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A Clinical Score for the Diagnosis of COVID-19

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ABSTRACT

This article is an overview of the different tools that clinicians can use to arrive at a diagnosis of COVID-19 and is aimed particularly to practitioners in countries of scarce resources.

Keywords

COVID-19, Clinical score, Signs and symptoms, Laboratory studies, Radiological studies, Laboratory studies.

The COVID-19 pandemic has affected a great number of countries all over the world including rich and poor countries. In response to this, multiple diagnostic manufacturers developed and begun selling rapid and easy-to-use devices to facilitate testing outside of laboratory-settings. These simple tests kits are based on detection of proteins from the COVID-19 virus in respiratory samples or detection of human antibodies in blood or serum [1]. Initially, long nasopharyngeal swabs capable of collecting a sample far back in the throat were used but required medical trained professionals exposing them to get contaminated as it happened in Germany where six physicians died from a COVID-19 infection.

The RT-PCR (reverse transcription polymerase chain reaction) is the most commonly used test but this test produces false negatives (FN) results sometimes due to failure to have enough viruses in the sample or to improper storage. Besides this, the results cannot be obtained in a short period of time due to logistic problems since it may take several days, particularly in poor-resource countries. Several studies have reported a high number of false-negative results for this test. For instance a rapid coronavirus test used by the White House to screen its staff could miss infections up to 48% of the time, according to a study by researchers at N.Y.U Langone [2].

Antibody tests have a low positive predictive value (PPV) when the prevalence in the population with antibodies is low. Antibodies are produced over days to weeks after infection with the virus. Studies suggest that the majority of patients develop antibody response only in the second week after onset of symptoms. This means that a diagnosis of COVID-19 infection based on antibody response will often only be possible in the recovery phase. In addition, antibody detection tests targeting COVID-19 may also cross-react with other human coronaviruses and give false-positive results.

According to the CDC, serological tests should not be used to make decisions about groups of persons residing in congregate settings, such as schools, dormitories or correctional facilities. Across local populations, testing produces more accurate results if the disease to be tested for is common in the population. The higher the test sensitivity, the fewer false negative results a test will give. The higher the specificity, the fewer false positives a test will give.

In a study from Italy, a group of investigators found that due to the large demand for rRT-PCR tests some limitations have been observed in the diagnosis on a large scale of the diagnosis of COVID-19 such as the long turnaround times (on average over 2-3 hours) and the need of certified laboratories, expensive equipment and trained personnel. In addition, the rRT-PCR test includes analytical and para-analytical issues which may jeopardize the

diagnostic accuracy of the test. Thus, the urgent need for alternative tests to quickly identify infected COVID-19 patients in order to prevent virus transmission and guarantee a prompt treatment. This group analyzed the blood results of 207 patients who were admitted to the San Rafaele Hospital in Milan, Italy, and were tested for the rRT-PCR. Of them, 105 tested positive and 102 were negative. They analyzed the plasma levels of white blood cells (WBC), platelets, C-reactive protein (CRP)- aspartame aminotransferase (AST), alanine aminotransferase (ALT), glutamyl trans peptidase (GGT), alkaline phosphatase (ALP), and lactate dehydrogenase (LDH). They found that the tests with a significant p-value of <0.001 were the following: a low WBC, a low neutrophil and monocyte count, and a high LDH. They concluded that a simple blood test might be helpful in identifying false positive or negative rRT-PCR tests that can be used in developing countries suffering from shortage of reagents and specialized laboratories [3].

Clinical presentation of COVID-19

The common signs and symptoms of COVID-19 overlap with other respiratory diseases including seasonal flu. The CDC has identified the percent of signs and symptoms observed in patients with confirmed COVID-19. They are the following: fever (83-99%), cough (59-82%), fatigue (44-70%), loss of appetite (anorexia) (40-84%), shortness of breath (31-40%), sputum production (28-33), and muscle aches (myalgia) (11-35%).

Importantly, many people with current infection may remain asymptomatic or only with mild symptoms yet can transmit the disease. Testing of both asymptomatic patients as well as individuals with known or high exposure is urgently needed to reduce opportunities for transmission.

The most common coronavirus symptoms from 55.924 cases in China, to 22 February, were as follow: fever (87.9%), dry cough (67.2%), fatigue (38.1%), sputum production (33.4%), shortness of breath (18.6%), muscle/joint pain (14.8), sore throat (13.9%), headache (13.6%), and chills (11.4%).

However, different figures are reported by Medical News Today. The prevalence of symptoms of COVID-19 appears to be: fatigue (68.3%), smell and taste disturbances (64.4%), dry cough (60.4%, fever (55.5%), muscle pain 44.6%), headache (42.6%), shortness of breath (41.1%), and sore throat (31.2%) [4].

