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Antibody response after first and second-dose of ChAdOx1-nCOV (Covishield™) and BBV-152 (Covaxin™) among health care workers in India: The final results of cross-sectional coronavirus vaccine-induced antibody titre (COVAT) study

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ABSTRACT

Background: We assessed the humoral immune response of both ChAdOx1-nCOV (Covishield™) and BBV-152 (Covaxin™) vaccines in Indian health care workers (HCW).

Methods: A Pan-India, Cross-sectional, Coronavirus Vaccine-induced Antibody Titre (COVAT) study was conducted that measured SARS-CoV-2 anti-spike binding antibody quantitatively, 21 days or more after the first and second dose of two vaccines in both severe acute respiratory syndrome (SARS-CoV-2) naïve and recovered HCW. Primary aim was to analyze antibody response (seropositivity rate, Geometric Mean Titre [GMT] and 95% Confidence Interval [CI]) following each dose of both vaccines and its correlation to age, sex, blood group, body mass index (BMI) and comorbidities. Here we report the results of anti-spike antibody response after first and two completed doses.

Results: Among the 515 HCW (305 Male, 210 Female) who took two doses of both vaccines, 95.0% showed seropositivity to anti-spike antibody. However, both seropositivity rate and GMT (95% CI) of anti-spike antibody was significantly higher in Covishield vs. Covaxin recipients (98.1 vs. 80.0%; 129.3 vs. 48.3 AU/mL; both $p < 0.001$). This difference persisted in 457 SARS-CoV-2 naïve and propensity-matched (age, sex and BMI) analysis of 116 participants. Age > 60-years, males, people with any comorbidities, and history of hypertension (HTN) had a significantly less anti-spike antibody GMT compared to age ≤ 60 years, females, no comorbidities and no HTN respectively, after the completion of two doses of either vaccine. Gender, presence of comorbidities, and vaccine type were independent predictors of antibody seropositivity rate and anti-spike antibody titre levels in multiple logistic and log transformed linear regression analysis. Both vaccine recipients had similar solicited mild to moderate adverse events and none had severe or unsolicited side effects.

Conclusions: Both vaccines elicited good immune response after two doses, although seropositivity rates and GMT of anti-spike antibody titre was significantly higher in Covishield compared to Covaxin recipients.

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1. Introduction

Nation-wide vaccination against the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection, the cause of Coronavirus disease 2019 (COVID-19) pandemic is currently ongoing across the globe. Vaccination with two candidate vaccines

namely Covishield™ and Covaxin™ in India has started from January 16, 2021 after the Emergency Use Approval (EUA). Covishield™ (ChAdOx1-nCoV or AZD1222, acquired from Oxford University and AstraZeneca, manufactured by Serum Institute of India, Pune) is a recombinant replication-deficient chimpanzee adenovirus-vectored vaccine encoding SARS-CoV-2 spike antigen produced in genetically modified human embryonic kidney (HEK) 293 cells. Each dose (0.5 ml) of Covishield contains 5×10^{10} viral spike particles. Covaxin™ (BBV-152, manufactured by Bharat Biotech, Hyderabad in collaboration with Indian Council of Medical Research [ICMR], India) is a β -propiolactone inactivated whole virion vaccine having all SARS-CoV-2 proteins adjuvanted with imidazoquinoline, a Toll-like receptor 7/8 (TLR 7/8) agonist, to boost the immune response. Each dose (0.5 ml) of Covaxin contains 6 μ g dose of whole virion inactivated corona virus protein of strain NIV-2020–770. The exact proportion of spike antigen in this whole-virus vaccine is not exactly known. While, early data from available phase 3 randomized clinical trials (RCTs) suggested that these two vaccines are safe and effective [1–3], there is still a paucity of information as to how much and how long, these novel vaccines can elicit an immune response, both at humoral and cellular level in the real-world settings. Moreover, the antibody kinetics after the first dose and completion of both doses of Covishield and Covaxin and thereafter, over a period of time is less well known. Here, we report the final results of ongoing Cross-sectional Coronavirus Vaccine-induced Antibody Titre (COVAT) study that assessed the anti-spike antibody humoral response 21-day after the first dose but before the second dose, and also after the completion of two doses of both Covishield and Covaxin [4].

2. Methods

2.1. Study design and participants

This report followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline for cross-sectional studies [5]. COVAT study is an ongoing, pan-India, cross-sectional study that was approved by the ethical committee of Thakershya Charitable Trust, Ahmedabad, Gujarat, India. Written informed consent were taken from all the participants who participated in this study, voluntarily. All adult health care workers of > 18 years of age who received the first dose of vaccine were eligible to participate in this study including those who had recovered from the COVID-19 in the recent past (> 6 weeks before the first dose). Individuals with current confirmed SARS-CoV-2 infection and those diagnosed within 6-weeks were excluded from the study. All subjects have received the first and second dose of either vaccine, 0.5 ml intramuscularly in the deltoid region. Data collection for this analysis started since the January 16, 2021 (first day of vaccination amongst HCW) until May 15, 2021 (data-lock date). The participants who acquired SARS-CoV-2 infection during the study period before the second sampling were excluded from the final analysis. India had nearly 25 million cases of COVID-19 with an average case reported per day ranging from 0.1 to 0.4 million during this period, with a peak of > 0.4 million cases on a single day on May 7, 2021.

2.2. Measurements

Clinical data was collected from all eligible participants including age, sex, blood groups, body mass index (BMI), past history of confirmed SARS-CoV-2 infection, any comorbidities, presence of diabetes mellitus (type 1 [T1DM] and type 2 [T2DM]), hypertension (HTN) including its duration and treatment received, dyslipidemia, ischemic heart disease (IHD), chronic kidney disease

(CKD) and cancer. Data was collected for any adverse events post-vaccination after the first and second dose. Additional data was also collected for subsequent SARS-CoV-2 infection including breakthrough infections. Accordingly, all participants were instructed to record and report the severity of conventional or solicited adverse events (fever; injection site pain, induration, swelling, redness; muscle pain; headache; excess fatigue; rash; pruritus or acute allergic reaction) to site investigators occurring within a week of vaccination after first and second dose. Severity of solicited adverse events was graded as nil, mild (recovered within 24 to 48-hour) to moderate (> 48-hour to < 7-days) and severe (requiring hospitalization), depending upon the intensity and duration of adverse event(s). Similarly, a record of unexpected or unsolicited adverse events of bleeding, thrombo-embolic episode, bells' palsy, seizure or other neurological manifestations, occurring from day 0 to 6 months after the second dose was also being recorded. Data collection for unsolicited adverse events and breakthrough infections is still ongoing and will be continued for 6-months after the second dose. Breakthrough infections are reported as per the given proforma that include- timing and severity, defined as mild (in-house or hospital treatment in anticipation of possible worsening but not actually requiring oxygen therapy), moderate (requiring oxygen supplementation but not requiring assisted ventilation, and severe (requiring ventilator).

Anti-spike antibody titre is being measured at four time-points: day 21 after the first dose until the day before the second dose; day 21–28 of second dose, day 83–97 (3-months) and day 173–187 (6-months) after the second dose. First blood sample (5 ml) were collected from eligible participants from day 21 after the first dose but before the second dose and second blood sample from day 21–28 after the second dose of each vaccine. An additional 7 days (21–36) for collection of second blood sample was allowed due to widespread lockdown. All samples were collected as either serum or plasma using EDTA vials from each participant and analyzed at Central laboratory of Neuberg, Supratech at Ahmedabad, Gujarat, India. The IgG antibodies to SARS-CoV-2 directed against the spike protein (S-antigen, both S1 and S2 protein) were assayed with LIAISON® S1/S2 quantitative antibody detection kit (DiaSorin Saluggia, Italy) using indirect chemiluminescence immunoassay (CLIA). The diagnostic sensitivity of this kit has been reported to be 97.4% (95% Confidence Interval [CI], 86.8–99.5%) > 15 days after SARS-CoV-2 infection with a specificity of 98.5% (95% CI, 97.5–99.2%) as per manufacturer's protocol. Antibody levels > 15.0 arbitrary unit (AU)/mL were considered as sero-positive, while antibody level \leq 15 AU/mL were considered as seronegative, as per the manufacturer's kit. This kit has found to have a concordance to neutralizing antibody (NAb) done by Plaque Reduction Neutralization Test (PRNT) with a positive agreement of 94.4% (95% CI, 88.8–97.2%) and negative agreement of 97.8% (95% CI, 94.4–99.1%) at a cut-off of > 15 AU/mL. The lower and upper limit of this quantitative spike antibody kit is 3.8 and 400 AU/mL respectively, as per the manufacturer's brochure [6].

2.3. Statistical analysis

Descriptive and inferential statistical analysis has been carried out for the present study. Normality of the data was assessed by Shapiro-Wilk test and visually by QQ plot for Covishield and Covaxin subgroups. Data on continuous scale was presented as Median (Interquartile range, IQR) and categorical data were presented as number (%). Mann-Whitney test was utilized to assess two non-parametric groups and Kruskal-Wallis test was used to compare the differences among two or multiple data group for data on continuous scale where it is presented as Median (Interquartile range, IQR). We also presented the log-transformed antibody titre data as geometric means along with its 95% confidence interval. For data

presented as geometric means, we used parametric tests (independent sample *t*-test and ANOVA test). We performed the analyses for the entire dataset and reported the main results. In order to confirm that the convenience sampling methodology did not creep in any bias in the results, we repeated the above analyses on the propensity matched dataset. A propensity score was generated taking into consideration age, sex and BMI of the all cohorts after the first dose and amongst the SARS-CoV-2 naïve cohorts after two complete doses of either vaccine. Participants having similar scores were matched and the two groups were compared accordingly. Chi-square test or Fischer's exact test was used to find the significance of study parameters on categorical scale between two or more groups. Furthermore, multiple logistic regression analysis was also conducted to find out whether any independent factors were associated with a blunted response to vaccine in anti-spike antibody generation following the first and after two doses of either vaccine. Additionally, in order to provide more reliable information on the independent predictors of antibody levels, explanatory variables were dummy coded and a log transformation of the outcome variable was done to perform multiple regression analysis. The β coefficients of the significant predictors were back transformed by taking an antilog to facilitate information of the data. A two-sided *P* value of < 0.05 was considered as statistically significant. To compare the antibody kinetics between two vaccines, we also presented the data as dot plot (present individual titers as points) as well as box-whisker plots, both after the first and the second dose. Entire statistical analysis was carried out with Statistical Package for Social Sciences (SPSS Complex Samples) Software Version 22.0 for windows, SPSS Inc., Chicago, IL, USA, with Microsoft Word and Excel being used to generate graphs and tables.

3. Results

Five hundred fifty-two participants who received first dose of either of the vaccine had complete set of data including anti-spike antibody, although only 515 who received two complete doses were included in the final statistical analysis after the exclusion of 37 cohorts from preliminary analysis. Fig. 1 depicts the flow diagram of participants disposition that entered from first to final analysis. The mean age of the participants was 44.8 ± 13.1 years, with 59.2% males (305/515) and 40.8% females (210/515). Out of 515 participants, 437 (84.9%) were aged ≤ 60 years and 78 (15.1%) were of age > 60 years. While 24.3% (125/515) had one or more comorbidities, 10.1% had T2DM, 18.3% had HTN, 4.7% had dyslipidemia and 2.5% had IHD. We had no participant having T1DM, CKD or cancer in our study cohort. Among all participants who completed two doses of either of the vaccine, 11.3% (58/515) had past history of confirmed SARS-CoV-2 (2-week prior to the first dose of vaccine). Participants who acquired SARS-CoV-2 infection after the first dose of either vaccine but before the collection of second blood sample (after second dose) were excluded. While there was no imbalance in baseline characteristics, a significantly larger proportion of participants had higher BMI, any comorbidities and past history of COVID-19 in Covishield compared to the Covaxin recipients. Table 1 summarizes the baseline characteristics of both 552 cohorts (who completed first dose of either of the vaccine) and 515 cohorts (who completed two doses of either of the vaccine).

