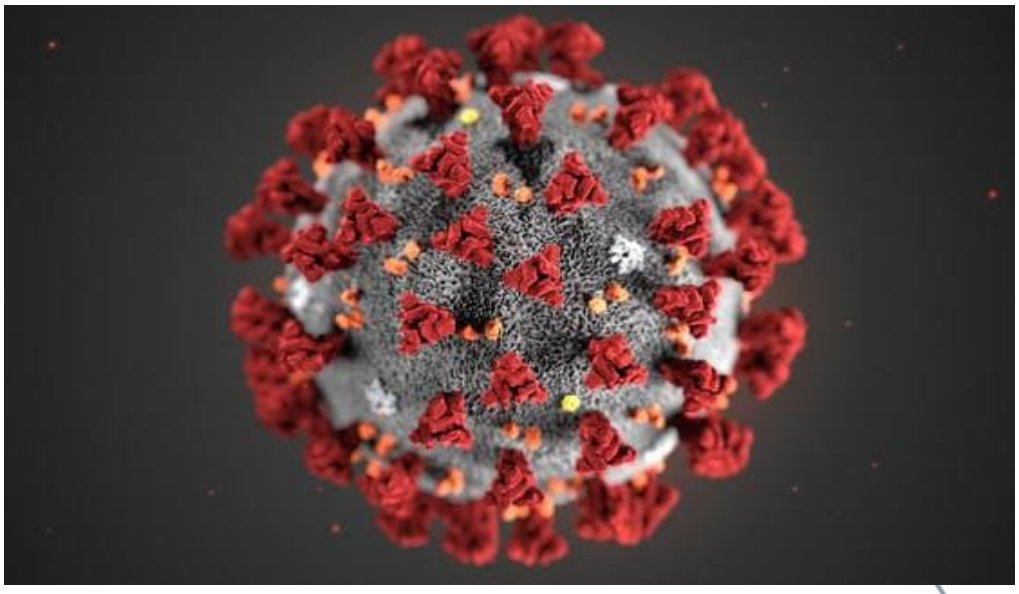
Ministry of Higher Education and Scientific Research

Thi qar University

Collage of Medicine

Department of Internal Medicine

Pattern Of Fever In patients with Covid 2019



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Introduction

Coronavirus disease 2019 (COVID-19) is defined as illness caused by a novel coronavirus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; formerly called 2019-nCoV), which was first identified amid an outbreak of respiratory illness cases in Wuhan City, Hubei Province, China.It was initially reported to the World Health Organization (WHO) on December 31, 2019. On January 30, 2020, the WHO declared the COVID-19 outbreak a global health emergency.On March 11, 2020, the WHO declared COVID-19 a global pandemic.

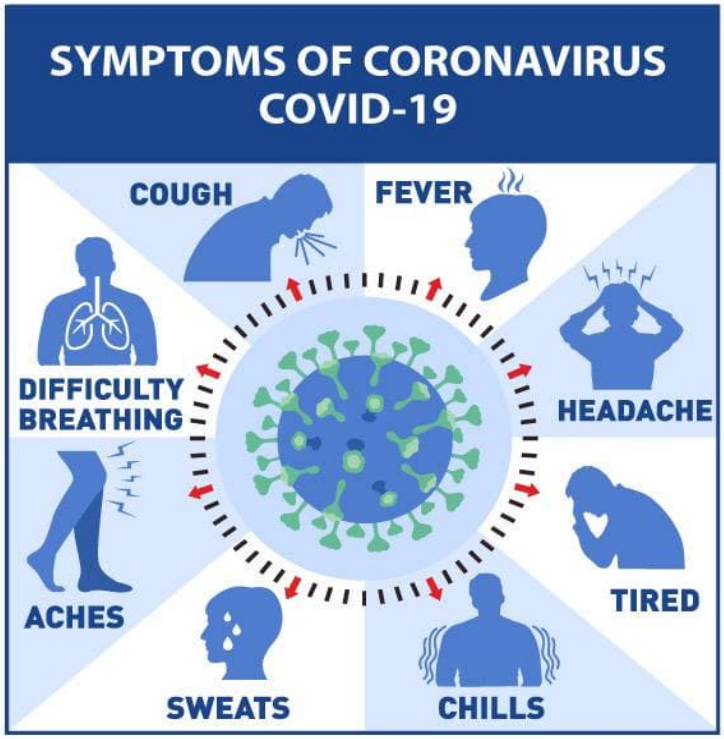
As of June 11,2021, confirmed COVID-19 infections number over 175 million individuals worldwide and have resulted in over 3.73 million deaths. In Iraq over 1.24 million infected individuals and over 16,614 deaths.