According to the European Centre for Disease Prevention and Control, the most common symptoms and signs are the following: headache 70%, nasal obstruction 67.8%, cough 63.2%, asthenia 63.3%, myalgia 62.3%, rhinorrhea 60.1%. gustatory dysfunction 54.2%, sore throat 52.9% and fever 45.4% [5].

In a study from the University of Leeds, researchers (from five universities including the University of Leeds in the UK) combined data from 148 separate studies to identify the common symptoms experienced by more than 24.000 patients from nine countries, including the UK, China and the US, and they found the following: fever 78%, cough 57%, fatigue 31%, loss of the ability to smell 25%, and difficulty to breath 23% [6].

As we can observe, from the figures cited above, there are some differences possibly due to ethnic and sociocultural characteristics of the populations involved. For instance, in a recent retrospective study on healthcare workers, a temperature of ≥ 37.5° was present in 85.0% of cases with a p-value of 0.002, followed by cough in 71% of cases with a p-value of 0.074, myalgia was present in 56.6% of cases with a p-value of 0.001, and anosmia/ageusia were present in 15.7% of cases but with a p-value of 0.001 which is considered statistically significant. Malaise was present in 56.6% of cases with a p-value of <0.055. In the same study they concluded that symptom and temperature reports are useful screening tools for predicting SARS-CoV-2 assay results in health care workers. Anosmia/ageusia and myalgia were the strongest independent predictors of positive assays, and that the absence of symptoms or symptoms limited to nasal congestion and sore throat were associated with negative assays [7]. In general, we can classify the most important signs and symptoms with prevalence above 55% and with a p-value near 0.001.

Regarding the loss of sense (anosmia) and taste (ageusia) that recently have emerged as important symptoms of COVID-19, British ear, nose and throat doctors, called on adults who lose their sense of smell to isolate themselves for seven days, even if they have no other symptoms, to slow the disease spread. These British physicians cited reports from other countries indicating that significant numbers of coronavirus patients experienced anosmia. For instance, in South Korea 30% of 2.000 patients experienced anosmia as the major presenting symptom.

In certain areas of Italy, doctors found that loss of taste and smell is indication that a person, who otherwise seems healthy, is in fact carrying the virus and may be spreading the disease to others. In Germany, at least two-thirds of more than 100 coronavirus patients experienced loss of smell and taste lasting several days. The American Academy of otolaryngology reported that reduced sense of smell and loss of taste are significant symptoms associated with coronavirus and these symptoms are present in patients who ultimately tested positive with no other symptoms [8].

In a study from Hong Kong, 27 patients with COVID-19 (45%) reported a taste dysfunction with 4 (6.67%) reporting ageusia and 23 (38.3%) reporting hypogeusia. Of these 27 patients, 22 (81.5%) reported 50% reduction of taste. In the same study, no ethnic differences in COVID-19 related smell and taste related dysfunction between Chinese and Caucasians was found. These symptoms were more specific for COVID-19 than fever, cough, and shortness of breath [9].

A growing number of case reports and series describe a wide array of neurological manifestations in patients with COVID-19 [10]. Early research from Wuhan, China, indicated that around 37% of those infected by COVID-19 displayed neurological symptoms. In

Brooklin, New York, loss of smell and taste are commonly reported in those with COVID-19. In addition, new onset of headaches, dizziness, weakness and unsteady gait, fatigue, muscle spasms, confusion and disorientation to time and place , altered level of consciousness, seizures, and stroke have been all observed [11].

Reports from China documented patients presenting with palpitations and chest pain without the typical fever and cough [12]. Accumulated evidence suggests that the cardiac involvement is common, particularly in a patient hospitalized with COVID-19 disease. Myocardial injury, evidenced by cardiac biological markers, such as elevated high sensitivity cardiac troponin I (hs-cTnl), was recognized among early cases in China [13].

In a systematic review and pooled analysis, Parasa et al. found that approximately 10 to 12 of patients with COVID-19 experienced GI symptoms, such as diarrhea (7.4%) and nausea and vomiting (4.6%). In addition, 30% to 50% of patients may have fecal swabs that test positive for the SARSCo2RNA confirming that the virus can be detected in other sites and therefore potentially transmitted in ways other than by respiratory droplets [14].

In a study from China, 25% of patients with COVID-19 experimented digestive symptoms such as pharyngalgia (sic), diarrhea, nausea, vomiting and abdominal pain which is lower than the percentage reported by other investigators [15].

