CIRCULATING ANTIBODY TITRES PREDICT INFECTION AND SEVERITY IN COVID-19 CLOSE CONTACTS

J Byrne[1,2], CM Gaillard[1], A Garcia-Leon[1], S Conlon[2], O Casey[2], SJ Kenny[3], G Kenny[1,2], L Gu[1], R Negi[1], G Saini[1], D Alalwan[1], T O'Gorman[1,4], S O'Regan[5,6], SF Fitzgerald[3], P Doran[7], C O'Broin[1,2], S Savinelli[1,2], ER Feeney[1,2], JA O'Halloran[1,2], M Horgan[4,7], AG Cotter[1,4], E de Barra[5,6], O Yousif[8], C Sadlier[9], A Landay[10], V Gautier[1], PWG Mallon[1,2]

on behalf of the All Ireland Infectious Diseases cohort study

1. Centre for Experimental Pathogen Host Research (CEPHR), University College Dublin, Belfield, Dublin 4, Ireland, 2. Department of Infectious Diseases, St Vincent's University Hospital, Elm Park, Dublin 4, Ireland, 3. Department of Clinical Microbiology, St Vincent's University Hospital, Elm Park, Dublin 4, Ireland, 4. Department of Infectious Diseases, Mater Misericordiae University Hospital, Eccles St, Dublin 7, Ireland, 5. Department of Infectious Diseases, Beaumont Hospital, Beaumont, Dublin 9, Ireland, 6. Department of International Health and Tropical Medicine, Royal College of Surgeons in Ireland, Dublin, Ireland, 7. School of Medicine, University College Dublin, Belfield, Dublin 4, Ireland, 8. Endocrinology Department, Wexford General Hospital, Carricklawn, Wexford, Ireland, 9. Department of Infectious Diseases, Cork University Hospital, Wilton, Co Cork, Ireland, 10. Department of Internal Medicine, Rush University, Chicago, Il, USA

All-Ireland Infectious Diseases cohort

CONTACT INFORMATION: joanne.byrne@ucd.ie

Background

- Higher anti-receptor binding domain (RBD) IgG antibodies are associated with greater host neutralisation against SARS-CoV-2, with a RBD threshold of 456IU/mL predicting clinically relevant host neutralising capacity[1].
- We aimed to explore whether higher RBD titres protected against incident infection in individuals with confirmed exposure to SARS-CoV-2 and establish a humoral correlate of protection from COVID-19, including against severe disease within a real-world setting.

Methods

- A multicentre, prospective cohort study enrolled close contacts of confirmed COVID-19 cases during hospital outbreaks from October 2021 to February 2022. All subjects were SARS-CoV-2 PCR negative at baseline and provided blood samples at exposure.
- Subjects underwent serial SARS-CoV-2 PCR testing over 14 days post exposure. Analysis was restricted to outbreaks where confirmed COVID-19 transmission occurred
- In those with incident infection, maximal disease severity was assessed as per World Health Organisation guidelines.
- Plasma RBD and full-spike (S) IgG were measured by electrochemiluminescence.
- We used Chi-squared test and Mann-Whitney to compare categorical variables and antibody titres, respectively, and Kaplan-Meier and Cox proportional hazard ratio (HR) to assessed survival analysis. Data is reported as median (interquartile range) or (n(%)) unless specified.

Results

- We identified 44 close contacts in 16 outbreaks of median age 77(63-83) years, 61% female, of whom 26(59%) became infected at 4.5(2-7) days, with 6(14%) experiencing moderate/severe COVID-19.

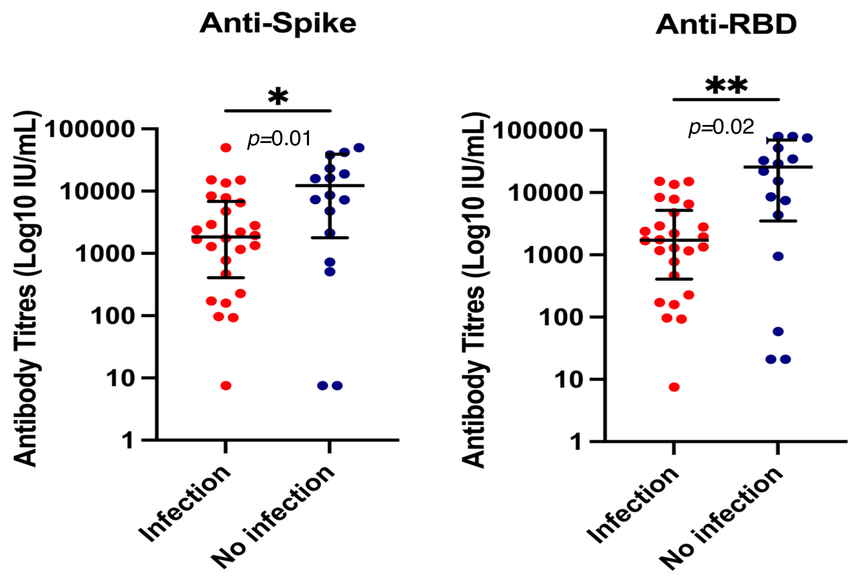
Table 1: Demographics of Study Population by Infection Status