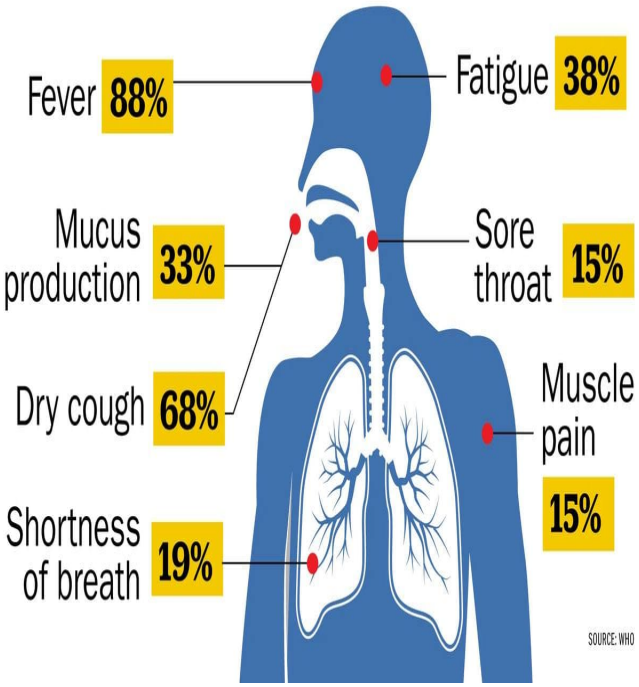
Presentations of COVID-19 range from asymptomatic/mild symptoms to severe illness and mortality. Symptoms may develop (2 days to 2 weeks) after exposure to the virus and the average incubation period is 5 days.

The main symptoms include:

- **Fever**
- **Coughing**
- **Shortness of breath**
- **Trouble breathing**
- **Fatigue**
- **Chills, sometimes with shaking**
- **Body aches**
- **Headache**
- **Sore throat**
- **Congestion/runny nose**

