Research Article

Serological Tests in Screening COVID-19

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Received Date: December 24, 2020
Publication Date: January 01, 2021

Abstract

Characteristically, after infection, antibodies are detected in the blood of individuals, particularly individuals with few or mild symptoms. In patients with varying symptoms of COVID-19 and negative results of reverse-transcriptase-polymerase-chain reaction (RT-PCR) tests, the testing has a significant clinical role when nasopharyngeal swabs are taken more than 5 days after symptom onset. The Royal College of Pathologists (RCPath) developed seven principles for the production of a COVID-19 testing strategy. Testing is carried out for a the purpose is one of these RCPath's principles. Nevertheless, denial of requesting SARS-CoV-2 (COVID-19) antibody tests for reassurance should be cautioned. With a lower antibody level, whether the protective immunity will be sustained is questionable. Several immune-based assays were developed against different SARS-CoV-2 (COVID-19) viral proteins as the followings: 1) Entire Spike (S) protein, IgG antibody from patient serum can cross-react with SARS-CoV and MERS-CoV, 2) S1 subunit of Spike (S) protein, IgA, IgG antibodies from patient serum can cross-react with SARS-CoV only,3) Receptor-binding domain (RBD), IgG antibody from patient serum can cross-react with SARS-CoV only, and 4) Nucleocapsid (N), IgG antibody from patient serum can cross-react with SARS-CoV only.

Long et al demonstrated in their study that IgG antibody and neutralizing antibody levels initiate decreasing within 2-3 months after infection in the majority of persons with recovery from SARS-CoV-2 (COVID-19) infection. Nevertheless, an analytical study of the dynamics of neutralizing antibody titers demonstrated reduced neutralizing antibodies around 6-7 weeks after illness onset. In conclusion, serological data greatly supplement the laboratory results from the quantitative reverse-transcriptase polymerase-chain reaction (qRTPCR), the design of virus elimination programs (seroepidemiology), the discovery of the monoclonal antibodies, and development of SARS-CoV-2 (COVID-19) vaccines.

Keywords: *COVID-19, SARS-CoV-2, test, serological.*

Abbreviations:

COVID-19: Coronavirus Disease 2019,

IgA: Immunoglobulin A,

IgG: Immunoglobulin G,

IgM: Immunoglobulin M,

MERS-CoV: Middle-East-Respiratory-Syndrome Coronavirus,

N: Nucleocapsid,

qRT-PCR: quantitative Reverse-Transcriptase-Polymerase-Chain Reaction,

RBD: Receptor-Binding Domain, RNA: Ribonucleic Acid,

RT-PCR: Reverse-Transcriptase-Polymerase-Chain Reaction,

S: Spike protein,

SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus type 2

Introduction

Characteristically, after infection, antibodies are detected in the blood of individuals, particularly individuals with few or mild symptoms. In patients with varying symptoms of COVID-19 and negative results of reverse-transcriptase-polymerase-chain reaction (RT-PCR) tests, the testing has a significantly clinical role when nasopharyngeal swabs are taken more than 5 days after symptom onset **(**1, 2**)**. The Availability and Accuracy of Antibody Tests Immunoglobulin M (IgM) rises soonest, whereas IgA and IgG persist. IgG alone. The maximum sensitivity for IgM alone, IgA alone, and IgG alone appear during the days 15-21 after the symptom onset that are 75.4 % (64.3-83.8), 98.7 % (39.0-100), and 88.2 % (83.5-91.8), respectively **(**3**)**, whereas the specificity at all times for IgM alone and IgG alone are 98.7 % (97.4-99.3) and 99.1 % (98.3-99.6), respectively **(**3**)** . The sensitivity and specificity of the antibody tests are critical due to false negative rates of RT-PCR that are between 2 % and 29 % **(**3**)**. A previous study on immunological assessment of SARS-CoV-2 (COVID-19) infections in China revealed that 81.1 % (30/37) and 62.2 % (23/37) of asymptomatic individuals tested positive for IgG and IgM, respectively and 83.8 % (31/37) and 78.4 % (29/37) of the symptomatic patients tested positive for IgG (around 3-4 weeks after COVID-19 exposure) and IgM, respectively **(**4**)**. In acute phase that the viral ribonucleic acid (RNA) can be identified in a respiratory sample, IgG levels in symptomatic patients were significantly statistical higher than those in the asymptomatic individuals **(**4**)**.

