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Short communication

IgG antibody production and persistence to 6 months following SARS-CoV-2 vaccination: A Northern Ireland observational study

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ABSTRACT

Background: This study evaluates spike protein IgG antibody response following Oxford-AstraZeneca COVID-19 vaccination using the AbC-19™ lateral flow device.
Methods: Plasma samples were collected from n = 111 individuals from Northern Ireland. The majority were >50 years old and/or clinically vulnerable. Samples were taken at five timepoints from pre-vaccination until 6-months post-first dose.
Results: 20.3% of participants had detectable IgG responses pre-vaccination, indicating prior COVID-19. Antibodies were detected in 86.9% of participants three weeks after the first vaccine dose, falling to 74.7% immediately prior to the second dose, and rising to 99% three weeks post-second vaccine. At 6-months post-first dose, this decreased to 90.5%. At all timepoints, previously infected participants had significantly higher antibody levels than those not previously infected.
Conclusion: This study demonstrates that strong anti-spike protein antibody responses are evoked in almost all individuals that receive two doses of Oxford-AstraZeneca vaccine, and which largely persist beyond six months after first vaccination.

1. Introduction

The global impact of the COVID-19 pandemic resulted in a race to find a safe and effective vaccine. In December 2020, the Pfizer BioNTech (PFZ) vaccine was approved for use in the UK, shortly followed by the ChAdOx1 Oxford-AstraZeneca (OAZ)[1] vaccine. The OAZ vaccine, an adenovirus vector vaccine is a modified, non-replicating, chimpanzee adenovirus which contains DNA coding for SARS-CoV-2 spike protein [1]. The first data on efficacy showed it was 64% effective after first dose and 70% after second [1]. SARS-CoV-2 neutralising antibodies were reported in 91% of participants following the first dose, and 99–100% following a second dose [2,3].

The UK Rapid Test Consortium (UK-RTC) was founded in response to a UK Government call for development of a rapid antibody test for use nationally. The consortium developed the AbC-19™ lateral flow device (LFD) antibody test now approved in Europe and UK for professional use and is available for sale. AbC-19™ is an easy-to-use, accurate and reliable neutralising antibody rapid test indicating positive antibody response post-infection or presence of neutralising antibodies post-vaccine [4]. Testing can take place in a wide range of environments and by a range of individuals from varying educational backgrounds as shown in our previously published data [5].

Antibody testing is vital to inform understanding of the prevalence of SARS-CoV-2 virus in the population. It is important for understanding response to emerging variants, detecting differences in levels of immunity (vaccinated immunity versus infection-acquired immunity) and their durability. Strategic antibody screening will inform the need for boosters and vaccination strategies globally [6].

This study assesses SARS-CoV-2 IgG antibody status at five timepoints during vaccination against COVID-19 disease with the OAZ vaccine using the AbC-19™. We also assess natural COVID-19 infection before and during these six months and report the impact of infection pre- and post-vaccination on antibody levels.

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[1] OAZ – Oxford-AstraZeneca ChAdOx1 COVID-19 Vaccine.

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2. Methods

The study was an observational study conducted over 5 time-points (up to 6 months post-first dose) on patients scheduled to receive the OAZ COVID-19 vaccine. The study was approved by the South Birmingham Research Ethics Service (REC 20/WM/0184, IRAS 286041) and all participants provided fully informed written consent prior to taking part. All work was carried out in accordance with the Declaration of Helsinki.

Participants were recruited by word-of-mouth or recruitment poster on the day of their first or second vaccination at a GP clinic in Belfast, Northern Ireland. A small number of participants (n = 12) were enrolled at the time of their second vaccination, so were only sampled at two timepoints. All participants provided informed consent, basic demographic information and details of any previous positive SARS-CoV-2 test result using REDCap electronic data capture tools hosted at Ulster University (*https://www.project-redcap.org/*). PANDEMIC study participants that had previously tested positive for COVID-19 were also invited to join the study via email. Participants were eligible for the study if they were over 18 years of age and could attend a blood sample clinic at the time of their first or second vaccination. Exclusion criteria included anyone with a blood disorder or contraindication to giving a blood sample, or anyone currently exhibiting symptoms of COVID-19. Samples were taken at five time-points: just before first vaccination (TP1), 3 weeks after first vaccination (TP2), just before second vaccination (TP3), 3 weeks after the second vaccination (TP4) and 6 months following first vaccination (TP5), as shown in Supplementary Table 1.