- **Loss of smell or taste**
- **Nausea**
- **Diarrhea**



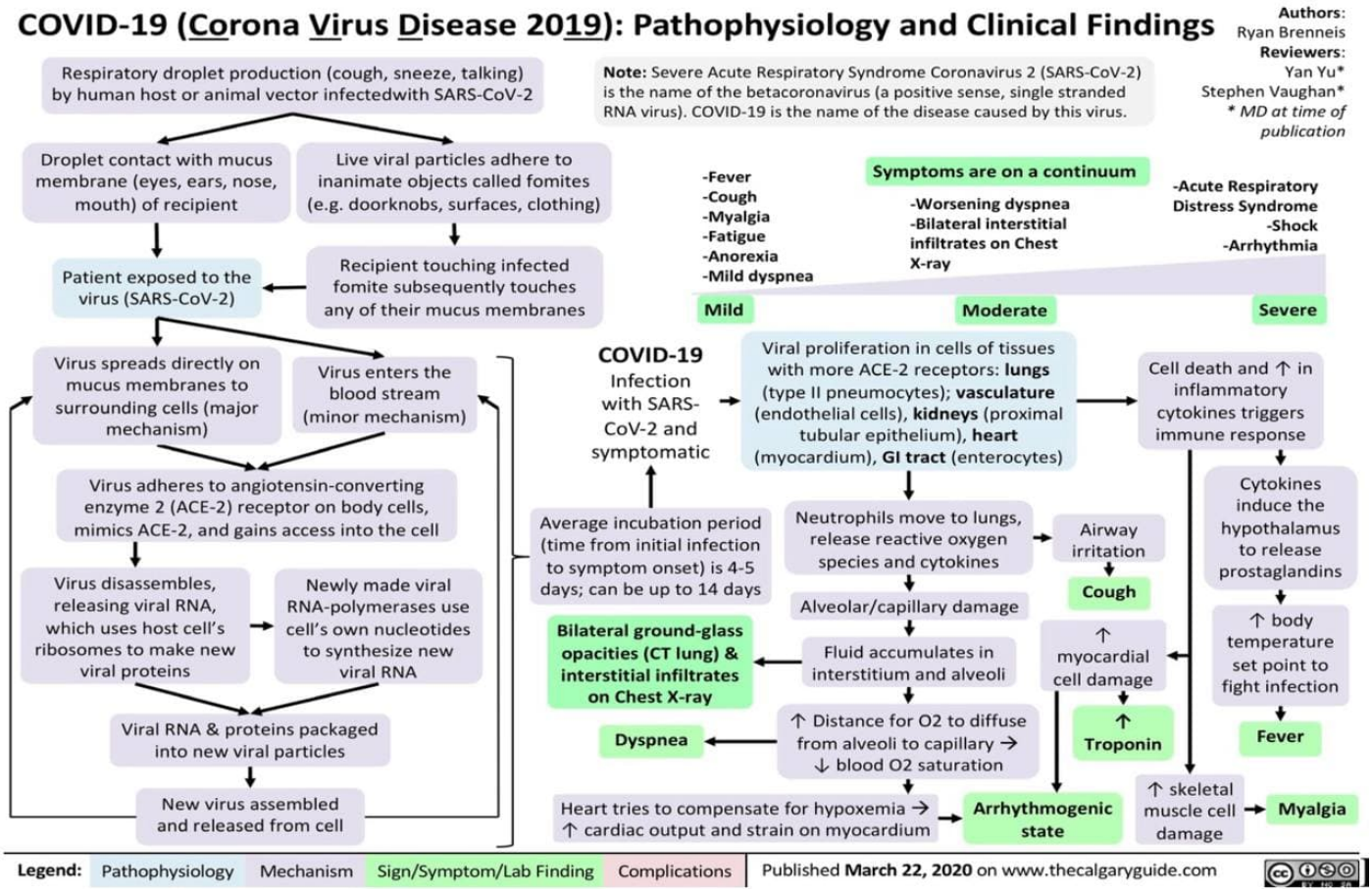


The virus can lead to pneumonia,respiratory failure, heart problems, liver problems, septic shock and death.

The principal mode by which people are infected with SARS-CoV-2 is through exposure to respiratory droplets carrying infectious virus (generally within a space of 6 feet). Additional methods include contact transmission (eg, shaking hands) and airborne transmission of droplets that linger in the air over long distances (usually greater than 6 feet).

Microbiologic (PCR or antigen) testing is required for definitive diagnosis.

Pathophysiology of COVID-19



Fever pattern in COVID-19

Fever is defined as a temperature of 38.0°C or higher.Fever is one of the most preserved evolutionary response over 600 million years to infections.It is a complex cytokine-mediated physiological response that stimulates both the innate and adaptive arms of immunity involving adrenergic stimulation pathways .Guan et al. reported fever in 42.8% at the time of admission and 88.7% of the COVID-19 patients at the time of hospitalization .This suggests although fever is the most common symptom in COVID-19 patients, the absence of fever at the time of initial screening does not exclude COVID-19.

Chen et al. reported the median duration of fever in COVID-19 patients; 10 days (95 confidential intervals [CIs]: 8–11 days. Resolution of fever coincided with PCR negativity of upper respiratory sample; 11 days (95 CIs: 10–12 days), radiological and clinical recovery. Those who received intensive critical care (ICU) services were more likely to have a longer duration of fever than the COVID-19 patients who did not receive ICU care (31 days vs. 9 days after onset of symptoms, respectively, P < 0.0001) .

Regular high fever in COVID-19 is considered to be an indicator of severe infection. In a study of 201 patients in Wuhan, high fever (>39°C) was associated with a higher likelihood of acute respiratory distress syndrome (HR, 1.77; 95% CI, 1.11–2.84), and lower risk of mortality (HR, 0.41; 95% CI, 0.21–0.82) .The preliminary results may point toward an association of improved prognosis in terms of mortality in severe COVID-19 patients with fever.

