HHS Public Access

Author manuscript

Ann Intern Med. Author manuscript; available in PMC 2024 January 24.

Published in final edited form as:

Ann Intern Med. 2020 November 17; 173(10): JC57. doi:10.7326/ACPJ202011170-057.

Antibody tests have higher sensitivity at ≥ 8 days after symptom onset and 99% specificity for detecting SARS-CoV-2

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Keywords

Antibodies; viral; Betacoronavirus; Coronavirus infections; Pneumonia; viral

Question

In primary or secondary care or in the community, how well do antibody tests detect severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection?

Review methods

Searched multiple databases to April 2020 for studies that assessed the accuracy of tests for detecting antibodies to SARS-CoV-2 for identification of current or past SARS-CoV-2 infection in patients. Studies with < 10 samples or patients were excluded.

Included studies

54 studies (15 976 samples and 8256 cases; mean or median age of cases 37 to 76 y; 26% to 87% men) met inclusion criteria. Studies included cases in the early phase of illness only (< 21 d after symptom onset) (23 studies), cases ≥ 21 days after symptom onset (2 studies), and mixed groups (23 studies); 6 studies did not report days after symptom onset. 48 studies used case-control designs and 6 were prospective studies in which it was not already known whether patients had SARS-CoV-2 infection.

Results: Diagnostic characteristics of antibody tests for detecting severe acute respiratory syndrome coronavirus 2 infection

Tests	Sensitivity (95% CI)					Specificity (CI)*
	1 to 7 d†	8 to 14 d†	15 to 21 d†	22 to 35 d†	> 35 d†	

Disclosures: The commentators have disclosed no conflicts of interest. The forms can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=ANN-NNNN

Tests	Sensitivity (95% CI)					Specificity (CI)*
	1 to 7 d†	8 to 14 d†	15 to 21 d†	22 to 35 d†	> 35 d†	
IgG	30% (22 to 39)	67% (58 to 74)	88% (84 to 74)	80% (72 to 86)	87% (80 to 92)	99% (98 to 100)
IgM	23% (15 to 34)	58% (46 to 70)	75% (64 to 84)	68% (55 to 79)	54% (38 to 69)	99% (98 to 99)
IgG/IgM‡	30% (21 to 41)	72% (64 to 80)	91% (87 to 94)	96% (91 to 98)	78% (66 to 86)	99% (97 to 99)
Total antibodies	25% (10 to 50)	84% (64 to 94)	98% (90 to 100)	70% (35 to 91)	79% (50 to 93)	99% (98 to 100)

CI defined in Glossary.

*Meta-analysis of 35 studies (8526 cases) across all time points.

†Days after symptom onset.

‡Positive if either IgG or IgM is positive.

Bottom line: Antibody tests have higher sensitivity at ≥ 8 days after symptom onset than at 1 to 7 days, and 99% specificity, for detecting SARS-CoV-2 infection.

Commentary

Reliable serologic testing is essential for understanding SARS-CoV-2 transmission and epidemiology, as well as confirming past infections for which nucleic acid amplification tests were either negative or not performed. Notably, connecting COVID-19 to pandemic-associated, multisystem inflammatory syndrome in children relied on antibody testing (1).

The meta-analysis by Deeks and colleagues provides valuable information about the state of serologic testing during a relatively early stage of the COVID-19 pandemic, but also raises important questions. Beyond confirming the variable and low sensitivity of serology in the first 14 days after infection, the authors noted a high risk for bias and raised concerns about the reference standards used in a majority of studies. Aside from separating testing based on IgM, IgG, or both antibody types combined, sensitivity analyses based on different antigen characteristics (mammalian cell produced, bacterial recombinant, or peptide) or targets (i.e., spike-protein or nucleocapsid-protein), as well as different testing platforms (i.e., ELISAs, lateral flow assays, and luciferase immunoprecipitation assays) was not possible, because many reports lacked those details. Importantly, these varying immunoassay formats will affect the time-dependent sensitivity and specificity of individual tests. For example, antibody to SARS-CoV-2 nucleocapsid has been reported to be more sensitive than spike protein early after infection (2).

As Deeks and colleagues acknowledge, the results of this meta-analysis of the operating characteristics of a heterogeneous mixture of assays should be interpreted with caution. Future studies will need to determine how well any immunoassay provides clinically useful information about protective immunity.

Funding

Department for International Development, UK; National Institute for Health Research, UK; and NIHR Birmingham Biomedical Research Centre at the University Hospitals Birmingham NHS Foundation Trust and the University of Birmingham, UK

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