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SYNOPSIS

03/25/2020

Review of "Profiling early humoral response to diagnose novel coronavirus disease (COVID-19)"

Article citation: Guo L, Ren L, Yang S, Xiao M, Chang, Yang F, et al. Profiling early humoral response to diagnose novel coronavirus disease (COVID-19). Clin Infect Dis. 2020 Mar 21 [Epub ahead of print]. Available from: https://dx.doi.org/10.1093/cid/ciaa310

One-Minute Summary

- This study examines **antibody (Ab) production** in coronavirus disease 2019 (COVID-19) patients and assesses the role of serology in diagnosis.
- **208 plasma samples** were collected from **82 confirmed** and **58 probable cases.**
- Of samples collected within 7 days post symptom onset (PSO) (i.e., acute phase), **35/41 (85.4%) were IgM-positive, 38/41 (92.7%) were IgA-positive**, and the **median time to detection for both was 5 days** (interquartile range [IQR] 3-6). Levels of IgM and IgA increased significantly from the first week to the second week of illness and plateaued by day 15 PSO.
- Of all samples (collected between day 1-39 PSO), **162/208 (77.9%) were IgG-positive** and the **median time to detection was 14 days** (IQR 10-18). Levels of IgG increased significantly in the first 3 weeks and then plateaued after 21 days PSO.
- **IgM positivity was higher in probable cases (54/58 [93.1%])** than in confirmed cases (62/82 [75.6%]).
- **Compared to PCR, the IgM detection rate was lower in the first 5 days PSO (100% for PCR vs. 71.4% for IgM) but was higher afterwards (44.3% for PCR vs 87.9% for IgM)**. When combining PCR and IgM, the overall detection rate increased to >90% compared to ~50% for PCR alone, for all samples tested within 25 days PSO.
- Among 26 confirmed cases with serial sampling, 6 had an initial PCR-negative throat swab but were IgM-positive. Additionally, investigation of a familial cluster (N=6) found that three members were PCR-negative but IgM-positive.
- The authors suggest that the **PCR supplemented with IgM can improve detection of COVID-19.**

Additional Information

- Paired throat swabs and blood samples were collected from **two cohorts of COVID-19 patients** taken between 1-39 days of disease onset: 1) 101 (n=169 samples) inpatients from Wuhan, China (January 2020), including 43 confirmed cases (20 severe, 23 mild/moderate) and 58 probable cases; and 2) 39 (n= 39 samples) confirmed cases from Beijing, China (8 severe, 31 mild).

- Confirmed cases were defined as detection of viral RNA by real-time PCR or sequencing. Probable cases were based on clinical manifestations, chest X-rays and epidemiological link to confirmed cases but RNA was not detected (i.e. PCR test was negative).
- Plasma from patients with non-COVID-19 acute lower respiratory tract infections (n=135) and healthy patients (n=150) were used as a control.
- Enzyme-linked immunosorbent assay (ELISA) was used for Ab detection using a recombinant nucleocapsid (N) protein from COVID-19. The **recombinant N protein did not cross-react with IgG against seasonal coronaviruses (CoV-229E, CoV-NL63, CoV-OC43, CoV-HKU1); however, there was cross reactivity with SARS-CoV Ab**.

PHO Reviewer's Comments

- The authors acknowledge that using cross-sectional sampling introduces variability in the timing of sample collection since symptom onset, leading to variation in appearance of antibodies.
- In the cross-reactivity studies, human plasma was tested at a dilution of 1:400. It is possible that cross-reactivity may be seen with undiluted plasma. Further, cross-reactivity with other viruses or other known interfering factors (e.g., Heterophile Ab, rheumatoid factor) was not determined.
- Higher IgM positivity in probable cases compared to confirmed cases is an interesting finding. It is possible that probable cases were diagnosed later in the course of illness when viral load is lower and therefore undetectable by PCR. This timing would correlate with the rise of IgM.

Citation

Ontario Agency for Health Protection and Promotion (Public Health Ontario). Review of "Profiling early humoral response to diagnose novel coronavirus disease (COVID-19)". Toronto, ON: Queen's Printer for Ontario; 2020.

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