Antibody Response To COVID-19 Infection and Vaccines

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Introduction

In this report, one of the first known comparisons is made between antibody responses in individuals vaccinated against or infected by the SARS-CoV-2 virus. Serum blood samples were collected from 7 individuals and tested with a surrogate virus neutralization test (sVNT). Samples from six of those individuals were also tested with SARS-CoV-2 S1 IgM and IgG ELISA.

The study includes men and women aged between 19 and 62 years old. Only one participant does not have a pre infection or vaccination sample. Post-vaccine samples were taken after the first vaccination. No boosters had been administered in the study cohort.

Results

Study Cohort

The cohort is composed of 4 vaccinated, 2 naturally infected and 1 PCR negative individual. Of the four who were vaccinated, all had a pre-vaccination baseline sample. Within the vaccine group, 2 received the Moderna vaccine and 2 received the Pfizer vaccine.

The natural infection group contains an individual who had both pre- and post-infection samples, as well as a PCR-positive test result. One other person had a post-infection sample, but not a baseline sample. This individual was assumed positive after a direct exposure and subsequent COVID-19 like illness.

This study participant who serves as the negative control submitted two samples, one of which was taken after a negative PCR result.

Average sample time after SARS-CoV-2 infection was 31.5 days. Post-vaccination sample timepoints after the first vaccination averaged 22.5 days and ranged from 14 days to 25 days. All vaccinated individuals received their first vaccination but not a booster shot.

Surrogate Virus Neutralization

All post infection and post vaccination samples were positive by the sVNT while the PCR negative control tested negative.

Each vaccinated individual tested positive for surrogate virus neutralization after previously testing negative (Figure 1). Their average neutralization value before vaccination was 0.03% but after vaccination it was 61%.

Both naturally infected individuals tested positive. Their average neutralization was 66%. The individual with both pre- and post-infection samples was negative prior to infection.

The average neutralization value for the two Pfizer vaccine recipients was 67%. For those receiving the Moderna vaccine the average value was 56%.