	Infection (n=26)	No Infection (n=18)	p Value
Age	78.5 (69.5-83)	75 (58-83)	0.36
Female sex	14 (54%)	13 (72%)	0.22
Prior COVID-19 infection			
Yes	0	4	0.01
No	26	14	
Vaccination status			
Vaccinated	25	17	0.79
Unvaccinated	1	1	
Number of vaccines.			
1	0	1	0.40
2	5	4	0.81
3	17	11	0.77
Unknown	3	1	0.50
Primary vaccination series			
Pfizer-BioNTech BNT162b2	19	14	0.72
Moderna mRNA-1273	1	0	0.22
AstraZenecaChAdOx1nCoV19	2	1	0.78
Janssen Ad26.COV2.S	0	1	0.40
Unknown	3	1	0.50
Predominant variant			
Delta (B.1.617.2)	5	3	0.83
Omicron (BA.1, BA.2)	21	15	
CT value of Index Case	15.4 (13.1-23.4)	13.2 (12.3-16.9)	0.25
Comorbidities	**Infection**	**No Infection**	
Immunosuppressed	8	2	0.13
Chronic Kidney Disease	11	3	0.07
Cardiovascular disease	9	6	0.93
Chronic Respiratory disease	7	4	0.73
Diabetes	3	4	0.34

Results (continued)

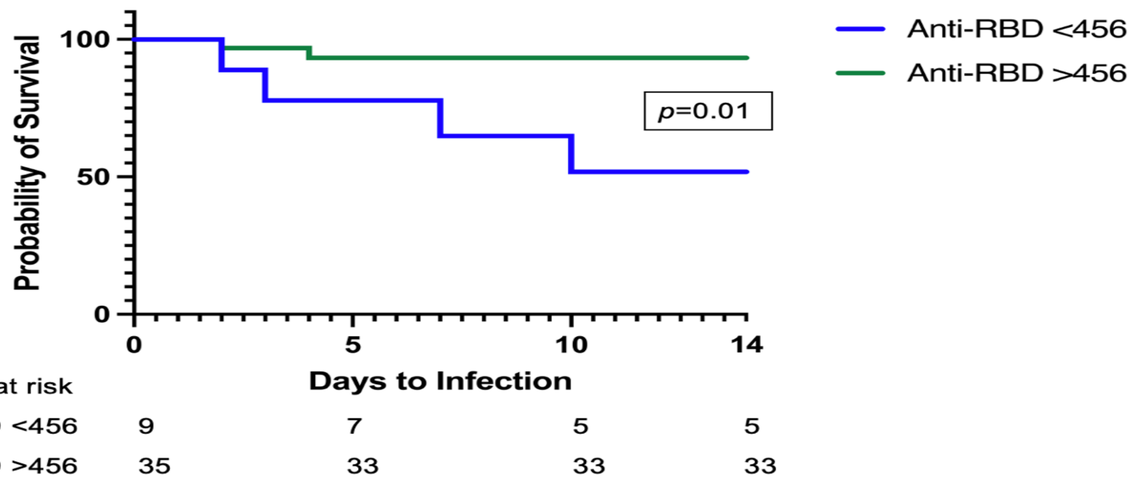
- No significant differences were observed in baseline clinical comorbidities, or index case CT value between those who did and did not become infected, Table 1.
- Subjects who became infected had significantly lower S and RBD titres than those who did not: S; 1714[544-4286]IU/ml versus 12246[2798-34441]IU/ml, *p*=0.006 and RBD; 3610[1100-6239]IU/ml versus 25676[5149-64216]IU/ml) *p*=0.015, Figure 1.
- In addition, an RBD IgG >456IU/ml (35(80%) subjects), was associated with an 84% risk reduction of developing moderate or severe COVID-19 (HR 0.16 (95%CI 0.03-0.87), *p*=0.03, Figure 2). This risk reduction strengthened with adjustment for age, sex, and prior COVID-19 (HR 0.09 (95%CI 0.01-0.55), *p*=0.01).

Figure 1: Significantly lower Anti-Spike IgG and Anti-RBD IgG in subjects who developed incident SARS-CoV-2 infection



Higher Spike and RBD Ab titres protect against SARS-CoV-2 infection post-exposure
RBD titres >456 IU/ml associated with 84% risk reduction in development of severe disease

Figure 2: Relationship between RBD threshold of 456IU/ml and development of moderate/severe COVID-19



Conclusions

- In individuals exposed to SARS-CoV-2, higher spike and RBD IgG antibody titres were associated with protection from infection.
- An RBD IgG titre >456IU/ml, was associated with an 84% reduced risk of developing moderate/severe COVID19, further supporting this threshold as a clinically relevant correlate of protection.

References and Acknowledgements

1. Kenny G, O'Reilly S, Wrigley Kelly N, Negi R, Gaillard C, Alalwan D, et al. Distinct receptor binding domain IgG thresholds predict protective host immunity across SARS-CoV-2 variants and time. Nature Communications. 2023;14(1).

Acknowledgements: The authors would like to thank the participants and investigators from the All Ireland Infectious Diseases study group.