Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Clinical Biochemistry 86 (2020) 34–35

Contents lists available at ScienceDirect

Clinical Biochemistry

journal homepage: www.elsevier.com/locate/clinbiochem

Letter to the Editor

Method comparison of SARS-CoV-2 serology assays involving three commercially available platforms and a novel in-house developed enzyme-linked immunosorbent assay

ARTICLE INFO

Keywords:
SARS-CoV-2
COVID-19
Serology
Antibody
ELISA
Comparison

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spurred the Coronavirus 2019 (COVID-19) global pandemic, causing clinical laboratories to rapidly implement tests for SARS-CoV-2. This testing rush led to the release of an abundance of SARS-CoV-2 serologic assays with questionable performance during the early months of the pandemic. These assays were distributed without requirement for prior review by the Food and Drug Administration (FDA) Emergency Use Authorization (EUA) pathway. Studies confirmed several assays had poor sensitivity and specificity, thus clinical laboratories had to exercise caution regarding which assays to adopt [1,2]. Given these issues, the University of Minnesota (UMN) developed an in-house serological SARS-CoV-2 assay in April [3]. In May, the FDA required all manufacturers to submit EUA applications for serologic testing which led to market removal of poorly performing tests and release of FDA-EUA approved assays. Therefore, we verified performance of three FDA-EUA approved commercial serological SARS-CoV-2 assays to provide high-throughput capability (> 10,000 tests/day), and compared them to our UMN method. Two assays detect "total" spike protein receptor binding domain (RBD) antibodies (UMN and Siemens ADVIA Centaur SARS-CoV-2 Total assay), and two detect nucleocapsid protein antibodies (Abbott SARS-CoV-2 IgG and Roche Cobas Anti-SARS-CoV-2). Commercial assays were performed according to manufacturer's instructions and the UMN assay was performed as previously described [3].

Results from 56 remnant serum specimens (N = 56 unique patients) are summarized in Table 1. 28 patients had COVID-19 infection confirmed by a polymerase chain reaction (PCR) assay. Negative patient specimens were either collected pre-pandemic (N = 25), had a negative PCR result (N = 1), or were tested for antibodies only (N = 2). Serum was collected an average of 16.7 (± 8.3) days after COVID-19 symptom onset (range: 6–35 days) and 9.7 (± 6.0) days after a positive PCR test (range: 2–22 days). In 22 of the 28 PCR-positive patients, antibodies were detected with all four assays. Two serum specimens from PCR-positive patients (collected 14 and 15 days post-symptom onset) were negative with all four tests. Additionally, one serum specimen (collected 6 days post-symptom onset) was positive for spike protein RBD antibodies (UMN/Siemens) and negative for nucleocapsid protein antibodies (Abbott/Roche). Another specimen (collected 7 days post-symptom onset) tested positive for nucleocapsid protein antibodies (Abbott/Roche) and negative for spike protein RBD antibodies (UMN/Siemens). In both cases, immature SARS-CoV-2 immune response could be the issue [3,4]. Two separate specimens tested positive with three of four assays, with one negative on the Siemens assay and the other negative on the Abbott assay.

In summary, all four SARS-CoV-2 serologic assays provided clinical sensitivities > 85%. The specificities and positive predictive values were 100% and negative predictive values were all > 87%. Reasons for discordance between assays are in need of further study, but likely derive from various factors including time from symptom onset or PCR positive result to collection, immune response variability, assay-specific cutoffs, or analytical performance. With the caveat of a small sample

Table 1
Sensitivity and specificity summary of SARS-CoV-2 antibody measurement procedures.

Measurement Procedure (Antigen, Ab* Isotype)	Positive Antibody Results/ Confirmed Positive PCR	Negative Antibody Results/ Prepandemic or Negative PCR	Sensitivity (95% CI)	Specificity (95% CI)	PPV*	NPV*
UMN (Spike RBD, Total Ab)	25/28	28/28	89.3% (71.8–97.7%)	100% (87.7–100%)	100%	90.3%
Siemens (Spike RBD, Total Ab)	24/28	28/28	85.7% (67.3–96.0%)	100% (87.7–100%)	100%	87.5%
Roche (Nucleocapsid, Total Ab)	25/28	28/28	89.3% (71.8–97.7%)	100% (87.7–100%)	100%	90.3%
Abbott (Nucleocapsid, IgG)	24/28	28/28	85.7% (67.3–96.0%)	100% (87.7–100%)	100%	87.5%

95% Confidence Intervals = 95% CI, were calculated using the Exact (Clopper-Pearson) formula.
* Antibody = Ab, PPV = Positive Predictive Value, NPV = Negative Predictive Value.

https://doi.org/10.1016/j.clinbiochem.2020.08.004
Received 14 July 2020; Accepted 8 August 2020
Available online 11 August 2020

size (N = 56 patients), this study suggests these four assays provide utility in detecting SARS-CoV-2 antibodies. These tests may provide critical data on COVID-19 prevalence to support pandemic countermeasure decision-making.

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