Serological Test Interpretation

The pre-test probability of infection has much influence on the interpretation of the serological test results not only influenced by the accuracy of the test itself. When screening suggestive symptomatic individuals, the pre-test probability will be much higher, compared to asymptomatic persons **(**5**)**.

Serological Testing Pitfalls

COVID-19 screening is essentially amounted by non-specific indication and population-based policies on testing. Inconsequences of testing with uncareful consideration, this risks the potential harm. In more affluent populations, the rates of testing will be higher **(**6**)** that limits the estimates of seroprevalence. The Royal College of Pathologists (RCPath) developed seven principles for the production of a COVID-19 testing strategy. Testing being carried out for a purpose is one of these RCPath's principles **(**7**)**. Nevertheless, denial of requesting SARS-CoV-2 (COVID-19) antibody tests for reassurance should be cautioned **(**8, 9**)**.

Immunity and Antibody Tests

In eliminating COVID-19, a combination of B and T cell immunity is likely to involve for the production of protective-immunity memory **(**5**)**. Nevertheless, currently, several longitudinal studies demonstrated waning of antibody levels **(**10**)**. With a lower antibody level, whether the protective immunity will be sustained is questionable **(**5**)**. A recent study revealed that produced antibodies can provide long-term immunity, whereas non-neutralizing antibodies can be generated. Antibody enhancement, a phenomenon that can facilitate a more severe-secondary infection **(**11**)**. This phenomenon is not to date with SARS-CoV-2 (COVID-19), but it has been demonstrated in other coronaviruses **(**11**)**. Immune-based Assays developed against different SARS-CoV-2 (COVID-19) Viral Proteins Several immune-based assays were developed against different SARS-CoV-2 (COVID-19) viral proteins as the followings : 1) Entire Spike (S) protein, IgG antibody from patient serum can cross-react with SARS-CoV and MERS-CoV **(**12**)**, 2) S1 subunit of Spike (S) protein, IgA, IgG antibodies from patient serum can cross-react with SARS-CoV only **(**12**)**, 3)Receptor-binding domain (RBD), IgG antibody from patient serum can cross-react with SARS-CoV only **(**12**)**, and 4) Nucleocapsid (N),IgG antibody from patient serum can cross-react with SARS-CoV only **(**12**)**.

Discussion

IgG antibody responses sustained for at least 34 months after outbreak in persons with laboratory-confirmed MERS-CoV infection **(**13**)**, whereas IgG levels in SARS-CoV-infected individuals were sustained for more than two years **(**14, 15**)**. Neutralizing antibodies that associate with the numbers of virus-specific T cells have been detected in most COVID-19 convalescent patients **(**16-19**)**. Long et al demonstrated in their study that IgG antibody and neutralizing antibody levels initiate decreasing within 2-3 months after infection in the majority of persons with recovery from SARS-CoV-2 (COVID-19) infection **(**4**)**. Nevertheless, an analytical study of the dynamics of neutralizing antibody titers demonstrated reduced neutralizing antibodies around 6-7 weeks after illness onset **(**20**)**.

Conclusion

Serological data greatly supplement the laboratory results from the quantitative reverse-transcriptase-polymerase-chain reaction (qRT-PCR), the design of virus elimination programs (seroepidemiology), the discovery of the monoclonal antibodies, and development of SARS-CoV-2 (COVID-19) vaccines.

References

1.Watson J, Whiting PF, Brush JE. "Interpreting a COVID-19 test result". BMJ 2020; 369 : m1808.

