

Laboratory and demographic findings among patients with coronavirus disease 2019: a review

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Abstract

Coronavirus disease 2019 (COVID-19) is the third known animal coronavirus, after severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome coronavirus (MERS-CoV). The mean age of the infected patients was estimated to be between 50 and 69 years old. Accordingly, the COVID-19 mortality rate was calculated as 15%. In this regard, the essential component of prevention and planning is knowledge of laboratory and demographic findings among COVID-19 patients; therefore, the present study was conducted to investigate laboratory and demographic

findings among these patients worldwide. This systematic review was performed on the articles published in English between January 1, 2019 and May 4, 2020, using MeSH-compliant keywords such as “COVID-19”, “Laboratory, coronavirus disease-19 testing”, and “demography” in international databases (PubMed, and web of science Scopus). Thereafter, the articles relevant to laboratory and demographic findings among COVID-19 patients were included in the final review. Reviewing the included articles showed changes in the mean lymphocytes count ranged from 0.7 to 39 in hospital or severe cases. Moreover, Leukopenia was not observed in patients with thrombocytopenia. In addition, C-reactive protein (CRP), leukocytes, D-dimer, fibrin degradation products (FDP), fibrinogen (FIB), neutrophils, aspartate aminotransferase (AST), serum creatinine, t-troponin, troponin I, and blood bilirubin levels showed increasing trends in most studies conducted on COVID-19 patients. Notably, the elevated lactate dehydrogenase (LDH) level was more common among children than adults. According to the results of the present study, and by considering the clinical characteristics of COVID-19 patients on the one hand, and considering the changes in laboratory samples such as lymphocytes and other blood markers due to the damaged myocardial, hepatic, and renal tissues on the other hand, it is recommended to confirm the diagnosis of this infection by evaluating the patients’ blood samples using other diagnostic methods like lung scan.

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Introduction

On December 31, 2019, China notified the World Health Organization (WHO) of a pneumonia of unknown etiology in Wuhan city, China. Afterward, Chinese government reported 440 cases of pneumonia of unknown etiology to WHO from December 31, 2019 to January 3, 2020. Subsequently, WHO received more information from the Chinese National Health Commission about the outbreak that was found to be associated with the exposure to a seafood market in Wuhan city. Correspondingly, Chinese authorities have identified it as a novel strain of coronavirus [1]. Initially, it was stated that the mortality rate of this novel coronavirus (2019-nCoV) was 15%. According to the results of the subsequent studies, this rate was lower than reported and between 4.3 and 11% [2, 3]. On March 11, 2020, WHO declared this disease a pandemic [4].

The coronaviruses' family can genotypically and serologically be divided into four genera of viruses: alpha, beta, delta, and gamma. The novel coronavirus (2019-nCoV) belongs to the beta-coronavirus category. Furthermore, it is the third known animal coronavirus disease, after SARS and MERS, both of which belong to the beta-coronavirus category [5]. The incubation period of this disease is 14 days, but is usually between 3 and 7 days [6]. Most of the patients with COVID-19 experience mild to moderate symptoms. Notably, it was shown that older people and those with some diseases such as cardiovascular disease, cerebrovascular disease, diabetes, chronic respiratory disease, and cancer are more likely to experience severe symptoms of the disease. Women also are less susceptible to the disease than men. Currently, there is vaccine not available to everyone or no treatment for COVID-19 [2,6,7]. The mean age of the infected patients was between 50 and 69 years old in a Chinese case-series [8]. The disease has also been reported among infants and children, and the latter tend to have milder symptoms compared to adults [9-11]. People's practice regarding home quarantine to prevent COVID-19 depends on a number of factors. Paying attention to the gender, attitude and occupation of individuals in policy making regarding home quarantine can improve the performance of the public [12]. Laboratory symptoms are as follows: COVID-19-positive throat, sputum, lower respiratory tract secretion, stool, and blood swab samples for nucleic acid [13]. Additionally, other laboratory symptoms include the elevated erythrocyte sedimentation rate (ESR) by 85%, C-reactive protein (CRP) by 63%, the decreased albumin by 98%, the elevated serum ferritin, the elevated liver function tests, and the elevated lactate dehydrogenase (LDH), the elevated D-Dimer, the elevated blood neutrophils, the elevated interleukin 6, and the elevated troponin, the decreased blood lymphocytes, the decreased or elevated leukocytes, the decreased or elevated platelets, the impaired coagulation tests, and the decreased hemoglobin [2,14]. Laboratory results vary according to patients' age and disease's severity. It is noteworthy that blood tests are usually normal in children, with transiently high or normal CRP and white blood-cell count (WBC) [10,15].

