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Research Article

# Prognostic and Diagnostic Importance of IgG and IgM Antibodies in COVID-19

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## Abstract

COVID-19 infection is a novel disease caused by SARS-CoV-2. It emerged in December 2019 in China and spread rapidly causing a worldwide pandemic. Extensive research is underway globally to obtain more information regarding the pathogenesis, diagnosis and treatment of the novel disease. The diagnosis of COVID-19 infection is done by detection of SARS-CoV-2 viral RNA by polymerase chain reaction (PCR) technique or nucleic acid hybridization-related strategies and by detection of antibodies by serological and immunological assays. Reverse transcription polymerase chain reaction (RT PCR) and rapid antigen tests from a throat swab or nasopharyngeal swab are the most common modalities for the diagnosis of COVID-19 infection. Immunological testing involving estimation of IgG and IgM antibodies is gaining importance for the diagnosis of the disease. The aim of the present study is to evaluate the levels of immunoglobulins (IgM and IgG) in symptomatic and asymptomatic patients for the diagnosis and prognosis of COVID-19 infection.

***Keywords:*** *Corona Virus 19 (COVID19); Immunoglobulin G (IgG); Immunoglobulin M (IgM); Prognostic and Diagnostic*

## Introduction

In December 2019, a novel coronavirus disease known as COVID-19, caused by SARS-CoV-2, emerged in China and rapidly spread worldwide. The World Health Organisation (WHO) declared COVID-19 as a pandemic disease. The mode of transmission of the disease is through airborne droplets. The disease spreads from human to human via the release of the virus in microdroplets during exhalation, talking, sneezing or coughing and also by contact with contaminated surfaces. Therefore, hand hygiene is crucial to prevent disease transmission. The common presentation of the disease is fever, sore throat, fatigue, cough or dyspnea. Some patients may progress to develop severe illness such as pneumonia and acute respiratory distress syndrome. The onset of symptoms takes around 2-14 days after exposure to the disease [1,2]. Though most of the patients recover with symptomatic treatment, it is still a threat to society.

The diagnosis of corona virus is widely done using reverse transcription polymerase chain reaction (RT PCR) and rapid antigen tests from a throat swab or nasopharyngeal swab. In some cases, it is also diagnosed on the basis of the clinical features, risk factors and a chest computerized tomography (CT) scan revealing lesions of pneumonia [3]. However, in addition to these diagnostic methods, there are other parameters for diagnosis such as Immunoglobulin G (IgG), immunoglobulin M (IgM), D-Dimer, Ferritin and C-reactive protein. The current study focusses on evaluation of levels of immunoglobulins i.e., IgG and IgM in infected cases (both symptomatic and asymptomatic) and also in people tested negative for corona virus. IgG and IgM are established for monitoring humoral immune responses to infections by viruses such as SARS-CoV-2 [4-10]. Better understanding of IgG and IgM antibodies in asymptomatic and symptomatic patients will assist early diagnosis and effective prevention against SARS-CoV-2 [11].

## Materials and Methods

### Study design and setting

Current study was undertaken in Benghazi, a city in the east of Libya. Samples were collected from patients attending Al Akeed laboratory, Benghazi, Libya. The collected samples were prospectively analyzed at the biochemistry laboratory. Measurement of IgG and IgM levels was done in samples of the patients.

### Subjects

The total number of patients taken for this study was 80, out of which 48 were positives cases and 31 were controls that tested negative, out of the 48 positive cases, 15 were asymptomatic and 33 were symptomatic. Amongst the 80 cases included in this study, 42 were females and 38 were males.

### Biochemical assessment

Venous blood samples were drawn from all the 80 patients. The blood was collected in plain tubes. The serum was separated and stored at 20°C until the assays were performed. IgG and IgM levels were measured in all patient samples using fully automated Mindray - CL-900i Chemiluminescence Immunoassay System.

## Results

The mean, standard deviation and median levels of IgG and IgM values of the total number of cases are shown in table 1. There is a significant increase of IgG concentration in cases when compared to controls ($p = 0.0001$). Also, there is a significant rise of IgM concentration in cases when compared to controls ($p = 0.0001$). The mean, standard deviation and median levels of IgG and IgM values of asymptomatic cases are shown in table 2. There is significant rise of IgG concentration in asymptomatic cases when compared with

controls (p+0.0001) and a significant rise of IgM concentration (p = 0.0059). The mean, standard deviation and median levels of IgG and IgM levels of symptomatic cases are shown in table 3. There is a significant rise of IgG in symptomatic cases when compared with controls (p = 0.0001) whereas IgM concentration is raised but not significant (p = 0.1079). We have observed significant difference of IgG among symptomatic and asymptomatic cases (p = 0.0001) but not IgM (p = 0.441). The mean, standard deviation and median levels of IgG and IgM levels of controls are shown in table 4.

