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Determination of Sero-Prevalence of SARS-CoV-2 antibody among immunized individuals with Covid-19 vaccine in a tertiary center, Nepal

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Abstract
Background: Coronavirus Disease 2019 (covid-19) is a highly contagious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). People who are infected with SARS-CoV-2 or are vaccinated with covid-19 vaccines are supposed to develop immunoglobulins and these immune responses in human body will determine the efficacy of the vaccines as well as help to discover new therapeutic options.
Methods: A cross-sectional study conducted between April to June, 2021, assessing serum antibody titer from participants who had taken the first dose of covishield™ vaccine (naïve as well as prior covid-19 infected individuals). Antibody testing was carried out with Roche Elecsys Anti-SARS-CoV-2 S electrochemiluminescence immunoassay on Roche Cobas e 601 module**.** Twenty-eight of these participants had follow up repeat antibody test after second dose of vaccine.
Results: A total of 122 participants with the first dose of Covishield™ vaccine were all tested seropositive, antibody titer ranging from minimum of 2.95 U/mL to maximum 2500 U/mL. Average antibody titer was 308.9 U/mL for naive cohort and 1604 U/mL for prior covid-19 infection. In twenty-eight participants who had antibody titer measured after 1 month of second dose, average titer was 1459.7 U/mL for naïve cohort and 1803.4 U/mL for prior covid-19 infected individuals, which was statistically significant compared to antibody response after the first dose.
Conclusions: Antibody responses against SARS-CoV-2 following immunization was 100%, with significant development after second dose in naïve population while robust immune response was present after first dose in prior SARS-CoV-2 infected individuals.

Keywords: Antibody, Covid-19, SARS-CoV-2, seroprevalence, vaccine

Introduction

Coronavirus Disease 2019 (covid-19) is a highly contagious disease and since its first identification in Wuhan, China, in December 2019, it has spread worldwide. It is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. Humoral immunity is a vital aspect of the immune system highly implicated in infection control. People who are infected with SARS-CoV-2 or are vaccinated with covid-19 vaccines are supposed to develop immune response against the corona virus and these antibodies (Ab) in human body will determine the efficacy of the vaccines [2]. Understanding the immune response to this virus is paramount to limit disease burden in the population, and to discover new therapeutic options. However, to date, the estimate of antibody longevity is from few weeks to months, with no exact consensus among different studies [3, 4].
Therefore, this study aims at finding the immune response against the SARS-CoV-2 (S-particle) following immunization among the Nepalese population, which could provide a better insight on estimating the immunogenic response and thus help discover new therapeutic options.

Methods

Design and Study Population

This is a cross-sectional study conducted at National Public Health Laboratory (NPHL), Kathmandu, Nepal, between April to June, 2021. All the participants presented during this time period for anti-SARS-CoV-2 antibody checkup were enrolled and only those meeting the inclusion criteria (who had taken the covishield™ vaccine and consented to participate in the study) were included in this study. Individual serum antibody titer was assessed with Roche Elecsys Anti-SARS-CoV-2 S electrochemiluminescence immunoassay (ECLIA) for the in vitro quantitative determination of antibodies (including IgG) against spike RBD of SARS-CoV-2, on Roche Cobas e 601 module**.** The results were interpreted using manufacturer's manual, as negative for anti-SARS-CoV-2-S if < 0.80 U/mL and positive if ≥ 0.80 U/mL with measurement range spanned from 0.4 U/mL to 2500 U/mL [5].

Ethical Approval

Ethical Approval for this research was obtained from Nepal Health Research Council (Reference no. 2984) and informed consent was taken from all the study population.

Statistical Analysis

The data were entered in Microsoft excel 2013 and statistical analysis were performed using the Statistical Package for Social Science (SPSS), version 23.0. Two-tailed Mann-Whitney and Kruskal Wallis Test (for independent variables) and Wilcoxon (for paired variables) tests were used to compare groups. Values lower than 0.4 U/mL were assumed as 0.4 and values higher than 2500 U/mL were reported as 2500; p values < 0.05 were considered statistically significant.

Results

A total of 122 participants (67 males and 55 females) who had taken the first dose of Covishield™ vaccine were included in the study. Of the total participants, 80 were naïve individuals with no prior covid-19 infection (mean age 39.4 years) while 42 participants with mean age of 37.9 years had prior history of covid-19 infection (Table 1).

All the study participants were tested seropositive with antibody titer ranging from minimum of 2.95 U/mL to maximum 2500 U/mL. The average antibody titer was 308.9 U/mL for naive cohort and 1604 U/mL for prior covid-19 infection. The average antibody titer was higher in each age group among the prior covid-19 infected participants compared to the naïve group (Figure 1).