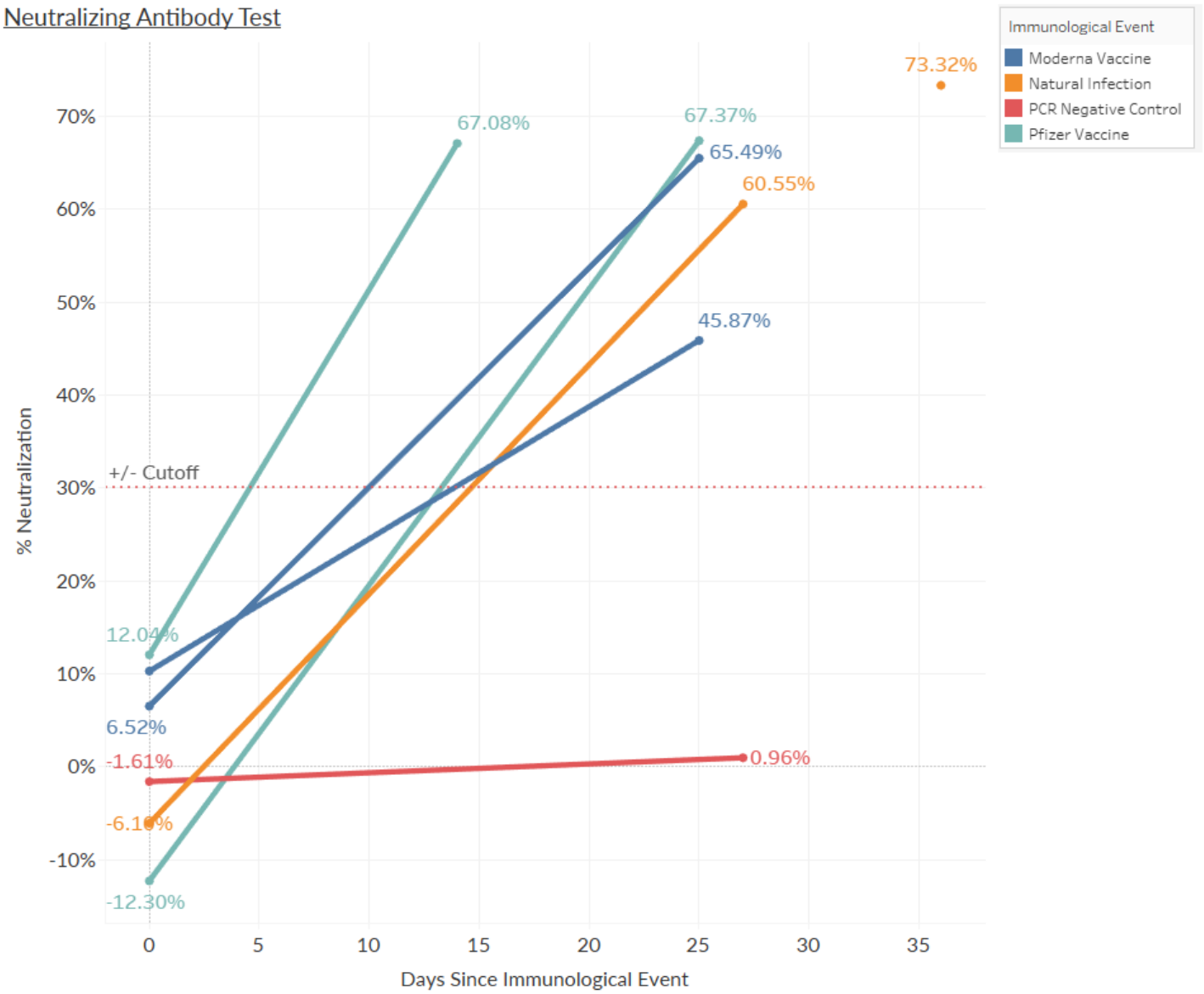

Figure 1. Percent neutralization from SARS-CoV-2 Spike S1 sVNT. The reference band at 30% represents the positive/negative cutoff generated by the negative control. The single orange point is from a naturally infected individual who does not have a matching pre-infection sample.

IgG and IgM ELISA

All samples that tested positive with the sVNT also tested positive for IgG antibodies (Fig 2). Only one sample tested positive for IgM antibodies.

The IgM positive sample also tested positive for neutralizing and IgG antibodies and was taken 14 days after the first Pfizer vaccine dose.

Before vaccination or natural infection, all samples were negative for both IgG and IgM.

One study participant was tested for sVNT but not IgG or IgM antibodies.

