Original article

Evaluation of SARS-CoV-2 Humoral Response Following Vaccination with ChAdOx1 nCoV-19 (Covishield™) and/or Sinopharm, BBIBP-CorV (Vero cell™)

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ABSTRACT

Background: Billions of doses of COVID-19 vaccine have been introducing in the world to prevent pandemic COVID-19. Higher efficacy but limited data are available for its longevity. We aimed to find out the IgG Anti-SARS Cov-2 antibody level among frontline healthcare workers after two doses of vaccines.

Methods: A cross-sectional study was carried among 170 HCPs of Seti Provincial Hospital of western Nepal, who were more than 18 years, and had taken two doses of either one of COVID 19 vaccine. All those participants, who were on leave during the data collection tenure (1st February 2022 to 28th February 2022) and/or did not consent to participate were excluded. Mindray SARS-CoV-2 S-RBD IgG assay kit based on CLIA method, was used whose target antigen is S-RBD (spike protein of receptor binding domain) antigen. The IgG immunoglobulin is detected and cut off value ≥10 AU/ml is considered positive.

Results: Based on the recommended cut off, the antibody was present in more than 90% across both groups of vaccinee i.e. the positive antibody titer at a mean duration of 7.31 months was 93.53% overall (93.75% and 93.44% in Vero cell™ and Covishield™ vaccinees respectively).

There were 3.92 times high odds of high antibody titer (≥250 AU/ml) in Covishield™ group (OR: 3.92, 95% CI: 1.86-8.26, P-value: <0.001) than in Vero cell™ group of vaccinee. Similarly, there were significant difference of high titer of antibody across groups with more than six months of elapse of vaccination (OR: 2.18, 95% CI: 1.06-4.49, P-value: <0.001) than with less than six months of elapse of vaccination.

Conclusions: The humoral response was higher among HCPs who received two-doses vaccination with ChAdOx1 nCoV-19 (Covishield™) and/or Sinopharm, BBIBP-CorV (Vero cell™) vaccine, and among those with six or more months of elapse of vaccination. The seroprevalence of SARS-CoV-2 following two-doses vaccination among HCPs was more than nine-tenths.

Keywords: antibody immunity; ChAdOx1 nCoV-19(Covishield™); receptor binding domain; seroprevalence; sinopharm.

INTRODUCTION

The outbreak of Coronavirus disease 2019 (COVID-19) was declared a Public Health Emergency of International Concern on January 30, 2020, and a global pandemic on March 11, 2020.[1] As of 21st June 2022, more than 536 million confirmed cases and 6.3 million deaths have been reported, and more than 11 billion vaccine doses have been administered.[2] Similarly, in Nepal, as of date 21st June 2022, 1.1 million populations are infected with case fatality rate of 1.22%, and 45 million doses of COVID-19 vaccines have been administered.[3]

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Different COVID-19 vaccines have been implemented to decelerate COVID-19 pandemic.[4] The first COVID-19 vaccination rolled out in Nepal on 27th January with the intention to vaccinate healthcare providers and security personnel in the first phase, and it was ChAdOx1 nCoV-19 (Covishield™).[5,6] Due to increasing vaccine to immunize the population, the Sinopharm COVID-19 vaccine (Vero cell™) was gradually rolled out in Nepal on 17th February 2021.[7]

This study was conducted to assess the humoral response following vaccination and factors affecting the humoral response.

METHODS

We carried out a cross-sectional study among the health care workers of Seti Provincial Hospital. This is a tertiary level hospital, situated in Sudurpashchim province of the western Nepal. The inclusion criteria were to include all the participants age more than 18 years, and who had taken two doses of COVID 19 vaccine either ChAdOx1 nCoV-19 (Covishield™) or Sinopharm, BBIBP-CorV (Vero cell™). All those participants, who were on leave during the data collection tenure (1st February 2022 to 28th February 2022) and/or did not consent to participate were excluded.

The number of hospital staffs who were vaccinated with two doses of either vaccine were 275. The Raosoft sample size calculator (http://www.raosoft.com/samplesize.html) was used to determine the size of the sample needed.[8] In the calculator, the 275-participants figure was used. In addition, the response duration was set to be 50%, and a margin of error 5% was allowed at 95% confidence interval. Hence, 161 was the minimum sample size needed. To reduce the erroneous results and enhance reliability, the target sample size was increased and 170 participants were included.