3.1. SARS-COV-2 anti-spike antibody positivity rates following one or two doses of vaccine

Of the 522 participant (325 male, 227 female), 456 and 96 received the first dose of Covishield and Covaxin respectively. Overall, 79.3% (438/552) had seropositivity (defined as anti-spike

antibody titre > 15 AU/mL measured at day 21 until day before second dose) for anti-spike antibody. The seropositivity rate was significantly higher in Covishield vs. Covaxin recipient (86.8 vs. 43.8% respectively, $p < 0.001$) after the first dose. Importantly, past history of SARS-CoV-2 infection resulted in a significantly greater antibody seropositivity rate compared to SARS-CoV-2 naïve individuals in overall cohort (96.7% vs. 77.2%, $p < 0.001$) after the first dose, irrespective of the type of vaccine received. Amongst the 515 participants (305 male, 210 female) who completed both doses of Covishield ($n = 425$) and Covaxin ($n = 90$) respectively, 95.0% (489/515) had seropositivity (defined as anti-spike antibody titre > 15 AU/mL measured at day 21–36 after the second dose) for anti-spike antibody. Notably, the seropositivity rate was significantly higher in Covishield vs. Covaxin recipients (98.1 vs. 80.0% respectively, $p < 0.001$) after two complete doses. Seropositivity rate was significantly ($p = 0.001$) higher in participants aged ≤ 60 years (96.3%) vs. > 60 years (87.2%), in overall cohorts. While no difference in seropositivity rate was observed for gender, BMI and presence of any comorbidities in overall study participants; females compared to males (100.0 vs. 96.8%, $p = 0.02$) and those having no comorbidities (any) compared to ones with any comorbidities had a significantly higher seropositivity rate (99.0 vs. 95.6%, $p = 0.02$) amongst Covishield recipients. Amongst the captured co-morbidities, people with T2DM had a significantly lower seropositivity rate compared to those without (84.6 vs. 96.1%, $p = 0.002$) in overall study participants, and this was consistent in both Covishield (91.3 vs. 98.9%, $p < 0.001$) and Covaxin recipients (33.3 vs. 83.3%, $p = 0.003$), respectively after the completion of two doses. No differential antibody seropositivity rate was observed in relation to types of blood group, presence or absence of dyslipidemia, IHD and treatment regime of DM and HTN. Table 2 summarizes the seropositivity rates after the first and second doses with either vaccine.

Interestingly, in a repeat analysis of 492 SARS-CoV-2 naïve participants after the first dose (after exclusion of subjects with a past history of COVID-19, $n = 60$), and 457 SARS-CoV-2 naïve participants after the two complete doses (excluding past history of COVID-19, $n = 58$) results were similar and consistent. Seropositivity rate to anti-spike antibody was significantly higher in SARS-CoV-2 naïve Covishield recipients compared to Covaxin, both after the first (85.5 vs. 41.9% respectively; $p < 0.001$) and two completed second dose (97.8 vs. 79.3% respectively; $p < 0.001$) (Supplementary table 1).

3.2. Comparison of SARS-CoV-2 anti-spike antibody seropositivity rate following one or two doses of vaccine in propensity matched analysis

In the propensity-matched analysis of 172 participants (86 participants in each arm) after the adjustment for age, sex and BMI who received the first dose of either vaccine; past history of SARS-CoV-2 infection and type of vaccine received were found to be associated with a different antibody seropositivity rate. Seropositive rates were found to be significantly higher in Covishield compared to the Covaxin recipients (88.4% vs. 43.0%, $p < 0.001$) in the propensity-matched analysis. Similarly, in the propensity-matched analysis of 116 SARS-CoV-2 naïve participants (58 recipients with each vaccine) after the adjustment for age, sex and BMI who received the two complete doses of either vaccine; seropositivity rates were significantly higher in Covishield compared to the Covaxin (98.3% vs. 82.8%, $p = 0.004$) recipients. Notably, age ≤ 60 years had higher seropositivity rate vs. > 60 -years (98.5 vs. 79.6%, $p = 0.001$) and the presence of T2DM was associated with a lower seropositivity rate compared to those without (92.0 vs. 50.0%, $p = 0.005$) in the propensity matched analysis after completion of two doses (Table 3).

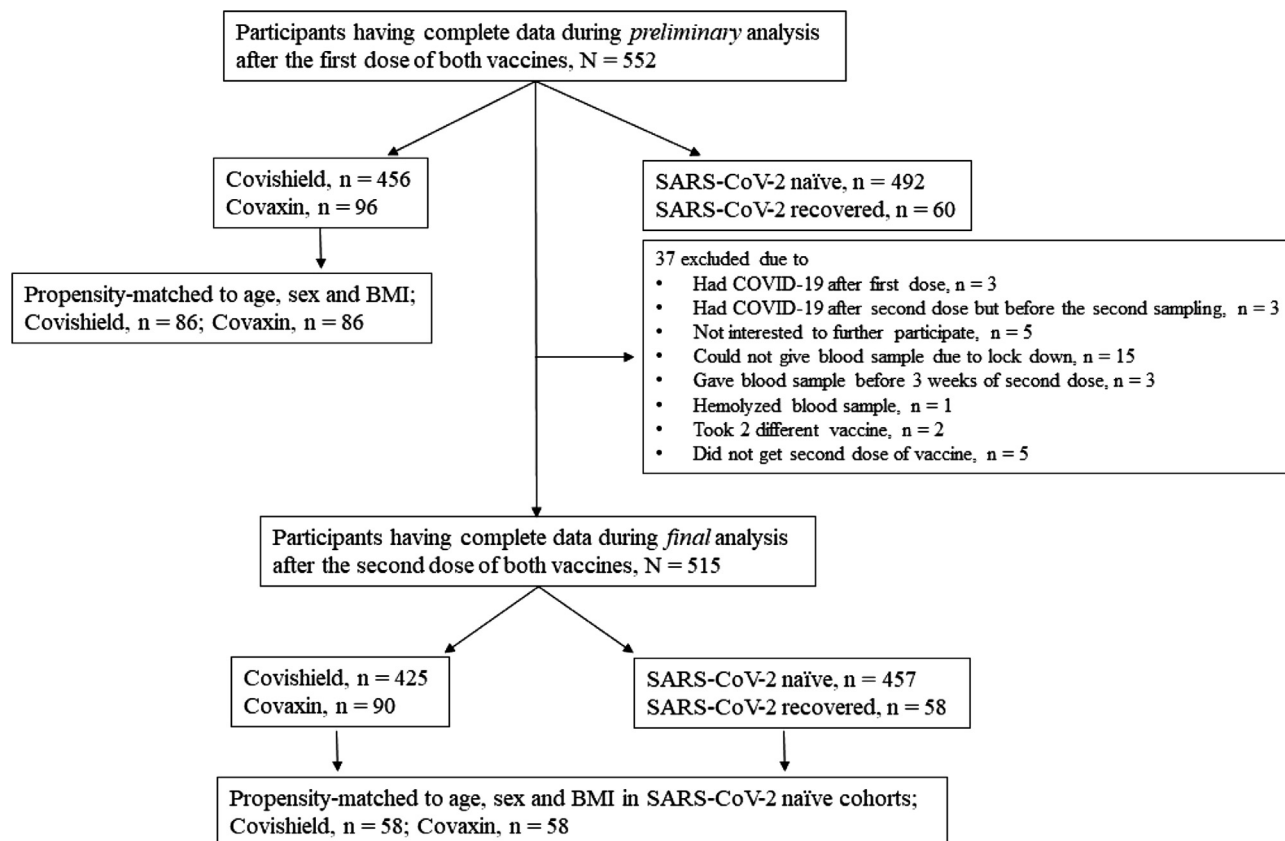


Fig. 1. Flow diagram for participants disposition after first and second dose of each vaccine.

3.3. Assessment of SARS-CoV-2 spike antibody titre following one or two doses of vaccine

The Geometric mean titre (GMT, 95% Confidence Interval) of anti-spike antibody was significantly higher in Covishield vs. Covaxin recipients, both after the first dose (GMT, 62.4 vs. 16.8 AU/mL, respectively; $p < 0.001$) and after the two complete doses (GMT, 129.3 vs. 48.3 AU/mL, respectively; $p < 0.001$). Subjects aged > 60 years, or HTN or of male sex had significantly lower anti-spike antibody GMT compared to those aged ≤ 60 years, without HTN or females, respectively after the completion of two doses of either vaccine (Table 4). Indeed, past history of SARS-CoV-2 infection elicited significantly higher antibody titre compared to SARS-CoV-2 naïve subjects, both after the first (GMT, 252.0 vs. 40.8 AU/mL; $p < 0.001$) and second dose (GMT, 302.7 vs. 95.6 AU/mL; $p < 0.001$), irrespective of the type of vaccine received. Notably, the GMT (95% CI) of anti-spike antibody was significantly higher in SARS-CoV-2 naïve participant who received Covishield compared to Covaxin both after first (GMT, 51.1 vs. 15.4 AU/mL, respectively; $p < 0.001$) and the completion of second dose (GMT, 114.0 vs. 45.3 AU/mL, respectively; $p < 0.001$) (Supplementary table 2). Furthermore, these GMT findings are consistent and concordant with an additionally calculated median (IQR) titre of anti-spike antibody among overall (Supplementary table 3) and the SARS-CoV-2 naïve cohorts (Supplementary table 4). Dot plot and Box-whisker plot (inbox) (Fig. 2) depicts the log antibody titre for different study parameters that were significantly different after the two complete doses of vaccine. Box-whisker plot (Fig. 3) depicts the long antibody titre for study parameters that were significantly different after first and second dose of vaccine. Supplementary Fig. 1 depicts the Dot plot and Box-whisker plot (inbox) for the log antibody titre for different study parameters that were

significantly different after the first dose of vaccine. No significant difference in the median (IQR) anti-spike antibody titre was observed when samples were analyzed between day 21–28 vs. day 29–36 vs. day 36–45 after the first dose of either vaccine (Supplementary table 5).

3.4. Comparison of SARS-CoV-2 anti-spike antibody titre following one or two doses of vaccine in propensity matched analysis

In the propensity (age, sex and BMI) matched analysis of 172 participants (86 participants in each arm) who received first dose of either vaccine; gender, past history of SARS-CoV-2 infection and type of vaccine received were found to be associated with a significantly different anti-spike antibody GMT. Anti-spike antibody was found to be significantly higher in Covishield compared to the Covaxin recipients (GMT, 62.0 vs. 16.4 AU/mL, respectively; $p < 0.001$) even in the propensity-matched analysis after the first dose. Furthermore, in the propensity-matched analysis of 116 SARS-CoV-2 naïve participants (58 recipients with each vaccine) after the adjustment for age, sex and BMI and after the two complete doses of either vaccine; GMT (95% CI) to anti-spike antibody were significantly higher in Covishield compared to the Covaxin (GMT, 112.6 vs. 46.8 AU/mL, respectively; $p < 0.001$) recipients. Notably, age > 60 -years, males, people with any comorbidities, and history of HTN had a significantly less anti-spike antibody GMT compared to age ≤ 60 years (76.8 vs. 111.5 AU/mL, respectively; $p = 0.02$), females (83.2 vs. 89.1 AU/mL, respectively; $p < 0.001$), no comorbidities (68.4 vs. 91.2 AU/mL, respectively; $p = 0.04$) and no HTN (79.7 vs. 116.2 AU/mL, respectively; $p < 0.001$) respectively, after the completion of two doses of either vaccine (Table 5).

Table 1
Baseline subject characteristics.

