Rapid Review Report

Review Title:	**How well does the presence and level of antibodies predict the clinical course of disease?**
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Key Findings

- Seroconversion occurs in majority of COVID-19 patients from the second week following symptom onset on.
- Between 7.8 - 43.6% of suspect cases and 4.7% of asymptomatic individuals with negative nucleic acid test (rt-PCR) test positive for antibodies against SARS-CoV-2.
- An increase in antibody titres correlates with a neutralizing antibody response and positive recovery of COVID-19 patients with mild to moderate symptoms.
- Although higher antibody titre and more robust antibody response are observed in severe and critically ill patients, those antibodies may not effectively clear virus and higher antibody levels may be associated with a worse clinical progress.

Limitations

- Some of the literature available is in the state of preprint, pending peer review.

GRADE of Evidence: B - Moderate

A grade of "B" is assigned when further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate. The review may include one high quality study and/or several studies with some limitations.

Background

Serological tests are implemented in several countries as an additional test for COVID-19 screening and diagnosis. It is presumed that individuals with serum antibodies against SARS-CoV-2 have protective immunity and can be deployed to take care of active COVID-19 patients. Nevertheless, the correlation of antibody levels with disease course is largely unknown.

Purpose

To investigate the correlation of antibody levels with clinical course.

Research Question(s)

How well does the presence and level of antibodies predict the clinical course of disease?

Method

This review was produced within 48 hours of request.

PICO Statement

P – Patients/Population	Not applicable
I – Intervention/Indication	Not applicable
C – Comparator/Control	Not applicable
O – Outcome	Not applicable

Search Strategy

(coronavirus* or corona virus* or coronovirus* or coronaviral or (wuhan adj1 virus) or (wuhan adj1 viral) or cov or covid or WN-CoV or ncov or 2019ncov or ncov2019 or ncovid or ncovid2019 or 2019ncovid or covid-19 or covid19 or covid 19 or corvid 19 or HCov-19 or HCov-2019 or hcov19 or hcov2019 or severe acute respiratory syndrome coronavirus 2 or severe acute respiratory syndrome corona virus 2 or SARS Coronavirus 2 or SARS Corona virus 2 or SARS-COV-2 or SARSCOV2 or SARSCOV 2 or SARS2 or SARS-2 or coronavirus disease 2019 or corona virus disease 2019 or 2019 novel coronavirus infection* or 2019 novel coronavirus disease or 2019-nCoV infection* or coronavirus disease-19 or new coronavirus or novel corona

Inclusion Criteria

- 2019-2020

Sources

medRxiv Google Google Scholar Medline
PubMed WHO Global Research on COVID-19
PHAC COVID-19 BMJ Best Practice

Summary of Evidence

Correlation of antibody levels with disease onset and recovery

IgG and IgM seroconversion usually begin 5-7 days post disease onset. The proportion of patients testing positive on IgG and/or IgM assays can be as low as 11.1% during week 1 [1], but rapidly increases from week 2 onward. Most (more than 80%) COVID-19 patients are positive for both IgG and IgM after week 3 [2-4]. IgM begins to decline after week 5 and may be undetectable after week 6-7 [5], whereas IgG titres continue to increase and persist [5]. Persistent high IgG titres indicate a protective humoral immune response [6].

Between 7.8 – 43.6% of suspect cases [1, 7] and 4.7% of asymptomatic individuals [7] with negative rt-PCR test results have been shown to be positive for antibodies. Therefore, IgM and/or IgG detection might be used as a supplemental diagnostic test for the patients with highly suspicious clinical symptoms or asymptomatic highly exposed close contacts.

There is no available evidence with which to estimate the durability of IgG protective immunity. However, if the immune response to SARS-CoV-2 resembles that toward SARS-CoV, this protective humoral immunity may persist for several years [8-11]. The prolongation of IgG production may indicate the significance of IgG in both humoral immune response to acute SARS-CoV infection and to the clearance of the remaining virus sources during recovery [11].

Correlation of antibody levels with clinical course

Multiple studies demonstrate that in COVID-19 patients with mild to moderate symptoms, rising of antibody levels correlate with a neutralizing antibody response and are accompanied by a decline in viral load, improvement of clinical symptoms and CT findings, [4, 12-15].

Although IgG and IgM titers are significantly higher in severe patients than non-severe patients, levels of antibodies are not always accompanied with RNA clearance, particularly in critically ill patients. Severe COVID-19 patients can develop faster peak antibody responses comparing with mild to moderate patients. However, the antibody neutralizing ability is impaired and viral clearance (estimated via rt-PCR) can be delayed [12, 15-16]. The Robust IgG antibody response that observed in critically ill patients is often associated with poor prognosis [16].

Conclusions

The majority of COVID-19 patients develop both IgM and IgG antibodies during the second week following disease onset. Some suspect cases and asymptomatic individuals with negative nucleic acid test nevertheless test positive for antibodies against SARS-CoV-2 virus. Rising of antibody levels correlate with a neutralizing antibody response and a favorable prognosis in COVID-19 patients with mild to moderate symptoms. Although higher antibody titer and more robust antibody response are observed in severe and critically ill patients, those antibodies may not effectively clean virus and higher titer of total antibody may be associated with a worse clinical prognosis.

References Included in Summary

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