2.Kucirka LM, Lauer SA, Laeyendecker O, Boon D, Lessler J. "Variation in false-negative rate of reverse transcriptase polymerase chain reaction-based SARS-CoV-2 tests by time since exposure". Ann Intern Med 2020; 173 : 262-267.

3.Arevalo-Rodriguez I, Buitrago-Garcia D, Simancas-Racines D, et al. "False-negative results of initial RT-PCR assays for COVID-19 :a systematic review". MedRxiv (Preprint) 2020. DOI : 10.1101/2020.04.16.20066787%.

4.Long Q-X, Tang X-J, Shi Q-L, Li Q, Deng H-J, Yuan J, et al. "Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections". Nature Medicine 2020; 26 : 1200-1204.

5.Watson J, Richter A, Deeks J. "Testing for SARS-CoV-2 antibodies". BMJ 2020; 370 : m3325. DOI : 10.1136/bmj.m3325

6.Hart JT. "The inverse care law". Lancet 1971; 1 : 405-412.

7.Martin J. COVID-19 testing : a national strategy. Royal College of Pathologists 2020. Available at : http://www.rcpath.org/uploads/assets/2e8d8771-f85a-408a-b5c8e68969cd21d5/cbcb4f30-d8f8-40fe-ba8cdef3e6803ee4/RCPath-COVID-19-testing-a-national-strategy.pdf (accessed on December 5, 2020).

8.Petrie KJ, Sherriff R. "Normal diagnostic test results do not reassure patients". Evid Based Med 2014; 19 : 14.

9.Rolfe A, Burton C. "Reassurance after diagnostic testing with a low pretest probability of serious disease : systematic review and meta-analysis". JAMA Intern Med 2013; 173 : 407-416.

10.Ibarrondo FJ, Fulcher JA, Goodman-Meza D, et al. "Rapid decay of anti-SARS-CoV-2 antibodies in persons with mild COVID-19". N Engl J Med 2020. DOI : 10.1056/NEJMc2025179

11.Fierz W, Walz B. "Antibody dependent enhancement due to original antigenic sin and the development of SARS". Front Immunol 2020; 11 : 1120.

12.Okba NMA, Muller MA, Li W, Wang C, GeurtsvanKessel CH, Corman VM, et al. "SARS-CoV-2 specific antibody responses in COVID-19 patients". Emerg Infect Dis 2020; 26. DOI : 10.1101/2020.03.18.20038059

13.Payne DC, et al. "Persistence of antibodies against middle-east- -respiratory-syndrome coronavirus". Emerg Infect Dis 2016; 22 : 1824-1826.

14.Guo X, et al. "Long-term persistence of IgG antibodies in SARS-CoV infected healthcare workers". Preprint available at : http://www.medrxiv.org/content/10.1101/2020.02.12.20021386v1 (2020)

15.Wu LP, et al. "Duration of antibody responses after severe acute respiratory syndrome". Emerg Infect Dis 2007; 13 : 1562-1564.

16.Ni L, et al. "Detection of SARS-CoV-2-specific humoral and cellular immunity in COVID-19 convalescent individuals". Immunity 2020. DOI : https://doi.org/10.1101/2020.03.17.20037713

17.Thevarajan I, et al. "Breadth of concomitant immune response prior to patient recovery : a case report of non-severe COVID-19". Nature Medicine 2020; 26 : 453-455.

18.Wu F, et al. "Neutralizing antibody response to SARS-CoV-2 in a COVID-19 recovered patient cohort and their implications". Preprint available at : http://www.medrxiv.org/content/10.1101/2020.03.30.20047365v2 (2020).

19.Suthar MS, et al. "Rapid generation of neutralizing antibody responses in COVID-19 patients". Preprint available at : http://www.medrxiv.org/content/10.1101/2020.05.03.20084442v1 (2020).

20.Wang X, et al. "Neutralizing antibodies responses to SARS-CoV-2 in COVID-19 patients and convalescent patients". Preprint available at : http://www.medrxiv.org/content/10.1101/2020.04.15.20065623v3 (2020).

Volume 2 Issue 1 January 2021