Characteristics	First dose of either vaccine			P value	Two completed doses of either vaccine			P value
	Overall, N = 552	Covishield, N = 456	Covaxin, N = 96		Overall, N = 515	Covishield, N = 425	Covaxin, N = 90	
Age								
Age (in years), Mean ± SD	44.85 ± 13.23	45.32 ± 12.97	42.25 ± 15.24	0.087	44.82 ± 13.09	45.15 ± 12.26	43.44 ± 16.04	0.286
Age ≤ 60 years, n (%)	464 (84.06)	384 (84.21)	80 (83.33)	0.831	437 (84.9)	361 (84.9)	76 (84.4)	0.905
Age > 60 years, n (%)	88 (15.94)	72 (15.79)	16 (16.67)		78 (15.1)	64 (15.1)	14 (15.6)	
Sex								
Male, n (%)	325 (58.88)	268 (58.77)	57 (59.38)	0.913	305 (59.2)	252 (59.3)	53 (58.9)	0.943
Female, n (%)	227 (41.12)	188 (41.23)	39 (40.63)		210 (40.8)	173 (40.7)	37 (41.1)	
Body mass index (BMI)								
BMI (kg/m ²), Mean ± SD	25.61 ± 4.36	25.57 ± 4.53	25.75 ± 3.31	0.751	25.42 ± 4.43	25.96 ± 4.87	24.02 ± 3.66	0.001
BMI < 25 kg/m ² , n (%)	379 (68.66)	309 (67.76)	70 (72.92)	0.556	353 (68.5)	287 (67.5)	66 (73.3)	0.531
BMI 25–29.9 kg/m ² , n (%)	106 (19.2)	89 (19.52)	17 (17.71)		96 (18.6)	81 (19.1)	15 (16.7)	
BMI ≥ 30 kg/m ² , n (%)	67 (12.13)	58 (12.72)	9 (9.38)		66 (12.8)	57 (13.4)	9 (10)	
Blood group (%)								
A + ve	108 (19.6)	89 (19.5)	19 (19.8)	0.052	104 (20.2)	86 (20.2)	18 (20)	0.319
B + ve	159 (28.8)	141 (30.9)	18 (18.8)		148 (28.7)	132 (31.1)	16 (17.8)	
AB + ve	30 (5.4)	25 (5.5)	5 (5.2)		29 (5.6)	24 (5.6)	5 (5.6)	
O + ve	225 (40.8)	172 (37.7)	53 (55.2)		205 (39.8)	155 (36.5)	50 (55.6)	
A-ve	7 (1.3)	7 (1.5)	0		7 (1.4)	7 (1.6)	0	
B-ve	10 (1.8)	10 (2.2)	0		9 (1.7)	9 (2.1)	0	
AB-ve	2 (0.4)	2 (0.4)	0		2 (0.4)	2 (0.5)	0	
O-ve	11 (2)	10 (2.2)	1 (1)		11 (2.1)	10 (2.4)	1 (1.1)	
Comorbidities								
Any Co-morbidities, n (%)	131 (23.73)	118 (25.88)	13 (13.54)	0.010	125 (24.3)	114 (26.8)	11 (12.2)	0.003
No Co-morbidities, n (%)	421 (76.27)	338 (74.12)	83 (86.45)		390 (75.7)	311 (73.2)	79 (87.8)	
Type 2 diabetes mellitus (T2DM)								
T2DM, n (%)	57 (10.33)	49 (10.75)	8 (8.33)	0.480	52 (10.1)	46 (10.8)	6 (6.7)	0.234
No T2DM, n (%)	495 (89.67)	407 (89.25)	88 (91.66)		463 (89.9)	379 (89.2)	84 (93.3)	
T2DM Duration								
Duration < 5 years, n (%)	11 (1.99)	10 (2.19)	1 (1.04)	0.605	8 (1.6)	8 (1.9)	0	0.409
Duration 5–10 years, n (%)	31 (5.61)	26 (5.7)	5 (5.2)		30 (5.8)	25 (5.9)	5 (5.6)	
Duration > 10 years, n (%)	15 (2.71)	14 (3.07)	1 (1.04)		14 (2.7)	13 (3.1)	1 (1.1)	
T2DM Control								
Optimum control, n (%)	55 (9.96)	48 (10.53)	7 (7.29)	0.307	51 (9.9)	45 (10.6)	6 (6.7)	0.470
No optimum control, n (%)	2 (0.36)	1 (0.21)	1 (1.04)		1 (0.1)	1 (0.2)	0	
T2DM Management								
Monotherapy, n (%)	16 (2.89)	13 (2.85)	3 (3.13)	0.563	15 (2.9)	13 (3.1)	2 (2.2)	0.615
Combination therapy, n (%)	35 (6.34)	32 (7.01)	3 (3.13)		32 (6.2)	29 (6.8)	3 (3.3)	
Insulin, n (%)	1 (0.18)	1 (0.21)	0		0	0	0	
No medication, n (%)	5 (0.9)	4 (0.87)	1 (1.04)		4 (0.1)	4 (0.9)	0	
Hypertension (HTN)								
Yes, n (%)	99 (17.93)	77 (16.89)	22 (22.91)	0.162	94 (18.3)	75 (17.6)	19 (21.1)	0.440
No, n (%)	453 (82.07)	379 (83.11)	74 (77.08)		421 (81.7)	350 (82.4)	71 (78.9)	
HTN Duration								
Duration < 5 years, n (%)	29 (5.25)	26 (5.7)	3 (3.13)	0.067	27 (5.2)	24 (5.6)	3 (3.3)	0.053
Duration 5–10 years, n (%)	48 (8.69)	31 (6.8)	17 (17.7)		46 (8.9)	31 (7.3)	15 (16.7)	
Duration > 10 years, n (%)	22 (3.99)	20 (4.39)	2 (2.08)		21 (4.1)	20 (4.7)	1 (1.1)	
HTN Management								
RAAS Blockers, n (%)	41 (7.43)	37 (8.11)	4 (4.16)	0.228	40 (7.8)	37 (8.7)	3 (3.3)	0.158
CCBs, n (%)	22 (3.99)	20 (4.39)	2 (2.08)		21 (4.1)	19 (4.5)	2 (2.2)	
Combined, n (%)	21 (3.81)	19 (4.17)	2 (2.08)		20 (3.9)	18 (4.2)	2 (2.2)	
No Medicine, n (%)	2 (0.36)	1 (0.21)	1 (1.04)		2 (0.4)	1 (0.2)	1 (1.1)	
Lipid abnormalities								
Dyslipidemia, n (%)	26 (4.71)	26 (4.71)	0	0.050	24 (4.7)	24 (5.6)	0	0.062
No Dyslipidemia, n (%)	526 (95.28)	430 (94.29)	96 (100)		491 (95.3)	401 (94.4)	90 (100)	
Ischemic heart disease (IHD)								
IHD, n (%)	13 (2.35)	13 (2.85)	0	0.094	13 (2.5)	13 (3.1)	0	0.093
No IHD, n (%)	539 (97.64)	443 (97.15)	96 (100)		502 (97.5)	412 (96.9)	90 (100)	
History of SARS-CoV-2 infection								
Past H/o COVID-19, n (%)	60 (10.87)	57 (12.5)	3 (3.12)	0.006	58 (11.3)	55 (12.9)	3 (3.3)	0.009
No Past H/o COVID-19, n (%)	492 (89.13)	399 (72.28)	93 (96.88)		457 (88.7)	370 (87.1)	87 (96.7)	

p < 0.05 considered as statistically significant, p computed by chi-square test or independent sample t-test to test the significance between Covaxin and Covishield, BMI- body mass index, T2DM- type 2 diabetes mellitus, HTN- hypertension, RAAS- Renin angiotensin aldosterone system, CCB- calcium channel blocker, IHD- ischemic heart disease, SARS-CoV-2- severe acute respiratory syndrome coronavirus-2, COVID-19- coronavirus disease 2019.

3.5. Independent variables associated with seropositivity to anti-spike antibody and titre level following two doses of vaccine

Multiple logistic regression analysis (to identify the independent predictors for non-seropositivity rate based on development

of SARS-CoV-2 Anti-spike antibody) suggests that amongst all the variables analyzed, three variables such as- sex, presence of comorbidities, and vaccine type were independent predictors of antibody seropositivity rate. Associated co-morbidities were significantly related to an increase in the non-seropositivity rate by > 4-fold

Table 2
Seropositivity to anti-spike antibody after the first dose and second dose of either vaccine.

Characteristics	First dose of either vaccine						Two completed doses of either vaccine					
	Overall, N = 552		Covishield, N = 456		Covaxin, N = 96		Overall, N = 515		Covishield, N = 425		Covaxin, N = 90	
	Seropositivity Rate	P	Seropositivity Rate	P	Seropositivity Rate	P	Seropositivity Rate	P	Seropositivity Rate	P	Seropositivity Rate	P
<i>Age</i>												
Age ≤ 60 years, n (%)	372/464 (80.2)	0.272	339/384 (88.3)	0.036	33/80 (41.2)	0.270	421/437 (96.3)	0.001	358/361 (99.2)	<0.001	63/76 (82.9)	0.110
Age > 60 years, n (%)	66/88 (74.4)		57/72 (79.2)		9/16 (56.2)		68/78 (87.2)		59/64 (92.2)		9/14 (64.3)	
<i>Sex</i>												
Male, n (%)	251/325 (77.2)	0.142	228/268 (85.1)	0.182	23/57 (40.4)	0.417	286/305 (93.8)	0.140	244/252 (96.8)	0.018	42/53 (79.2)	0.830
Female, n (%)	187/227 (82.4)		168/188 (89.4)		19/39 (48.7)		203/210 (96.7)		173/173 (100)		30/37 (81.1)	
<i>Body mass index (BMI)</i>												
BMI < 25 kg/m ²	301/379 (79.4)	0.731	273/309 (88.3)	0.375	27/70 (38.6)	0.150	338/353 (95.8)	0.441	285/287 (99.3)	0.028	53/66 (80.3)	0.984
BMI 25–29.9 kg/m ²	85/106 (80.2)		74/89 (83.1)		11/17 (64.7)		90/96 (93.8)		78/81 (96.3)		12/15 (80)	
BMI ≥ 30 kg/m ²	57/67 (85.1)		49/58 (84.5)		4/9 (44.4)		61/66 (92.4)		54/57 (94.7)		7/9 (77.8)	
<i>Blood groups</i>												
A + ve, n (%)	84/108 (77.8)	0.826	79/89 (88.8)	0.930	5/19 (26.3)	0.400	99/104 (95.2)	0.799	86/86 (100)	0.569	13/18 (72.2)	0.396
B + ve, n (%)	130/159 (81.8)		121/141 (85.8)		9/18 (50)		142/148 (81.8)		127/132 (96.2)		15/16 (93.8)	
AB + ve, n (%)	23/30 (76.7)		21/25 (84)		2/5 (40)		26/29 (89.7)		23/24 (95.8)		3/5 (60)	
O + ve, n (%)	175/225 (77.8)		149/172 (86.6)		26/53 (49.1)		193/205 (94.1)		153/155 (98.7)		40/50 (80)	
A-ve, n (%)	7/7 (100)		7/7 (100)		-		7/7 (100)		7/7 (100)		-	
B-ve, n (%)	8/10 (80)		8/10 (80)		-		9/9 (100)		9/9 (100)		-	
AB-ve, n (%)	2/2 (100)		2/2 (100)		-		2/2 (100)		2/2 (100)		-	
O-ve, n (%)	9/11 (81.8)		9/10 (90)		0/1 (0)		11/11 (100)		10/10 (100)		0/1 (0)	
<i>Comorbidities</i>												
Any Co-morbidities, n (%)	95/131 (72.5)	0.027	92/118 (78)	0.001	3/13 (23.1)	0.092	116/125 (92.8)	0.207	109/114 (95.6)	0.021	7/11 (63.6)	0.148
No Co-morbidities, n (%)	343/421 (81.5)		304/338 (89.9)		39/83 (47)		373/390 (95.6)		308/311 (99)		65/79 (82.3)	
<i>Type 2 diabetes mellitus (T2DM)</i>												
T2DM, n (%)	42/57 (73.7)	0.265	39/49 (79.6)	0.112	3/8 (37.5)	0.710	44/52 (84.6)	0.002	42/46 (91.3)	<0.001	2/6 (33.3)	0.003
No T2DM, n (%)	396/495 (80)		357/407 (87.7)		39/88 (44.3)		445/463 (96.1)		375/379 (98.9)		70/84 (83.3)	
<i>T2DM Duration</i>												
T2DM Duration < 5 years, n (%)	9/11 (81.8)	0.751	8/10 (80)	0.994	1/1 (100)	0.214	8/8 (100)	<0.001	8/8 (100)	<0.001	-	0.008
T2DM Duration 5–10 years, n (%)	21/31 (67.74)		20/26 (76.92)		1/5 (20)		23/30 (76.7)		21/25 (84)		2/5 (40)	
T2DM Duration > 10 years, n (%)	11/15 (73.3)		11/14 (78.6)		0/1 (0)		13/14 (92.9)		13/13 (100)		0/1 (0)	
<i>T2DM Control</i>												
T2DM-Optimum control, n (%)	40/55 (72.7)	0.390	38/48 (79.2)	0.609	2/7 (28.6)	0.168	43/51 (84.3)	0.369	41/45 (91.1)	0.568	2/6 (33.3)	0.762
T2DM-No optimum control, n (%)	0/2 (0)		1/1 (100)		1/1 (100)		1/1 (100)		1/1 (100)		0 (0/0)	
<i>T2DM Management</i>												
Monotherapy, n (%)	14/16 (87.5)	0.287	12/13 (92.3)	0.414	2/3 (66.7)	0.155	14/15 (93.3)	0.151	13/13 (100)	0.201	1/2 (50)	0.103
Combination therapy, n (%)	24/35 (68.6)		24/32 (75)		0/3 (0)		26/32 (81.2)		26/29 (89.7)		0/3 (0)	
Insulin, n (%)	1/1 (100)		1/1 (100)		-		-		-		-	
No medication, n (%)	3/5 (60)		3/4 (75)		0/1 (0)		4/5 (80)		3/4 (75)		1/1 (100)	
<i>Hypertension (HTN)</i>												
HTN, n (%)	65/99 (65.7)	0.001	56/77 (72.7)	<0.001	13/22 (55.4)	0.760	86/94 (91.5)	0.090	72/75 (96)	0.137	14/19 (73.7)	0.438
No HTN, n (%)	373/453 (82.3)		340/379 (89.7)		41/74 (88.9)		403/421 (95.7)		345/350 (98.6)		58/71 (81.7)	
HTN Duration < 5 years, n (%)	17/29 (58.6)	0.549	17/26 (65.4)	0.414	0/3 (0)	0.482	27/27 (100)	0.008	24/24 (100)	0.010	3/3 (100)	0.152
HTN Duration 5–10 years, n (%)	33/48 (68.8)		25/31 (80.6)		8/17 (47.1)		39/46 (84.8)		28/31 (90.3)		11/15 (73.3)	
HTN Duration > 10 years, n (%)	15/22 (68.2)		14/20 (70)		1/2 (50)		20/21 (95.2)		20/20 (100)		0/1 (0)	
<i>HTN Management</i>												
RAAS Blockers, n (%)	28/41 (68.3)	0.944	27/37 (73)	0.928	1/4 (25)	0.704	37/40 (92.5)	0.958	35/37 (94.6)	0.352	2/3 (66.7)	0.695
CCBs, n (%)	14/22 (63.6)		14/20 (70)		0/2 (0)		20/21 (95.2)		18/19 (94.7)		2/2 (100)	
Combined, n (%)	14/21 (66.7)		14/19 (73.7)		0/2 (0)		19/20 (95)		18/18 (100)		1/2 (50)	
No Medicine, n (%)	1/2 (50)		1/1 (100)		0/1 (0)		2/2 (100)		1/1 (100)		1/1 (100)	

