Evaluation of Three Anti-SARS-CoV-2 Serologic Immunoassays for Post-Vaccine Response

Article:
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Guest: Drs. Ashley Di Meo and Jessica Miller are second year clinical chemistry fellows in the Department of Laboratory Medicine and Pathobiology at the University of Toronto.

Randye Kaye: Hello, and welcome to this edition of JALM Talk from the *Journal of Applied Laboratory Medicine*, a publication of the American Association for Clinical Chemistry. I'm your host, Randye Kaye.

COVID-19 vaccines have now been widely administered and many countries are recommending booster doses. However, questions still remain about the longevity and variability of antibody responses to vaccination in different individuals.

Further, there are now several commercially available SARS-CoV-2 antibody tests. Many of these tests provide quantitative detection of antibodies to the virus but further studies are needed to be able to better interpret these quantitative results in the context of vaccine response and immunity.

An original article in the January 2022 JALM Special Issue on Autoimmune Diagnostics described the evaluation of quantitative serologic antibody response in a cohort of 98 participants following the administration of either a single dose or both doses of an mRNA SARS-CoV-2 vaccine. The study compared the participants' antibody test results across three different anti-SARS-CoV-2 immunoassays.

On today's podcast, we are joined by the co-first authors of this article, Drs. Ashley Di Meo and Jessica Miller are second year clinical chemistry fellows in the Department of Laboratory Medicine and Pathobiology at the University of Toronto. They completed the study under the mentorship of the article's senior author, Dr. Vathany Kulasingam.

Welcome Drs. Di Meo and Miller. Dr. Miller, the first question is for you. Can you tell us about what led you to conduct this study and how it was designed?

Jessica Miller: Thank you for having us on your podcast today. And then regarding what led us to conduct the study, we

actually had the fortunate opportunity working at University Health Network. And so we had access to a large population of health care workers that had early access to the vaccine, and then we are also fortunate to have access to the antibody assays against SARS-CoV-2 from three companies so including Roche Diagnostics, DiaSorin as well as Abbott.

And so because of this, we set out to compare the diagnostic performance of these assays in our study cohort as well as analyzing the changes in antibody titers over time. And then posing the question of whether extended time between doses actually had an effect on these antibody titers. And then in terms of our study design, we actually set a selection criterion where only those that had received their first dose of the vaccine at least three weeks prior could participate.

And so, in total we had 98 serum samples, 88 of them came from healthcare workers from the University Health Network. And then all 88 of these healthcare workers had received the COVID-19 vaccine from Pfizer, specifically; 39 of them had received only the first dose, while 49 of the 88 had received both doses of the vaccine.

And then finally, we also had a really unique opportunity to have access to 10 serum samples from patients who had received solid organ transplants. And so, in terms of this study cohort, there were 10 patients, 5 of them had received 2 doses of the Pfizer vaccine and then 5 had received 2 doses of the Moderna vaccine.

Randye Kaye: All right, thank you. So, let's talk about your results. What did the results tell you about the antibody levels in healthcare workers after their first and their second vaccine doses?

Jessica Miller: Yeah, for sure. So first, I'll just quickly talk about the assay performance and how we compared the different assay from the different companies. So among the 88 health care workers, we use the predefined assay-specific threshold to consider a result as either positive or negative.

And then all 88 of the patient samples had antibody levels considered positive by Roche, and so that would mean that it had a sensitivity of 100%. 86 of the 88 were considered positive by DiaSorin so that had a sensitivity of 98%. And then 87 of the 88 participants

were considered positive by Abbott so having a sensitivity of 99%. And so overall, the ability of these assays were really able to correctly identify positive antibody titers in these participants and so had a really high sensitivity.

And then one thing I just want to point out is that the absolute values that are generated from each of these assay platforms are not interchangeable so the test does lack standardization and harmonization. And so you can really only consider the raw results within the context of each specific platform and their reference intervals and the package inserts.

And then, in terms of the antibody titers for our results, our results match other publications. So, there's a statistically significant decrease in antibody levels over time which we sort of are well aware of now.

