Review Article

Clinical and laboratory findings of COVID-19

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Abstract:

The pandemic of coronavirus disease-19 started in Wuhan City of China in December 2019 and quickly spread all over the world, infecting almost two million people. The clinical presentation of the disease is mild/moderate in 80% of cases; however, it leads to a critical clinical presentation by 20%, which is severe or very severe disease requires intensive care. The mortality is high, especially in cases with advanced age, comorbidities, and pneumonia-related acute respiratory distress syndrome and respiratory failure, while children are often with subclinical manifestations. The most common clinical findings are fever, cough, fatigue, and shortness of breath. The incubation period ranges from 2 to 14 days. The most common laboratory findings are lymphocytopenia and thrombocytopenia. Elevated D-dimer, ferritin, troponin I, lactate dehydrogenase and interleukin-6, and hypoxia (O_2 saturation $\leq 90\%$) were identified as "poor prognostic factors" associated with severe disease and mortality. The monitoring of such parameters was reported to be beneficial for determining patients with risk and potentially high mortality.

Keywords:

Clinical presentations, coronavirus disease-19, laboratory findings, prognostic factors

Introduction

In December 2019, a novel coronavirus (COVID-19), was identifed as a outbreak of acut respiratory illness in China. COVID-19 displays symptoms ranging from mild to severe pneumonia that can lead to death in some individuals.

Clinical Findings

Following the incubation period, the most common clinical findings in Coronavirus disease-19 (COVID-19) are fever, dry cough, and fatigue. It may cause a clinical presentation progressing to acute respiratory distress syndrome (ARDS) with shortness of breath and respiratory failure in more severe cases.[1] The presence of typical upper respiratory tract infection findings (rhinorrhea, nasal congestion, and sore throat, etc.) has been rarely reported in COVID-19, but the presentation does not refuse the diagnosis. Several studies reported an altered sense of smell, such as anosmia and hyposmia as early disease symptoms. To a rare extent, neurological symptoms (headache, confusion, and changes in consciousness, etc.) and gastrointestinal symptoms such as diarrhea, especially in children, have been identified in COVID-19 infection [Table 1].[1-3]

Incubation period

The time from exposure to the onset of symptoms, is between 2 and 14 days (average: 4–5 days).[1,4-7] An analysis of 181 cases in China reported that the incubation period was 2.2 days and 11.5 days in 2.5% and 97.5% of the cases, respectively, with a median of 5.1 days. The incubation period has been reported to differ among patients with clinically severe and mild/moderate

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How to cite this article: Komurcuoglu B. Clinical and laboratory findings of COVID-19. Eurasian J Pulmonol 2020;22:S16-8.

Table 1: Coronavirus disease-19 symptom frequency

Clinical symptoms	All cases (%)	Severe disease (%)	Nonsevere disease (%)
Fever	88.7	91.9	88.1
Cough	67.8	70.5	67.3
Fatigue	38.1	39.9	37.8
Sputum	33.7	35.3	37.8
Shortness of breath	18.7	37.6	15.1
Myalgia/arthralgia	14.9	17.3	14.5
Sore throat	13.9	13.3	14
Headache	13.6	15	13.4
Chills	11.5	15	10.8
Nausea-vomiting	56	6.9	4.6
Nasal congestion	4.8	3.5	5.1
Diarrhea	3.8	5.8	3.5

disease and be similar to severe acute respiratory syndrome (SARS) in general terms. A long incubation period is believed to be the reason for the easy spread of the disease.[4,5]

Infectivity

For COVID-19 infection, infectivity is based on the detection of viral RNA in the respiratory tract and other specimens. The viral RNA reaches its peak level in the upper respiratory tract specimens right after the onset of the symptoms and gradually decreases in the following days of the disease. An infected person is believed to infect an average of 2–5 people.[2,8]

Clinical severity of the disease

The clinical manifestations of the COVID-19 infection can be classified as mild, moderate, severe, very severe disease (critical disease).[9,10]

a. Mild/Moderate disease: Cases with mild symptoms and without pneumonia or with mild pneumonia. This manifestation accounts for 81% of all cases
b. Severe disease: Cases with severe symptoms such as dyspnea and hypoxia, or with more than 50% of lungs affected within the first 24–48 h. This manifestation accounts for 14% of all cases
c. Critical disease (very severe disease): Cases requiring intensive care monitoring due to a severe clinical presentation such as respiratory failure, shock, and multiple organ dysfunction. This manifestation accounts for 2.3% of all cases.