The initial presentation of the fever in COVID-19 in the first week, during the viral phase of the illness, is likely a manifestation of the body's immune response to the viral replication to augment immunity. However, if the viral infection does not resolve in due course, the disease process is complicated by the viral triggered state of dysregulated inflammation described as cytokine storm or secondary hemophagolymphocytosis, heralded by unremitting fever.

A study conducted in Singapore by Deborah et al examined the characteristics of fever and their correlation to cytokine levels and adverse outcomes in COVID-19. There were two patterns of fever identified. One was prolonged fever which persisted into the second week of illness and the second, saddleback fever where the fever recurs, after defervescence beyond day 7 of illness, to last less than 24 hours. Those patients who did not have fever were taken as controls.

Patients with prolonged fever had more hypoxia (27.8% vs 0.9%, p<0.01) and ICU admission (11.1% vs 0.9%, p= 0.05) compared to cases in the control group. Saddleback fever was significantly associated with hypoxia (14.3% vs 0.9%, p=0.03) but not ICU admission (0.9% vs 0.0 %,

p= 1.00) compared to those in the control. Cases with prolonged fever were found to have higher levels of anti-inflammatory interleukin (IL)-1 receptor antagonist (IL-1RA), pro-inflammatory IL-6, chemokine interferon γ induced protein 10 (IP-10) compared to controls.

This suggested that in patients with prolonged fever, close monitoring for hypoxemia should be instituted, while patients with saddleback fever without desaturation generally do well. Even though the numbers studied are quite low, the study points towards diligent oximetry monitoring and perhaps admission and more aggressive interventions in Covid patients who have fever persisting for more than a week.

Treatment of COVID-19

- **Mild to Moderate Disease :**

Patients with a mild clinical presentation (absence of viral pneumonia and hypoxia) may not initially require hospitalization, and most patients will be able to manage their illness at home. The decision to monitor a patient in the inpatient or outpatient setting should be made on a case-by-case basis. This decision will depend on the clinical presentation, requirement for supportive care, potential risk factors for severe disease, and the ability of the patient to self-isolate at home. Patients with risk factors for severe illness should be monitored closely given the possible risk of progression to severe illness, especially in the second week after symptom onset. The patients should quarantine themselves till the symptoms are subsided or at least for 10-14 days .