And then, in particular, following administration of a single dose of the Pfizer vaccine, the antibody levels had significantly decreased four weeks after receiving the vaccine. And then in those that received both doses of the vaccine, the antibody titer significantly decreased after about five weeks of administration.

Which I say is pretty interesting because at the time of the study this was first carried out, so this was in March of last year when we started this study, both the Pfizer and Moderna vaccines were approved for a 2-dose schedule with either 21 or 28 days apart but due to limited vaccine supply at the time the public health officials had actually extended the time between dose.

And so, showing one result that we showed in our study is that with increasing time between dose one and dose two there is actually higher antibody titers. And so this really actually supported the decision made by the public health officials at the time.

Randye Kaye: All right. Thank you. So, Dr. Di Meo, let me ask you this one. Dr. Miller mentioned that cohort of solid organ transplant patients. So, what can you tell us about the vaccine response in that cohort?

Ashley Di Meo: So, of the ten patients that were included in the cohort, five received both doses of the Pfizer vaccine while the remaining five received both doses of the Moderna vaccine. So, although this cohort was small, we did observe significantly decreased antibody

responses in these patients compared to our cohort of healthcare workers.

So this has also been observed in the context of other vaccine programs with patients who have received a solid organ transplant. In fact, previous reports also suggest that transplant recipients generate a less robust immune response to vaccines compared with non-transplant patients regardless of the type of vaccine.

So, solid organ transplant recipients have relative humoral response rates that are approximately 50 to 70% of those seen in non-transplant populations, which supports the findings of our study.

Randye Kaye: Wow. Thank you. That's very interesting. So, besides that, what would you say are the clinical implications of your study?

Ashley Di Meo: So, with the increasing availability of the vaccinations against SARS-CoV-2, it is important to compare the clinical performance of serological assays that detect antibodies to SARS-CoV-2.

And in this study, we really compared the post vaccination antibody response in 98 participants across 3 serologic SARS-CoV-2 immunoassays and all 3 assays, while not interchangeable, showed greater than 90% sensitivity for detecting vaccine response. So, we also demonstrated that antibody levels decreased with increased time between vaccine administration and blood draw for the first and second dose.

While there have been significant changes to the COVID-19 situation since our study was completed, including the emergence of this new Omicron variant and the implementation of additional vaccine boosters, our study does help to showcase that the decreasing antibody titers with time. Thus supporting the need for vaccine boosters in order to maintain immunity and help protect individuals against COVID-19.

Randye Kaye: All right. Thank you. So, here's my final question. What do you think the future holds for SARS-CoV-2 serology testing? What value will this testing serve in the future?

Ashley Di Meo: This is a great question Randye. So with the introduction of COVID-19 vaccines, I think we can all agree that there was a lot of excitement surrounding

the potential role of serology testing. Could a simple blood test reveal whether the vaccine was working, or later be used as an indicator to guide the rollout vaccine boosters?

So, we now know that the presence of SARS-CoV-2 antibodies does not necessarily correlate with COVID-19 immunity. And so, as we start to look to the future of SARS-CoV-2 serology testing, not only will it be important to establish an international standard to allow direct comparison of assay between laboratories, but population-based studies linking quantitative serology results to clinical outcomes will also be necessary to help determine what level of antibody correlates with COVID-19 immunity.

And then looking forward to the value of serology testing in the future, I think it will continue to support evidence-based decision-making for public health recommendations.

Randye Kaye: All right, very interesting. Thank you both so much for joining us today.

Ashley Di Meo: Thank you Randye.

Jessica Miller: Thank you Randye.

Randye Kaye: That was Drs. Ashley Di Meo and Jessica Miller from the University of Toronto discussing the JALM original article entitled "Evaluation of Three Anti-SARS-CoV-2 Serologic Immunoassays for Post-Vaccine Response." This article is part of JALM's January 2022 Special Issue entitled: "Autoimmune Diagnostics: Fundamentals to Cutting Edge". Thanks for tuning in to this episode of JALM Talk. See you next time, and don't forget to submit something for us to talk about.