Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Journal of Infection 83 (2021) e18–e3

Contents lists available at ScienceDirect

Journal of Infection

journal homepage: www.elsevier.com/locate/jinf

Letter to the Editor

Cross reactivity of serological response to SARS-CoV-2 vaccination with viral variants of concern detected by lateral flow immunoassays

Dear Editor

The Coronavirus 2 (SARS-CoV-2) pandemic continues to affect almost every country in the world (1). In the UK, two main vaccines have formed the basis of the national immunisation strategy: the AstraZeneca ChAdOx1 nCoV-19 vaccine (AZ) (2) and the Pfizer-BioNtech COVID-19 vaccine (PFZ)(3). Both elicit immune responses targeting the viral spike protein and both have been shown to reduce the incidence of severe disease in early trials (2,3). With the emergence of several variants of concern (VOC) such as the B.1.1.7 (United Kingdom - Alpha), that have increased transmissibility (4,5), it is necessary to understand whether current vaccines will provide protection against VOC. Detection of serum IgG against SARS-CoV-2 spike protein correlates with future protection against COVID-19 infection ([6,7]) but does IgG induced by the wild-type spike protein interact with the spike protein from VOC and give protection against infection by VOC? Immunodiagnostic tests to measure vaccine responses are available in specialised laboratories whilst lateral flow tests (LFTs) can also be made available at point of care and easily deployed in resource poor settings. Here we have used LFTs to examine IgG antibody levels against spike protein from the SARS-CoV-2 wildtype (Wuhan) and from four VOC: B.1.1.7 (United Kingdom - Alpha), B.1.351 (South Africa – Beta), P.1. (Brazil - Gamma) and B.1.617.2 (Indian – Delta). We have used serum from donors with ELISA confirmed anti-spike antibody induced by natural infection (NI) and from donors who had received two doses of the AZ or PFZ vaccines.

LFTs targeting SARS-CoV-2 wildtype (AbC-19^{TM}) (8) and the four VOC, Alpha, Beta, Gamma and Delta (prototype LFTs) were provided by Abingdon Health for use in this analysis. The five different SARS-CoV-2 spike antigens sprayed onto the nitrocellulose test lines were stabilised full trimeric spike protein made by mammalian cell culture using HEK cells. The LFTs were identical except for the nature of the spike protein and that the AbC-19^{TM} (Wild-type) LFT was CE marked and the variant LFTs were prototypes. All LFTs used the same colloidal gold-labelled anti-IgG signal and run buffer and all were used according to manufacturer instructions. Each assay was scored after 20 min using a line-intensity score – an ordinal, semi-quantitative assessment of reactivity - by three independent observers; scores of 0–10 with 0 negative, 1–3 weak and 4 and above as medium to strong (Supplementary figure 1). An enzyme-linked immunosorbent assay (ELISA) measured total antibody response against the spike glycoprotein (MK654; The Binding Site).

Serial dilutions at 1 in 2 (1000 – 7.8 IU/mL) of the WHO standard NIBSC 20/136 (9), were made into pre-2019 negative control serum. Antibody responses from 3 groups were assessed: 10 otherwise healthy individuals (median age 49 yrs, range 28–60) bled 4–12 weeks after a non-hospitalised COVID-19 infection (NI) with a positive PCR result via swab test during Spring 2020 when the Wuhan strain was prevalent; 20 individuals (median age 47 yrs, range 28–60) post second dose of PFZ (median time between vaccination and sampling 30.5 days, range 25-47) (London-Camden & Kings Cross Research Ethics Committee (20/HRA/1817) 20 individuals (median age 72 yrs, range 64–81) post second dose of AZ (median time between vaccination and sampling = 27.8 days, 4 - 37) (North West ethics committee, Preston CIA UPH IRAS approval (REC 20\NW\0240)). Two-way ANOVA was performed on the data to analyse the statistical relationship between each group and the intrinsic differences between variants.

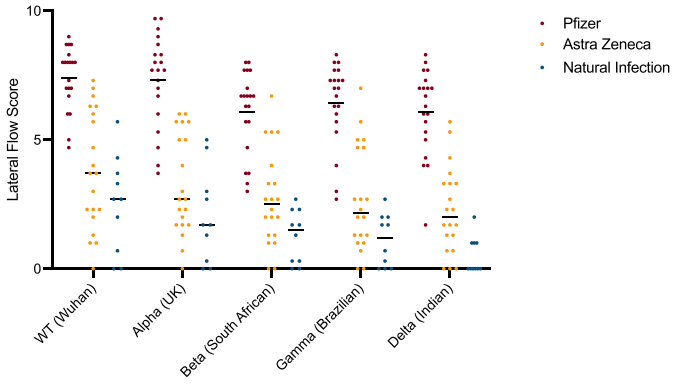

Fig. 1. Lateral flow score (mean) against each variant: Wuhan (wild type WT), Alpha, Beta, Gamma, Delta. Differences between groups are shown above (**** = p <0.0005; *** = p = 0.0004).

