Original Article

Observational study of SARS-CoV-2 antibody immune response in a cohort of patients at a North Suburban Chicago, Illinois, in a physician's practice

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ABSTRACT

Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused a global pandemic. The application of point of care serological testing can help determine past infection and assist healthcare workers assess patient risk.

Method: An observational study of 114 subjects in North Suburban Chicago, Illinois, was performed using the Clungene® lateral flow immunoassay (LFI). Patients' PCR test results and clinical symptoms were used to compare the seroconversion rate of this patient population with the surrounding community.

Results: Excluding 1 aberrant result, there was 100% positive agreement (10) between PCR and antibody (IgG or IgM) test results. There were 7 patients who did not have a prior PCR test who were positive for IgG; 5 of the 7 had clinical symptoms consistent with possible exposure and 2 were asymptomatic. There was 1 person with a suspected exposure to an infected person who was IgM positive. Ninety-five asymptomatic patients were seronegative. The overall rate of 15.9% seroconversion (IgG or IgM) is consistent with other community-based testing results in the North Suburban Chicago, Illinois area.

Conclusion: Rapid screening tests to identify antibody positive patients recovered from coronavirus disease-2019 can be a useful tool for healthcare professionals to determine or confirm past infection.

Statement of novelty: Limited data is available on the use of point of care serological testing to assist healthcare professionals with the assessment of their patient population regarding past SARS-CoV-2 infectivity and seroconversion. The present study successfully investigated the use of a point of care antibody test in a physician's office to determine which patients have developed antibodies, indicating an immune response to SARS-CoV-2, and to assist with decisions on whether patients should pursue normal social and workplace activities.

Background

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused a global pandemic. The percentage of infected individuals who seroconvert is unknown. Serological tests can help determine whether a person or population of people have developed antibodies indicative of an adaptive immune response to SARS-CoV-2. In April and May of 2020, 2 internist gerontology general practitioner's offices in

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Submitted 3 July 2020
Accepted 5 August 2020
Available online 6 August 2020

LymphoSign Journal 7:104–108 (2020)
dx.doi.org/10.14785/lymphosign-2020-0007

North Suburban Chicago, Illinois, tested a cohort of patients to determine their SARS-CoV-2 antibody immune response. North Suburban Chicago consists of communities north of Chicago, bordering the shores of Lake Michigan. Previously reported SARS-CoV-2 results by a North Suburban Chicago, Illinois community hospital suggested an 18% infectivity rate during this same period (Seidenberg 2020).

Introduction

SARS-CoV-2 has caused over 162 748 infections and 7301 deaths in Illinois State at the time of writing this report (Illinois Department of Health 2020). To avoid spread of SARS-CoV-2 and to help standardize definitions of clearance, it is important to understand the development of antibodies to infection (Ragnesola et al. 2020). Serology (antibody) tests may detect different types of antibodies. The most common are IgM and IgG. Published data suggests that 95% of patients with a confirmed PCR test (either documented result or self-reported) have a positive IgG antibody (Wajnberg et al. 2020). Another study found 3 types of IgM seroconversion: synchronous seroconversion of IgG and IgM, IgM seroconversion earlier than that of IgG, and IgM seroconversion later than that of IgG (Long et al. 2020).

Positive antibody results from appropriately validated serology tests that are designed to be very specific to the SARS-CoV-2 virus can indicate whether a patient has had recent or prior SARS-CoV-2 infection (Long et al. 2020). In addition, while there is uncertainty with this new virus, it is possible that the use of antibody tests and clinical follow-up can provide the medical community with more information on whether or not, and how long, a person who has recovered from the virus is at lower risk of infection if they are exposed to the virus again (FDA 2020).

Methods

Two physician practices in North Suburban Chicago, Illinois, tested 114 study participants: 11 of whom had a positive PCR test of which 10 had some reported coronavirus disease-2019 (COVID-19)-like symptoms, 6 were symptomatic or had exposure risk, and 97 were asymptomatic. The age of the subjects ranged from 3 to 84. Serological testing was performed between 22 April 2020 and 26 May 2020. Inclusion criteria included patients routinely managed by the practicing physicians who consented to a serological test. Using a whole blood sample drawn from a lancet, subjects were tested for the detection of SARS-CoV-2 antibodies (IgG and IgM) using the point of care CLUNGENE® SARS-COV-2 VIRUS (COVID-19) IgG/IgM Rapid Test Cassette lateral flow immunoassay (LFI). Previously, the manufacturer of the LFI validated this immunoassay for the qualitative detection of antibodies to SARS-CoV-2 and the data was submitted to the US FDA consistent with the requirements of the Emergency Use Authorization (FDA 2020). See Figure 1, a schematic diagram showing the location of the sample well, buffer well, and control and test lines of the Rapid Test Cassette.