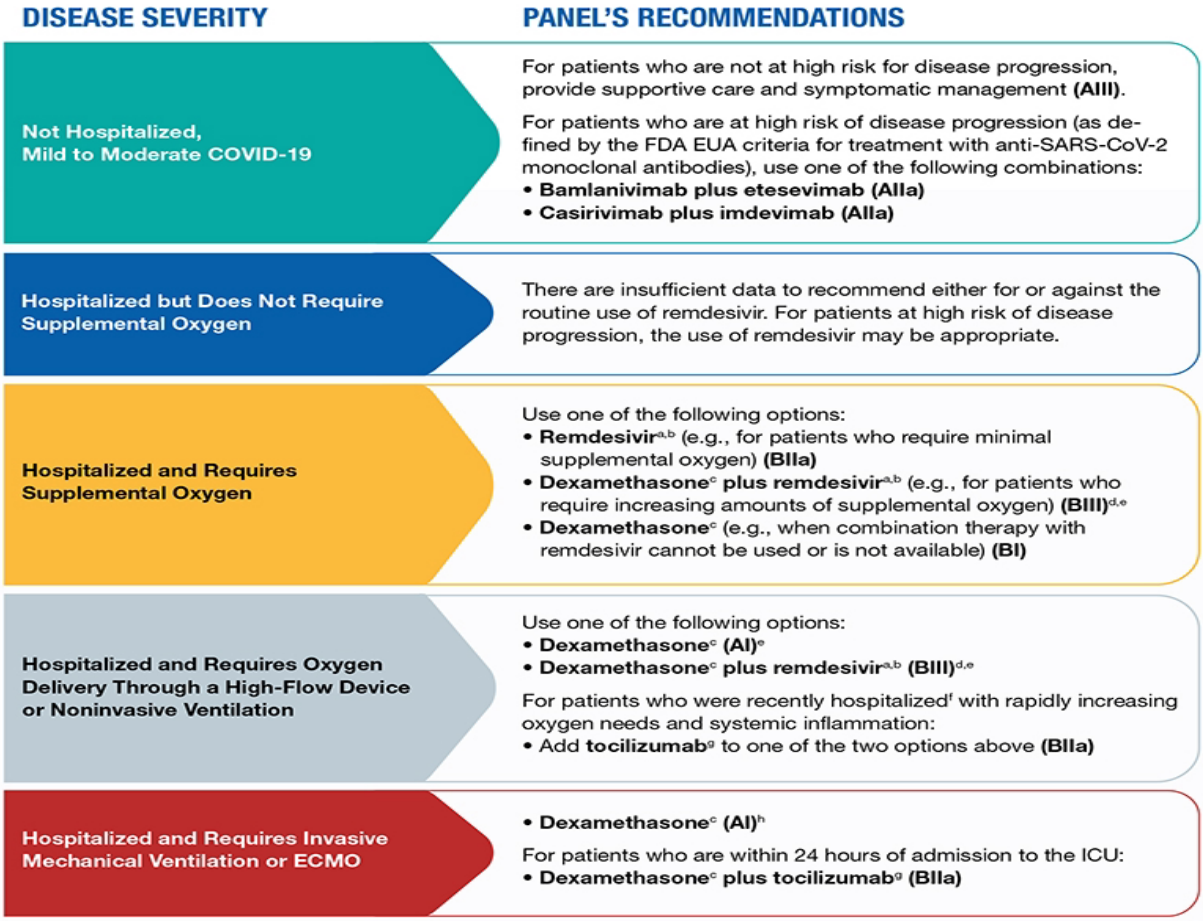
- **Severe Disease:**

Some patients with COVID-19 will have severe disease requiring hospitalization for management. Inpatient management includes supportive management of the most common complications of severe COVID-19: pneumonia, hypoxemic respiratory failure/ARDS, sepsis and septic shock, cardiomyopathy and arrhythmia, acute kidney injury, and complications from prolonged hospitalization, including secondary

bacterial and fungal infections, thromboembolism, gastrointestinal bleeding, and critical illness polyneuropathy/myopathy.

Figure 1. Pharmacologic Management of Patients with COVID-19 Based on Disease Severity

Doses and durations are listed in the footnotes.



Rating of Recommendations: A = Strong; B = Moderate; C = Optional
Rating of Evidence: I = One or more randomized trials without major limitations; IIa = Other randomized trials or subgroup analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = Expert opinion

[a] The remdesivir dose is 200 mg IV for one dose, followed by remdesivir 100 mg IV once daily for 4 days or until hospital discharge (unless the patient is in a health care setting that can provide acute care that is similar to inpatient hospital care). Treatment duration may be extended to up to 10 days if there is no substantial clinical improvement by Day 5.

[b] For patients who are receiving remdesivir but progress to requiring oxygen through a high-flow device, noninvasive ventilation, invasive mechanical ventilation, or ECMO, remdesivir should be continued until the treatment course is completed.

[c] The dexamethasone dose is 6 mg IV or PO once daily for 10 days or until hospital discharge. If dexamethasone is not available, equivalent doses of other corticosteroids (e.g., prednisone, methylprednisolone, hydrocortisone) may be used. See the Corticosteroids section for more information.

[d] The combination of dexamethasone and remdesivir has not been studied in clinical trials.