Table 1: Demographic data of naïve participants and prior covid-19 infected participants following 1st dose of vaccine.

Participants	No of cases	Antibody titer range (U/mL)		Mean antibody titer (U/mL)	Median antibody titer (U/mL)	P Value*
		Min.	Max.			
Naïve individuals	80	2.95	2500	308.9	57.5	<0.001
Prior covid-19 positive	42	13.69	2500	1604	1837	

**Mann-Whitney Test*

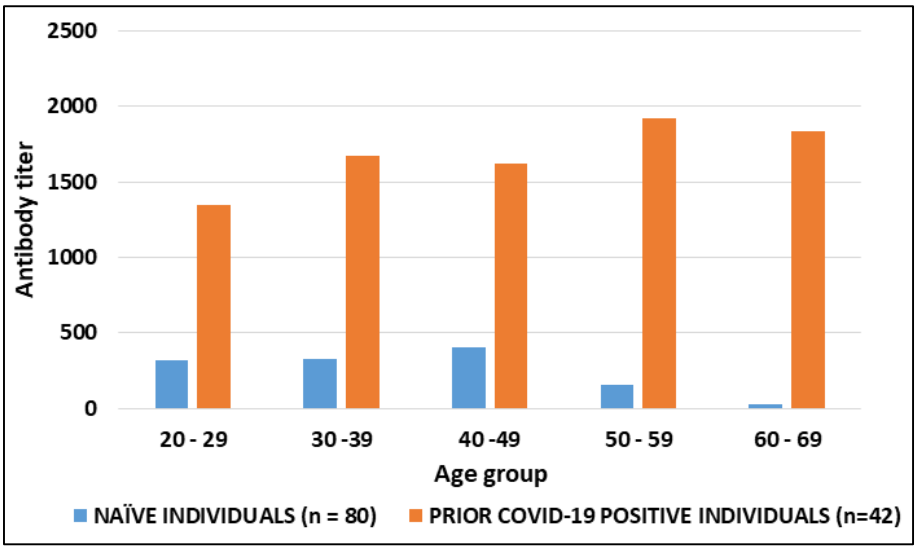

Fig 1: Comparing average antibody titer in naive and prior covid-19 positive participants by age group.

The antibody titer was not significantly different when measured at <8 weeks to 12 weeks interval after first dose of vaccine in both the naïve as well as prior covid-19 infected groups (Figure 2). The average antibody titer measured among the prior covid-19 positive participants, irrespective of their time duration of covid-19 infection to antibody testing following first dose of covid-19 vaccine were not significant (p=0.64) (Table 2).

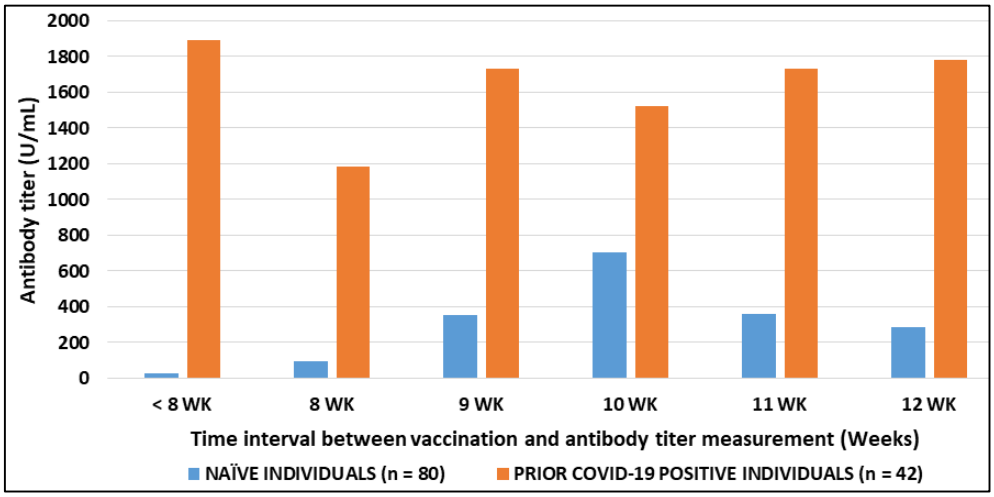

Fig 2: Comparing average antibody titer among naïve and prior covid-19 infected participants with regard to time interval after vaccination.