| | IgG | IgM |
|---|---|---|
| Mean | 134.8956 | 2.655 |
| STD | 101.2434 | 2.557406 |
| Median | 123.895 | 1.975 |
| Number | 48 | 48 |
| p-Value | 0.0001 | 0.0001 |

***Table 1:*** *Mean, standard deviation and median of IgG and IgM levels of total cases.*

| | IgG | IgM |
|---|---|---|
| Mean | 38.93667 | 3.761333 |
| STD | 27.72358 | 6.84764 |
| Median | 28.52 | 1.22 |
| Number | 15 | 15 |
| p-Value | 0.0001 | 0.0059 |

***Table 2:*** *Mean, standard deviation and median of IgG and IgM in asymptomatic cases.*

| | IgG | IgM |
|---|---|---|
| Mean | 207.2942 | 11.71242 |
| STD | 137.1822 | 39.97337 |
| Median | 188.8 | 3 |
| Number | 33 | 33 |
| p-Value | 0.0001 | 0.1079 |
| p-Value | 0.0001 | 0.441 |

***Table 3:*** *Mean, standard deviation and median of IgG and IgM in symptomatic cases.*

| | IgG | IgM |
|---|---|---|
| Mean | 0.61 | 0.269677 |
| STD | 0.699643 | 0.203461 |
| Median | 0.4 | 0.23 |
| Number | 31 | 31 |

***Table 4:*** *Mean, standard deviation and median of IgG and IgM in controls.*

## Discussion

The manifestation of COVID-19 infection ranges from asymptomatic carriers, mild symptoms such as cough, fever and fatigue to severe illness such as pneumonia or acute respiratory distress syndrome. The transmission of the infection is via airborne droplets during close contact. Not only the symptomatic patients but also the asymptomatic carriers can transmit the disease. It has been suggested that asymptomatic carriers are important sources of infection [12]. Therefore, early diagnosis of the disease is crucial to prevent spread of the disease. Researchers worldwide are constantly working to develop rapid and accurate testing methods. Since COVID-19 manifests in several different ways, it is important to diagnose the positive cases in the early stages of the disease to prevent spread of the virus and also to prevent unnecessary quarantining of negative cases. In addition, early diagnosis will enable better management of patients with co-morbidities with a high risk of complications. Currently, the testing for COVID-19 infection is done in two ways: the first is by detection of SARS-CoV-2 viral RNA by polymerase chain reaction (PCR) technique or nucleic acid hybridization-related strategies and the second is by detection of antibodies by serological and immunological assays. RT-PCR is the most widely used testing procedure to detect the presence of viral RNA. Several other nucleic acid assays such as isothermal amplification assays, hybridization microarray assays, amplicon-based metagenomics sequencing, Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) based technologies are also under investigation or are approved to be used for testing purposes in some places. Though RT-PCR is widely used for the diagnosis of the disease, its limitation is that it cannot be used for prognosis of the disease or to evaluate past infection or immunity [13]. Also, false negative reports with RT-PCR are seen in 20 - 67% of the patients. Factors resulting in false negative reports include technique of specimen collection, source of specimen, and time of collection of specimen following exposure to the virus. A study reported that the sensitivity of RT-PCR 4 days after exposure is 33%, at the onset of symptoms it is 62% and 3 days after the appearance of the symptoms it is 80% [12].

Alternative methods such as serological testing for IgG and IgM antibodies for COVID-19 are being increasingly used for diagnosis. These antibodies are detectable after 4 - 5 days of infection. Approximately 70% of symptomatic patients show positive IgM antibodies by 8 - 14 days and 90% of patients show positive results by 11 - 24 days. More than 98% of patients show positive IgG antibodies after several weeks [14]. IgM is an indicator of early stages of the disease and IgG indicates current or past infection. In the current study, there was a significant increase in IgG levels in symptomatic cases as compared to control. In asymptomatic cases, there was a significant increase in IgG as well as IgM levels. It has also been reported that a higher antibody titre implicates poor prognosis, since patients with worse clinical presentation have higher antibody response and higher levels of inflammatory markers [15]. Serological testing is advantageous because it detects IgG and IgM antibodies uniformly and is not dependent on sample collection factors and thereby there are lesser false negative reports as seen with RT-PCR. In addition, serological tests are easy to perform, rapid, samples are easy to obtain and pose lesser risk to the operator. Therefore, they can be used for diagnostic purposes [16]. The demand for diagnosis of symptomatic and asymptomatic individuals infected with COVID-19 with the use of immunological testing of IgG and IgM antibodies is increasing. The results of the present study indicate that IgG and IgM antibodies can be used not only for diagnosis of COVID-19, but also its prognosis.

## Conclusion

Research is underway to develop robust, serological assays for the diagnosis of COVID-19. Detection of IgG and IgM antibodies can prove to be useful in diagnosis of asymptomatic individuals also. They can be used for seroepidemiological purposes to determine the extent of the disease. They are also useful for determining prognosis of the disease. Thus, serological testing can assist the healthcare workers for containing the spread COVID-19.

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