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Review Article

Clinical, Radiological, and Laboratory Findings in Patients Infected With 2019 Novel Coronavirus (SARS-CoV-2)

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Abstract

The outbreak of a novel coronavirus disease 2019 (COVID-19) began in China in December 2019 and spread worldwide. The current review summarized clinical, radiological, and laboratory findings of patients infected with COVID-19. Based on many studies, the main symptoms of the disease include respiratory symptoms, fever, cough, and dyspnea; there is also a wide range of biochemical, hematological, and radiological changes in the patients. The signs (or symptoms) and other variables in the early stage or the mild stage of the disease appear in a highly heterogeneous and non-specific manner. Identifying the clinical and paraclinical symptoms of COVID-19 can be effective in controlling it.

Keywords: Coronavirus disease 2019, Severe acute respiratory syndrome, Clinical symptoms, Laboratory findings, Radiological features

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Introduction

The outbreak of coronavirus disease 2019 (COVID-19) began in Wuhan, China in December 2019, and eventually turned into a worldwide pandemic (1). It is caused by becoming infected with a specific type of coronavirus. The International Committee of Taxonomy of Viruses (ICTV) named this virus as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (2). Coronaviruses (CoVs) are a group of RNA viruses that cause diseases in mammals and birds. They are single-stranded positive-sense RNA viruses belonging to the Coronaviridae family (3). Asymptomatic carriers of the coronavirus are the main source of the virus (4). COVID-19 spreads most often when an infected person is in close contact with another person. The virus spreads through the air, primarily via respiratory droplets or aerosols, when the infected person sneezes, coughs, speaks, or breathes heavily. Moreover, it may be transmitted via contaminated surfaces (4-6). The incubation period may range from 1 to 14 days but mostly occurs from day 3 to 7 (7). The disease is associated with clinical symptoms of viral pneumonia, and the most common symptoms are fever, fatigue, dry coughs,

and shortness of breath (6, 8). Other symptoms, such as runny nose, nasal congestion, and diarrhea have been reported less frequently; in more severe cases, dyspnea is also seen. Moreover, acute respiratory distress syndrome (ARDS), septic shock, difficulty to compensate metabolic acidosis, and coagulative dysfunction develop rapidly (9). COVID-19 has a mild to severe spectrum. Also, mortality rates vary from country to country, and it has been reported between 0.4%–3.4 % (10). On January 30, 2020, the World Health Organization (WHO) announced the epidemic of COVID-19 as a global health emergency (11).

Due to the lack of a completely effective drug or vaccine for COVID-19, timely identification of patients and their isolation from the healthy population can prevent its rapid spread (12). Currently, molecular tests are the standard methods to confirm COVID-19, but in negative reverse transcription-polymerase chain reaction (RT-PCR) test patients, a combination of travel history of the individual to the affected areas as well as clinical symptoms along with typical CT imaging and laboratory findings are used (12, 13). Moreover, using biosensors in detecting COVID-19 is a new view that can improve the diagnostics procedure in the future (14). The current review focused on the manifestations and symptoms of COVID-19 in various tests.

Clinical Findings

People with COVID-19 have had a wide range of symptoms. Fever (88%-98%), dry coughs (60%-82%), dyspnea (31%-55%), chest tightness (31%-40%), sudden loss of smell (anosmia) and/or taste (ageusia) (30%-60%) are the most common symptoms of the disease (15-18). Other signs and symptoms included: sputum production (28%-29.33%), fatigue (22%-44%), myalgia (11%-44%), headache (8%), haemoptysis (5%), diarrhea (2%-3%), poor appetite (12.0%), shortness of breath, rash, sore throat, face pain, nasal obstruction, throat congestion, tonsil swelling, enlargement of lymph nodes, vomiting, consciousness disorder, paresthesia, and stomachache (3, 18-24). Severe cases of COVID-19 may experience worsened symptoms, such as coagulation dysfunction, irreversible bleeding, ARDS, septic shock, and refractory metabolic acidosis (21).