A 5ml of blood was collected through venipuncture following standard operating protocol. After preparation of serum by centrifuging, quantitative IgG antibody against the RBD (Receptor Binding Domain) of the spike protein were analyzed by chemiluminescence immunoassay (CLIA) method. *Mindray SARS-CoV-2 S-RBD IgG* assay kit was used whose target antigen is S-RBD antigen. The IgG immunoglobulin is detected and cut off value ≥10 AU/ml is considered positive. Out of all those who become positive, they were categorized into two groups viz., high titer (≥250 AU/ml) and low titer (<250 AU/ml). Assays were done according to the manufacturer's instructions mentioned in the WHO International Standard for COVID-19 serological tests. The manufacturer states the clinical specificity and sensitivity of the *Mindray SARS-CoV-2 S-RBD IgG* assay kit was 99.6% (95% CI: 99.3%-99.8%) and 99.6% (95% CI 98.9%-99.8%). The whole two-step CLIA for quantitative determination of SARS-CoV-2 S-RBD IgG in human serum or plasma is performed on the fully automated Mindray CL 1200i analytical system (Mindray Bio-Medical Electronic Co Ltd, Shenzhen, China).[9]

Data was collected through pretested semi-structured questionnaire which included age, gender, ethnicity, professional roles, types and duration of vaccination, COVID-19 infection pre- and post-vaccination state, and lab report of SARS COV2 antibody quantitative level. The pre-vaccination or post-vaccination COVID-19 infection were assessed by their previous recall of test with rapid antigen test kit or rt-PCR following symptoms of COVID-19. Entered data of excel sheet was analyzed using Statistical Packages for Social Sciences (SPSS), IBM SPSS® v21 (IBM, Armonk, New York). Frequency, percentage, and mean ± SD (range) were used to express descriptive statistics. Chi square test and binary logistic regression was used to identify the association with antibody status.

The ethical clearance for the study was obtained from the apex ethical review board of the nation viz., Nepal Health Research Council (NHRC) (Ref no.1909). Written informed consent was taken from each participant, and were assured of their voluntary participation. The permission letter from the Seti Provincial Hospital was obtained and submitted to NHRC to conduct and facilitate the research.

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

RESULTS

The mean age of the participants immunized with either Vero cell™ or Covishield™ were comparable (33.65± 10.27 v/s 34.35± 9.67 respectively, P-value: 0.674). More than half of the vaccinees of either vaccine group (70.83% in Vero cell™ v/s 69.67% in Covishield™ group) were below 40 years of age. The minimum and maximum age of the participants for overall vaccination were 19 and 63 years respectively. About half of the participants of each vaccine group were female (54.17% in Vero cell™ v/s 50.00% in Covishield™). Most of the participants were Brahmin (22.92% v/s 35.25%) in each vaccine group. By professional roles, majority of the participants were

nursing staffs (41.67% Vero cell™ v/s 36.07% in Covishield™). (Table 1)

Table 1. Socio-demographic characteristics of the participants who received vaccination with ChAdOx1 nCoV-19 (Covishield™) and BBIBP-CorV, Sinopharm (Vero cell™) (N=170).

Characteristics	[1]Vero cell™ (n, %)	[2]Covishield™ (n, %)	Overall
Age			
Mean ± SD	33.65± 10.27	34.35± 9.67	34.15 ± 9.82
Median (Min, Max)	30.00 (20, 59)	33.00 (19, 63)	33.00 (19, 63)
<40 years	34 (70.83)	85 (69.67)	119 (70.00)
≥ 40 years	14 (29.17)	37 (30.33)	51 (30.00)
Gender			
Female	26 (54.17)	61 (50.00)	87 (51.17)
Male	22 (45.83)	61 (50.00)	83 (48.82)
Ethnicity			
Brahmin	11 (22.92)	43 (35.25)	54 (31.76)
Chhetri	13 (27.08)	24 (19.67)	37 (21.77)
Tharu	6 (12.50)	19 (15.57)	25 (14.71)
Thakuri	5 (10.42)	10 (8.20	15 (8.82)
Others[3]	13 (27.08)	26 (21.31)	39 (22.94)
Professional roles			
Office assistants	8 (16.67)	18 (14.75)	26 (15.29)
Administrative staffs	5 (10.41)	12 (9.84)	17 (10.00)
Paramedics	12 (25.00)	32 (26.23)	44 (25.88)
Nursing staffs	20 (41.67)	44 (36.07)	64 (37.65)
Doctors (≥MBBS)	3 (6.25)	16 (13.11)	19 (11.18)

[1] BBIBP-CorV, Sinopharm (Vero cell™) Inactivated COVID-19

[2] ChAdOx1 nCoV-19 (Covishield™)

[3] Others: Dalit, Gurung, Limbu, Magar, Muslim, Newar, Rai, Tamang and Terai-madhesi

About three-fifths of the participants (61.18%,104) did not have COVID-19 before vaccination. Similarly, four-fifths of the participants (82.94%, 141) were tested positive with COVID-19 infection (79.17% in Vero cell™ v/s 84.43% in Covishield™) following vaccination. The IgG type against S-RBD was negative in less than 10% (6.47%, 11). The mean duration of measurement of IgG following two doses of either Vero cell™ or Covishield™ vaccine was approximately 6 and 9 months respectively (5.81 months in Vero cell™ v/s 8.59 months in Covishield™ respectively). (Table 2)

