

## Clinical and Diagnostic Criteria of COVID 19; a Study of 4659 Patients Evaluating Diagnostic Testing and Establishing an Algorithm

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**Received:** April 02, 2020; **Published:** April 10, 2020

### Abstract

**Background:** COVID 19 is a pandemic that has crippled the world. The disease process started in the Hubei province of China, but has been successfully confirmed in over 170 countries at the time of this article. There does not exist a treatment for this disease. The hallmark of therapy has been early detection, immediate isolation and supportive care. The crux of this management regimen is the early diagnosis of patients. Given the novel nature of this disease, there have been multiple reports attempting to address early diagnosis, however there has yet to be a consensus.

**Purpose:** The purpose of our study was to review and compile the literature to achieve a large sample size and propose a diagnostic algorithm.

**Methods:** We reviewed PubMed and Google Scholar and evaluated over 100 articles. 22 articles were chosen, where the diagnosis and diagnostic tests with results were stratified and studied.

**Results:** There were 4659 patients identified in our data. Clinical symptoms in order of most importance were fever, cough and fatigue. Laboratory data on COVID 19 positive patients included lymphopenia, elevated CRP and elevated ESR. The gold standard in the literature is the RT-PCR, however the accuracy of this test is approximately 60%. CT Chest was sensitive and specific greater than 90% of the time, in particular when coupled with the clinical symptoms.

**Discussion:** Given the high false negative rate of RT-PCR, and the time component involved in obtaining the results, we proposed an alternative diagnosis pathway. Patients presenting with two of the following clinical symptoms: fever, cough, fatigue, should undergo an immediate CT scan of the chest. Should the classic findings of COVID 19 be appreciated, an immediate working diagnosis of COVID 19 must be entertained. A negative CT chest does not exclude COVID 19, but entails a repeat CT Chest to be performed 48 hours later. The disease has a propensity to peak in symptoms, laboratory findings and imaging close to day 10 of presentation. Until a therapeutic regimen or vaccine is discovered, early diagnosis and isolation remain the mainstay of therapy.

**Citation:** Ali Mahmood, Charisma Gajula and Prianka Gajula. (2020). "Clinical and Diagnostic Criteria of COVID 19; a Study of 4659 Patients Evaluating Diagnostic Testing and Establishing an Algorithm". *Journal of Medicine and Surgical Sciences* 2.1.

DOI: 10.5281/zenodo.3755546

## Background

COVID 19, caused by SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), is pandemic that started in the Hubei region of China. The disease has been documented in 785,709 patient's worldwide, accounting for 37,686 deaths, with an incredible 2202 occurring just today. [1] The origin of the virus was a fish market in Wuhan, China, and while that index epicenter has been deemed disease free, the remainder of the world continues to report increasing and a staggering number of cases. Italy and Spain remain in critical quarantine, with mortality reported as high as 40-50%. [2] The number of cases in the United States, at the time of this research, had climbed to 139,675, with 2457 deaths, as per the data at Johns Hopkins University Coronavirus Resource Center. [2]

COVID 19 was first reported in the winter of 2019. There is very little consensus data and/or information regarding its exact etiology, epidemiology, diagnostic testing and treatment regimens. Much of the literature stems from small case volumes, thus contributing to a wide variety of opinions regarding presenting symptoms, diagnostic testing and pertinent findings. Without an accurate diagnosis, treatment can often be delayed, or wrongfully initiated, leading to catastrophic complications, morbidity and/or death. Lack of containment and quarantine of positive COVID 19 cases can lead to subsequent spread to immune deficient patients and lead to unnecessary mortality.

The purpose of our study was to review the literature and combine a multitude of quality studies to create a firm foundation for the treating clinicians. We wanted to provide a framework of clinical symptoms to recognize, tests to order and most important, provide an algorithm of results for clinicians to reference for accurate diagnosis, isolation and treatment purposes.

## Methods and Results

We reviewed 22 studies, published over a 3 month period. There were 4659 COVID 19 cases reviewed. [3-22] The number of diagnostic tests was far greater, due to many patients undergoing serial CT scans and laboratory tests to study the extent and chronological progression of the disease process. The majority of the literature was representative of the cases from the Hubei region in China, however there was a study from South Korea.