An EDTA-plasma (10 ml) sample was collected at each time point from each participant. All blood samples were processed within 2 h of collection in refrigerated centrifuges (15 min, 3000 rpm, 4 °C). Samples were stored at −80 °C until analysis. Analyses were performed on AbC-19™ at Ulster University according to manufacturer's instructions. Assays were performed with samples in batches of 10, with one researcher adding 2.5 μL of EDTA-plasma to the assay and a second adding 100 μL of buffer immediately following sample addition. After 20 min, the strength of resulting test line was scored, independently by three experienced blinded observers, from 0–10 according to a visual score card (Figure S1). In qualitative mode, a score ≥1 is positive. Using the semi-quantitative approach, scores of 1, 2 and 3 are low positive whilst scores of 4, 5, 6, 7, 8, 9 and 10 are high positive.

All data was analysed using Microsoft Excel and GraphPad Prism 9 with figures generated in Prism. Differences between RT-PCR positive and no RT-PCR results were analysed using two tailed unpaired Welchs *t*-test and 6 months post vaccine group compared by Brown-Forsythe and Welch one-way ANOVA.

3. Results

We assessed SARS-CoV-2 IgG antibody status in a total of 111 participants using the AbC-19™ at five timepoints to determine antibody response to OAZ vaccination. AbC-19™ results were graded quantitatively, then classified semi-quantitatively as directed by the manufacturer: test lines were graded as negative, low positive or high positive as described above (Figure S1).

The initial samples were collected at a Belfast GP clinic during March 2021, when access to vaccination was limited to those aged 50 years and above, or those classified as vulnerable or clinically extremely vulnerable. A small number of participants were recruited from previous PANDEMIC study phases who were eligible for vaccination and previously tested positive for COVID-19 [4]. The cohort consisted of 55% female (n = 61, aged 28–89 years, median 51 years) and 45% male (n = 50, aged 24–82 years, median 51 years) subjects, with an overall age range of 24–89 years (median 51 years old). A total of n = 14 participants had tested positive by RT-PCR for SARS-CoV-2 infection before being vaccinated, with a range of 47–219 days (median 104 days) between the positive result and first vaccination.

Samples were collected from n = 94 participants at the time of first vaccination (TP1) with n = 75 (79.7%) scoring negative by AbC-19™ (n = 4 previously infected, Fig. 1). 14 samples scored low positive (14.9%) and 5 scored high positive (5.3%). Of the 19 participants with a positive result (n = 14 low positive, n = 5 high positive) at 1st dose, 8 had previously reported that they had been infected with COVID-19 (n = 5 low, n = 3 high; Fig. 1).

Participants (n = 89) were sampled again at 3-weeks post-first vaccination (TP2). By this time, 86.5% (77/89) of participants had antibodies detectable by AbC-19™: 45/77 were scored as low positive and 32/77 as high positive. All previously infected participants had detectable antibodies (Fig. 1). Two of the three participants, not reported as previously RT-PCR positive but AbC-19™ positive, and presumably seropositive at 1st dose, had a robust IgG response, comparable to RT-PCR positive participants, with low positive AbC-19™ scores at TP1 and high positive scores at TP2 (Figure S2).

At time of second vaccination (TP3), antibody levels had fallen. The number scoring as high positive reduced to 16 (from 32 at TP2) and the number scoring negative for SARS-CoV-2 IgG increased to 25 (from 12 at TP2). Overall, 75.7% (78/103) of participants showed detectable antibodies as either low or high positive.

Three weeks after the second dose (TP4), all but one participant showed antibodies detectable by AbC-19™ (99%, 101/102). 30 participants had low positive scores (29.4%) while 71 had high positive scores (69.6%). These data indicate a robust IgG response to OAZ vaccination (Fig. 1).

Participants were sampled again 6 months after receiving their first vaccination (TP5), and antibody levels remained detectable in 86/95 (90.5%) of participants, including all who were infected prior to first vaccination (n = 10 sampled). The proportion of high positive AbC-19™ scores reduced somewhat to 38/95 (40%) while 47/95 (49.5%) had low positive antibody levels.

