COVID 19: Clinical Presentation
• SARS-CoV-2 Infection: COVID-19
• COVID-19 Epidemiology
• COVID-19 Disease Course and Symptoms
• Risk Factors for Severe COVID-19 Infection
• Hospitalization with COVID-19: Presenting Symptoms
• Special Populations: Paediatrics
• Special Populations: Immunosuppressed Patients
• Special Populations: Pregnancy
• Summary
SARS-CoV-2 Infection: COVID-19
• On 11 February 2020, WHO officials announced a new infectious disease named COVID-19 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)\(^1\)

• ‘CO’ stands for corona, ‘VI’ for virus, and ‘D’ for disease and the 19 for the year 2019 when it was first diagnosed\(^2\)

• Guidelines agreed by the WHO, the World Organisation for Animal Health and the Food and Agriculture Organisation of the United Nations stated that the disease name must:
  • Be pronounceable
  • Be related to the disease
  • Not refer to a geographical location, animal, individual or group of people

---

COVID-19 Epidemiology
Following the emergence of the first case of infection in China, cases of SARS-CoV-2 infection spread rapidly across the globe.

- Over 200 countries have reported cases of COVID-19
- Over 225 million cases reported Worldwide
- Over 4.6 million deaths

---

Cases of, and deaths from, COVID-19 continue to increase globally

<table>
<thead>
<tr>
<th>Confirmed Cases</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Global:</strong> 213,912,908</td>
<td><strong>Global:</strong> 4,463,734</td>
</tr>
<tr>
<td>US: 38,223,029</td>
<td>US: 632,272</td>
</tr>
<tr>
<td>India: 32,558,530</td>
<td>Brazil: 576,645</td>
</tr>
<tr>
<td>Brazil: 20,645,537</td>
<td>India: 436,365</td>
</tr>
<tr>
<td>France: 6,757,783</td>
<td>Mexico: 255,452</td>
</tr>
<tr>
<td>Russia: 6,709,605</td>
<td>Peru: 197,944</td>
</tr>
<tr>
<td>UK: 6,621,799</td>
<td>Russia: 175,328</td>
</tr>
<tr>
<td>Turkey: 6,273,651</td>
<td>UK: 132,323</td>
</tr>
<tr>
<td>Argentina: 5,155,079</td>
<td>Indonesia: 129,293</td>
</tr>
<tr>
<td>Colombia: 4,897,150</td>
<td>Italy: 128,914</td>
</tr>
<tr>
<td>Spain: 4,815,205</td>
<td>Colombia: 124,474</td>
</tr>
</tbody>
</table>

COVID-19 Disease Course and Symptoms
COVID-19 Disease Course

Infection → Symptoms → Severe Disease → Recovery

- Infection: 5-6 days*
- Symptoms: 14 days†
- Severe Disease: 7 days‡
- Recovery: 2–8 weeks‡
- Recovery: 3–6 weeks†
- Death

*mean; † median; ‡ unknown average type

The signs and symptoms experienced by patients are determined by the disease pathogenesis, with milder illness correlating with viral replication, and more severe illness correlating with the body’s inflammatory response.
### Clinical Symptoms Reported Across the Global Population*

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Studies Reporting (n)</th>
<th>% of Presenting Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>144</td>
<td>59</td>
</tr>
<tr>
<td>Cough</td>
<td>139</td>
<td>55</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>99</td>
<td>31</td>
</tr>
<tr>
<td>Sore throat</td>
<td>62</td>
<td>14</td>
</tr>
<tr>
<td>Headache</td>
<td>76</td>
<td>12</td>
</tr>
<tr>
<td>Fatigue</td>
<td>78</td>
<td>28</td>
</tr>
<tr>
<td>Myalgia</td>
<td>69</td>
<td>17</td>
</tr>
<tr>
<td>Sputum/secretion</td>
<td>57</td>
<td>25</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>85</td>
<td>10</td>
</tr>
<tr>
<td>Chest pain</td>
<td>27</td>
<td>11</td>
</tr>
<tr>
<td>Nasal congestion</td>
<td>19</td>
<td>5</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>17</td>
<td>2</td>
</tr>
<tr>
<td>Rhinorrhea</td>
<td>32</td>
<td>8</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>16</td>
<td>5</td>
</tr>
<tr>
<td>Confusion</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Anorexia</td>
<td>18</td>
<td>20</td>
</tr>
</tbody>
</table>

*Data from a systemic review of most common clinical manifestations in patients diagnosed with COVID-19 that included 152 publications, a total of 41,409 individuals from at least 23 countries; Percentages rounded to nearest integer value. Mesquita R et al. Clinical manifestations of COVID-19 in the general population: systematic review. Wien Klin Wochenschr. 2021 Apr;133(7-8):377-382.
Primary Symptoms of COVID-19\textsuperscript{1,2}

- Headache
- Cough, sore throat
- Shortness of breath or difficulty breathing
- Nausea or vomiting, diarrhea
- Congestion or runny nose, new loss of taste or smell
- Fatigue, muscle or body aches, fever or chills

Monocytes and macrophages can be infected by SARS-CoV-2.