Radiological studies

Chest CT scan

Definitive diagnosis of coronavirus of Covid-19 requires a positive RT-PCR test or a chest CT scan. However, current best practice advices that a chest CT scan is not used to diagnose COVID-19 but may be helpful in assessing for complications. The non-specific imaging findings are most commonly of atypical or organizing pneumonia often with a bilateral, peripheral and basal predominant distribution. The use of CT as a primary screening tool is discouraged because, according to a recent meta-analysis, the pooled sensitivity was good (94%) but the specificity was poor (37%) [16].

In a recent study, the Fleischer Institute Society recommended that imaging is not indicated in patients with suspected COVID-19 and mild clinical features unless they are at risk for disease progression such as worsening of respiratory status. In a resource-constrained environment, imaging is indicated for medical triage of patients with suspected COVID-19 who present with moderate-severe clinical features and a high pretest probability of disease. The primary findings of CT in adults are the following: ground-glass (GGO), crazy paving appearance and septal thickening, air space consolidation, bronco vascular thickening in the lesion, and traction bronchiectasis. The ground-glass opacities and consolidated opacities are usually bilateral, peripheral and basal in distribution. The chest CT findings that have the highest discriminatory value ($p<0.001$) are: peripheral distribution, ground-glass opacity, and bronchovascular thickening in the lesions [16].

Chest radiography

According to Radiopedia Organization, chest radiography is typically the first-line imaging modality used for patients with suspected COVID-19. For ease of decontamination, use of portable radiography units is preferred. Chest radiographs may be normal in early or mild disease. Of patients with COVID-19 requiring hospitalization, 69% had abnormal chest radiography at the initial time of admission, and 80% had radiographic abnormalities sometime during hospitalization. Findings are more extensive about 10-12 days after symptom onset.

The most frequent findings are airspace opacities, whether described as consolidation or, less commonly, ground-glass opacities (GGO). The distribution is most often bilateral, peripheral, and lower zone predominant.

COVID-19 score

Based on the above-mentioned information, I decided to construct a clinical score for the diagnosis of COVID-19 that could be helpful to decide which patients should be observed and which should be tested. Those with a low score can be observed at home because chances are that they may have a different disease. Those with a high score should be tested and possibly sent to the hospital for further evaluation.

The main advantage of the score is that it can be done in different settings around the world without straining the economic and technical resources of the health facilities particularly in countries of the third world. This score uses common clinical signs and symptoms and common laboratory tests that have a good statistical significance ($p<0.001$). The same way, the score uses the chest X-ray that is available in many hospitals of scarce resources.

In this score, fever which is the most common reported symptom, is defined as >37.5°C (p-value 0.001). The cluster of respiratory symptoms includes dyspnea or shortness of breath that could be interpreted in different ways so I decided to represent it in a more objective form by using the oxygen saturation (<92%), when possible. (Now these days, pulse oximetry is available in different settings and can be used for monitoring purposes at home). The cluster of musculoskeletal symptoms includes myalgia (p-value <0.001), fatigue, asthenia, and malaise.

This clinical score could also be helpful to facilitate the issue of death certficates in countries in the middle of catastrophic conditions such as it happened in some European and South American countries.

I should mention that the in the construction of this score, the clinical signs and symptoms of COVID-19 have been subjected to several changes and adjustments due to its protean manifestations that involve different organs. Therefore it is possible that more changes may be needed in the near future.

Clinical Score for the Diagnosis of COVID-19 (TOCSMANAGLLI)	Points	p-value
Temperature (>37.5°C) (Fever and/or chills)	2	<0.002
Oximetry (<92%) and/or dyspnea	2	<0.001
Cough and/or sore throat	1	<0.074
Stuffy and/or runny nose, sneezing	1	<0.001
Myalgia and/or fatigue, asthenia, malaise	1	<0.001
Anosmia and/or Ageusia	1	<0.001
Neurological: headache and/or brain fog, dizziness	1	?
Arrhythmia and/or palpitations, chest pain. myocardial damage	1	?
GI symptoms: anorexia and/or nausea, vomiting, diarrhea	1	?
Laboratory studies		
Lymphopenia and/or monocytopenia, neutropenia	1	<0.001
LDH and/or CRP increase, D-dimer and troponin elevated	1	<0.001
Imaging		
Imaging (chest X-ray and/or chest CT)	1	<0.001
Total	14	
*mnemonics to facilitate memorization of the score		

Interpretation of the Covid-19 score

A score of 1-4 indicates a low probability of the disease. A score of 5-6 indicates a possible presence of the disease. A score of 7-11 indicates a probable presence of the disease, and a score of 12-14 indicates a high probability of the disease.

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