Considering the increasing incidence of this disease, and since most of the previous studies have been conducted in a specific area with a limited sample size, the essential component of prevention and planning is knowledge of laboratory and demographic findings among COVID-19 patients. Therefore, the present study was conducted to investigate laboratory and demographic findings among the patients with COVID-19 worldwide.

Materials and Methods

Eligibility criteria

The present narrative review study was performed on full-text original English articles published in foreign journals from January 1, 2019 to May 4, 2020.

Information sources

Articles were selected from databases (PubMed, Web of Science and Scopus).

Search

Study selection

Those articles related to laboratory and demographic findings among COVID-19 patients were reviewed. The results of these

studies are presented in the tables. It should be noted that we excluded unrelated studies.

Data collection process

Summary and full text of the included articles were reviewed by two relevant researchers independently. Moreover, the checklist information including author's name, year of publication, place of study, sample size, demographic characteristics (age and sex), and laboratory findings were recorded.

Data items

Articles were selected from international databases using all MeSH-compliant keywords including "COVID-19", "Laboratory, Coronavirus disease-19 testing", and "Demography".

Summary measures

The articles conducted on demographic characteristics and laboratory findings from January 1, 2019 to May 4, 2020, were selected and the results were presented in tabular form.

Synthesis of results

A total of 2675 articles were initially reviewed. It should be noted that 675 articles were duplicates, 800 articles were fully read, and 740 articles were irrelevant, so 60 articles were finally included in the study (Figure 1).

Results

SARS-CoV-2 is an emerging pathogen that caused a high incidence of pneumonia in the infected individual [16]. Understanding the clinical and laboratory characteristics of patients will be helpful in diagnosis and treatment of this disease.

Lymphocytes and cytokines

In this study, the mean lymphocyte counts in hospital or in more severe cases ranged from 0.7 to 39 (Table 1). Changes in lymphocyte count may be related either to the severity or to the prognosis of COVID-19 [17]. Lymphocytopenia commonly occurs in patients with SARS-CoV-2 [18]. In addition, T lymphocytes act as antivirus and balance immune responses. CD8 β T cells play a vital role in SARS-CoV virus killing in the patients' lungs [19,20]. IL-6 is also known as a key cytokine that plays an important role in host defense by stimulating the immune response, bleeding, and immune responses. It should be noted that IL-6 levels dramatically increase during infection [21,22]. The results of studies conducted on SARS-CoV indicated that the reduction of CD4 β T cells plays a role in reducing lymphocyte uptake and cytokine production, which also has a negative effect on improving SARS-CoV symptoms [23]. Cytokines play important roles in viral infections. In fact, cytokine level significantly increases in patients with more severe disease [24].

White blood-cell count, D-dimer, fibrin degradation products, fibrinogen, and C-reactive protein

In the present study, except in patients with thrombocytopenia, leukopenia (white blood cell (WBC) count $<4 \times 10^9 / L$) was not observed in the patients (Table 1). In other studies, it was found that the elevated WBC count occurs more in children than in adults, which indicates leukopenia in most cases, while lymphocyte count decreases in adults [25]. The results show that D-dimer,

FDP, and FIB have increased in COVID-19 patients in most studies, which is somewhat consistent with the results of the other relevant studies [26,27]. The CRP level has also increased in most studies. It was shown that the elevated CRP levels also occur more frequently than alanine aminotransferase (ALT), AST, creatine kinase, and D-dimer (Table 1), which is consistent with the findings of the other studies conducted on patients with MERS-CoV and SARS-CoV [28-30].

Serum creatinine, troponin T, troponin I, blood bilirubin, lactate dehydrogenase leukocytes, and neutrophils

In the present study, the findings demonstrated an increase in AST, serum creatinine, troponin T, troponin I, and blood bilirubin, which indicate damages to myocardial, liver, and kidney of the COVID-19 patients. Accordingly, elevated AST, ALT, and γ -GT levels among COVID-19 patients are often associated with liver damage [31]. Moreover, the decreased lymphocytes and the elevated CRP, IL-6, ESR, and d-dimer can be associated with liver, kidney, and myocardial damages as well [32]. The elevated blood urea and creatinine levels have been reported in the blood of patients before death [17]. In a study by Du *et al.*, it was found that more than half of COVID-19 patients experience impaired renal function [33], due to the elevated blood urea and creatinine levels. The increased LDH could also indicate the fact that SARS-CoV-2 infection is associated with cardiopulmonary tissue damage among children. Consistently with the other studies, the results of the present study show the elevated LDH in children compared to adults. The elevated LDH and blood sugar levels are two important factors in the diagnosis of COVID-19 patients [34]. On the other hand, reduc-