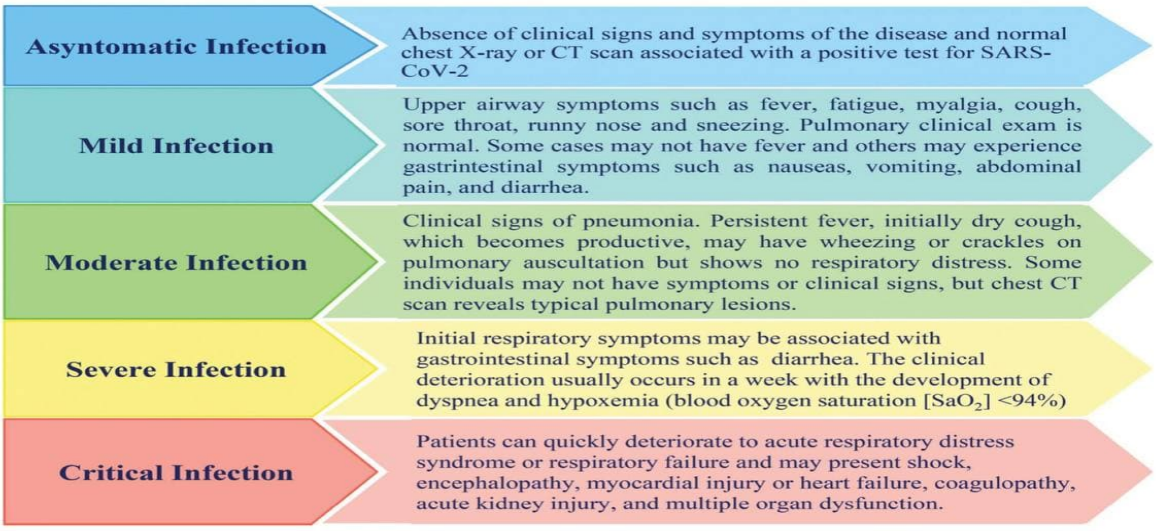
[e] In the rare circumstances where corticosteroids cannot be used, **baricitinib plus remdesivir** can be used **(BIIa)**. The FDA has issued an EUA for baricitinib use in combination with remdesivir. The dose for baricitinib is 4 mg PO once daily for 14 days or until hospital discharge.

[f] For example, within 3 days of hospital admission. See the Interleukin-6 Inhibitors section for more information.

[g] The tocilizumab dose is 8 mg/kg of actual body weight (up to 800 mg) administered as a single IV dose. Tocilizumab should not be combined with baricitinib and should be avoided in certain groups of patients who are at increased risk for complications. See the Interleukin-6 Inhibitors section for more information.

[h] The combination of **dexamethasone plus remdesivir** may be considered for patients who have recently been intubated **(CIII)**. The Panel **recommends against** the use of remdesivir monotherapy in these patients.

Key: ECMO = extracorporeal membrane oxygenation; EUA = Emergency Use Authorization; FDA = Food and Drug Administration; ICU = intensive care unit; IV = intravenous; the Panel = the COVID-19 Treatment Guidelines Panel; PO = orally



Prevention of COVID-19

Avoidance is the principal method of deterrence.

General measures for prevention of viral respiratory infections include the following:

1-Hand-washing with soap and water for at least 20 seconds. An alcohol-based hand sanitizer may be used if soap and water are unavailable.

2-Individuals should avoid touching their eyes, nose, and mouth with unwashed hands.

3-Individuals should avoid close contact with sick people.

4-Sick people should stay at home (eg, from work, school).

5-Coughs and sneezes should be covered with a tissue, followed by disposal of the tissue in the trash.

6-Frequently touched objects and surfaces should be cleaned and disinfected regularly.

The FDA has granted EUAs for 3 SARS-CoV-2 vaccines since December, 2020. Two are mRNA vaccines – BNT-162b2 (Pfizer) and mRNA-1273

(Moderna), whereas the third is a viral vector vaccine – Ad26.COV2.S (Johnson & Johnson). Other vaccines are in or nearing phase 3 trials.

Conclusions

Coronavirus disease (COVID-19) is an pandemic infectious disease caused by a newly discovered coronavirus.

Most people infected with the COVID-19 virus will experience mild to moderate respiratory illness and recover without requiring special treatment. Older people, and those with underlying medical problems like cardiovascular disease, diabetes, chronic respiratory disease, and cancer are more likely to develop serious illness.

Prolonged fever beyond 7 days from onset of illness can identify patients who may be at risk of adverse outcomes from COVID-19. Patients with saddleback fever appeared to have good outcomes regardless of the fever.

The best way to prevent and slow down transmission is to be well informed about the COVID-19 virus, the disease it causes and how it spreads. Protect yourself and others from infection by getting vaccinated,washing your hands or using an alcohol based rub frequently and not touching your face .

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