Molecular Test

Nucleic acid testing is the primary method of diagnosing COVID-19. It is done by RT-PCR or determining the viral gene sequence in the sputum, throat swabs, feces, or blood samples (2, 6).

Respiratory tract sampling is the best way to perform the COVID-19 diagnosis test. Until recently, the specimens were taken mostly from the lower respiratory tract (3). But, sampling of the lower respiratory tract is more difficult and requires skilled medical staff. It can also cause airway damage and bleeding and is painful for the patients. Instead, collecting upper respiratory specimens included nasopharyngeal, oropharyngeal, and nasal swab specimens is safe, rapid, and straightforward (20). Therefore, several researchers investigated the bio-distribution of COVID-19 in different samples and different stages after illness onset.

In a study conducted by Wang et al , the bio-distribution of 2019-nCoV in different types of clinical specimens was investigated using real-time RT-PCR methods. Their findings showed that bronchoalveolar lavage fluid specimens (93%), sputum (72%), and nasal swabs (63%) had the highest positive rates, respectively; and fiber bronchoscope brush biopsy (46%), pharyngeal swabs (32%), feces (29%), and blood (1%) followed them. Moreover, none of the urine samples were positive (21).

Yang et al showed that in the first 14 days after onset of the disease the sputum (74.4%-88.9%) and nasal swabs (53.6%-73.3%) had the highest positive rate, respectively. Sputum and nasal swabs had a positive rate ranging from 42.9% to 61.1%, 15 days after disease onset. Moreover, the positive rate of throat swabs was low 8 days after disease onset (22).

Various studies have shown that the positive rate of RT-PCR for throat swab specimens was about 30-60%. It depends on the procedure of sample collection, transportation, specimens' source, sampling time (different period after disease onset), and the type of utilized kit (20-23).

Zhang et al evaluated the patients during the medical treatment period using molecular methods. Their finding indicated that 53.3% had positive oral swabs, 26.7% had positive anal swabs, 40% were blood positive, 20% were serum positive, and 2 patients had both anal and oral swabs positive on day 0 (25). On day 5, they found only 25% positive oral swabs. In contrast, 37.5% of anal swabs were positive. These findings suggested that at the beginning of the disease, the patient spreads the virus through the respiratory tract, and over time from the onset of the disease, the virus spreads more through the anal route (25, 26). Therefore, infected patients can potentially spread the virus through the respiratory tract, body fluid, and oral-fecal routes.

Serological Test

As mentioned, nasal and throat specimens are tested to identify people infected with COVID-19 using the RT-PCR method. In some cases, the RT-PCR method cannot detect the infection (false-negative result); therefore, additional tests can be used to detect COVID-19 infection in people with a negative RT-PCR result. These include evaluating clinical signs, imaging tests, and serological tests (2).

Numerous researchers have developed serological methods for measuring antibody titers in patients' serum. In a study, Zhou et al used SARSr-CoV Rp3 NP as antigen to develop an anti-SARS-CoV IgG and IgM ELISA kit (26).

In another study, Wang et al used a kind of nucleocapsid protein (NP) to developed IgM and IgG detection kit (27). These serological methods showed that the viral antibody titer increased over time from the onset of the disease (26).

For example, Zhang et al showed that the antibodies titer (IgM and IgG titer) was very low or even unmeasurable on the first day. In addition, an elevation of viral antibodies titer was seen in all patients on the fifth day. They suggested that both viral IgM and IgG serological test and the molecular test are needed to identify patients and carriers (25).

In general, the sensitivity of antibody tests in the first week after the onset of symptoms is very low and cannot play a major role in diagnosing COVID-19. It can also play a complementary role in other tests in people who show disease symptoms, though RT-PCR test is negative or not performed. If antibody tests are used on day 15 or later after the onset of symptoms, it can play an important role in diagnosing a previous SARS-CoV infection. However, the duration of antibody enhancement is currently unknown, and we found very little data for more than 35 days from the onset of symptoms (28).