Monocytes from COVID-19 patients show an activated phenotype, and can produce cytokines IL-6, IL-10 and TNF.

A high level of cytokines triggers a cytokine storm, leading to more severe disease, and possibly death.
**Pulmonary Manifestations of COVID-19**

**Symptoms**
- Fatigue
- Cough
- Dyspnea

**Signs**
- Increased breathing rate
- Decreased oxygen saturation
- Sputum production
- Respiratory failure
- Acute Respiratory Distress Syndrome (ARDS)
- Low $\text{PaO}_2/\text{FiO}_2$
- Imaging shows lung infiltrates

$\text{PaO}_2/\text{FiO}_2$ ratio of arterial partial pressure of oxygen to fraction of inspired oxygen

Extrapulmonary Manifestations of COVID-19

Dermatologic
- Petechiae
- Livedo reticularis
- Erythematous rash
- Urticaria
- Vesicles
- Pernio-like lesions

Cardiac
- Takotsubo cardiomyopathy
- Myocardial injury/myocarditis
- Cardiac arrhythmias
- Cardiogenic shock
- Myocardial ischemia
- Acute cor pulmonale

Endocrine
- Hyperglycemia
- Diabetic ketoacidosis

Gastrointestinal
- Diarrhea
- Nausea/vomiting
- Abdominal pain
- Anorexia

Neurologic
- Headaches
- Dizziness
- Encephalopathy
- Guillain-Barré
- Ageusia
- Myalgia
- Anosmia
- Stroke

Cardiovascular
- Deep vein thrombosis
- Pulmonary embolism
- Catheter-related thrombosis

Hepatic
- Elevated ALT/AST
- Elevated bilirubin

Renal
- Acute kidney injury
- Proteinuria
- Hematuria

### NIH Guidelines: The COVID-19 Severity Spectrum

#### Stage | Characteristics
--- | ---
Asymptomatic or pre-symptomatic | Positive test for SARS-CoV-2 but no symptoms
Mild illness | Varied symptoms (e.g., fever, cough, sore throat, malaise, headache, muscle pain) but no shortness of breath, dyspnea or abnormal imaging
Moderate illness | $\text{SpO}_2 \geq 94\%$ and evidence of lower respiratory disease during clinical assessment or imaging
Severe illness | $\text{SpO}_2 < 94\%$, $\text{PaO}_2/\text{FiO}_2 < 300 \text{mmHg}$, respiratory rate $>30$ breaths/min, or lung infiltrates $>50\%$ on imaging
Critical illness | Respiratory failure, septic shock, and/or multiorgan dysfunction

NIH, National Institutes of Health; $\text{PaO}_2/\text{FiO}_2$, ratio of arterial partial pressure of oxygen to fraction of inspired oxygen; $\text{SpO}_2$, oxygen saturation.

• Data suggest that:
  • 80% of cases are asymptomatic or mild\(^1\),
  • 15% are severe\(^1\), and
  • 5% are critical\(^1\)

• Data on the percentage of people with COVID-19 who require hospital admission is difficult to estimate, as people who are asymptomatic may not get tested and confirmed as being infected\(^2\)
  • A recent study based on US COVID-19 cases estimated the infection-hospitalization ratio at 2.1%, although varies based on age and race\(^2\)

• Of hospitalized patients:
  • Median hospital stay has been estimated at 5 days\(^3\)
  • 86.4% recover\(^3\)
  • 21.9% admitted to ICU\(^3\)
  • 16.9% required invasive mechanical ventilation\(^3\)
  • 13.6% die\(^3\)

Risk Factors For Severe COVID-19 Infection
Risk Factors For Severe Illness from COVID-19 Infection

- **Older adults**: risk increases with age from 50 years onwards, those aged ≥85 years are at the highest risk

- **Racial/ethnic minority groups and people with disabilities**: risk increases with increase in likelihood of comorbidities, reduced healthcare access and increased likelihood of living in a congregate setting

- **People with medical conditions**: including cancer, chronic kidney disease, chronic lung diseases, dementia and other neurological conditions, diabetes, down syndrome, heart conditions, HIV, immunocompromised, liver disease, obesity, SCD, transplant recipient, CVD

- **Pregnant and recently pregnant people**: Pregnant people with COVID-19 are more likely to experience preterm birth and other poor outcomes related to pregnancy versus pregnant people without COVID-19

Hospitalization with COVID-19: Presenting Symptoms
### Presenting Symptoms: Hospitalized Patients