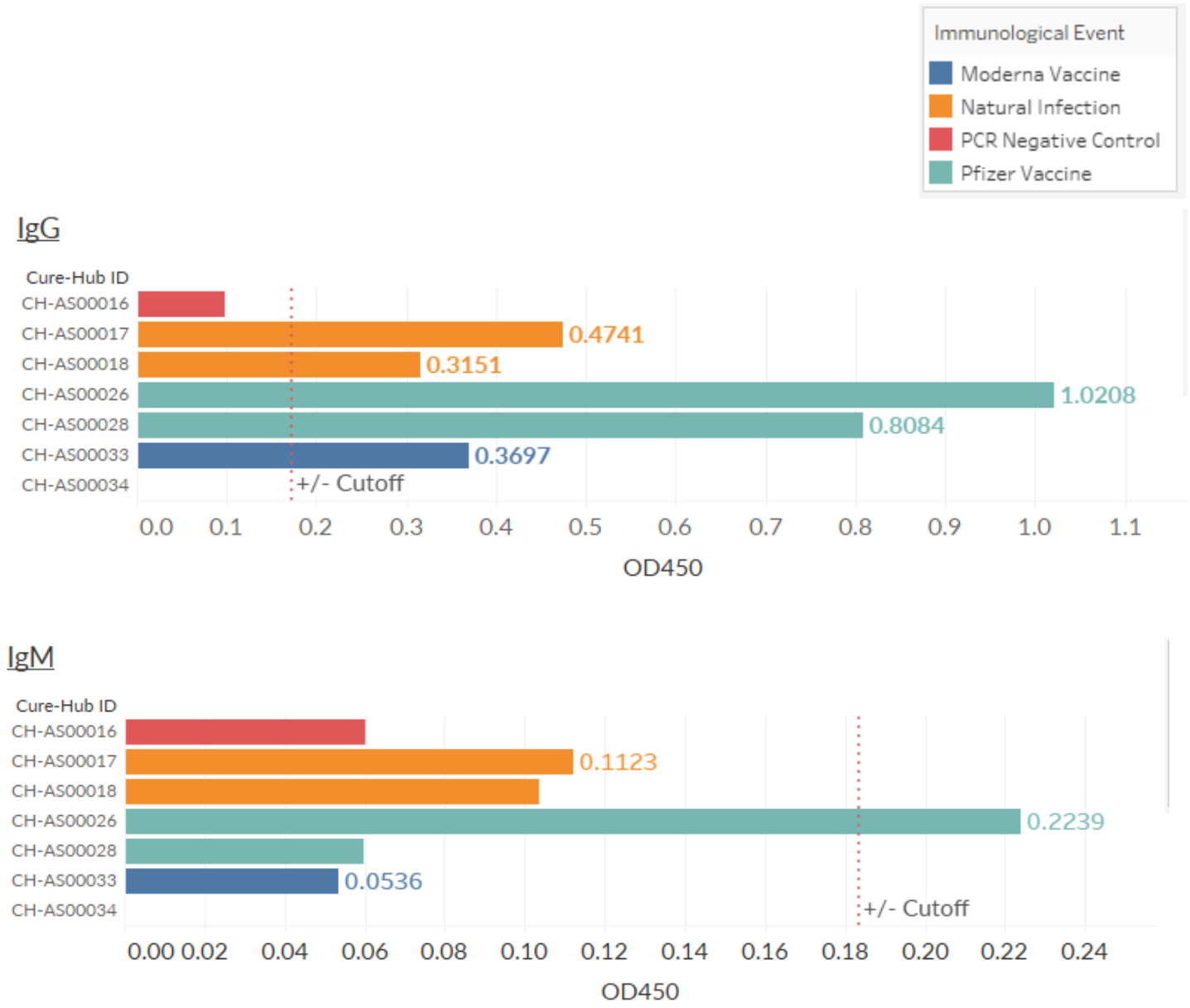

Figure 3. Optical Density 450nm values from SARS-CoV-2 S1 IgG and IgM ELISAs.

Methods

After informed consent was obtained, blood was collected by fingerstick or venipuncture into a lithium heparin coated microtainer or a marble top SST tube.

Fingerstick Sample Collection

The Cure-Hub sample collection kit was mailed or given to individuals for capillary, whole blood collection. Samples were obtained with a fingerstick and lithium heparin microtainer with PST gel. Samples were either mailed or given back to Cure-Hub. After Cure-Hub received the study participant's sample tube, the microtainer was centrifuged for 5 minutes at 1600xg. The serum layer was removed and stored at -20deg C˚.

Venipuncture sample collection

After venous collection into a marble top SST tube, blood was allowed to clot for 30min-60min, then centrifuged for 10 minutes at 1600xg. The serum layer was removed and stored at -20deg C˚.

IgG and IgM ELISA

SARS-CoV-2 Spike S1 IgG and IgM ELISA (Genscript, Catalog # L00831) was performed on all samples. Prior to running the ELISA, all reagents were brought up to room temperature. Serum samples were diluted in kit manufacturer's dilution buffer. Samples were diluted 1:100 and 100uL was run on the ELISA according to the manufacturers protocol. Optical Density (OD) values were read with 450nm absorbance on a plate reader.

Surrogate Virus Neutralization Test

Serum neutralization of SARS-CoV-2 S1 RBD was tested with the Genscript cPASS sVNT kit (Catalog # L00847). Prior to running the sVNT assay, all samples and reagents were brought up to room temperature. Samples were diluted 1:100 in the kit manufacturer's dilution buffer. A stock solution of RBD-HRP reporter was made with a 1:1,000 dilution in RBD-HRP dilution buffer. Then 60uL of diluted sample was combined with 60uL of the stock RBD-HRP solution. The 120uL neutralization reaction was performed at 37deg C˚ for 45 minutes, then 100uL of the reaction was loaded on the extracellular ACE2 coated capture plate and incubated for 20 minutes at 37deg C˚. After washing and development with TMB, OD values were read with 450nm absorbance on a plate reader. Interpretation of results was carried out according to manufacturer's provided calculation:

$$\text{Inhibition \%} = (1-(\text{OD Value of Sample}/\text{OD Value of Negative Control})) \times 100$$

Background

SARS-CoV-2 emerged from Wuhan, China in the Winter of 2019. On March 11, 2020, the World Health Organization (WHO) declared COVID19, the disease caused by SARS-CoV-2, to be a global pandemic. To this date COVID-19 has infected tens of millions of people and caused over a million deaths.

Mitigation efforts have varied widely, between countries and even within the United States. Despite the various efforts to stop or slow the virus, a vaccine has always been the best hope to put the COVID-19 pandemic behind us.

In the Spring of 2020, the United States government launched Operation Warp Speed. The goal of this program was to accelerate production of therapeutics and develop vaccines in record time.

On December 11th, 2020, nine months after the WHO declared COVID-19 to be a global pandemic, Pfizer, was granted Emergency Use Authorization (EUA) for their vaccine, Tozinameran. One-week later another pharmaceutical company, Moderna, was granted an EUA for their own COVID-19 vaccine.

Vaccine distribution was initiated and in December of 2020, the most high-risk groups received their first vaccinations.

With vaccine rollout, there are questions about vaccine effectiveness and how immune protection compares between vaccines and natural infections.

To address these questions Cure-Hub tested serum from vaccinated and naturally infected individuals with a surrogate virus neutralization test and IgG and IgM ELISAs. Serum samples were obtained from individuals who agreed to participate in the Cure-Hub citizen science project.

Discussion

The data presented here is the first known, direct, head-to-head comparison between the immune response generated by both COVID-19 vaccines and natural infections.

Despite the small sample size, the results indicate that just one dose of the Pfizer and Moderna vaccines can elicit an antibody response comparable to an individual who has had COVID-19.

Although there is variation between vaccines, this variation is within the expected inter-assay variability.

A larger sample size may smooth out those differences.

A results dashboard can be viewed at: Vaccines vs Natural Infection | Cure-Hub (cure-hub.com).

The dashboard will be a 'living figure' that is updated and modified as more data comes in.