Laboratory Profiles

Finding of complete blood counting (CBC) on admission demonstrated that 16-25% of patients had leucopenia (white blood cell < 4×10^9/L); and over half of the patients (53.33%-63%) showed lymphopenia (lymphocyte count below 1.0×10^9/L) (3, 6, 20). CD4+ lymphocyte count decreased significantly. Moreover, in some patients, the CD4+ lymphocyte /CD8+ lymphocyte ratio was lower than normal (19). Changes in hemoglobin and platelet counts have also been reported, which increased in some patients and were above the normal range, and reduced in some other patients (19). Coagulation impairments were observed in many patients, so that 58.67% of them had increased activated partial thromboplastin time and 40% had prolonged prothrombin time (19). Severe cases showed high D-dimer levels and prothrombin time (3, 7, 19). Furthermore, 20-43 % of patients developed liver dysfunctions, and the levels of alanine aminotransferase and aspartate aminotransferase were increased in their serum (7, 19, 20). These elevations were much higher in ICU patients (62%) than non-ICU patients (25%) (3, 19).

Some patients had an elevated rate of creatine kinase, hypersensitive troponin I (hs-cTnI), and lactate dehydrogenase (LDH). The procalcitonin level was normal in most of them (3, 4, 19, 20). Moreover, the elevation of the erythrocyte sedimentation rate and C-reactive protein (CRP) was reported (4, 6, 7, 19).

In the study of Zhao et al, patients with elevated interleukin 6 (IL-6) showed significant decreases in the LYM%, CD4+, and CD8+ T cell count (19). In addition, 7-20% of patients developed renal complications associated with elevated serum creatinine and blood urea nitrogen levels. These findings suggested that the internal organs could also be potential targets of COVID-19 (19, 20).

ICU-admitted patients had higher levels of white blood cells, especially neutrophils, as well as higher levels of D-dimer, creatine kinase, and creatine compared to non-ICU patients (18, 29).

Radiology finding

Due to the large number of patients referring to healthcare systems in countries involved in the recent pandemic of COVID-19, the use of non-invasive diagnostic tools, fast, available, and with acceptable safety along with RT-PCR is very important for better and faster management of patients. One of these diagnostic tools is the use of non-enhancing chest CT-scans (12). Various studies have shown that chest scans have higher sensitivity (86%-98%) for diagnosis of COVID-19 compared with initial RT-PCR (18, 28-33).

A study conducted by Ai et al identified that 75% of patients, who had a negative RT-PCR results, had symptoms of COVID-19 on the chest CT scan (12). Moreover, 60-93% of cases had COVID-19 symptoms on the chest CT scan prior to or paralleled to the initial positive RT-PCR results (12). Several studies also showed that almost all patients with COVID-19 had characteristic symptoms on the chest CT scan (5, 12, 34).

In a study conducted by Huang et al on 2019-nCoV infected patients, all patients had pneumonia with chest CT scan abnormalities (27). The hallmarks of COVID-19 infection on imaging were bilateral and peripheral ground-glass and consolidative pulmonary opacities (6, 18, 20, 27, 35). For instance, several prospective analyses revealed that 71%-98% of the patients had bilateral involvements (3, 8, 12, 20), 46%-85% had ground-glass opacities, and 19%-50% had consolidations (8, 9, 12, 20). Moreover, opacities with a rounded morphology (33%), reticulation (14%), peripheral location of the opacities (33%), consolidation with ground-glass opacities (29%), and crazy-paving pattern (19%) had been reported (8). In addition, it was found that as the disease progressed, the range of CT findings increased (9, 35).

The main features of chest CT scans of ICU patients on admission were subsegmental consolidation and bilateral multiple lobular areas. In contrast, non-ICU patients showed bilateral ground-glass opacity and subsegmental areas of consolidation. Subsequent chest CT scans showed bilateral ground-glass opacity, and the consolidation was resolved (3).