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Table 2 (continued)

Characteristics	First dose of either vaccine				Two completed doses of either vaccine					
	Covishield, N = 456		Covaxin, N = 96		Overall, N = 515		Covishield, N = 425		Covaxin, N = 90	
	Seropositivity Rate	P	Seropositivity Rate	P	Seropositivity Rate	P	Seropositivity Rate	P	Seropositivity Rate	P
<i>Dyslipidemia</i>	23/26 (88.5)	0.437	23/26 (88.5)	0.897	23/24 (95.8)	0.954	23/24 (95.8)	0.692	-	(*)
No Dyslipidemia, n (%)	415/526 (78.89)		373/430 (86.7)		466/491 (94.9)		394/401 (98.2)		72/90 (80)	
<i>Ischemic heart disease (IHD)</i>	11/13 (84.6)	0.635	11/13 (84.6)	0.810	13/13 (100)	0.400	13/13 (100)	0.612	-	(*)
IHD, n (%)	427/539 (79.2)		385/443 (86.9)		476/502 (94.8)		404/412 (98.1)		72/90 (80)	
No IHD, n (%)	58/60 (96.7)	<0.001	55/57 (96.5)	0.023	58/58 (100)	0.062	55/55 (100)	0.271	3/3 (100)	0.378
<i>History of SARS-CoV-2 infection</i>	380/492 (77.2)		341/399 (85.5)		431/457 (94.3)		362/370 (97.8)		69/87 (79.3)	
Past H/o COVID-19, n (%)	396/456 (86.8)	<0.001	42/96 (43.8)		417/425 (98.1)	<0.001	72/90 (80)		-	
No Past H/o COVID-19, n (%)										
<i>Types of vaccine</i>										
Covishield, n (%)										
Covaxin, n (%)										

p < 0.05 considered as statistically significant; p computed by chi-square test; BMI- Body mass index; T2DM- Type 2 diabetes mellitus; HTN- Hypertension; RAAS- Renin angiotensin aldosterone system; CCB- Calcium channel blocker; IHD- Ischemic heart disease; SARS-CoV-2- Severe acute respiratory syndrome coronavirus-2; COVID-19- Coronavirus disease 2019; NA- Not applicable; (*) - No statistics is computed.

(Odds Ratio [OR] 4.68; 95% CI, 1.382–15.839; p = 0.013), while male gender also showed a significant increase in the non-seropositivity rate by > 3-folds (OR 3.37; 95% CI, 1.221–9.321; p = 0.019). Notably, recipients of Covishield had a significantly lower non-responder rate by 41% (OR 0.59; 95% CI, 0.021–0.659; p < 0.001), compared to those who received Covaxin (Table 6).

In a multiple linear regression model with log transformed antibody levels as outcome variable, we found presence of comorbidity, sex, vaccine type and past history of COVID-19 infection as independent predictors of antibody titre. The R value of the model represents the simple correlation and is 0.493, which indicates a moderate degree of correlation. The overall R² value of 0.247 indicating 24.7% of the total variation in the dependent variable (antibody titre) can be explained by our model. The multiple regression analysis (to identify the independent predictors for SARS-CoV-2 Anti-spike antibody titre) suggests that amongst all the variables analyzed, four variables such as- presence of comorbidity, sex, past history of SARS-CoV-2 infection and vaccine type were independent predictors of antibody levels. While presence of comorbidity resulted in decrease in the antibody titre by 13% (β = 0.87; 95% CI, 0.79–0.97; p = 0.010), female gender was found to have 9% greater antibody titre compared to males (β = 1.09; 95% CI, 1.02–1.17; p = 0.018). SARS-CoV-2 naïve participants were associated with significantly lower antibody titre by 37% (β = 0.63; 95% CI, 0.57–0.71; p < 0.001). Notably, recipients of Covaxin had a significantly lower antibody titre by 32% ((β = 0.68; 95% CI, 0.62–0.74; p < 0.001), as compared to those who received Covishield (Table 7).

3.6. Post-vaccination adverse events

Covishield recipients had higher proportions of any mild to moderate side-effects as compared to Covaxin (46.7% vs. 31.2%, p = 0.006) after the first dose. Higher rates of mild to moderate side effects were observed with Covishield compared to the Covaxin recipients (50.0 % vs. 30.2%, p = 0.008) even in the propensity-matched participants after the first dose. Although Covishield recipients also reported a higher incidence of mild to moderate side-effects in 18.1% (77/425) compared to 11.1% (10/90) in Covaxin recipients after the second dose of vaccine, it did not reach statistical significance (p = 0.11). Notably, in the propensity-matched cohort, any side-effects (mild to moderate) post vaccination was also similar (p = 0.13) in the Covishield arm 8/58 (13.79%) vs. Covaxin arm 6/58(10.34%). No serious solicited and any unsolicited side effects were noted after the first and second dose until the data lock (Supplementary table 6). Since this study is still ongoing, we will keep on reporting the details of any unsolicited side effects with either vaccine until 6 months after the second dose.

3.7. Post-vaccination SARS-CoV-2 infection

From Jan 16, 2021 (Day 1 of vaccination) until May 15, 2021 (Day 21–36 after second dose, data-locking date), a total of 30 (30/492, 6.1%) HCW have reported to have COVID-19 among SARS-CoV-2 naïve cohorts (n = 492) after the first dose of vaccination. Of the 30 participants 4 had suspected (symptomatic and positive signs on High Resolution Computed Tomography [HRCT] of chest but negative to either Reverse Transcription Polymerase Chain Reaction [RT-PCR] or Rapid Antigen Test [RAT]) and 26 had confirmed (RT-PCR or RAT positive) COVID-19. Three had SARS-CoV-2 infection before the second dose, while 27 had acquired SARS-CoV-2 infection after the second dose. Breakthrough infections (defined as SARS-CoV-2 infection > 2 weeks after the second dose) were reported in 4.9% (24/492) of cases following both vaccines. Breakthrough infections were noted in 5.5% (22/399) cohorts

Table 3
Seropositivity to anti-spike antibody in propensity score (age, sex, BMI) matched analysis after the first dose of either vaccine in total cohorts and after the second doses of either vaccine in SARS-CoV-2 naïve cohorts[#]

