Determination of Immunological Memory Responses to COVID19 in patients with mild disease: a prospective study.

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Introduction

- In 2020 the World Health Organisation declared Covid-19 outbreak as a global pandemic, to date it has affected more that 165.9 million people worldwide. Knowledge of immunity of a COVID-19 infection has been limited and the antibody response against SAR-CoV-2 infection remains poorly understood.
- The main research question asked in this study is how long immunity to COVID-19 would last in patients that previously had a mild infection of the virus. The secondary research question to this study is how Lateral Flow devices compare to that of the Roche Elecsys automated antibody assay in people who had previously had mild cases of SARS-CoV-2.

Method

- This study was approved by Walse Health and Care Research Committee (Reference No. 20/YH/0190). A prospective follow up of seventy nine COVID-19 positive patients looking at antibody responses monthly post infection. For all participants the antibody responses were tested on at least 4 occasions. Serological responses were tested with two commercially independent assays. SARS-CoV-2 antibodies were measured using Roche Elecsys e602 platform which provides a qualitative detection of combined IgM/IgG antibodies against a nucleocapsid protein and MP Rapid Lateral Flow immunoassay, which provides a qualitative detected of IgM and IgG for Spike protein and nucleocapsid protein separately. Roche Elecsys nucleocapsid protein assay is a qualitative assay. Linearity studies (data not presented in the poster) showed that the Roche assay to be linear.

Results

- Seventy nine non-hospitalised subjects (51 (65%) female, 28 (35%) male) who were infected with COVID-19 in March and April 2020 participated in the study.
- For the majority of the patients (86%) a three phase immune response against the nucleocapsid protein was observed. An initial increase of antibodies in the first three months followed by a period plateaux, before a decrease in antibodies which was seen after 6 months. The remaining 14% showed a different immune response with an extended period of increasing antibodies lasting up 6-7 months before a decrease was seen.

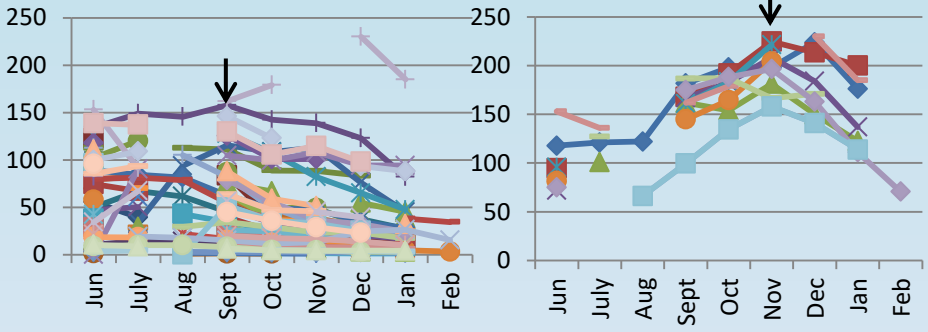
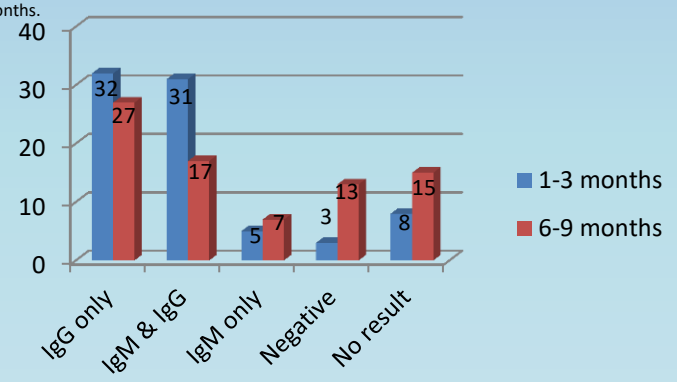


Figure 1 : SARS-CoV-2 antibodies measured using Roche Elecsys e602 showing the immune response seen in the majority of patients

Figure 2 : SARS-CoV-2 antibodies measured using Roche Elecsys e602 showing the immune response seen in the other 14% of patients

- This study showed a good concordance 99.3% (Kappa Cohen 0.987 (*CI* 0.963-1) between the two methods in the early phase (1-3 months) of this study. However, approximately 6-9 months post infection method agreement reduced to 90% (Kappa Cohen 0.899 (*CI* 0.831-0.967).
- In the monthly follow up testing of these patients, 73% lost IgM prior to IgG; however 22 % of patients had persistent IgM and IgG until 9 months post the infection date. 2.5% of patients gained IgM only after 6-9 months which suggests that these patients were subject to reinfection at some point in this time frame. Like the majority of patients in the study these patients also showed a three phase immune response.

Figure 3: the antibody response seen using the MP Rapid Lateral Flow immunoassay at 1-3 months and 6-9 months.



Discussion

- For those who recovered from COVID-19, our data shows humoral immune response to the virus can last for at least 6-9 months, and may last longer (given the rate of decline of antibodies).
- In a previous study which has been conducted in hospitalised patients, we showed that the analytical performance of MP-rapid for SARS-CoV-2 antibodies was comparable to Roche Elecsys (with 98.5% agreement (Cohen's Kappa 0.96. (95% *CI* 0.92-0.99)), with sensitivity a of 100% at day 21 and specificity of greater than 98.5%.[1] However, in ambulant mild cases of Sars-CoV-2 infection, such as this study, there was a poor agreement between the two methods evident by a reduction in Cohen and Kappa agreement to (Cohen's Kappa 0.851 (95% *CI* 0.688-0.967). [2]
- At the beginning of the study (1-3 months) only 5 participants had IgM only antibodies in 6-9 months 7 patients had IgM only. This finding may indicate re-infection despite presence of antibodies to SARS-CoV-2 virus.
- Two distinct different immunological memory responses have been observed. The appearance of IgM long after the acute phase of the infection is a phenomenon may need further investigation.

References

1. N Jassam, J H Barth, V Allgar et al. Evaluation of the MP Rapid 2019-NCOV IgM/IgG combo POCT test vs. an established platform-based method. Ann Clin Biochem 2021. doi: 10.1177/0004563221995551.
2. Farnsworth CW, Anderson NW. SARS-CoV-2 serology: much hype, little data. Clin Chem 2020; 66(7):875-877.