Cytokine

Measurement of cytokines in the acute phase of COVID-19 disease showed that plasma concentrations of TNFα, PDGF, MIP1B, MIP1A, MCP1, IP10, GCSF, GMCSF, IFNγ, IL10, IL9, IL8, IL7, IL1RA, IL1B, and VEGF were evaluated in these patients. Moreover, plasma

Table 1. Clinical Symtoms, Laboratory and Radiological Findings of Patients Infected With COVID-19 (2, 5, 6, 8, 18, 19, 22, 25, 27, 28, 30-33)

Disease Assessment Methods	Findings	
	Suggestive Findings	**Inconsistent Findings**
Radiological findings	- Ground glass opacities (Bilateral, Multifocal, Unilateral, Uniform) - Peripheral distribution or less likely peribronchovascular distribution - Multifocal/bilateral consolidation (predominantly in late stage) - Patterns of organizing pneumonia, reverse halo, linear opacities and crazy-paving (might show in late stage)	- Tree-in-bud opacities - Centrilobular nodules - Predominantly peribronchovascular distribution - Predominantly reticular opacities - Cavity - Lymphadenopathy - Pleural effusion
Molecular findings	RT-PCR positive result, viral gene sequencing	
Hematological findings	leukopenia, lymphopenia	Reduced CD4+/CD8+ ratio, coagulation disfunction
Biochemical findings		Increased ALT, AST, hs-cTnI, creatine kinase, LDH, CRP, ESR
Serological findings	Elevation of viral IgM and IgG antibody some days after disease onset	
Cytokine findings	Elevation of TNFα, PDGF, MIP1B, MIP1A, MCP1, IP10, basic FGF, IFNγ, GMCSF, GCSF, IL10, IL9, IL8, IL7, IL1RA, IL1B, and VEGF	Elevation of TNFα, MIP1A, MCP1, GCSF, IP10 IL7, IL10, and IL2
clinical findings	fever, dry cough, dyspnea, chest tightness, anosmia, ageusia	Sputum production, fatigue, myalgia, headache, haemoptysis, diarrhoea,poor appetite, rash, sore throat, shortness of breath, face pain, nasal obstruction, throat congestion, tonsil swelling, enlargement of lymph nodes, vomiting, consciousness disorder, paresthesia, stomach ache

concentrations of TNFα, MIP1A, MCP1, IP10, GCSF, IL7, IL10, and IL2 were higher in ICU patients than non-ICU cases (3, 27).

Patients infected with 2019-nCoV also had high amounts of IL1B, IFNγ, IP10, and MCP1. Additionally, ICU-admitted patients had higher concentrations of GCSF, IP10, MCP1, MIP1A, and TNFα, suggesting that the cytokine storm was associated with disease severity (3).

In some patients with elevated IL-6, LYM%, CD4+, and CD8+, T cell counts were significantly decreased, and NEU%, CRP, and LDH levels increased significantly. Elevated IL-6 may be an important factor leading to T lymphocyte damage and cellular immune deficiency. IL-6 could also be used as an indicator to evaluate infection severity (19).

Clinical symptoms, laboratory, and radiological findings of patients infected with COVID-19 are summarized in Table 1.

Conclusion

The reviewed studies showed that COVID-19 has a wide range of symptoms that occur in different people with different kinds of severity. The use of only one diagnostic method lacks sensitivity and accuracy and cannot diagnose COVID-19 with certainty, especially in the early stages of the disease. The main symptoms of the disease include respiratory symptoms, fever, cough, and dyspnea; moreover, there is a wide range of biochemical, hematological, and radiological changes in the patients. Finally, the signs (or symptoms) and other variables in the early stage or the mild stage of the disease appear in a highly heterogeneous and non-specific manner.

Conflict of Interest Disclosure
None to declare.

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Ethical Statement
Not applicable.

Authors' Contributions
JF, IA, PM, HF, EZ, LK, ZF, and AF: Substantial contributions to the conception and design of the work; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. JF, ZF, HH, and HF: Analysis, interpretation of data for the work, final approval of the version to be published. MGB, MRB, SBN, and HM: Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; final approval of the version to be published.

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Informed Consent
Informed Consent Not applicable because it was based on searching in databases

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