Characteristics	First dose of either vaccine						Two completed doses of either vaccine [#]					
	Overall, N = 172		Covishield, N = 86		Covaxin, N = 86		Overall, N = 116		Covishield, N = 58		Covaxin, N = 58	
	Seropositivity Rate	P	Seropositivity Rate	P	Seropositivity Rate	P	Seropositivity Rate	P	Seropositivity Rate	P	Seropositivity Rate	P
<i>Age</i>												
Age ≤ 60 years, n (%)	98/148 (66.2)	0.722	67/73 (91.2)	0.019	31/75 (41.3)	0.409	66/67 (98.5)	0.001	43/43 (100)	0.088	23/24 (95.8)	0.027
Age > 60 years, n (%)	15/24 (62.5)		9/13 (69.2)		6/11 (54.5)		39/49 (79.6)		14/15 (93.3)		25/34 (73.5)	
<i>Sex</i>												
Male, n (%)	52/81 (64.2)	0.696	36/40 (90)	0.661	16/41 (39)	0.475	47/51 (92.2)	0.593	23/23 (100)	0.414	24/28 (85.7)	0.565
Female, n (%)	61/91 (67)		40/46 (87)		21/45 (46.7)		58/65 (89.2)		34/35 (97.1)		24/30 (80)	
<i>Body mass index (BMI)</i>												
BMI < 25 kg/m ²	78/124 (62.9)	0.402	55/62 (88.7)	0.938	23/62 (37.1)	0.116	84/92 (91.3)	0.836	50/51 (98)	0.933	34/41 (82.9)	0.996
BMI 25–29.9 kg/m ²	22/29 (75.9)		12/14 (85.7)		10/15 (66.7)		15/17 (88.2)		6/6 (100)		9/11 (81.8)	
BMI ≥ 30 kg/m ²	13/19 (68.4)		9/10 (90)		4/9 (44.4)		6/7 (85.7)		1/1 (100)		5/6 (83.3)	
<i>Blood group</i>												
A + ve, n (%)	22/37 (59.5)	0.655	17/18 (94.4)	0.368	5/19 (26.3)	0.264	22/24 (91.7)	0.948	14/14 (100)	0.894	8/10 (80)	0.581
B + ve, n (%)	34/47 (72.3)		28/33 (84.8)		6/14 (42.9)		30/32 (93.8)		17/18 (94.4)		13/14 (92.9)	
AB + ve, n (%)	3/6 (50)		2/2 (100)		1/4 (25)		8/9 (88.9)		7/7 (100)		1/2 (50)	
O + ve, n (%)	53/80 (66.2)		28/31 (90.3)		25/49 (51)		40/46 (87)		15/15 (100)		25/31 (80.6)	
A-ve, n (%)	-		-		-		1/1 (100)		1/1 (100)		-	
B-ve, n (%)	1/2 (50)		1/2 (50)		-		2/2 (100)		2/2 (100)		-	
AB-ve, n (%)	-		-		-		-		-		-	
O-ve, n (%)	-		-		-		2/2 (100)		1/1 (100)		1/1 (100)	
<i>Comorbidities</i>												
Any Co-morbidities, n (%)	19/33 (57.6)	0.274	18/22 (81.8)	0.266	1/11 (9.1)	0.015	7/9 (77.8)	0.174	4/4 (100)	0.784	3/5 (60)	0.202
No Co-morbidities, n (%)	94/139 (67.6)		58/64 (90.6)		36/75 (48)		98/107 (91.6)		53/54 (98.1)		45/53 (84.9)	
<i>Type 2 diabetes mellitus (T2DM)</i>												
T2DM, n (%)	8/17 (47.1)	0.088	7/11 (63.6)	0.006	1/6 (16.7)	0.176	2/4 (50)	0.005	2/2 (100)	0.849	0/2 (0)	0.002
No T2DM, n (%)	105/155 (67.7)		69/75 (92)		36/80 (45)		103/112 (92)		55/56 (98.2)		48/56 (85.7)	
<i>T2DM Duration</i>												
T2DM Duration < 5 years, n (%)	3/4 (75)	0.114	2/3 (66.7)	0.059	1/1 (100)	0.156	1/1 (100)	0.143	1/1 (100)	0.982	0/0 (0)	0.902
T2DM Duration 5–10 years, n (%)	4/8 (50)		4/4 (100)		0/4 (0)		1/3 (33.3)		1/1 (100)		0/2 (0)	
T2DM Duration > 10 years, n (%)	1/5 (20)		1/4 (25)		0/1 (0)		-		-		-	
<i>T2DM Control</i>												
Optimum control, n (%)	7/16 (43.8)	0.121	6/10 (60)	0.052	1/6 (16.7)	0.176	2/4 (50)	(*)	2/2 (100)	(*)	0/2	(*)
No optimum control, n (%)	1/1 (100)		1/1 (100)		-		-		-		-	
<i>T2DM Management</i>												
Monotherapy, n (%)	4/6 (66.6)	0.085	3/3 (100)	0.198	1/3 (33.3)	0.364	1/1 (100)	0.933	1/1 (100)	0.982	-	(*)
Combination therapy, n (%)	3/10 (30)		3/7 (42.9)		0/3 (0)		1/3 (33.3)		1/1 (100)		0/2	
Insulin, n (%)	1/1 (100)		1/1 (100)		0/1 (0)		-		-		-	
No medication, n (%)	-		-		-		-		-		-	
<i>Hypertension (HTN)</i>												
HTN, n (%)	93/137 (67.9)	0.232	64/72 (88.9)	0.735	29/65 (44.6)	0.600	9/12 (75)	0.053	1/1 (100)	0.894	8/11 (72.7)	0.328
No HTN, n (%)	20/35 (57.1)		12/14 (85.7)		8/21 (38.1)		96/104 (92.3)		56/57 (98.2)		40/47 (85.1)	
<i>HTN Duration</i>												
HTN Duration < 5 years, n (%)	4/8 (50)	0.645	4/5 (80)	0.634	0/3 (0)	0.362	4/4 (100)	0.054	1/1 (100)	(*)	3/3 (100)	0.101
HTN Duration 5–10 years, n (%)	13/22 (59.1)		5/5 (100)		8/17 (47.1)		5/7 (71.4)		-		5/7 (71.4)	
HTN Duration > 10 years, n (%)	3/5 (60)		3/4 (75)		1/1 (0)		0/1 (0)		-		0/1 (0)	
<i>HTN Management</i>												
RAAS Blockers, n (%)	4/8 (50)	0.749	4/5 (80)	0.788	0/3	0.155	1/2 (50)	0.124	1/1 (100)	0.894	0/1 (0)	0.380
CCBs, n (%)	3/6 (50)		3/4 (75)		0/2		3/3 (100)		-		3/3 (100)	
Combined, n (%)	4/6 (66.7)		4/4 (100)		0/2		-		-		-	
No Medicine, n (%)	1/2 (50)		1/1 (100)		0/1		-		-		-	

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Table 3 (continued)

Characteristics	First dose of either vaccine			Two completed doses of either vaccine ^a		
	Overall, N = 172	Covishield, N = 86	Covaxin, N = 86	Overall, N = 116	Covishield, N = 58	Covaxin, N = 58
	Seropositivity Rate	P	Seropositivity Rate	P	Seropositivity Rate	P
Dyslipidemia	8/10 (80)	0.768	6/6 (100)	0.102	2/4 (50)	0.864
Dyslipidemia, n (%)	107/162 (66.04)		63/80 (78.75)		44/82 (53.69)	
No Dyslipidemia, n (%)	3/4 (75)	0.692	3/4 (75)	0.393	0/0	0.393
Ischemic heart diseases (IHD)	110/168 (65.5)		73/82 (89)		37/86 (43)	
IHD, n (%)						
No IHD, n (%)						
History of SARS-CoV-2 infection	12/12 (100)	0.009	9/9 (100)	0.250	3/3 (100)	0.042
Past H/o COVID-19, n (%)	101/160 (63.1)		67/77 (87)		34/83 (41)	
No Past H/o COVID-19, n (%)						
Types of vaccine						
Covishield, n (%)	76/86 (88.4)	<0.001			57/58 (98.3)	0.004
Covaxin, n (%)	37/86 (43)				48/58 (82.8)	

p < 0.05 considered as statistically significant, p computed by chi-square test; BMI- Body mass index, T2DM- Type 2 diabetes mellitus, HTN- Hypertension, RAAS- Renin angiotensin aldosterone system, CCB- Calcium channel blocker, IHD- Ischemic heart disease, SARS-CoV-2- Severe acute respiratory syndrome coronavirus-2, COVID-19- Coronavirus disease 2019, NA- Not applicable, (*) - No statistics is computed.

in Covishield and 2.2% (2/93) of Covaxin recipients, although there were no significant statistical differences (p = 0.21) in breakthrough infections between two vaccine recipients until the data lock. The majority of vaccine recipients had mild (28/30) to moderate (2/30) COVID-19 infections and all recovered. None of the cohort who had COVID-19 following either vaccine had severe COVID requiring mechanical ventilation (Supplementary Table 7). Since this study is still ongoing, we will report every detail of breakthrough infection with either vaccine until 6 months after the second complete doses.

4. Discussion

Summarily, this cross-sectional COVAT study reported an overall 95.0% (489/515) seropositivity rate after two complete doses of both vaccines in entire study participants that include both SARS-CoV-2 naïve and recovered individuals (Covishield 98.1% and Covaxin 80.0%, respectively). While seropositivity rates after two complete doses was 97.8% and 79.3% with Covishield and Covaxin, respectively in SARS-CoV-2 naïve individuals; 100% of study participants with a past history of SARS-CoV-2 were seropositive after two doses of either vaccine. Notably, while both vaccines showed an increase in seropositivity rate, GMT (95% CI) and median (IQR) anti-spike antibody titre after the second dose, Covaxin gained a significant increase in both seropositivity and antibody titre only after the two doses. Contrarily, Covishield showed a good seropositivity rate and a > 3-fold rise in anti-spike antibody GMT even after a single dose. One dose of either vaccine yielded a very high seropositivity and anti-spike antibody titre in SARS-CoV-2 recovered individuals (Table 8). There was no significant difference in seropositivity rate with regard to age, sex, BMI, blood group and any comorbidities including its duration and treatment, except that the participants with T2DM had a significantly less seropositive rate compared to those without. Importantly, GMT (95% CI) and median (IQR) titre of anti-spike antibody was significantly lower in age > 60 years, males and people with history of HTN compared to age ≤ 60 years, females and no history of HTN, respectively. Notably, no difference in seropositivity rate was observed amongst SARS-CoV-2 naïve vs. SARS-CoV-2 recovered participants after the two completed doses of either vaccine. Any adverse side effects post-vaccination was similar in Covishield and Covaxin recipients after second dose, although it was higher with former after the first dose compared to later but were mild to moderate in nature. Surprisingly, the seropositivity rate, GMT and median anti-spike antibody titre was significantly higher in Covishield recipients, compared to the Covaxin. Whether this differential finding between two vaccines is related to a lesser number of Covaxin participants compared to the Covishield, or due to the difference in characteristics of participants, or due to the difference between the type of vaccine- vector-based vs. inactivated whole virion, or related to differential immunogenic response due to the difference in spike antigen dose in each vaccine - is not exactly known - and need further studies. Nevertheless, even in age- sex- and BMI-matched propensity analysis, seropositivity rate, GMT and median anti-spike antibody titre continued to remain significantly higher with Covishield compared to Covaxin in SARS-CoV-2 naïve recipients. Notably, sex, presence of comorbidities, and the type of vaccine used were independent predictors of antibody kinetics in multiple regression analysis.

Our findings are similar to published evidence in randomized controlled trials (RCTs) and real-world studies, although only few studies correlated it with other variables such as age, sex, BMI or presence or absence of comorbidities. In phase 2 RCT, 96.6% (95% CI, 92.8–98.8) had seropositivity (defined as post-vaccination IgG anti-spike antibody titre 4-fold higher than the baseline) to IgG

Table 4
Geometric Mean (SD) anti-spike antibody titre after the first dose and second doses of either vaccine.

