BRIEF REPORT

COVID-19 IgG/IgM antibody testing in Los Angeles County, California

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Abstract
Evidence suggests that asymptomatic and mild SARS-CoV-2 infections comprise > 95% of all cases. Developing a test that indicates past infection and possible immunity against the virus is important. We administered 244 antibody tests to three groups of high-risk population. The test consisted of an IgG component and an IgM component. The overall IgM/IgG positivity for patients with none, mild, moderate, and severe symptoms were 21.1%, 21.8%, 14.2%, and 26.9%, respectively. Those with moderate or severe symptoms were no more or less likely to have positive antibody tests than those with no or mild symptoms.

The emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) or COVID-19 has presented a substantial threat to healthcare system all over the world. Many countries have initially declared restrictive measures, such as lockdown or stay-at-home orders, in an attempt to contain the pandemic at the local level by reducing individual contact. Now, the world has already started exiting the lockdown, including the USA, while the number of confirmed cases rises. Based on the WHO latest COVID-19 report as of end of July 2020, there are over 16,600,000 confirmed cases worldwide, out of which more than 4,400,000 cases are in the USA. But this report does not include the COVID-19 cases with little to no symptoms that never got tested or confirmed positive. According to Takahashi et.al., evidence suggests that asymptomatic and mild SARS-CoV-2 infections together comprise > 95% of all COVID-19 infections [1].

The RT-PCR test remains the gold standard and most accurate test to diagnose active COVID-19. But as this test provides no information on past infections, developing a test that can identify past exposure and possible established immunity against the virus is very important. Such a test may be helpful in supporting the exit from lockdown or identifying people who could return to their on-site jobs, or those who might be ready to handle a job that is of higher exposure [2]; this comes through serology testing, also known as antibody testing.

A serology test looks for the presence of antibodies, which are specific proteins made in response to infections. Antibodies are known to be specific, which means that an antibody is able to recognize, bind to, and destroy specific antigen only. This feature allows the using of antibodies as a screening tool for past exposure to specific antigens, such as the SARS-CoV-2, as they are detected in the blood of people who are tested after infection.

Another important feature of antibodies is providing immunological memory. After an infection, the cells producing those specific antibodies against the infection significantly increase in number, which allows for the protection of the body against repeated infections [3].

In this paper, we report the results of 244 antibody tests we administered in Los Angeles (LA) county, between April 21 and May 22, 2020. We used One Step SARS-CoV2 (COVID-19) IgG/IgM Rapid Test, which is a qualitative membrane-based immunoassay for the detection of IgG and IgM antibodies to SARS-CoV-2 in whole blood, serum, or plasma specimen. The test has 96% sensitivity for IgG, 88% for IgM, and a specificity of 100% for both IgG and IgM. Sensitivity is the chance that a person who tests positive has actually been infected, while specificity is the chance that a person who tests negative has actually not been infected in the past [4]. The test detected IgG antibody as low as 1:40, IgM antibody as low as 1:8.

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The One Step SARS-CoV2 (COVID-19) IgG/IgM Rapid Test consists of two components, an IgG component and an IgM component. If the specimen contains SARS-CoV-2 IgG antibodies, a colored line will appear in IgG test line region. If the specimen contains SARS-CoV-2 IgM antibodies, a colored line will appear in IgM test line region. If the specimen does not contain SARS-CoV-2 antibodies, no colored line will appear in either of the test line regions, indicating a negative result [5].

We administered the test to 244 participants from three groups, those with past exposure/possible infection, healthcare professionals at an LA County hospital, and first responders (firefighters, police officers, and paramedics). The average age of the study participants was 51.1 years and 50% were males. Our study population consisted of 40 first responders, 56 healthcare workers, and 148 participants of general population with past exposure/possible infection. A total of 122 participants overall were asymptomatic, while 55 had mild symptoms, 28 had moderate symptoms, and 27 had severe symptoms.

Overall, 51 of the 244 (20.9%) tested positive for antibodies. Seven out of the 244 were previously PCR-confirmed as COVID-19 positive (3 hospitalized, 4 outpatients) and were all found to have antibodies present.

Among 40 first responders, 8 were positive for IgM and/or IgG (20%). Of these, 5 out of 8 were asymptomatic; the rest were equally distributed between mild, moderate, and severe symptoms at time of infection. Among those 8, 5 had IgM only present, 2 had IgG only, and 1 had both present.