Table 2: Comparing antibody titer of prior covid-19 infected participants after first dose vaccination from time of covid-19 infection interval

Time interval after covid-19 infection to first dose vaccination	No of cases	Ab titer range (U/mL)		Mean Ab titer (U/mL)	P value**
		Min.	Max.		
3 – 5 Months	8	55.61	2500	1350.4	0.64
6 – 8 Months	31	13.69	2500	1665.4	
9 Months and more	3	245	2500	1646	

** *Kruskal Wallis Test*

The data of 28 participants who had follow-up antibody titer measured after 1 month of the second dose of vaccine were also included, of which 19 were naïve individual and 9 had prior covid-19 infection. Comparing the antibody titer among the naive participants, the average antibody titer was 1459.7 U/mL after the 2nd dose which was significantly higher compared to that from first dose which was 166.1U/mL (p <0.001). The average antibody titer of the 9 participants with prior covid-19 infected individuals was 1803.4 U/mL after the second dose of vaccine which was high compared to 953.6 U/mL after first dose (p=0.04) (Table 3). In contrast to this finding, two participants with prior covid-19 infection had lower antibody titer after the second dose compared to that from first dose. These two participants had antibody titer of 1280 U/mL and 2124 U/mL after second dose of vaccination compared to 1576 U/mL and 2494 U/mL respectively measured after the first dose of vaccination.

Table 3: Comparing vaccine immune response of 28 participants following first and second dose of covid-19 vaccine.

Participants	Vaccine	No of Cases	Ab titer range (U/mL)		Mean Ab titer (U/mL)	P value***
			Min.	Max.		
Naïve individuals	1ST DOSE	19	2.95	1937	166.1	<0.001
	2ND DOSE	19	292.3	2500	1459.7	
Prior Covid-19 infected	1ST DOSE	9	13.69	2500	953.6	0.04
	2ND DOSE	9	1280	2500	1803.4	

*** *Wilcoxon Signed Ranks Test*

Discussion

This study was conducted to assess the immune response following covid-19 (Covishield™) vaccination in context to Nepalese population and the results showed that all the 122 participants had developed immune response with antibody titer ranging from 2.95 U/mL to 2500 U/mL. These findings were comparable to study done by Binay et al which also showed seropositivity in 100% of the study participants [6]. Antibody titer measured at different time interval after first dose of vaccine showed similar immune response in prior covid-19 infected individuals as well as in naïve cohort. This might support the vaccination policy of some countries who are giving the second dose of covid-19 vaccine at 8-12 weeks interval as it shows a good antibody response, thus enabling a larger number of people to receive the first dose [7].

Unsurprisingly, vaccinated individuals with evidence of prior COVID-19 infection led to a boost response just after the first dose of covid-19 vaccine, achieving antibody titers approximately 2 to 4-fold magnitude higher compared with naïve individuals as shown in figure 2. The average antibody titer measured were similar among the prior covid-19 positive participants, irrespective of their time duration of covid-19 infection to antibody testing following first dose of covid-19 vaccine (Table 2), further suggesting the first prime vaccine dose acted as a boost. This has led to some researcher argue that a first prime vaccine dose would effectively act as a boost, so a second dose might not be needed in those populations [8-10]. Moreover, two participants in this study with history of proven SARS-CoV-2 infection, had lower antibody titer measured 4 weeks after the second dose of vaccination. In contrast to this, a robust immunogenic response was seen only after the second dose of vaccine in the majority of naïve individuals. Thus, a significant increase in antibody response after second dose vaccine in our study supports the evidence that most vaccine platforms use a two-dose prime boost approach to generate an immune response

against the virus S1 spike protein [8, 11].

However, the duration of long-term immunity to SARS-CoV-2 following infection or vaccination, as well as the level of antibody required for immunity, is currently unknown [12]. Thus, with the current limited understanding of correlates of immunity, prevalence of disease, and durability of immunity, antibody testing should remain a tool of public health until more is understood about long-term impacts of SARS-CoV-2 on the immune system [13]. Limitations of this study include a small sample size and thus, a large-scale study needs to be conducted in order to obtain a better insight on the development of immunogenicity and vaccine efficacy.

Conclusions

All the participants had developed antibody responses against SARS-CoV-2 following immunization as early as first dose which is very reassuring in preventing and treating COVID-19 disease that is not fully understood till date. Moreover, in naïve individuals, second dose of vaccine developed a remarkable and statistically significant immune response while the first dose alone had a similar robust immune response in prior SARS-CoV-2 infected individuals.

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Conflict of Interest

The authors declared no potential conflict of interest with respect to the research, authorship and/or publication of this article.

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