Characteristics	First dose of either vaccine						Two completed doses of either vaccine					
	Overall, N = 552		Covishield, N = 456		Covaxin, N = 96		Overall, N = 515		Covishield, N = 425		Covaxin, N = 90	
	Antibody Titer, Geometric Mean (95% CI), in AU/mL	P value	Antibody Titer, Geometric Mean (95% CI), in AU/mL	P value	Antibody Titer, Geometric Mean (95% CI), in AU/mL	P value	Antibody Titer, Geometric Mean (95% CI), in AU/mL	P value	Antibody Titer, Geometric Mean (95% CI), in AU/mL	P value	Antibody Titer, Geometric Mean (95% CI), in AU/mL	P value
<i>Age</i>												
Age ≤ 60 years	51.84 (51.47–52.21)	0.10	66.17 (65.83–66.51)	0.02	16.07 (14.94–17.19)	0.54	114.81 (114.56–115.06)	0.002	136.99 (136.75–137.22)	0.001	51.76 (51.01–52.50)	0.22
Age > 60 years	39.63 (38.75–40.51)		45.51 (44.62–46.39)		21.28 (18.56–23.99)		77.62 (76.79–78.44)		93.28 (92.49–94.07)		32.94 (30.37–35.51)	
<i>Sex</i>												
Male	44.15 (43.69–44.61)	0.02	55.44 (55.01–55.87)	0.02	15.12 (13.77–16.47)	0.44	97.72 (97.39–98.05)	0.009	117.49 (117.17–117.81)	0.01	41.69 (40.71–42.67)	0.22
Female	58.82 (58.31–59.33)		73.79 (73.32–74.26)		19.71 (18.08–21.34)		125.89 (125.54–126.24)		147.57 (147.24–147.89)		58.61 (57.52–59.69)	
<i>Body-mass Index (BMI), Kg/m²</i>												
< 25	47.98 (47.57–48.39)	0.70	63.25 (62.88–63.62)	0.92	14.17 (12.99–15.35)	0.20	107.15 (106.86–107.43)	0.75	128.82 (128.56–129.08)	0.87	45.71 (44.84–46.58)	0.91
25–29.9	53.62 (52.86–54.38)		59.58 (58.82–60.34)		30.86 (28.17–33.54)		109.65 (109.04–110.25)		123.03 (122.44–123.61)		53.70 (51.69–55.70)	
≥ 30	53.54 (52.46–54.62)		62.09 (60.99–63.18)		20.61 (17.22–23.99)		117.49 (116.75–118.22)		134.89 (134.14–135.64)		51.29 (49.38–53.19)	
<i>Blood group</i>												
A + ve	53.74 (52.85–54.63)	0.87	76.54 (75.77–77.31)	0.70	10.25 (8.09–12.41)	0.36	120.23 (119.71–120.75)	0.23	149.97 (149.50–150.43)	0.50	45.08 (43.49–46.66)	0.66
B + ve	52.48 (51.89–53.07)		59.43 (58.85–60.01)		19.84 (17.55–22.13)		117.22 (116.79–117.65)		125.31 (124.85–125.76)		67.76 (66.52–68.99)	
AB + ve	46.30 (44.71–47.89)		64.99 (63.46–66.52)		8.50 (6.53–10.47)		91.62 (90.27–92.97)		118.85 (117.68–120.02)		26.12 (21.12–31.12)	
O + ve	45.69 (45.16–46.22)		58.17 (57.68–58.66)		20.86 (19.35–22.37)		95.50 (95.1–95.9)		120.50 (120.13–120.87)		46.77 (45.71–47.83)	
A-ve	98.88 (97.01–100.75)		98.88 (97.01–100.75)		-		156.67 (155.24–158.09)		156.67 (155.24–158.09)		-	
B-ve	48.64 (45.53–51.75)		48.64 (45.53–51.75)		-		131.52 (129.60–133.43)		131.52 (129.60–133.43)		-	
AB-ve	43.83 (38.53–49.12)		43.83 (38.53–49.12)		-		77.27 (75.41–79.13)		77.27 (75.41–79.13)		-	
O-ve	46.61 (44.15–49.07)		59.59 (57.46–61.71)		4.00		169.39 (168.39–170.54)		186.21 (185.06–187.36)		64.86 (NP)	
<i>Any Comorbidities</i>												
Yes	40.71 (39.94–41.48)	0.07	49.37 (48.62–50.12)	0.02	7.06 (5.59–8.53)	0.04	98.15 (97.61–98.69)	0.20	114.71 (114.21–115.20)	0.09	19.49 (17.27–21.71)	0.01
No	52.84 (52.46–53.22)		67.69 (67.34–68.03)		19.30 (18.14–20.46)		112.20 (111.93–112.47)		135.11 (134.85–135.37)		54.70 (53.96–55.44)	
<i>Type 2 diabetes mellitus (T2DM)</i>												
Yes	39.52 (38.31–40.73)	0.20	50.37 (49.17–51.56)	0.21	8.93 (6.75–11.10)	0.26	92.47 (91.36–93.58)	0.23	121.25 (120.33–122.17)	0.61	11.63 (7.64–15.62)	0.004
No	51.00 (50.64–51.36)		64.00 (63.67–64.33)		17.84 (16.73–18.95)		110.84 (110.59–111.08)		130.32 (130.08–130.56)		53.63 (52.93–54.33)	
<i>Duration of DM</i>												
< 5 yrs.	52.42 (50.39–54.44)	0.43	53.58 (51.17–55.98)	0.58	5.50 (42.64–51.28)	0.26	164.06 (162.33–165.78)	0.04	162.18 (160.45–163.90)	0.13	-	(*)
5–10 yrs.	32.97 (31.27–34.67)		47.34 (45.71–48.97)		4.00 (3.78–7.22)		67.29 (165.71–168.87)		91.20 (89.85–92.54)		14.39 (9.59–19.18)	
> 10 yrs.	45.28 (42.42–48.14)		53.84 (51.09–56.58)		-		131.52 (129.33–133.71)		172.19 (170.62–173.75)		4.00	
<i>Control of DM</i>												
Optimum	39.24 (37.98–40.49)	0.86	51.25 (50.03–52.47)	(*)	6.28 (4.68–7.88)	(*)	90.99 (89.95–92.13)	(*)	119.67 (118.73–120.60)	(*)	11.63 (7.64–15.62)	(*)
Not optimal	48.06 (43.87–52.24)		21.99		105.00		212.81		212.81		-	
<i>T2DM Management</i>												
Monotherapy	46.10 (44.39–47.80)	0.56	63.53 (61.89–65.16)	0.53	11.48 (8.65–14.31)	0.67	125.89 (124.32–127.46)	0.31	177.34 (176.38–178.29)	0.10	14.28 (5.89–22.66)	0.002
Combination	38.33 (36.67–39.99)		45.90 (44.26–47.54)		9.05 (4.93–14.97)		84.14 (82.56–85.72)		114.55 (113.30–115.79)		4.31 (3.02–5.6)	
Insulin	-		-		-		-		-		-	
No medication	30.09 (26.54–33.64)		49.83 (43.20–56.45)		4.00 (*)		65.31 (61.14–69.48)		52.84 (47.37–58.31)		151.98	
<i>Hypertension (HTN)</i>												
HTN	31.46 (30.61–32.31)	<0.001	37.91 (37.16–38.66)	<0.001	16.38 (14.09–18.66)	0.93	80.72 (80.12–81.32)	0.002	100.51 (109.96–111.06)	<0.001	34.17 (32.40–35.94)	<0.001
No HTN	54.89 (54.52–55.25)		69.00 (68.62–69.38)		16.98 (15.80–18.15)		116.14 (115.88–116.40)		136.46 (136.20–136.71)		52.84 (52.04–53.63)	

(continued on next page)

Table 4 (continued)

Characteristics	First dose of either vaccine						Two completed doses of either vaccine					
	Overall, N = 552		Covishield, N = 456		Covaxin, N = 96		Overall, N = 515		Covishield, N = 425		Covaxin, N = 90	
	Antibody Titer, Geometric Mean (95% CI), in AU/mL	P value	Antibody Titer, Geometric Mean (95% CI), in AU/mL	P value	Antibody Titer, Geometric Mean (95% CI), in AU/mL	P value	Antibody Titer, Geometric Mean (95% CI), in AU/mL	P value	Antibody Titer, Geometric Mean (95% CI), in AU/mL	P value	Antibody Titer, Geometric Mean (95% CI), in AU/mL	P value
<i>Duration of HTN</i>												
< 5 yrs.	24.56 (23.18–25.93)	0.003	30.28 (28.95–31.61)	0.001	4.00 (*)	0.47	80.35 (79.23–81.47)	0.01	89.35 (88.53–90.17)	0.04	34.72 (33.02–36.42)	0.24
5–10 yrs.	35.22 (33.94–36.49)		47.42 (46.13–48.71)		20.46 (17.75–23.17)		72.44 (71.46–73.42)		98.08 (97.14–99.02)		38.72 (36.55–40.89)	
> 10 yrs.	34.10 (32.15–36.05)		35.88 (33.87–37.89)		20.49 (6.52–34.46)		103.28 (101.92–104.63)		120.23 (119.09–121.36)		5.00 (*)	
<i>HTN Management</i>												
RAASB	31.36 (30.22–32.49)	0.02	35.33 (34.21–36.45)	0.003	10.41 (5.73–15.08)	(*)	81.28 (80.46–82.09)	0.23	92.17 (91.41–92.93)	0.08	19.94 (15.71–24.17)	0.40
CCBs	27.72 (25.69–29.75)		33.64 (31.63–35.65)		4.00		90.99 (89.73–92.25)		98.56 (97.20–99.92)		42.66 (40.83–44.49)	
Combined	37.96 (36.04–39.88)		48.11 (46.33–49.89)		4.00		97.49 (96.24–98.73)		120.78 (119.81–121.74)		14.28 (7.43–21.13)	
No Medicine	15.62 (6.11–25.12)		60.99 (*)		4.00		51.17 (45.94–56.39)		130.92 (*)		19.93 (*)	
<i>Dyslipidemia</i>												
Yes	52.18 (50–85–53.51)	(*)	52.18 (50.85–53.51)	(*)	-	(*)	97.72 (96.61–98.83)	(*)	98.63 (97.52–99.74)	(*)	-	(*)
No	21.99		21.99		-		212.81		212.81		-	
<i>Ischemic heart disease (IHD)</i>												
Yes	41.13 (39.21–43.05)	0.63	41.13 (39.20–43.05)	0.22	16.84 (15.80–17.88)	(*)	112.25 (111.03–113.47)	0.91	112.25 (111.03–113.47)	0.56	-	(*)
No	49.89 (49.54–50.24)		63.14 (62.81–63.46)		-		108.64 (108.39–108.89)		129.89 (129.65–130.13)		48.26 (47.53–48.99)	
<i>History of SARS-CoV-2 infection</i>												
Past H/O -Yes	251.99 (251.28–252.70)	<0.001	250.55 (249.80–251.30)	<0.001	239.75 (239.26–240.03)	0.002	302.69 (302.28–303.09)	<0.001	302.90 (301.58–303.42)	<0.001	256.25 (254.72–256.68)	0.009
Past H/O -No	40.75 (40.42–41.08)		51.13 (50.82–51.44)		15.38 (14.37–16.39)		95.59 (95.34–95.84)		113.95 (113.71–114.19)		45.28 (44.55–46.00)	
<i>Types of vaccines</i>												
Covishield	62.37 (62.05–62.69)	<0.001					129.30 (129.07–129.53)	<0.001				
Covaxin	16.84 (15.80–17.88)						48.26 (47.46–48.92)					

p < 0.05 considered as statistically significant, p computed by independent sample t-test or ANOVA test, BMI- body mass index, T2DM- type 2 diabetes mellitus, HTN- hypertension, RAAS- Renin angiotensin aldosterone system, CCB- calcium channel blocker, IHD- ischemic heart disease, SARS-CoV-2- severe acute respiratory syndrome coronavirus-2, COVID-19- coronavirus disease 2019, (*) - No statistics is computed.

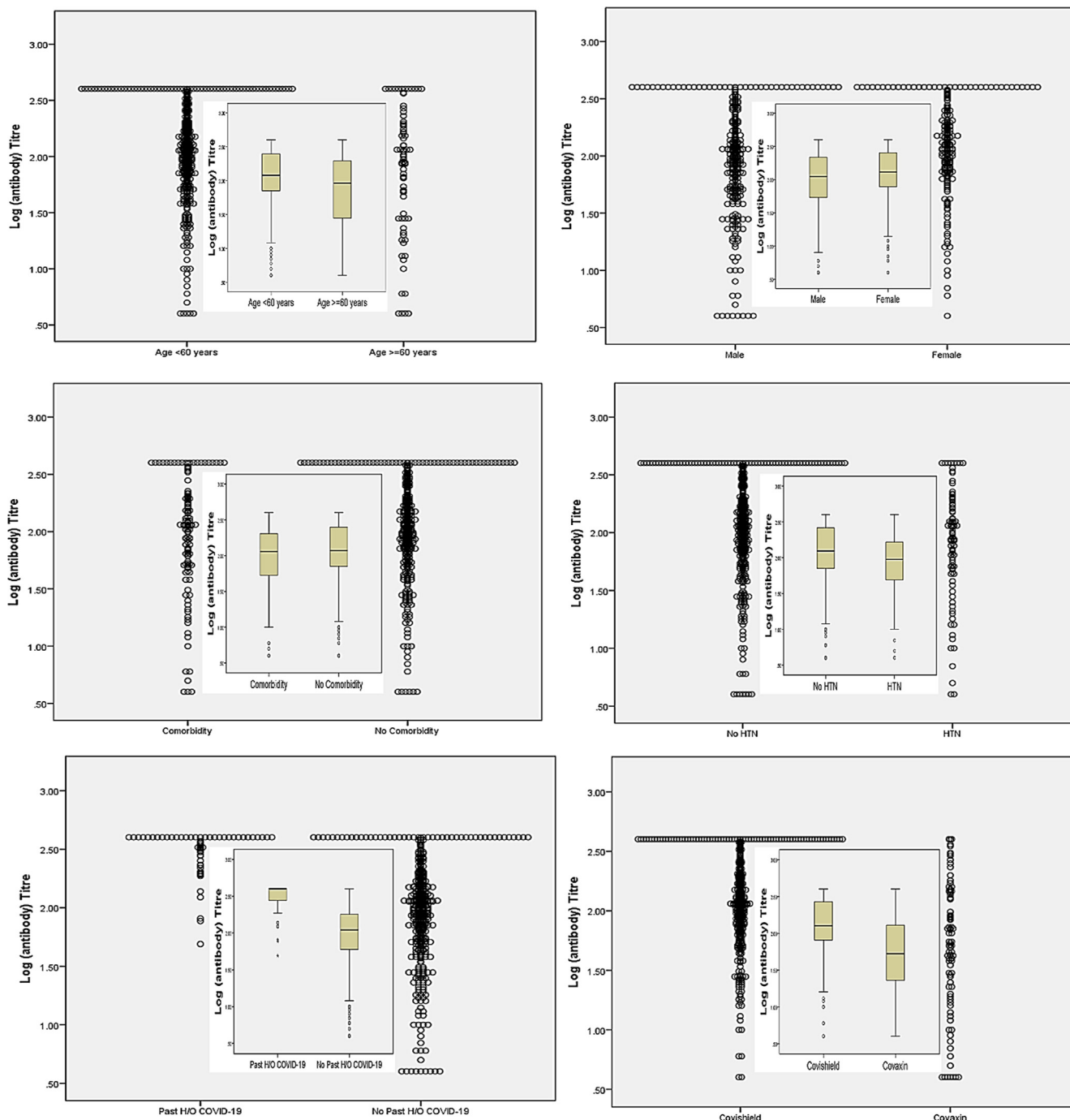


Fig. 2. Dot plot and Box-whisker plot (inbox) demonstrating log antibody titer by study parameters after two complete doses of either vaccine.