The tests were performed by a trained health professional. The results were visually analyzed according to the manufacturers' instructions for use.

Results

Eleven patients had a confirmed PCR test indicating prior infection. The common clinical manifestation of these PCR patients was fever and fatigue. Serological testing was performed between 27 and 42 days post PCR SARS-CoV-2 positive result for 10 of the patients. See Table 1. Ten of the 11 PCR positive patients were IgG (10) or IgM (1) antibody positive (91%).

The 1 PCR positive patient who was seronegative (antibody negative) was evaluated again by a second serological test and was also IgG and IgM negative (CLUNGENE 2020; Quest Diagnostics 2020). Based on an overall clinical evaluation, it was determined that the patient was SARS-CoV-2 infected but had Waldenstrom's macroglobulinemia (WM), a cancer of the immune system in which antibodies are over produced in an unregulated fashion. Individuals with this type of disease do not respond in a normal fashion to immunologic stimuli. The fact that this patient did not produce measurable antibodies to the coronavirus is not surprising and consistent with this disease. Therefore, this WM patient was excluded from the result data.

There were 6 patients who did not have a prior PCR test but were symptomatic or had exposure risk; all were positive for IgG or IgM. The rate of seroconversion for the symptomatic, exposed or PCR positive subpopulation was 100% (16/16). There were 2 IgG positive asymptomatic patients and 95 asymptomatic seronegative

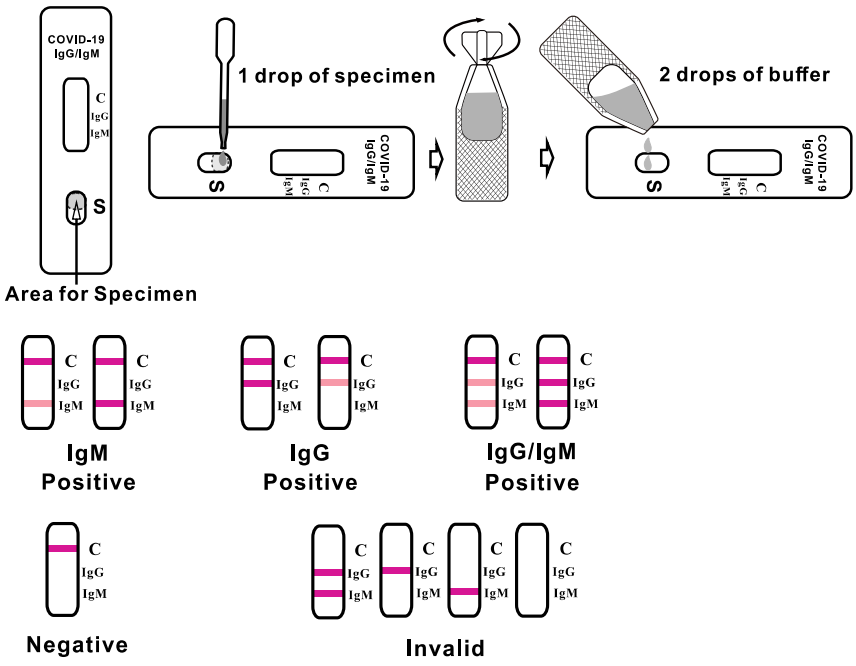

Figure 1: A schematic diagram showing the location of the sample well, buffer well, and control and test lines of the Rapid Test Cassette.