100% of Pfizer vaccinated individuals showed pan specificity to all spike variants tested here (20/20). 85% of Astra Zeneca vaccinated individuals (17/20) and 40% of individuals whom have recovered from first wave infection (4/10) also displayed pan specificity to the five spike variants used here. Reactivity correlated with measurement of total IgG, IgA and IgM ant-Wuhan spike protein by laboratory ELISA test (10) with the exception of two NI samples that were ELISA positive and negative on all four virus variant LFTs. All 20 PFZ group sera reacted against each VOC; and mean scores from the PFZ group were Wuhan 7.4, Alpha 7.3, Beta 6.1, Gamma 6.5 and Delta 6.1. These scores were greater than both the 20 AZ group sera that were Wuhan 3.8, Alpha 3.3, Beta 2.7, Gamma 2.7 and Delta 2.3 and the 10 NI group sera that were Wuhan 2.5, Alpha 2.0, Beta 1.3, Gamma 1.1 and Delta 0.5 (p<0.0001) (Fig. 1). Titration of the WHO standard NIBSC 20/136 sera showed positive results to all variants down to 15 IU/ml and at 7 IU/ml only failed to detect the Delta variant (Fig. 2, Supplementary figure 1).

https://doi.org/10.1016/j.jinf.2021.07.020

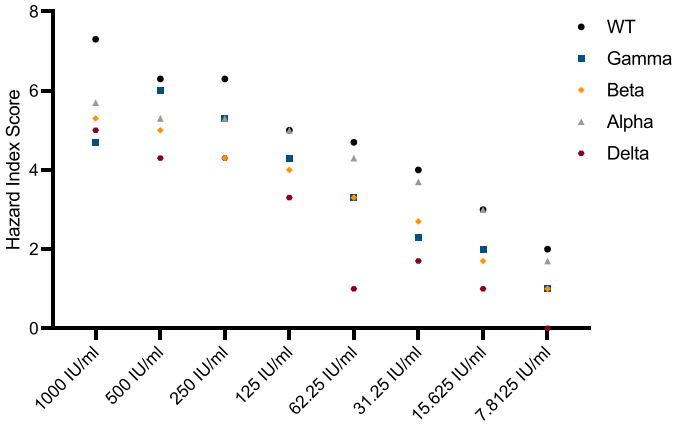

Fig. 2. Lateral flow score against each variant: Wuhan (wild type WT), Alpha, Beta, Gamma, Delta for a titration of the WHO standard NIBSC 20/136.

We have shown the use of the AbC-19™ rapid IgG LFT (Abingdon Health) can successfully determine seropositivity for SARS-CoV-2 in all 40 individuals aged 28–81 years of age tested following second dose of vaccine, and 8/10 health care workers following natural infection. IgG antibody levels were greatest after PFZ vaccination (median age 47 years) and lowest after natural infection (median age 49 years). PFZ induced greater antibody levels than AZ vaccination but donors within the AZ cohort were older (median 71 years) which may have impacted on antibody response. The IgG anti-spike antibody in these three groups had been induced by the Wuhan spike protein. We assessed its cross-reactivity with spike protein from the Alpha, Beta, Gamma and Delta variants using spike protein from each variant in LFTs otherwise identical to the AbC-19™ LFT. All 48 serum samples that were positive in the AbC-19™ LFT were positive against three variant LFTs (Alpha, Beta and Gamma) albeit at lower levels; taking the mean of all the variant LFT scores these means were a percentage of the mean Wuhan score 88%, 71% and 49% respectively for PFZ, AZ and NI. In the Pfizer group 100% (20/20) of individuals showed specificity to the delta variant, whereas 85% of AZ and only 40% of NI group showed reactivity to the Delta variant. The WHO standard NIBSC 20/136 derived from hospitalised donors most likely infected by the Wuhan virus had reactivity to all VOC down to 15 IU/ml.

Ethics approval and consent to participate

London-Camden & Kings Cross Research Ethics Committee (20/HRA/1817)

North West ethics committee, Preston CIA UPH IRAS approval (REC 20\NW\0240)

Consent for publication

Not applicable.

Availability of data and material

Not applicable.

Funding

None.

Authors contributions

All authors have contributed to the manuscript.

Authors information

None.

Patient and public involvement

None, paper is of interest to patients and public in light of current pandemic. An observational study.

Transparency declaration

The author affirms the manuscript is an honest accurate and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Declaration of Competing Interests

Drayson, Plant and University of Birmingham own stock in Abingdon Health

Acknowledgements

We thank the staff of University Hospitals Birmingham NHS Foundation Trust who kindly volunteered for this study. We would also like to thank the research staff of the Birmingham Wellcome NIHR Clinical Research Facility who undertook the staff facing assessments. We would like to thank colleagues at the Clinical Immunology Service for overseeing recruitment, sample processing and LFA scoring.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jinf.2021.07.020.

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