Less than one-third of the vaccinees with Vero cell™ (29.17%, 14) had elapsed more than six months of duration following immunization with two doses with COVID-19 vaccination. However, majority of the vaccines with Covishield™ (92.62%, 113) had elapsed more than six months of duration following immunization with two doses with COVID-19 vaccination. (Table 2)

Table 2. Vaccine related characteristics of the participants who received vaccination with ChAdOx1 nCoV-19 (Covishield™) and BBIBP-CorV, Sinopharm (Vero cell™) (N=170).			
Characteristics	**[1]Vero cell™ (n, %)**	**[2]Covishield™ (n, %)**	**Overall**
Pre-vaccination COVID19 Infection			
No	27 (56.25)	77 (63.11)	104 (61.18)
Yes	21 (43.75)	45 (36.89)	66 (38.82)
Post-vaccination COVID19 Infection			
No	38 (79.17)	103 (84.43)	141 (82.94)
Yes	10 (20.83)	19 (15.57)	29 (17.06)
Antibody status (IgG)			
No (<10 AU/ml)	3 (6.25)	8 (6.56)	11 (6.47)
Yes (≥10 AU/ml)	45 (93.75)	114 (93.44)	159 (93.53)
Timing of IgG Measurement[3]			
Mean ± SD	5.81± 1.53	8.59± 0.91	7.81± 1.68
Median (Min, Max)	6.00 (2, 9)	9.00 (5, 9)	9.00 (2, 9)
≤6 months	34 (70.83)	9 (7.38)	43 (25.29)
>6 months	14 (29.17)	113 (92.62)	127 (74.71)

[1]BBIBP-CorV, Sinopharm (Vero cell™) Inactivated COVID-19, [2] ChAdOx1 nCoV-19 (Covishield™), [3] **In months**

There were 3.92 times high odds of high antibody titer (≥250 AU/ml) in Covishield™ group (OR: 3.92, 95% CI: 1.86-8.26, P-value: <0.001) than in Vero cell™ group of vaccinee. Similarly, there were significant difference of high titer of antibody across groups with more than six months of elapse of vaccination (OR: 2.18, 95% CI: 1.06-4.49, P-value: <0.001) than with less than six months of elapse of vaccination. The rest of the socio-demographic and vaccine related characteristics did not have significant association with antibody titer level. **(Table 3)**

Table 3. Association of socio-demographic, and vaccine related characteristics with antibody response to vaccination (n= 159).					
	Antibody response		**Univariable model[1]**		
Parameters	**Low (10-249 AU/ml)**	**High (≥250 AU/ml)**	**OR**	**95% CI**	**P-value**
Age					
<40 years	54 (48.21)	58 (51.79)	1 (Ref.)		
≥ 40 years	22 (46.81)	25 (53.19)	1.06	0.54-2.09	0.871
Gender					
Female	41 (49.40)	42 (50.60)	1 (Ref.)		
Male	35 (46.05)	41 (53.95)	1.14	0.61-2.13	0.673
Ethnicity					
Brahmins	22 (44.00)	28 (56.00)	1 (Ref.)		
Chhetri	17 (47.22)	19 (52.78)	0.88	0.37-2.08	0.767
Others[2]	37 (50.68)	36 (49.32)	0.76	0.37-1.58	0.466
Professional roles					
Office assistants, staffs & paramedics	40 (49.38)	41 (50.62)	1 (Ref.)	0.57-2.12	
Nursing staffs & doctors	36 (46.15)	42 (53.85)	1.14	0.61-2.12	0.684
Pre-vaccination COVID19					
No	42 (45.16)	51 (54.84)	1 (Ref.)		

Table 3. Association of socio-demographic, and vaccine related characteristics with antibody response to vaccination (n= 159).					
	Antibody response		Univariable model[1]		
Yes	34 (36.36)	32 (51.52)	0.78	0.41-1.46	0.430
Post-vaccination COVID19					
No	64 (48.85)	67 (51.15)	1 (Ref.)		
Yes	12 (42.86)	16 (57.14)	1.27	0.56-2.90	0.565
Vaccine type					
Vero cell™	32 (71.11)	13 (28.89)	1 (Ref.)		
Covishield™	44 (38.60)	70 (61.40)	3.92	1.86-8.26	**<0.001**
Timing of IgG Measurement					
≤6 months	26 (34.21)	16 (19.28)	1 (Ref.)		
>6 months	50 (65.79)	67 (80.72)	2.18	1.06-4.49	**0.035**

