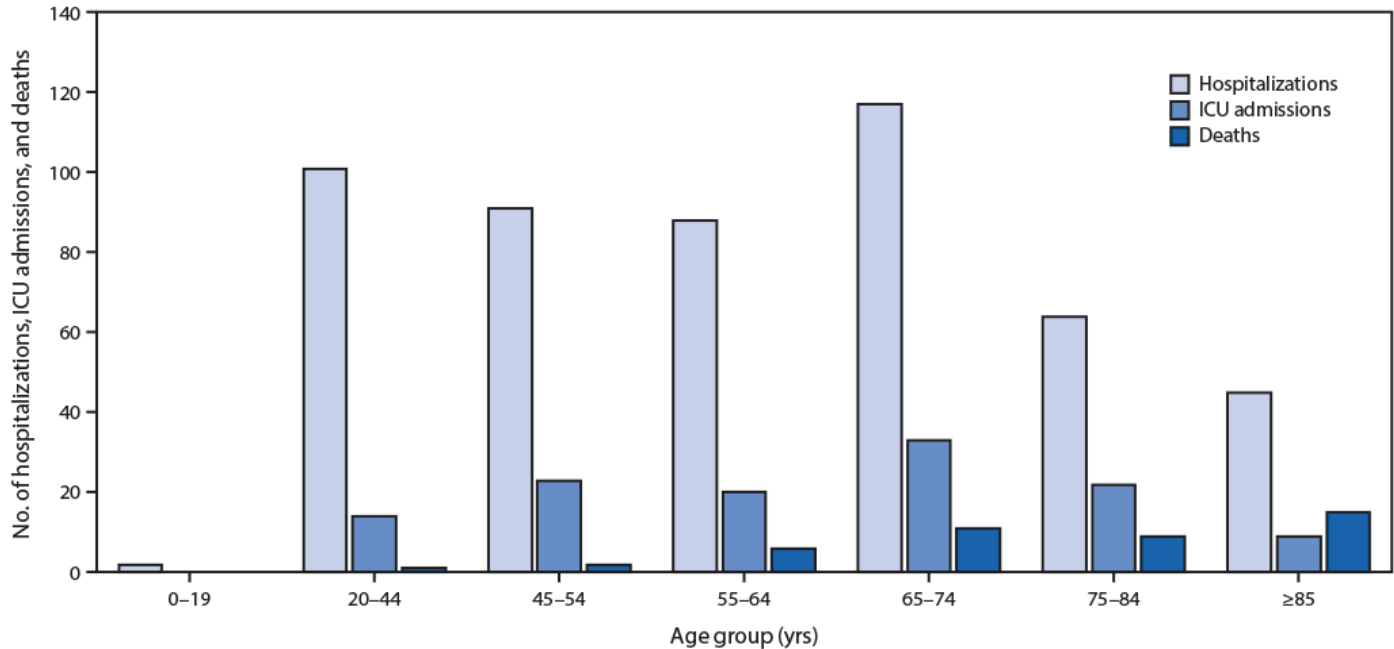
Risk Factors for ARDS ²¹	Risk Factors for Death
Older age (>65y)	Older age (>60 ^{6,21-24} -65y ²)
Diabetes Mellitus	Male Sex ^{6,21,24}
D-dimer elevation (>1.0ug/mL)	Hypertension ⁶
Ferritin (>300ng/mL)	Diabetes mellitus ⁶
Lymphopenia (0.37 x 10 ⁹ /L)	D-dimer elevation (>1.0ug/mL) ^{6,20}
	Ferritin (>300ng/mL) ^{6,20}
	Lymphopenia (<0.02x10 ⁹ /L) ¹ (0.37X10 ⁹ /L) ²⁰
	High sensitivity troponin I (>28pg/mL) ⁶

DISEASE PROGRESSION

- 76% patients placed on NIV progressed to invasive ventilation.⁴
- Worse outcomes with septic shock, ARDS & AKI⁵
- Watch for sudden cardiac deterioration after lung recovery
- Median hospital LOS in severe patients 13 days (11.5 - 17.0) vs 11 days (10.0 - 13.0) in nonsevere patients⁵
- Respiratory failure, circulatory failure, and combined failure are the commonest causes of death²⁵

PROGNOSIS

- The disease presentation and prognosis may vary significantly with 81% of people having mild pneumonias or no respiratory issues, 14% of cases having severe disease requiring supplemental oxygen and 5% being critical cases characterized by respiratory failure, shock or multiorgan dysfunction.³
- Older age, high Sequential Organ Failure Assessment (SOFA) score, and blood d-dimer levels >1 µg/mL are risk factors for poor prognosis and in-hospital mortality in patients with COVID-19.⁶
- The MuLBSTA score may be useful in predicting poor prognosis in patients with COVID-19. The factors included in this score are multilobular infiltration, lymphopenia, bacterial co-infection, smoking history, hypertension, and age.^{2, 26}
- Of the patients who recover, a significant number of patients will still have radiological abnormalities (ground-glass opacities on CT) at time of discharge.²⁷
- Other serious complications other than acute respiratory distress syndrome ARDS (29%) included anemia (15%), acute cardiac injury (12%) and secondary infection (10%).³
- The current overall all-cause mortality rate in patients with COVID is 4.2%²⁸ – ranging from 0.5% to 5.9% depending on the country and the percentage of the population being tested in that country.
- Mortality also varies significantly depending on the age of the patient. Among people under 49, 0.2% of those who contracted the disease died, compared to 14.8% of those who were 80 and older.²⁹ Young children appear to be mildly affected but may serve as a vector for transmission.
- In the US, out of a total of 4,226 COVID-19 cases, there are 44 known deaths. Among these, 15 (34%) deaths were reported among adults aged ≥85 years, 20 (46%) among adults aged 65–84 years, and nine (20%) among adults aged 20–64 years.³⁰