Symptoms

Asymptomatic infection was reported in COVID-19. Such cases are believed to be an important source of disease spread, especially as carriers and infectors. Nevertheless, the incidence of asymptomatic individuals is unknown.[1-3] A series of more than 70 thousand cases reported the polymerase chain reaction (PCR) positive case rate without any clinical symptoms to be 1%.[7] Another study assumed that 18% of the estimated cases

might be asymptomatic based on a modeling system.[9] Thoracic computed tomography (CT) of asymptomatic cases revealed typical findings such as ground-glass appearance in 50% and atypical findings in 20%, and 20% of cases developed symptoms in the following days.[8] A study of 55 diseases established pneumonia on CT in 67% of asymptomatic cases.[10] It is very difficult to report an asymptomatic case percentage with available data. It is believed that at least half of these cases are symptomatic on monitoring, and may develop manifestations progressing to pneumonia and respiratory failure.[8,10]

The complaints most commonly reported by studies include fever, fatigue, dry cough, anorexia, myalgia, dyspnea, and sputum. Specifically, high fever, cough, and dyspnea should be carefully examined as they indicate a "severe or critical case."[1-3,7]

The study by Guan et al. found fever to be the most commonly detected symptom (88.7%–99%) ($\geq 38.3°C$). Nevertheless, the identified number of nonfebrile or subfebrile cases (20%) is higher than SARS and Middle East respiratory syndrome infections.[1] Cough occurs in 2/3 of cases. The cough was usually identified as dry and with expectoration to a rarer extent.[1,3] Upper respiratory tract symptoms (rhinorrhea, nasal congestion, sneeze, and sore throat) are rarer with COVID-19 infection than with other viral agents. Yet, anosmia and hyposmia are reported to be early diagnostic findings and early findings suggestive of COVID-19 infection.[7,10] The study by Zhou et al. demonstrated that the median duration of fever and cough was 12 days (8–13 days) and 19 days (12–23 days), respectively, among patients hospitalized and survived.[11]

COVID-19 may occur with various clinical manifestations. A study identified 11 different clinical types: type with asymptomatic infection, no mild pneumonia, PCR negative but antibody positive; type with PCR positive after recovery; type complicated with secondary bacterial pneumonia, mild pneumonia symptoms; type with allergic rhinitis and pneumonia, atopic dermatitis and pneumonia, starting with pneumonia and diarrhea in COPD cases.[12]

Laboratory Findings

The most common laboratory findings at diagnosis are lymphocytopenia (83.2%), thrombocytopenia (36.2%), and leukopenia (33.7%)[1-3] [Table 2]. Reported findings among infectious markers are elevated C-reactive protein, liver function tests (alanine transaminase/aspartate transaminase), and D-dimer. The level of procalcitonin is often within the normal range at initial diagnosis unless a bacterial infection is added; however, it has been shown to elevate in intensive care patients.[13-15]

Table 2: Laboratory findings of coronavirus disease-19 cases with severe and non-severe disease

Laboratory findings (%)	All cases (%)	Severe disease (%)	Nonsevere disease (%)
WBC <4000/mm³	33.7	61.1	28.1
Lymphocytes <1.500 mm³	83.2	96.1	80.4
Platelets <150.000 mm³	36.2	57.7	31.6
CRP ≥10 mg/l	60.7	81.5	56.4
LDH ≥250 u/l	41	58.1	37.1
AST >40 u/l	22.2	39.4	37.1
D-dimer ≥500 mg/dl	46.6	59.6	43.2

WBC: White blood cell, CRP: C-reactive protein, LDH: Lactate dehydrogenase, AST: Aspartate transaminase

Severe lymphocytopenia at initial diagnosis and ongoing during the disease was found associated with mortality. Elevated D-dimer and lymphopenia were found associated with mortality. Likewise; D-dimer, serum levels of ferritin, troponin I, Lactate dehydrogenase, interleukin-6, and PaO$_2$ ≤ 90 mmHg, which was elevated at initial diagnosis and increased during follow-up, were identified as "poor prognostic factors" associated with severe disease and mortality.[14-16] Monitoring of such parameters, especially in severe pneumonia cases was reported to be beneficial in terms of "cytokine storm" caused by overstimulated immune system and progression to ARDS.[13-16]

Sixty-one COVID-19 patients were prospectively assessed; severe disease and intensive care admission were found significantly higher in the group with an advanced age (≥50 years) and a neutrophil-to-lymphocyte ratio (NLR) of ≥3.13, and NLR was considered as an independent risk factor related to the disease.[17]

In conclusion, COVID-19 infection is associated with high mortality, especially in cases developing ARDS and respiratory failure at an advanced age. Close monitoring of clinical findings suggestive of severe pneumonia (such as high fever, cough, shortness of breath, and hypoxia) and laboratory findings indicative of poor diagnosis is a guide to identify patients with a potentially high mortality and to administer an effective treatment in time.

Financial support and sponsorship

Conflicts of interest
There are no conflicts of interest.

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