[1] Binary logistic regression

[2]Ethnicity others: Tharu, Thakuri, Dalit, Gurung, Limbu, Magar, Muslim, Newar, Rai, Tamang and Terai-madhesi

DISCUSSION

All the immune-competent individuals after being infected with SARS CoV-2 will develop immunity against it.[10] Compared to the general population, HCPs have risk of acquiring infection either from the healthcare settings or community settings. Exposure to a large number of patients may be the common cause of infection for healthcare providers.[11, 12]

In this study, 170 healthcare workers were included. We analyzed SARS-CoV-2 humoral response following vaccination with two doses of two different types of vaccine viz., Vero cell™ and Covishield™ among healthcare providers of the Sudurpaschim province of the western Nepal. Based on the cut-off recommended in the *Mindray SARS-CoV-2 S-RBD IgG* assay kit[9] , the antibody was present in more than 90% across both groups i.e. the positive antibody titer at a mean duration of 7.31 months was 93.53% overall (93.75% and 93.44% in Vero cell™ and Covishield™ vaccinees respectively). According to the "Enhanced Surveillance on Sero-prevalence of SARS-CoV-2 in General Population, 2020" by the Ministry of Health and Population, Nepal Government in collaboration with WHO, the national crude sero-prevalence in general population was 11.9%. with the highest being 27.3% in the Madhesh pradesh, and the lowest being 5.3% in the Sudurpaschim province reported in the second and third week of October 2020.[13] However, the study by Aryal et. al. at a tertiary center of Nepal showed a seroprevalence of 22.2 % among healthcare providers from November 2020 to January 2021.[14] The study from the Switzerland by Stringhini et. al., showed a total seroprevalence of 66.1% in general population following 6 months of immunization[15]. Our study reported a higher seroprevalence likely because of development of immunity with vaccination over a definite time period and long term exposure to cases with COVID-19[14,16]

In our study, the age, gender, ethnicity and COVID-19 infection pre- and post-vaccination did not show significant association with antibody response. Following two doses covid-19 vaccination. But, one study from Iran by Balou showed that participants in the age group of 35–54 years were significantly more likely to have a positive anti-SARS-CoV-2 antibody test than the age group of 20–34 years (odds ratio = 1.53, 95% CI: 1.04–2.25, P-value: 0.029), and also physicians were significantly more likely to have a positive antibody test than office workers (odds ratio = 1.92, 95% CI: 1.04–3.54, P-value: 0.037).[17] In mixed effect model study by Anastassopoulou et. al., after immunization with the BNT162b2 vaccine in a cohort of healthcare workers (HCWs, n = 439) from Greece, female participants, who were also younger than male participants [mean (SD) age = 47.9 (8.9) *vs.* 49.9 (10.5) years, p = 0.0085], had higher antibody titers compared to males (60,967 *vs.* 54,325, p = 0.012) following first dose of immunization.[18]

Similarly, the study by Aryal et. al., showed statistically significant association of antibody positivity with previous history of SARS-CoV-2 infection and the presence of flu-like symptoms in preceding six months.[14]

The protective efficacy of both vaccines is variable and even variable with state of the recipient and number of doses received. The real-world data from the UK showed that the ChAdOx01 nCoV-19 vaccine had 91% efficacy against hospitalisation-associated infection by the delta (B.1.617.2) variant, 74% efficacy against symptomatic infection by the alpha (B.1.1.7) variant, and 67% efficacy against symptomatic infection by the delta variant.[19,20] Similarly, the Sinopharm vaccine 14 days after the second dose was efficient in reducing the risk of symptomatic COVID-19 infection by 94.3% in elderly population.[21] The vaccine effectiveness in fully vaccinated individuals of the emirate of Abu Dhabi with Sinopharm's BBIBP-CorV vaccine was 80%, and 92% in preventing COVID-19-related hospital admissions, and critical care admissions, respectively, when compared to the non-vaccinated group.[22]

Our study had also some limitations, the first being its study design which is a cross-sectional nature. The others were small sample size, single center study, including only healthcare providers. We had not incorporated the comorbidities of the participants. We had also not considered the BMI (body mass index) of the vaccinees. In addition, the cellular immunity post-vaccination could not be assessed.

CONCLUSIONS

The humoral response was higher among healthcare providers who received two-doses vaccination with ChAdOx1 nCoV-19 (Covishield™) and/ or Sinopharm, BBIBP-CorV (Vero cell™) vaccine. Both ChAdOx1 nCoV-19 (Covishield™) and BBIBP-CorV, Sinopharm (Vero cell™) vaccinated groups showed high seropositive for SRB neutralizing antibodies. The humoral response was higher among those with six or more months of elapse of vaccination. The seroprevalence of SARS-CoV-2 following two-doses vaccination among healthcare providers was more than nine-tenths.

COMPETING INTERESTS

None

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