Overall, antibody levels increased at 3 weeks after each dose of vaccine, while there was a slight drop in AbC-19™ score before the second dose and a larger drop over the 6 months following second dose (Figure S2). Individuals with a reported previous COVID-19 infection had a significantly higher quantitative AbC-19™ score than those without at all timepoints ($p < 0.05$ to $p < 0.0001$), with the largest difference seen between these groups at TP2 (Fig. 2a-e). After providing a sample at TP4, five participants became infected with SARS-CoV-2 (and tested positive by RT-PCR) all of whom scored high positive by AbC-19™ at TP5, with scores significantly higher than doubly vaccinated, uninfected participants ($p < 0.0001$, Fig. 2e). Infection prior to vaccination had no signifi-

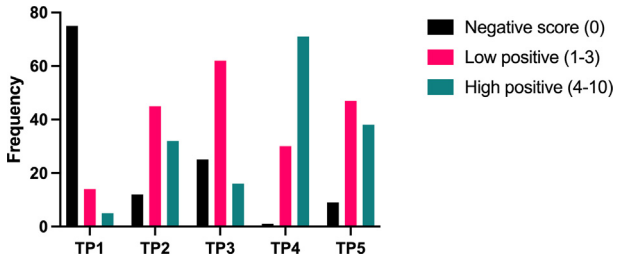

Fig. 1. Semi-quantitative scoring of AbC-19™ result for participants at five time points. TP1 = before 1st vaccination, TP2 = 3 weeks after 1st vaccination, TP3 = before 2nd vaccination, TP4 = 3 weeks after 2nd vaccination and TP5 = 6 months after 1st vaccination.

