Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Seroprevalence: Navigating the Absence of a Gold Standard

Sahar Saeed[1], Sheila O'Brien[1], Anne-Claude Gingras[2], Karen Colwill[2], Kento Abe[2], David Fisman[3], Ashleigh Tuite[3], Heidi Wood[4], QiLong Yi[1], Steven Drews[1]

[1]Canadian Blood Services, Ontario, Canada

[2] Lunenfeld-Tanenbaum Research Institute at Mt. Sinai Hospital, Sinai Health System, Ontario, Canada

[3] Dalla Lana School of Public Health, University of Toronto, Ontario, Canada

[4] National Microbiology Laboratory, Public Health Agency of Canada, Winnipeg, Manitoba, Canada

Purpose /Objective

- Multiple assays to detect SARS-COV-2 antibodies are available but no gold standard exists.
- Due to many factors including waning antibodies and differences in test designs, discordance between SARS-CoV-2 serology assays is common.
- Given these limitations we used multiple assays and methodological approaches to estimate SARS-COV-2 seroprevalence during the first COVID-19 wave in Canada.

Methods

- This serial cross-sectional study was conducted using residual plasma from healthy blood donors between April-September 2020.
- We compared seroprevalence rates by multiple composite reference standards (CRS) and by a series of Bayesian Latent Class Models (BLCM) (using uninformative, weakly and informative priors).
- Using the BLCM we estimated assay characteristics, bimonthly to evaluate changes over time.

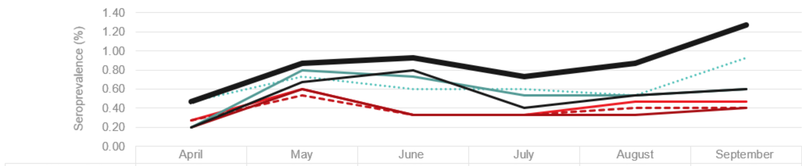
Table 1. Assay Characteristics.

Assay	Assay platform	Capture Antigen (IgG)	Manufacture	Cut-offs (positive)	Cut-off reference*
Abbott-NP	Chemiluminescent microparticle immunoassay	Nucleocapsid	Abbott	≥1.40	Manufacture
Spike	Chemiluminescent ELISA	spike	Gingras Lab	≥0.190	3 SD + negative mean
RBD	Chemiluminescent ELISA	RBD	Gingras Lab	≥0.186	3 SD + negative mean
NP	Chemiluminescent ELISA	Nucleocapsid	Gingras Lab	≥0.396	3 SD + negative mean

Results

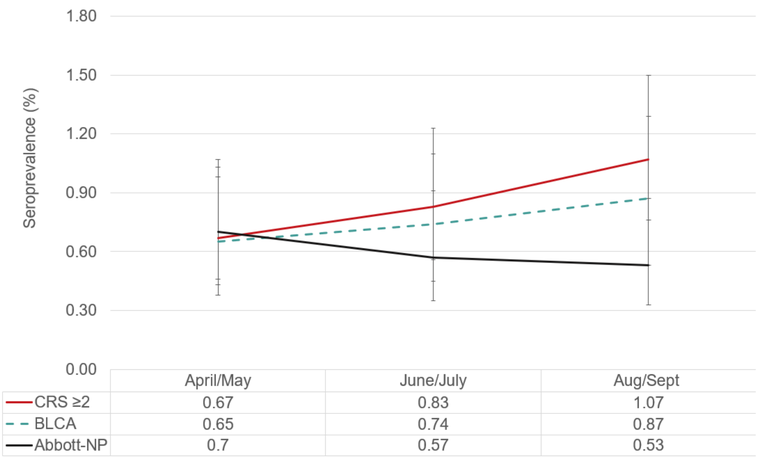
- In total, 8999 blood samples were tested.
- The Abbott-NP assay consistently estimated seroprevalence to be lower than the ELISA-based assays.
- Assay characteristics varied considerably over time.
- Overall RBD had the highest sensitivity 82.2% (69.3, 92.9%) with a specificity of 99.6% (99.4, 99.7%).
- In contrast the sensitivity of the Abbott-NP assay was the lowest and waned from 63.2% (41.4, 83.1%) in April/May to 33.9% (19.7, 53.1%) by August/September.

Figure 1. Seroprevalence by month over the first COVID-19 wave in Canada by various composite reference standards (results from four anti-SARS-CoV-2 immunoassays).



	April	May	June	July	August	September
Abbott+Spike	0.27	0.60	0.33	0.33	0.47	0.47
Abbott+RBD	0.27	0.53	0.33	0.33	0.40	0.40
Abbott+NP	0.20	0.60	0.33	0.33	0.33	0.40
Spike+RBD	0.47	0.73	0.60	0.60	0.53	0.93
Spike+NP	0.2	0.8	0.73	0.53	0.53	0.6
RBD+NP	0.20	0.67	0.80	0.40	0.53	0.60
Any two or more	0.47	0.87	0.93	0.73	0.87	1.27

Figure 2. Fig 3. Summary comparison of seroprevalence rates by analytical methods.



	April/May	June/July	Aug/Sept
CRS ≥2	0.67	0.83	1.07
BLCA	0.65	0.74	0.87
Abbott-NP	0.7	0.57	0.53

Discussion

- In the absence of a gold standard, we evaluated multiple assays and methodological approaches to estimate SARS-CoV-2 seroprevalence in healthy Canadian blood donors.
- None of the individual assays resulted in seroprevalence increasing monotonically over time.
- Seroprevalence estimates were similar by either BLCM or a composite reference standard when at least two positive assays (out of four) were used to determine a "true" result.
- However, by using the BLCM, we were able to derive time-updated test characteristics that could be used to adjust for waning antibody signals.

Summary/Conclusions

- Regardless of the analytical method we found at the end of the first COVID-19 wave, SARS-CoV-2 seroprevalence among a healthy population of blood donors was low (<2%).
- While the sensitivity of all assays waned, the rates did vary.
- We found significant limitations to using a single assay to estimate SARS-CoV-2 seroprevalence in a low prevalence setting, such as healthy Canadian blood donors during the first wave of the COVID-19 pandemic.

References

Sahar Saeed et al.
medRxiv 2021.05.11.21256992; doi: https://doi.org/10.1101/2021.05.11.21256992

Abstract ID: 9260
Poster number: P-PH-3

Acknowledgements

The authors would like to thank CBS and NML operations staff for undertaking laboratory testing. SJD received funding through the Canadian Institutes of Health Research (VR2-172723) and Alberta Innovates (G2020000360 Drews), ACG received funding through the Krembil Foundation to the Sinai Health System Foundation. The robotics equipment used for the ELISA assays is housed in the Network Biology Collaborative Centre at the Lunenfeld-Tanenbaum Research Institute (ACG), a facility supported by Canada Foundation for Innovation funding, by the Ontarian Government and by Genome Canada and Ontario Genomics (OGI-139). Commercial Abbott Architect SARS-Cov-2 IgG assay kit costs were partially supported by Abbott Laboratories, Abbott Park, Illinois. Abbott analyzers used at Canadian Blood Services were provided by the COVID-19 Immunity task Force (CITF). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Canadian Blood Services
BLOOD PLASMA STEM CELLS ORGANS & TISSUES