

# General Symptoms with COVID-19

Subjects: Pathology

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Coronavirus disease 2019 (COVID-19) due to the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has become an epidemiological threat and a worldwide concern. SARS-CoV-2 has spread to 210 countries worldwide and more than 3,000,000 confirmed cases and 228,513 deaths have been reported, while the number of both confirmed and fatal cases is continually increasing. COVID-19 is a viral disease that can affect every age group – from infants to the elderly – resulting in a wide spectrum of various clinical manifestations. COVID-19 might present different degrees of severity – from mild or even asymptomatic carriers, even to fatal cases. The most common complications include pneumonia and acute respiratory distress syndrome. Fever, dry cough, muscle weakness, and chest pain are the most prevalent and typical symptoms of COVID-19. However, patients might also present atypical symptoms that can occur alone, which might indicate the possible SARS-CoV-2 infection. The aim of this paper was to review and summarize all of the findings regarding clinical manifestations of COVID-19 patients and those include respiratory, neurological, olfactory and gustatory, gastrointestinal, ophthalmic, dermatological, cardiac, and rheumatologic manifestations, as well as specific symptoms in pediatric patients.

Keywords: COVID-19 ; Sars-Cov-2 ; coronavirus ; COVID-19 symptoms ; clinical manifestations ; specific manifestations ; non-specific manifestations ; symptoms ; outbreak ; diagnosis ; public health ; symptoms of COVID-19

## 1. Introduction

The majority of patients with COVID-19 present common symptoms that include fever, shortness of breath, cough (either with or without sputum), sore throat, nasal congestion, dizziness, chills, muscle ache, arthralgia, weakness, fatigue or myalgia, chest tightness, excessive mucus production with expectoration, hemoptysis, and dyspnea<sup>[1][2][3][4][5][6][7]</sup>. Even though fever is not the only initial clinical manifestation of SARS-CoV-2 infection, it is considered to be critical<sup>[8][9]</sup>. Fever, cough, and fatigue are the three most prevalent symptoms in COVID-19 patients<sup>[10][11]</sup>. Other less characteristic symptoms include headache, diarrhea, abdominal pain, vomiting, chest pain, rhinorrhoea, or pharyngalgia<sup>[12][13][14][15]</sup>. Approximately 90% of the patients present more than one symptom<sup>[16][17]</sup>. An approximate proportion of severe versus common cases of COVID-19 is estimated to 1:4<sup>[18]</sup>. It is suggested that an early onset of shortness of breath constitutes a poor prognostic factor for patients. Among 81 fatal cases of patients from Wuhan, the most common cause of death was a respiratory failure (46.91%), followed by septic shock (19.75%), multiple organ failure (16.05%), and cardiac arrest (8.64%). Rarer death causes were acute coronary syndrome, malignant arrhythmia, or disseminated intravascular coagulation (DIC)<sup>[19]</sup>. Zhou et al. reported a case of a COVID-19 patient with a spontaneous pneumomediastinum and subcutaneous emphysema<sup>[20]</sup>. Clinical characteristics might differ between critically ill and non-critically ill patients<sup>[21][22]</sup>.

## 2. Radiological Findings

The majority of patients show bilateral pneumonia and only a small percentage of COVID-19 patients show unilateral pneumonia. The most frequent computed tomography (CT) findings are bilateral patchy shadows and ground-glass opacities (GGO); multilobe involvement and focal lesions (patches, stripes, or nodules) are also very characteristic<sup>[23][24][25][26]</sup>. Less characteristic CT findings include centrilobular nodules, tree-in-bud sign, cystic change, pleural effusion, interstitial fibrosis, or lymphadenopathy. CT examinations show that lesions are more likely to be localized in the periphery than in the center of the lungs and the lesions are more patchy than oval<sup>[27][28]</sup>. Other CT findings include either pure GGO or GGO with reticular and/or interlobular septal thickening, GGO with consolidation, or pure consolidation<sup>[29][30]</sup>. Less common, but still characteristic, CT findings include ground-glass followed by irregular or halo sign, air bronchogram, bronchovascular bundle thickening, grid-form shadow, and hydrothorax<sup>[23]</sup>. Ground glass-like shadows, fibrous stripes, patchy shadow, and pleural thickening are observed both in common-type and severe or critical-type patients, independent to the severity of the COVID-19 course<sup>[31]</sup>. Single or multiple lobes of a single lung or both lungs (without a characteristic pattern) can be affected; interestingly, some of the studies showed that severe critical-type patients exhibit lesions primarily in the right lung<sup>[32]</sup>.