Table 1: **PCR positive patients.**

Date of PCR test	Date of serological test	No. of days between tests	Antibody results
3/27/2020	4/22/2020	27	IgG+
3/24/2020	4/22/2020	29	IgG+
4/5/2020	4/23/2020	19	IgG+
3/26/2020	4/24/2020	29	IgG+
3/23/2020	4/24/2020	31	IgG- (2x)[a]
3/26/2020	4/27/2020	32	IgG+
3/16/2020	4/27/2020	42	IgG+
3/28/2020	4/27/2020	31	IgG+
3/19/2020[b]	4/24/2020	35[b]	IgG+
3/19/2020[b]	4/27/2020	38[b]	IgG+
Unknown	4/28/2020	Unknown	IgM+

[a]Patient was SARS-CoV-2 infected but had Waldenstrom's macroglobulinemia and, as expected, did not produce measurable antibody when tested with 2 different antibody test systems.
[b]Exact date of PCR test unknown; estimated number of days between tests.

patients. The rate of seroconversion for the asymptomatic subpopulation was 2% (2/97). The overall rate of seroconversion for the entire population (IgG or IgM) was 15.9% (18/113). See Table 2. This overall rate is consistent with other community-based testing results in the North Suburban Chicago, Illinois area.

Discussion

Our study analyzed whole blood samples for SARS-CoV-2 from a cohort of patients presenting at 2 physician offices during April and May of 2020. The patients were tested to determine antibodies related to potential infection and recovery from SARS-CoV-2. The CLUNGENE® SARS-COV-2 VIRUS (COVID-19) IgG/IgM Rapid Test Cassette was reportedly simple to implement with adequately trained clinical staff. Results were obtained within 15 minutes and the red procedural control line confirmed that adequate specimen volume, sufficient membrane wicking, and error-free procedural technique were used. With the exception of 1 unusual patient, clinically documented infected patients with a confirmed SARS-CoV-2 PCR test were 100% in positive agreement with the presence

Table 2: **Summary of results.**

Measure	Value
PCR positive, symptomatic, or exposed	
Positive PCR/IgG or IgM positive	10
Clinically suggestive positive/IgG positive	5
Exposed patient: IgM positive	1
Subtotal (symptomatic)	16/16 (100%)[a]
Asymptomatic	
Asymptomatic/IgG positive	2
Asymptomatic IgG/IgM negative	95
Subtotal (asymptomatic)	2/97 (2.1%)
Overall seroconversion rate	18/113 (15.9%)

[a]Waldenstrom's macroglobulinemia patient excluded from results.

of the IgG antibody. These results are consistent with the manufacturer's clinical performance data showing 97.4% positive IgG agreement with SARS-CoV-2 infected patients with a known positive PCR test as reported in the Instructions for Use, and 100% sensitivity when confirmed PCR infected patients were tested 15–42 days following infection in a separate study submitted to the US FDA (FDA 2020). Consistent with recently published data, IgM can persist more than 23 days after symptom onset (Wajnberg et al. 2020).

There have been 3 prior publications evaluating the CLUNGENE® test. One showed lower sensitivity (Vásárhelyi et al. 2020); however the cassettes used in this study were a previous generation assay with lower sensitivity and the PCR test used to determine positive agreement had "logistical problems during the PCR analysis and the suppliers of reagents used for certain component changed"[1]. Therefore, the results are not comparable. A second study analyzed blood samples from COVID-19 convalescent plasma donors and determined that the CLUNGENE® test possessed high sensitivity and specificity for COVID-19 antibodies (Ragnesola et al. 2020). A third evaluated CLUNGENE®'s diagnostic performance and reported a specificity of 99% and sensitivity of 97.4% for IgM or IgG 14 days following infection which are consistent with this observational study (Van Elslande et al. 2020).

Limitations

Our study has several limitations. Samples were not tested for virus neutralization; therefore neutralizing activities of the detected IgG antibodies are not known. The small sample size of patients makes it difficult to draw a definitive conclusion or determine the relationship between antibody response and clinical course. It should be emphasized that the CLUNGENE® test is only a qualitative serological test and not quantitative. At the time of this publication there are no approved quantitative serological tests (CDC 2020).

Conclusion

Rapid screening tests to identify antibody positive people recovered from coronavirus disease-2019 can be a useful tool for healthcare professionals. Confirming suspected antibody formation in SARS-CoV-2 cases with the help of serological testing can reduce exposure risk. This study highlights the relevance of serological testing to assess patient immunity by antibody detection and assist with decisions on whether to pursue normal social and workplace activities.

Disclosures

Christopher C. Lamb, PhD, worked with the manufacturer of the Clungene® test on the Emergency Use Authorization submission to the US FDA.

Funding

No external funding was received for this work.

Acknowledgements

The author acknowledges Ryan Dagenais for assistance with literature review and editorial support with the manuscript; his efforts were funded by BioSolutions Services.

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[1]Translated from original language of Hungarian to English via Google Translate.

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