Among 56 healthcare workers, 10 (17.8%) were positive for IgM and/or IgG. And they were equally distributed among those with no symptoms ($n = 3$), and those with mild, moderate, or severe symptoms.

Among 148 subjects of general population with concerning symptoms or exposure to the virus, 33 tested positive (22.3%), 18 of them were asymptomatic, 9 reported mild symptoms, and the rest were distributed among moderate or severe symptoms.

In total, 51 subjects of the 244 tested positive (20.9%), 15 of which had both IgM and IgG antibodies present.

The overall IgM/IgG positivity for patients with none, mild, moderate, and severe symptoms were 21.1%, 21.8%, 14.2%, and 26.9%, respectively.

Generally speaking, antibody testing is not relied upon for the diagnosis of acute COVID-19, as it takes few days until the immune response develops. Also the availability of the RT-PCR with its high sensitivity during the first 5.5 days after onset does not necessitate the use of antibody testing to diagnose acute infections. However, IgM against SARS-CoV-2 may be useful in suspected COVID-19 patients negative by molecular methods after this time point [6]. A study recently showed that IgM antibodies were detectable in 85% of COVID-19-confirmed patients 1 to 7 days after the onset of their symptoms [7]. The same study also found that IgG was detected 14 days (IQR 10–18) after symptom onset. IgG is an antibody that is responsible for long-term immunity after infection; it also enhances disease outcome in situations where patients have pre-existing IgG against the same antigen.

There are multiple factors that can affect the results of an antibody test, such as the population demographics including age and occupation, the time elapsed between sampling and the onset of symptoms, and the administered test's characteristics such as sensitivity, specificity, or cross-reactivity. Cross-reactivity occurs when two different antigens share similar structural regions, which makes the same antibody able to recognize both of them.

Another factor that can also affect the test result is the severity of symptoms. In our study, 21.3% of participants with no or mild symptoms tested positive ,while 78.7% tested negative. Among the participants with moderate or severe symptoms, 20% tested positive for IgG/IgM. Our findings suggest that patients with moderate or severe symptoms are not likely to have more or less positive antibody tests than those with no or mild symptoms, suggesting that potential immunity and virologic response may not be best judged by severity of disease at onset.

Another important factor to discuss here is age. Multiple studies have shown that the incidence of COVID-19 increased with age [8, 9]. In our study, the mean age for the individuals who tested positive was 53.6 years. Forty years or less of age were 21.5%, while 78.4% were above 40. This percentage hints towards that young individuals may not only have less incidence of developing the COVID-19, but might also be less likely to develop antibodies.

Overall, 20.9% of the tested individuals were found to have antibodies present, indicating their past infection. However, it is very important to emphasize that the factors discussed above might have contributed to this high prevalence in LA County.

The main limitation of this study was the sample size, which was not large enough to study the test performance more thoroughly. In addition, there was only single serology test used in this study; using different serology tests from different manufacturers and comparing their results would have further increased the credibility of the reported results.

Also, the One Step SARS-CoV2 (COVID-19) IgG/IgM Rapid Test is a qualitative test; neither the quantitative value nor the rate of increase in the concentration of IgG or IgM antibodies to SARS-CoV-2 can be determined by this test.

Another limitation to mention here is the lack of T cell measurements, so future follow-up on the ability of T cells to wear off future infections would not be possible in this study.

In summary, a positive antibody response to SARS-CoV-2 can assist in diagnosing COVID-19, including subclinical cases [7]. Our test demonstrated accurate performance in detecting IgG/IgM antibodies in individuals with previous exposure to COVID-19. An antibody test might not be a 100% specific or 100% sensitive, but it could definitely assist in making decisions that depend on whether someone had been previously exposed to the virus and aid in making decisions related to easing lockdowns. Meanwhile and as long as the virus continues to spread, the world should continue to practice social distancing and follow all preventive guidelines in place to protect themselves and people around them.

Compliance with ethical standards

Conflict of interest   The authors declare that they have no conflicts of interest.

Ethical approval   This study received the ethical approval from The Lundquist Institute IRB.

Informed consent   All of the study participants signed the informed consent prior to enrollment.

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