### 3. Laboratory Findings

Generally, COVID-19 patients tend to have normal or decreased white blood cell counts, lymphopenia, or thrombocytopenia<sup>[33][34]</sup>. Zhang et al. showed that patients with high leukocyte count ( $>10 \times 10^9/L$ ), higher neutrophil count ( $>7 \times 10^9/L$ ), and lower lymphocyte count ( $<0.4 \times 10^9/L$ ) are much more prone to severe COVID-19 pneumonia and composite endpoint (which was the admission to an intensive care unit, mechanical ventilation, or death)<sup>[35]</sup>. Besides, higher levels of C-reactive protein ( $>150 \text{ mg/L}$ ) and increased D-dimer levels ( $>1 \text{ mg/L}$ ) are also strongly associated with an increased risk of COVID-19 pneumonia and the composite endpoint. Additional laboratory indicators of increased risk are higher alanine aminotransferase (ALT) activity ( $>80 \text{ U/L}$ ), higher aspartate aminotransferase (AST) activity ( $>80 \text{ U/L}$ ), higher  $\alpha$ -hydroxybutyrate dehydrogenase activity ( $>540 \text{ U/L}$ ), higher lactate dehydrogenase activity ( $>720 \text{ U/L}$ ), higher creatine kinase activity ( $>600 \text{ U/L}$ ), and lower total protein level ( $<60 \text{ g/L}$ ). So far, researchers have not observed a significant statistical association between altered platelet counts and creatinine levels with an increased risk of COVID-19-related pneumonia. As opposed to numerous studies, Zhang et al. showed that COVID-19 pneumonia and composite endpoint are associated with leukocytosis rather than leukopenia<sup>[35]</sup>. However, the abovementioned results differ among COVID-19 patients. Du et al. observed that the majority of COVID-19 patients (81.2%) had lowered eosinophil count and many patients had decreased hemoglobin and hematocrit, as well as decreased activated partial prothrombin time (APTT) and increased prothrombin time (PT)<sup>[19]</sup>. Among studied patients, 22.4% had increased procalcitonin levels and elevated levels of blood urea nitrogen or serum creatinine. It is still speculated whether eosinophilopenia might constitute a prognostic factor for COVID-19 patients. Some patients present progressive lymphopenia with a concurrent progressive neutrophilia<sup>[36]</sup>. However, among the most common reported laboratory findings, those of the highest prevalence include elevated levels of C-reactive protein and erythrocyte number, as well as increased myohemoglobin, liver enzymes, and muscle enzymes<sup>[10]</sup>. Additionally, patients with a severe course of COVID-19 usually have elevated D-dimer levels, increased procalcitonin, increased leukocyte number, and lymphocytopenia<sup>[37][38]</sup>. In some cases, lymphocytes and white blood cell levels might remain within physiological ranges. The decrease in the number of lymphocytes is generally observed in the CD4<sup>+</sup> subpopulation. No significant changes are stated in the case of CD8<sup>+</sup> and B cell subpopulations<sup>[39]</sup>. Further, interleukin 10 (IL-10), interleukin 6 (IL-6), interleukin 1 (IL-1), interleukin 2R (IL-2R), and tumor necrosis factor alpha (TNF- $\alpha$ ) levels might exceed the upper limit in COVID-19 patients<sup>[40][41][42][43]</sup>. Chemokines, such as interferon gamma-induced protein 10 (IP-10) and monocyte chemoattractant protein 1 (MCP1), are also overexpressed during the course of COVID-19<sup>[44]</sup>.

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