Coronavirus disease 2019 (COVID-19) hospitalizations, intensive care unit (ICU) admissions, and deaths, by age group — United States, February 12– March 16, 2020 Source: CDC Morbidity and Mortality Weekly Report (MMWR) March 18th 2020

REFERENCES

1. Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA*. 2020
2. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*. 2020;395(10223):507-513.
3. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;395(10223):497-506.
4. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med*. 2020.
5. Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med*. 2020.
6. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020.
7. Wu C, Chen X, Cai Y, et al. Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. *JAMA Intern Med*. 2020.
8. Arentz M, Yim E, Klaff L, et al. Characteristics and Outcomes of 21 Critically Ill Patients With COVID-19 in Washington State. *JAMA*. 2020.
9. Young BE, Ong SWX, Kalimuddin S, et al. Epidemiologic Features and Clinical Course of Patients Infected With SARS-CoV-2 in Singapore. *JAMA*. 2020.
10. Livingston E, Bucher K. Coronavirus Disease 2019 (COVID-19) in Italy. *JAMA*. 2020.
11. Lippi G, Plebani M. Laboratory abnormalities in patients with COVID-2019 infection. *Clin Chem Lab Med*. 2020. DOI: 10.1515/CCLM-2020-0198.
12. Wang Z, Yang B, Li Q, et al. Clinical Features of 69 Cases with Coronavirus Disease 2019 in Wuhan, China. *Clin Infect Dis*. 2020. DOI: 10.1093/cid/ciaa272.
13. Kanne JP, Little BP, Chung JH, et al. Essential for Radiologists on COVID-19: An Update-Radiology Scientific Expert Panel. *Radiology*. 2020. DOI: 10.1148/radiol.2020200527
14. Salehi S, Abedi A, Balakrishnan S, et al. Coronavirus Disease 2019 (COVID-19): A Systematic Review of Imaging Findings in 919 Patients. *AJR*. 2020;215:1-7. DOI: 10.2214/ajr.20.23034.
15. Li Y, Xia L. Coronavirus Disease 2019 (COVID-19): Role of Chest CT in Diagnosis and Management. *AJR*. 2020;214:1-7. DOI: 10.2214/AJR.20.22954.

REFERENCES

(CONTINUED)

16. Peng QY, Wang XT, Zhang LN. Findings of lung ultrasonography of novel coronavirus pneumonia during the 2019-2020 epidemic. 2020. *Inten Care Med*. 2020. DOI: 10.1007/s00134-020-05996-6.
17. Huang Y, Wang S, Liu Y. A Preliminary Study on the Ultrasonic Manifestations of Peripulmonary Lesions of Non-Critical Novel Coronavirus Pneumonia (COVID-19). 2020. DOI: 10.2139/ssrn.3544750.
18. Poggiali E, Dacrema A, Bastoni D, et al. Can Lung US Help Critical Care Clinicians in the Early Diagnosis of Novel Coronavirus (COVID-19) Pneumonia?. 2020. *Radiology*. DOI: 10.1148/radiol.2020200847.
19. Chan JF, Yuan S, Kok KH, To KK, Chu H, Yang J, Xing F, Liu J, Yip CC, Poon RW, Tsoi HW, Lo SK, Chan KH, Poon VK, Chan WM, Ip JD, Cai JP, Cheng VC, Chen H, Hui CK, Yuen KY. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet*. 2020;395(10223):514. Epub 2020 Jan 24.
20. Wu, C et al. *JAMA Intern Med*. 2020 Mar 13. doi: 10.1001/jamainternmed.2020.0994
21. Onder, G, Rezza, G, Brusaferro S, *JAMA* 2020 Mar 23. doi:10.1001/jama.2020.4683
22. Chinese CDC. <http://weekly.chinacdc.cn/en/article/id/e53946e2-c6c4-41e9-9a9b-fea8db1a8f51>
23. Korean CDC. <https://www.cdc.go.kr/board/board.es?mid=a30402000000&bid=0030>
24. NYC DOH. <https://www1.nyc.gov/assets/doh/downloads/pdf/imm/covid-19-daily-data-summary.pdf>
25. Ruan, Q, Yang, K., Wang, W. et al. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. *Intensive Care Med* (2020). <https://doi.org/10.1007/s00134-020-05991-x>
26. Guo L, Wei D, Zhang X, Wu Y, Li Q, Zhou M, Qu J. Clinical Features Predicting Mortality Risk in Patients With Viral Pneumonia: The MuLBSTA Score. *Front Microbiol*. 2019 Dec 3;10:2752. doi: 10.3389/fmicb.2019.02752.
27. Wang Y, Dong C, Hu Y, Li C, Ren Q, Zhang X, Shi H, Zhou M. Temporal Changes of CT Findings in 90 Patients with COVID-19 Pneumonia: A Longitudinal Study. *Radiology*. 2020 Mar 19:200843. doi: 10.1148/radiol.2020200843.
28. WHO situation report 60 (https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200320-sitrep-60-covid-19.pdf?sfvrsn=d2bb4f1f_2) accessed on 21 March 2020.
29. The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. The Epidemiological Characteristics of an Outbreak of 2019 Novel Coronavirus Diseases (COVID-19) — China, 2020[J]. *China CDC Weekly*, 2020, 2(8): 113-122.
30. Severe Outcomes Among Patients with Coronavirus Disease 2019 (COVID-19) — United States, February 12–March 16, 2020. *MMWR Morb Mortal Wkly Rep*. ePub: 18 March 2020. DOI: <http://dx.doi.org/10.15585/mmwr.mm6912e2>