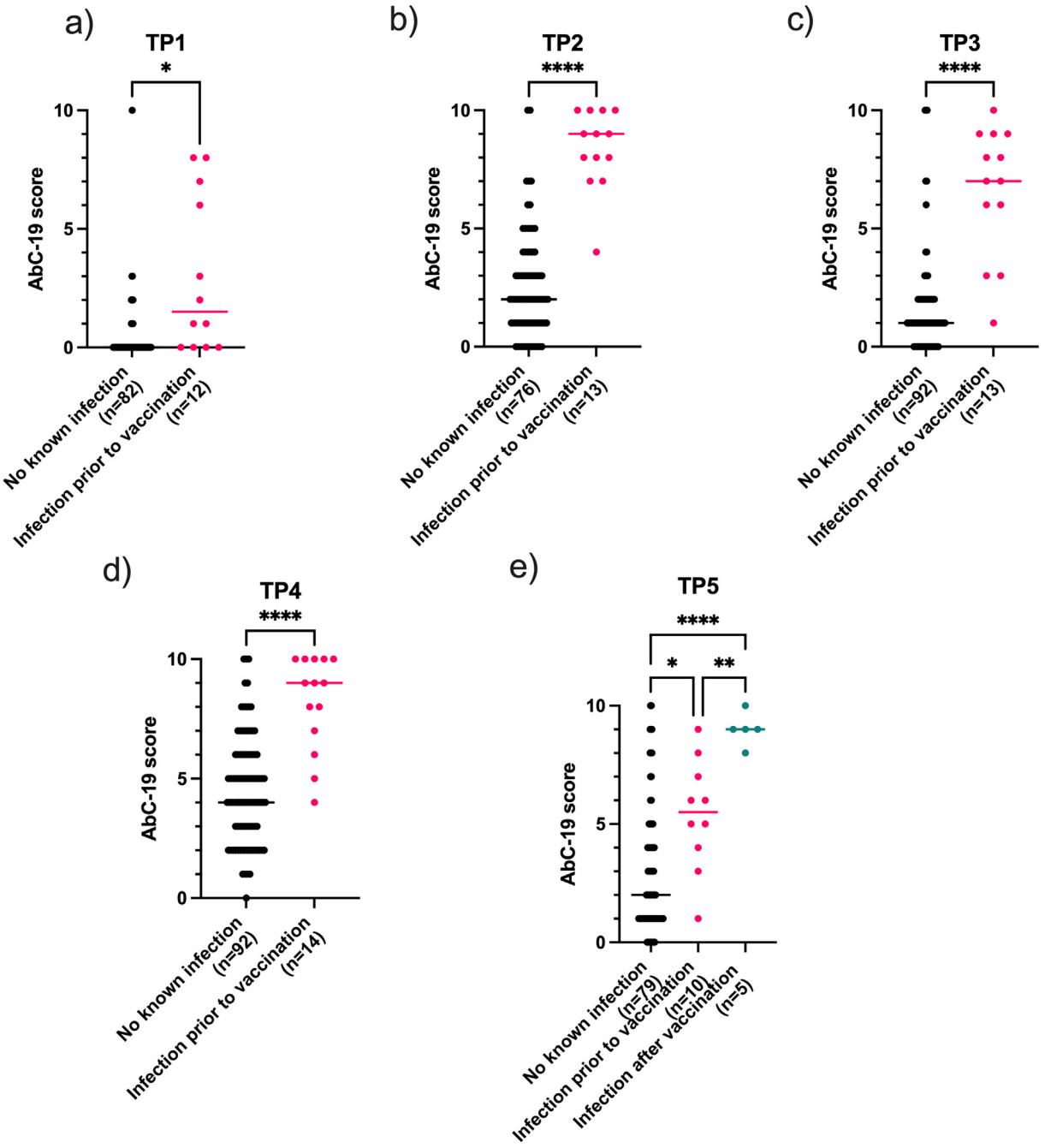

Fig. 2. AbC-19™ quantitative score between previously RT-PCR positive, no known infection groups and infection after vaccination at all time points (where relevant). TP1 = before 1st vaccination, TP2 = 3 weeks after 1st vaccination, TP3 = before 2nd vaccination, TP4 = 3 weeks after 2nd vaccination and TP5 = 6 months after 1st vaccination. Differences in means analysed using Welchs two-tailed unpaired *t*-test or Brown-Forsythe and Welch ANOVA (median *=p < 0.05, **P < 0.01, ****=p < 0.0001).

cant effect on the reduction in AbC-19™ scores observed between the two final timepoints (no infection- mean change −1.772, infection prior to vaccination mean change −3.1, p = 0.128, Fig. 3).

4. Discussion

We have previously shown good laboratory validation performance metrics for AbC-19™ detection of SARS-CoV-2 spike protein IgG antibody in a laboratory-based setting with a sensitivity of 97.58% (95% CI, 95.28%-98.95%) on a cohort of known positives, and specificity of 99.59% (95% CI, 98.53 %- 99.95%) on known negatives, including 223 pre-pandemic samples [4]. We demonstrated excellent overall agreement between antibody levels when measured by three other immunoassays (Roche Elecsys Anti-SARS-CoV-2 IgG/IgA/IgM against the SARS-CoV-2 Nucleocapsid antigenic region (Roche Diagnostics, Basel, Switzerland), the Abbott SARS-CoV-2 IgG assay against the same antigenic region (Abbott Diagnostics, Abbott Park, Illinois, USA) and EuroImmun Anti-SARS-CoV-2 ELISA-IgG against the S1 domain of the spike (antigenic) protein of SARS-CoV-2 (EuroImmun UK, London, UK). We also demonstrated that detectable spike protein IgG antibody may persist for more than 10 months after RT-qPCR-confirmed infection especially in cases where initial antibody reading was high on a scale of 1 to 10. The kinetics of antibody response following vaccination have been examined but have largely concentrated on mRNA vaccines (PFZ and Moderna). In a study using AbC-19™