## Clinical Features

COVID 19 exhibited an equal affinity for male and female patients. Some studies reported the male to female distribution to be 52/48

respectively, while other studies documented 43/57, but overall the consensus arrived from the summation of the studies was 50/50. [6,7] The mean age varied, with the two widest ranges reported in the literature between ages 26-83 to 21-90 years. [8,20] Interestingly, the majority of the mean ages were less than 50, contradicting the thought process that this was a disease impacting the elderly only. Fever and cough were the two most common clinical symptoms appreciated. Fatigue followed afterwards, with some reports mentioning patients who had presented with diarrhea. [13].

## Diagnostic Studies

COVID 19 patients underwent a battery of laboratory tests. Pertinent findings included findings of lymphopenia, elevated ESR (erythrocyte sedimentation rate) and elevated CRP (C-reactive protein). [13] The real time reverse transcription polymerase chain reaction (RT-PCR) had been heralded as the confirmatory test, however after compilation of data, this test was reported to be only 60% confirmatory in multiple reports. [5,20,22] CT scans were undertaken, and often repeated, in the majority of patients who presented with a suspicion of COVID 19. Key findings described on CT included ground glass opacities, consolidation, lineal opacities, paving pattern, and bronchial wall thickening. [15,16] Ground glass opacities were described in upwards of 80% of patients with COVID 19, with some multiple larger studies reporting a higher 97% present. [7,14, 21,22] The peripheral and posterior distribution of ground glass opacities was the most common finding. These were most prevalent on the 10th day following the diagnosis being made. The ground glass opacities were found to be bilateral with a predilection for the lower lobes. [12] In many studies, patients that were found to be COVID 19 positive had radiological findings confirm the diagnosis before the RT-PCR turned positive. Pneumothorax was appreciated in patients with aggressive disease or severe disease states. [4]

## Discussion

COVID 19 is a new disease entity that has caused a pandemic. While much of the literature published has attempted to help the medical community at large, there exist varying opinions, recommendations and findings. The purpose of our study was to review the prevailing literature and present a large case series with pertinent findings and results that would primarily aid the clinician in suspecting, establishing and confirming a diagnosis. Our number of patients evaluated, 4659 is the largest number in the literature, at this point. We recommend that any patient presenting with two

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of the following symptoms of fever, cough and/or fatigue undergo a CT scan of the chest. The RT-PCR should be done if available, however the sensitivity of the CT findings is significantly more sensitive when coupled with the clinical findings, with a misdiagnosis as low as 3.9%. [8] A CT scan with COVID 19 findings, along with the clinical symptoms warrants immediate isolation of the patient and notification of the contacts. We further advocate that a high clinical suspicion warrants a repeat CT scan in 48 hours because the disease progression will eventually show ground glass opacities greater than 85% after day 10 of diagnosis. [8-10] it has been well established that the disease has a significant increased mortality for patients with co-morbidities and therefore until a cure of vaccine is developed, isolation with symptomatic treatment are mandatory to prevent further spread and contamination. Lopinavir and ritonavir along with interferon and Chinese medicine have been used with limited success and virtually no reproducibility.

The authors recognize that a significant portion of this manuscript pertains to diagnostic imaging. This is not a bias towards radiology, rather a recognition that imaging provides the best media for an accurate diagnosis. This is the largest study to date in the literature and while there is not a pathognomonic test, CT Chest imaging coupled with clinical symptoms has provided the best diagnostic yield by far, trumping RT-PCR, even to our surprise.

## Conclusion

Patients that present with 2 of the following: fever, cough, fatigue, need to undergo a CT scan of the chest. A CT scan with ground glass opacities is enough to establish a working diagnosis of COVID 19. Negative CT imaging does not rule out COVID 19 in the midst of clinical symptoms and suspicions, but warrants a repeat CT scan in 48 hours. While this may seem aggressive, until there is a cure for this disease entity, the danger of disease progression, or worse, diffuse community spread, mandate repeat and significant testing. Obtaining blood for lymphocyte counts, ESR, CRP and performing RT-PCR are helpful, if available, but based on the large data reviewed, the greatest efficacy arises from the clinical evaluation of the patient coupled with diagnostic imaging.

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