anti-spike antibody titre at day 56 (28-days after the second dose), measured by ELISA in 177 participants who received 6 mcg dose of Algel-IDMG Covaxin. Moreover, seroconversion rate to NAb measured by PRNT₅₀ rose to 98.3% 28-days after the second dose, compared to 47.5% 28-days after the first dose. However, no difference in NAb titre was observed in relation to gender and age [7,8]. In phase 1/2 RCT, two doses of ChAdOx1 nCoV-19 (Covishield) vaccine elicited a significant increase in anti-spike IgG antibody at

day 56 (Median 639 EU, IQR 360–792) compared to its median titre (210.7 EU, 149.4–206.8) at 28-days, as measured by ELISA in 10 prime-boost participants [9]. Similarly, in phase 2/3 RCT there was a significant increase in anti-spike IgG antibody in 1593 cohorts who took 2 standard doses of ChAdOx1 nCoV-19 measured by multiplex immunoassay [1,2]. In a cross-sectional community survey from England (REal-time Assessment of Community Transmission-2 program, REACT-2) that studied IgG anti-spike

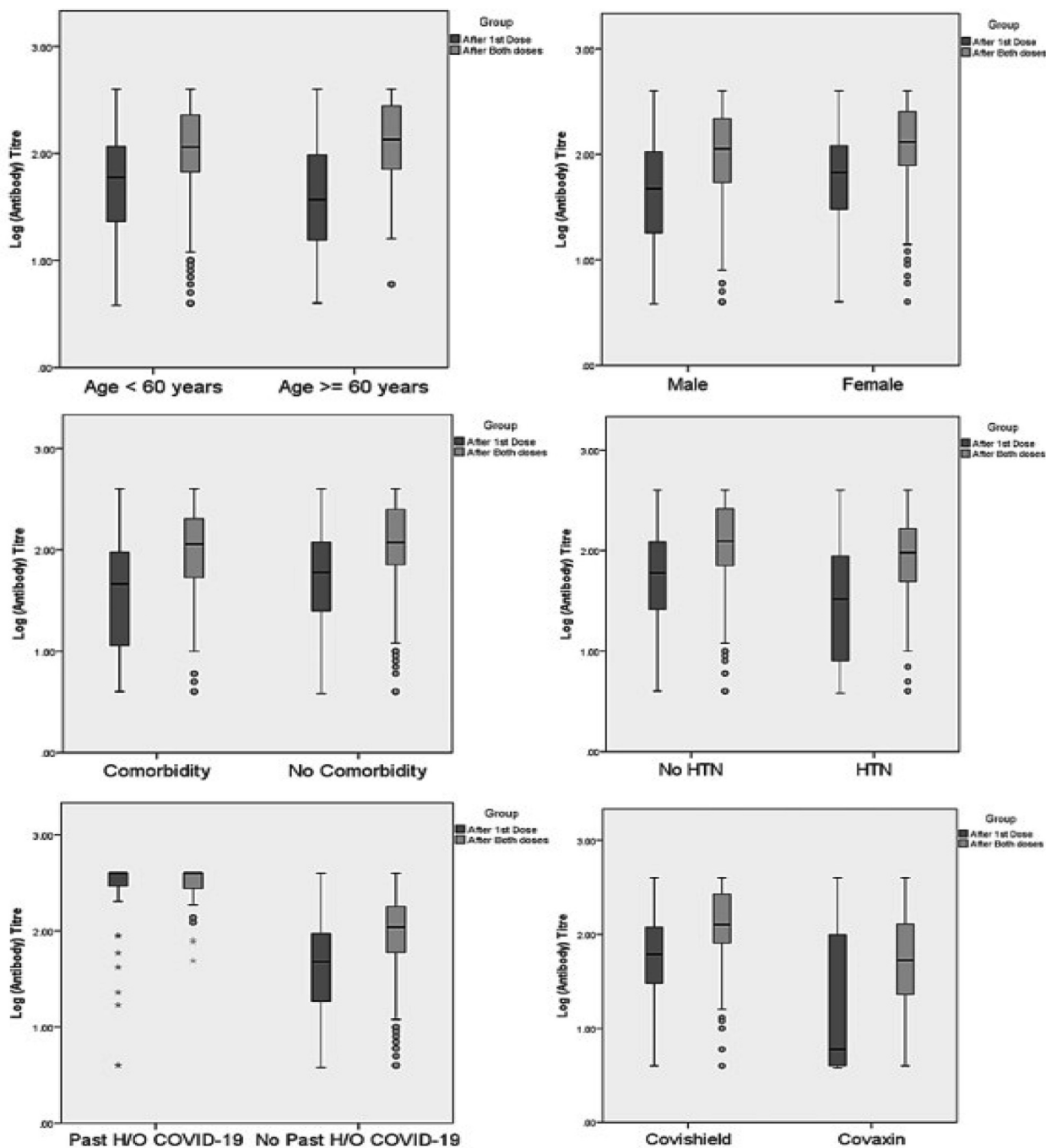


Fig. 3. Box-whisker plot demonstrating log antibody titer by study parameters after first and second doses of either vaccine.

antibody kinetics after two doses of Pfizer-BioNTech vaccine, involving 971 participants, found 91.1% seropositivity across all age groups. There was also a consistent decreasing trend in IgG positivity with the increasing age in REACT-2 study [10]. A high IgG seropositivity of 90.1% to a single dose of Pfizer-BioNTech vaccine was observed in people with past confirmed or suspected COVID across all age groups. Notably, none of these studies reported the antibody response in relation to comorbidities. Recent

studies have reported a significantly diminished anti-spike antibody titre in hemodialysis patients compared to healthy control even after the two completed doses of both Pfizer-BioNTech vaccine and Moderna vaccines [11–13]. One study found highly attenuated humoral response to anti-spike antibody after two completed doses of Pfizer-BioNTech vaccine in people receiving disease-modifying drugs such as Ocrelizumab and Fingolimod for the treatment of multiple sclerosis [14]. In a recent small study

Table 5
Propensity score (age, sex, BMI) matched analysis of Geometric Mean (95% CI) anti-spike antibody titre after the first dose of either vaccine in total cohorts and after the second doses of either vaccine in SARS-CoV-2 naïve cohorts[#]