tion of CD8 T cells and loss of eosinophils due to SARS-CoV-2 are effective on causing eosinopenia and eventual death resulted from chronic respiratory diseases, because IL-5 produced by CD8 T cells helps in proliferating and activating eosinophils [35,36]. The results of the present study show an increase in leukocyte and neutrophil levels. The increased neutrophil counts were also observed in severe pneumonia caused by COVID-19 [37]. In fact, it can be said that laboratory changes in patients indicate the progression of the disease. Therefore, it is very important to perform the relevant tests on COVID-19 patients.

Discussion

Blood biochemical indicators such as C-reactive protein, lymphocytes, AST, ALT neutrophils, FDP and FIB, D-dimer, LDH, C-reactive protein are the best predictors of disease progression in patients with Covid-19 [38]. Coagulation is a physiological response to infections [30,39-41]. In patients, coagulation increases excessively due to increased levels of D-dimer, FDP, and FIB [42].

In addition, studies showed that the coronavirus can induce the body to produce oxidative stress and release a large amount of active oxygen free radicals, which can, on one hand, make the virus replicate unceasingly, but, on the other hand, the excessive free radicals can damage the body's biological membrane lipid peroxidation, enzyme, amino acid, and oxidative protein, leading to injury to the organs, such as the lung, heart, liver, kidney [43].

One of the limitations of the present study is the lack of sys-

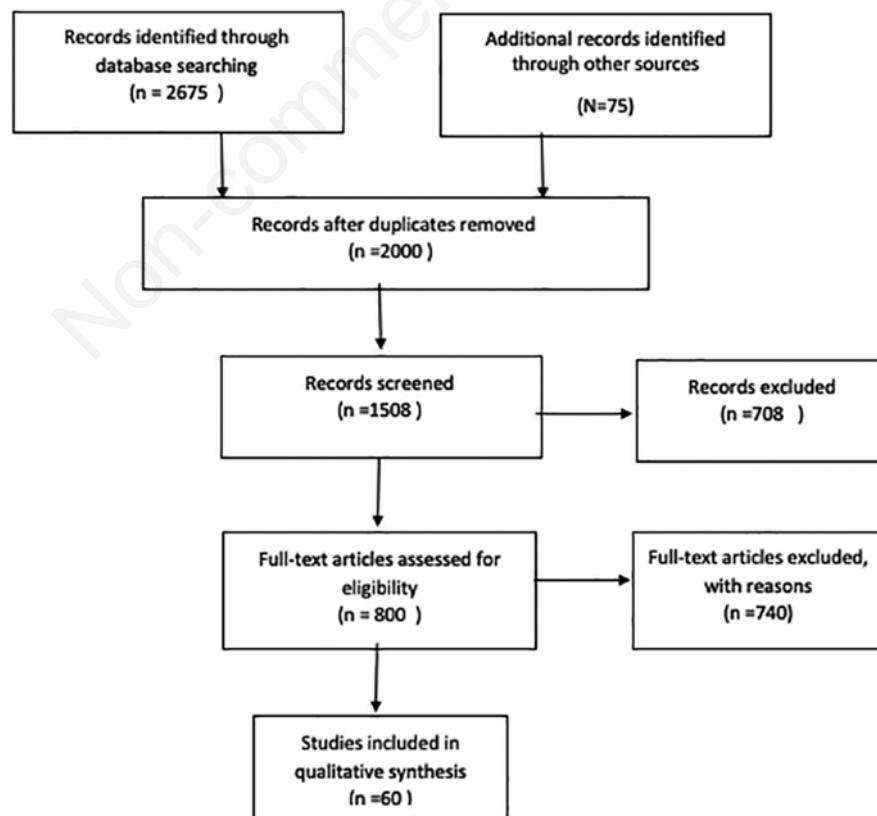


Figure 1. Flowchart of articles included in this review.

tematic reviews of articles that have simultaneously reported lung scan information of patients in order to provide more comprehensive information to researchers.

Conclusions

According to the results of the present study, considering the clinical characteristics of COVID-19 patients on the one hand, and changes in laboratory samples such as lymphocytes and other blood markers due to damages to myocardial, hepatic, and renal tissues on the other hand, it is recommended to confirm the diagnosis of this infection by evaluating the patients' blood samples using other diagnostic methods like lung scan.

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