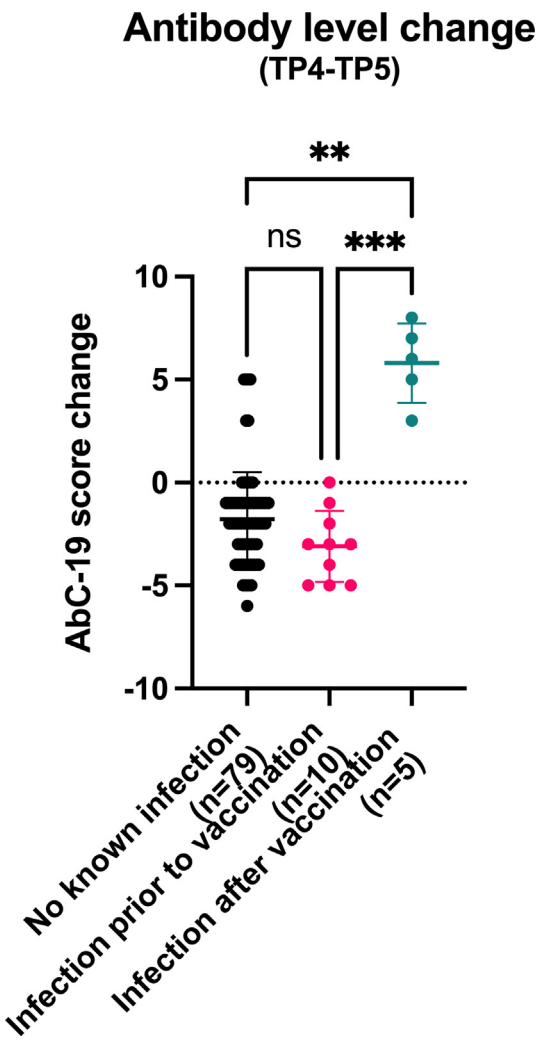

Fig. 3. Change in AbC-19™ quantitative score between TP4 (3 weeks after 2nd vaccination) and TP5 (6 months after first vaccination). Differences in means analysed using Brown-Forsythe and Welch ANOVA. ns = not significant, **=P < 0.01, ***=p < 0.001.

to compare IgG antibodies in participants double-vaccinated with either PFZ or OAZ vaccination, Ebanks et al (2021) showed a greater antibody response following PFZ, though a higher OAZ cohort median age may account for the reduced IgG response observed [7].

Here, we used the AbC-19™ to determine the kinetics of the response to the OAZ vaccination at various timepoints through the vaccination program. 86.5% of participants mounted a detectable IgG antibody response to the first vaccine dose, falling to 74.7% immediately prior to the second dose, and rising to 99% after it, with previously infected participants having a significantly higher quantitative AbC-19™ score than those without at all timepoints. These results are in close agreement with similar studies of antibody response to the OAZ, PFZ and Moderna vaccines measured using a variety of assays – LFD, chemiluminescent immunoassays (CLIA), and chemiluminescent microparticle assays (CMIA) [8–13]. In all studies, almost all participants mount a detectable antibody response to two doses of vaccine that is greater in previously infected individuals (either known RT-PCR positive or seropositive at baseline).

Antibody levels have been shown to decline over time following vaccination, but remain detectable for more than 6 months after second vaccination [9,14,15]. Titres of neutralizing antibodies have been shown to decay faster in never infected vaccinated individuals than in those infected prior to vaccination [16]. No significant difference in the reduction of AbC-19™ scores between previously infected and never infected individuals was observed in this study (Fig. 3).

Infection following the second dose of vaccine in previously uninfected individuals results in a high IgG antibody titre with a mean increase in AbC-19™ score of 5.8, significantly higher ($p<0.0001$) than the mean decrease in AbC-19™ score of 1.7 observed in doubly vaccinated, uninfected individuals (Fig. 3). Similar immune responses to post-vaccination infection were observed in nursing home residents infected following a second dose of PFZ vaccine [17].

The present study has limitations. Firstly, the largest portion of participants came from the 50+ year old age group being called for vaccination at the time of the study and were representative of the ethnic diversity of the area of Belfast, in which they were recruited (2.2% belonging to minority ethnic groups) [18]. The data that was obtained from younger participants was limited to those individuals called for vaccination due to underlying health problems. Secondly, we assessed antibody levels semi-quantitatively with the AbC-19™, a device which we already demonstrated to have a good correlation between other commercially available assays (Roche, Abbott, EuroImmun) [4]. Additionally, a drop in antibody levels in undiluted serum of individuals with high positive (10) scores may not be detected. Dilution of serum samples by 10- or 100-fold may be necessary [11]. Thirdly, only the humoral (antibody) immune response was measured in this study; cellular (T cell) responses to vaccination were not investigated. Two vaccine doses have been shown to be required for maximal T cell response, which importantly appear to be directed against SARS-CoV-2 epitopes conserved between the SARS-CoV-2 variant used in the OAZ vaccine and the variants of concern that have subsequently emerged [19].

In summary, this study demonstrates via AbC-19™ that two doses of the OAZ ChAdOx1 vaccine elicits strong anti-spike protein antibody responses in almost all vaccinated individuals which persist for most individuals beyond six months after first vaccination. The utility of the 20-minute response time AbC-19™ rapid test in confirming this antibody response is also demonstrated. Further follow-up of this cohort at later time points will monitor further decline in antibody levels and help inform the likely need for additional vaccine or booster doses, particularly tailored to emerging strains or for people in whom the greatest decline in antibody levels is seen with time.

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Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Professor Tara Moore acted as a consultant for Abingdon Health during the final period of sampling. At time of conception and commencement of this study, none of the authors received payment from Abingdon Health.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2022.02.087.

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