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>71.6</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>71.2</td>
</tr>
<tr>
<td>Cough</td>
<td>68.9</td>
</tr>
<tr>
<td>Fatigue</td>
<td>45.5</td>
</tr>
<tr>
<td>Confusion</td>
<td>26.7</td>
</tr>
<tr>
<td>Cough (sputum)</td>
<td>26.2</td>
</tr>
<tr>
<td>Muscle ache</td>
<td>20.6</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>20.4</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>19.8</td>
</tr>
<tr>
<td>Chest pain</td>
<td>14.6</td>
</tr>
<tr>
<td>Headache</td>
<td>12.5</td>
</tr>
<tr>
<td>Wheeze</td>
<td>10.9</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>10.2</td>
</tr>
<tr>
<td>Sore throat</td>
<td>9.8</td>
</tr>
</tbody>
</table>

**Symptoms associated with viral pneumonia**

Special Population: Paediatrics
• Children appear more likely to be asymptomatic than adults
  • Studies describe rates of asymptomatic infection as high as 13%, but true prevalence remains unknown

• Most commonly reported symptoms in children similar to those in adults
  • Fever, cough, shortness of breath, myalgia, fatigue and headache
  • Sore throat or pharyngeal erythema (5–50%), myalgia (10–25%), rhinorrhea/nasal congestion (4–30%) and headache (3–28%) have also been described
  • Gastrointestinal pain, nausea/vomiting and diarrhoea seem to occur less commonly in children (5–10%)
  • Anosmia and ageusia have not yet been reported
    • possibly due to challenges eliciting this type of symptomatology from younger children

• The overlap of symptoms with other respiratory tract viral infections common in children, such as influenza and respiratory syncytial virus, poses additional challenges to recognition of COVID-19.

Children with COVID-19: A Systematic Review

• A meta-analysis of 48 studies\(^1\) in paediatric patients with COVID-19 (n=5,829), exploring most common clinical and laboratory findings

• Children of all ages at risk of COVID-19\(^1\)

• Main illness classifications\(^1\):
  • Asymptomatic: 20% (95% CI: 14–26%)
  • Mild: 33% (95% CI: 23–43%)
  • Moderate: 51% (95% CI: 42–61%)

• The most prevalent symptom was fever, followed by cough, nasal symptoms, diarrhea, and nausea/vomiting\(^2\)

---

Special Population: Immunosuppressed Patients
Due to impaired immune defenses from both underlying disease and treatment, immunocompromised patients with respiratory virus infection are at risk of: 1

- More severe infection
- Increased rates of bacterial and fungal superinfection

Similar concerns exist regarding immunosuppressed patients infected with SARS-CoV-2. 1, 2

However, association between COVID-19 and intense cytokine release raises the possibility that immunosuppression may temper the exuberant inflammatory response in this infection.

Important issues remain, specifically:

- Possibility of atypical clinical manifestations in the immunocompromised
- Attributable risk of immunosuppression versus other comorbidities on COVID-19 severity

Patients with cancer appear to have an increased risk of severe outcomes. 1, 2

Well-treated HIV is not associated with an excess risk of severe COVID-19. 3

---

Special Population: Pregnancy
• Pregnant people are at greater risk of having severe illness following COVID-19 infection, particularly if there are other factors that put them at greater risk – such as having underlying medical conditions\(^1\)

• Compared with pregnant people without COVID-19, those with COVID-19 are more likely to experience adverse pregnancy outcomes, including:\(^1,2\)
  • Preterm birth\(^1,2\)
  • Pregnancy loss\(^1\)
  • Stillbirth\(^2\)
  • Preeclampsia\(^2\)

• In addition, compared with pregnant people with mild COVID-19, those with severe COVID-19 during pregnancy are at greater risk of:\(^2\)
  • Gestational diabetes\(^2\)
  • Low birth weight\(^2\)

Summary
• COVID-19 primarily impacts the respiratory system, though most organ systems can be involved\(^1\)
  • Symptom onset ranges from 2–14 days after exposure to SARS-CoV-2\(^3\)
• Patients are at risk of disease transmission before onset of symptoms\(^4\)
• Patients infected with SARS-CoV-2 can be asymptomatic or present with a range of clinical signs and symptoms ranging from mild to critical\(^1,3,4\)
• The patient journey varies according to disease severity\(^5\)
• Children appear more likely to be asymptomatic than adults, yet the commonly reported symptoms in children are similar to those in adults\(^6\)
• Due to impaired immune defenses from both underlying disease and treatment, immunocompromised patients with respiratory virus infection are at risk of more severe infection and increased rates of bacterial and fungal superinfection\(^7\)
• Compared with pregnant people without COVID-19, those with COVID-19 are more likely to experience adverse pregnancy outcomes, including preterm birth, pregnancy loss, stillbirth and preeclampsia\(^8,9\)