Characteristics	First dose of either vaccine						Two completed doses of either vaccine [#]					
	Overall, N = 172		Covishield, N = 86		Covaxin, N = 86		Overall, N = 116		Covishield, N = 58		Covaxin, N = 58	
	Antibody Titer, Geometric Mean (95 %CI) in AU/mL	P	Antibody Titer, Geometric Mean (95 %CI) in AU/mL	P	Antibody Titer, Geometric Mean (95 %CI) in AU/mL	P	Antibody Titer, Geometric Mean (95 %CI) in AU/mL	P	Antibody Titer, Geometric Mean (95 %CI) in AU/mL	P	Antibody Titer, Geometric Mean (95 %CI) in AU/mL	P
<i>Age (Years)</i>												
≤ 60	51.48 (49.17–52.59)	0.102	67.95 (63.44–69.38)	0.021	18.08 (17.92–19.90)	0.612	111.48 (111.17–112.56)	0.022	132.65 (131.88–134.36)	0.002	49.76 (48.92–49.90)	0.223
> 60 years	38.84 (36.72–39.11)		48.62 (47.29–48.87)		21.73 (21.04–22.92)		76.84 (76.79–77.01)		88.35 (87.19–88.74)		31.73 (31.04–32.29)	
<i>Sex</i>												
Male	43.25 (43.05–45.74)	0.018	41.25 (40.69–42.85)	0.034	16.19 (15.29–17.12)	0.496	83.17 (83.05–83.41)	<0.001	114.54 (114.45–114.64)	0.012	41.48 (41.29–41.67)	0.446
Female	59.72 (58.81–60.91)		54.54 (54.15–56.64)		19.56 (17.69–21.04)		89.13 (88.91–89.57)		141.35 (140.44–142.75)		54.88 (54.69–55.04)	
<i>Body-mass Index (BMI)</i>												
< 25 kg/m ²	47.09 (46.67–47.54)	0.792	64.04 (63.48–65.32)	0.601	13.3 (12.04–14.82)	0.359	87.09 (86.66–87.14)	0.728	124.82 (123.48–125.18)	0.933	43.1 (42.84–43.27)	0.323
25–29.9 kg/m ²	51.92 (50.86–52.07)		61.9 (60.47–62.39)		26.42 (23.89–24.82)		91.2 (90.96–92.07)		121.03 (120.64–121.76)		52.81 (51.89–53.47)	
≥ 30 kg/m ²	53.86 (51.83–54.18)		62.38 (61.35–63.28)		20.62 (19.21–21.39)		79.18 (78.83–80.18)		138.89 (137.7–139.14)		50.83 (49.05–51.79)	
<i>Blood group</i>												
A + ve	54.72 (52.07–55.75)	0.902	73.12 (71.76–73.73)	0.712	11.16 (10.49–13.43)	0.393	119.63 (118.07–120.75)	0.710	147.12 (146.37–148.73)	0.467	45.08 (43.49–46.66)	0.282
B + ve	51.23 (50.49–52.44)		61.43 (60.95–62.32)		18.76 (16.52–18.99)		117.22 (115.91–117.88)		124.43 (123.95–125.16)		67.76 (66.52–68.99)	
AB + ve	46.06 (44.54–48.24)		64.48 (64.25–65.98)		7.12 (6.12–9.12)		91.03 (90.27–92.54)		117.48 (116.25–117.92)		26.12 (21.12–31.12)	
O + ve	45.17 (44.65–46.04)		55.11 (54.43–56.79)		20.77 (19.71–22.43)		95.08 (94.33–96.02)		118.11 (117.83–119.57)		46.77 (45.71–47.83)	
A-ve	96.34 (94.51–97.28)		99.67 (94.21–100.19)		-		156.67		156.67		-	
B-ve	47.29 (46.84–48.31)		43.52 (42.62–45.03)		-		131.52 (129.84–132.03)		131.52 (129.84–132.03)		-	
AB-ve	43.52 (41.69–43.99)		43.96 (42.12–44.57)		-		-		-		-	
O-ve	46.78 (44.29–47.93)		57.21 (55.2–58.97)		-		169.39 (168.23–170.24)		172.21		64.86	
<i>Any Comorbidities</i>												
Yes	40.63 (38.38–40.89)	0.595	49.71 (47.58–50.54)	0.022	9.48 (8.37–10.93)	0.065	68.4 (68.05–69.63)	0.042	107.71 (106.68–108.31)	0.022	15.48 (14.03–15.93)	0.010
No	53.67 (52.39–53.97)		67.81 (65.75–69.92)		19.23 (17.91–21.2)		91.20 (90.12–92.68)		131.11 (129.87–132.92)		53.23 (52.91–53.96)	
<i>Type 2 diabetes mellitus (T2DM)</i>												
T2DM	40.63 (38.38–40.89)	0.187	48.55 (47.32–49.28)	0.202	9.47 (9.15–11.85)	0.262	79.20 (78.62–80.44)	0.129	88.55 (87.32–89.52)	0.141	9.47 (9.15–11.85)	0.079
No T2DM	53.67 (52.39–53.97)		67.32 (64.16–69.95)		17.09 (16.7–18.75)		103.84 (102.61–103.90)		132.32 (131.46–132.95)		57.09 (56.27–58.66)	
<i>Duration of DM</i>												
< 5 years	51.62 (50.68–53.81)	0.393	54.62 (53.21–55.63)	0.612	46	(*)	145.62	(*)	145.62	(*)	-	(*)
5–10 years	29.73 (27.71–31.83)		47.20 (46.19–48.3)		5.5 (4.46–12.8)		59.73 (57.71–61.93)		71.20		12.2 (7.46–22.8)	
> 10 years	44.75 (42.58–45.68)		53.12 (51.7–54.89)		4		-		-		-	
<i>Control of DM</i>												
Optimum	36.83 (34.43–39.84)	(*)	57.42 (53.73–60.93)	(*)	6.84 (5.81–7.94)	(*)	86.54 (84.62–89.78)	(*)	106.42 (103.21–107.36)	(*)	9.42 (7.81–10.69)	(*)
Not optimum	24.65		24.65		-		-		-		-	
<i>T2DM Management</i>												
Monotherapy	46.91 (44.35–48.09)	0.197	62.91 (59.48–64.31)	0.245	11.53 (10.58–13.17)	0.262	112.91	(*)	112.91	(*)	-	(*)
Combination	38.46 (37.43–40.27)		44.55 (43.59–45.24)		9.09 (7.92–9.96)		80.46 (78.84–84.13)		114.55		4.09 (2.92–4.96)	
Insulin	-		-		-		-		-		-	
No medication	-		-		-		-		-		-	
<i>Hypertension (HTN)</i>												
HTN	32.92 (30.01–33.6)	<0.001	38.26 (37.6–39.74)	<0.001	15.07 (14.14–18.28)	0.871	79.72 (79.01–80.65)	<0.001	100.51 (99.6–102.93)	<0.001	34.07 (32.86–38.28)	0.456
No HTN	56.37 (54.14–57.08)		70.32 (68.97–71.88)		15.98 (14.03–17.83)		116.19 (114.28–117.04)		135.65 (133.7–136.58)		52.98 (50.12–53.54)	
<i>Duration of HTN</i>												
< 5 years	24.35 (22.31–25.41)	0.004	28.61 (26.51–29.87)	0.003	4	0.395	79.85 (77.31–80.76)	0.034	87.61	(*)	39.72 (37.02–41.42)	0.158
5–10 years	34.14 (32.96–36.42)		-		19.72 (18.55–21.89)		72.44 (71.46–73.42)		-		35.72 (34.55–37.89)	
> 10 years	35.5 (32.83–36.57)		46.56 (44.12–46.25)		19.5 (17.86–20.38)		5.5		-		5.5	
<i>HTN Management</i>												
RAAS Blockers	32.28 (30.46–33.18)	0.001	34.17 (32.08–36.54)	0.002	9.98 (7.02–11.05)	(*)	74.28 (70.46–78.09)	0.215	82.17	(*)	39.84	(*)
CCBs	26.87 (24.47–28.51)		-		4		36.12 (34.73–39.25)		-		36.12 (34.73–39.25)	
Combined	36.84 (35.24–38.08)		32.6 (31.58–33.24)		4		-		-		-	
No Medicine	14.67 (14.01–16.15)		48.25 (46.8–49.27)		4		-		-		-	

(continued on next page)

Table 5 (continued)

Characteristics	First dose of either vaccine			Two completed doses of either vaccine*		
	Overall, N = 172	Covishield, N = 86	Covaxin, N = 86	Overall, N = 116	Covishield, N = 58	Covaxin, N = 58
	Antibody Titer, Geometric Mean (95 %CI) in AU/mL	P	Antibody Titer, Geometric Mean (95 %CI) in AU/mL	P	Antibody Titer, Geometric Mean (95 %CI) in AU/mL	P
Dyslipidemia						
Yes	52.92 (51.48–53.69)	0.071	60.99	-	-	-
No	59.11 (58.17–60.2)		52.92 (51.48–53.69) 114.81 (113.12–115.41)	(*)	114.81 (113.12–115.41)	(*)
Ischemic heart disease (IHD)						
Yes	43.56 (42.19–44.65)	0.581	43.56 (42.19–44.65) 63.83 (61.38–64.79)	(*)	118.48 (116.79–119.29)	(*)
No	51.67 (50.07–52.75)		16.56 (14.27–19.85)		-	-
History of SARS-CoV-2 infection:						
Yes	251.19 (251.04–251.30)	<0.001	251.55 (250.25–302.68) 41.83 (40.58–42.87)	0.012	112.64 (111.50–113.92) 46.79 (45.91–47.83)	<0.001
No	39.74 (38.71–40.02)		256 (255.84–257.91) 15.14 (14.96–15.78)		-	-
Types of vaccine						
Covishield	62.01 (61.19–63.92)	<0.001				
Covaxin	16.38 (15.91–17.46)					

p < 0.05 considered as statistically significant, p computed by independent sample t-test or ANOVA test, BMI- body mass index, T2DM- type 2 diabetes mellitus, HTN- hypertension, RAAS- Renin angiotensin aldosterone system, CCB- calcium channel blocker, IHD- ischemic heart disease, SARS-CoV-2- Severe acute respiratory syndrome coronavirus-2, COVID-19- coronavirus disease 2019, (*) - No statistics is computed.

(n = 136) that assessed immunogenicity with Covishield and Covaxin in Indian people with rheumatoid arthritis reported a significantly lower median (IQR) anti-spike antibody titre with later compared to the former, measured by ELISA [15].

The larger question is whether the humoral antibody response to a vaccine correlates with the efficacy (reduction in attack rates, severity and mortality due to COVID-19). Although the correlation of antibody titre to the vaccine efficacy is less well understood, NAb targeting different epitopes of spike glycoprotein have been found to protect from COVID-19 with ChAdOx1 nCoV-19 (Covishield) and Moderna mRNA-1273 vaccine. Moreover, NAb titre following vaccination highly correlates with the NAb titre in convalescent post-SARS-CoV-2 infection. Furthermore, Anti-spike antibody titre is reported to highly correlate with in-vitro virus neutralization test measured by PNT [16]. Indeed, a strong correlation (r range 0.87–0.94) between NAb responses measured by PNT against the spike glycoprotein and those detected by ELISAs have been reported in patients with RT-PCR confirmed COVID-19 [17]. Contrarily, a longitudinal study found no relationship between post-vaccination serum binding-antibody in SARS-CoV-2 naïve individuals [18]. Collectively, it is not exactly known as to what level of binding and neutralizing antibody protects human from COVID-19 [19].

To the best of our knowledge, this Pan-India cross-sectional COVAT study would be the first of its kind that has involved HCW from 13 States and 22 cities and reporting anti-spike antibody kinetics after two completed doses of two different vaccines. However, we also acknowledge several limitations. First, in the present study, we have used a convenience sampling amounting to selection bias. A community-based study in a larger population with multi-stage sampling would be an ideal sampling method. Second, we did not have dilution and neat values for those sample that hit both the upper and lower limit of kit that assessed anti-spike antibody. This could have likely underestimated the GMT in Covishield recipients, since many participants had undiluted plateaued value when compared to Covaxin recipients. Third, we used a binary logistic regression (to identify the predictors of non-response to vaccines) which primarily assumes linearity between the explanatory variable and the outcome variable, hence this model may miss out any predictor variable which may have non-linear relationship with the outcome variable. Fourth, we have measured only anti-spike binding antibody and could not assess NAb and cell-mediated immune response such as Th-1 and Th-2 dependent antibody or cytokines (primarily due to the lack of standardized commercial labs in India). Although a recent study has demonstrated a high correlation between spike protein-based ELISA and different antibody classes including NAb in COVID-19 patients [20]. Fifth, we could not measure the baseline anti-spike antibody titre prior to the vaccination, because of logistic issue due to lockdown. Due to the missing pre-vaccination titre, both seroconversion rates and mean-fold titre increases could not be calculated. Finally, two values of short-term anti-spike antibody as evaluated in this report may not necessarily predict the efficacy of vaccine, nor the absence of seropositivity confer failure of vaccine in the absence of NAb and T-cell response assessment.

In conclusion, this cross-sectional study suggests that both vaccines induce seropositivity to anti-spike antigen in 95% of SARS-CoV-2 naïve and recovered individuals, 3-weeks after completion of two doses. Notably, Covishield recipients had a significantly higher rate of seropositivity and GMT of anti-spike antibody compared to Covaxin both after first and second doses. Whether any real difference in inducing immunogenicity and corresponding efficacy exists between two vaccines can only be meaningfully demonstrated through a head-to-head RCT.

Table 6
Multiple logistic regression to identify the independent predictors for non-seropositivity after first and second dose (based on development of SARS-CoV-2 Anti-spike antibody).

First dose: Variables in the Equation								
	B	S.E.	Wald	df	P value	Exp(B)	95% C.I. for EXP(B)	
							Lower	Upper
Age	0.019	0.327	0.003	1	0.954	1.019	0.537	1.935
Sex (ref = female)	0.281	0.250	1.263	1	0.261	1.324	0.811	2.161
BMI	-0.022	0.176	0.016	1	0.900	0.978	0.692	1.382
Associated comorbidities	1.004	0.434	5.366	1	0.021	2.730	1.167	6.386
Type 2 diabetes	0.163	0.470	0.120	1	0.729	1.177	0.468	2.958
Hypertension	-0.323	0.383	0.714	1	0.398	0.724	0.342	1.532
Ischemic heart disease	-0.236	0.950	0.062	1	0.803	0.789	0.123	5.084
Dyslipidaemia	0.000	0.000	2.333	1	0.127	1.000	1.000	1.000
Past H/O Covid-19	-1.947	0.744	6.848	1	0.009	0.143	0.033	0.613
Covishield vs. Covaxin	-2.206	0.274	64.631	1	<0.001	0.110	0.064	0.189
Constant	6.929	1.884	13.528	1	0.0001	1021.857		
Second dose: Variables in the Final Equation								
Age	-0.425	0.472	0.810	1	0.368	0.654	0.259	1.650
Sex (ref = female)	1.216	0.518	5.503	1	0.019	3.374	1.221	9.321
BMI	-0.205	0.280	0.536	1	0.464	0.815	0.471	1.410
Associated comorbidities	1.543	0.622	6.152	1	0.013	4.679	1.382	15.838
Type 2 diabetes	-0.552	0.620	0.793	1	0.373	0.576	0.171	1.941
Hypertension	0.718	0.595	1.458	1	0.227	2.051	0.639	6.579
Ischemic heart disease	-0.286	0.950	0.062	1	0.893	0.789	0.423	6.084
Dyslipidemia	0.000	0.000	3.401	1	0.065	1.000	1.000	1.000
Past H/O Covid-19	0.732	0.609	1.444	1	0.230	2.078	0.630	6.854
Vaccine type (ref = Covaxin)	-2.825	0.522	29.296	1	<0.001	0.590	0.021	0.659

a. Variable(s) entered on regression step: Age, Sex, BMI (body mass index), Associated Comorbidities, Type 2 diabetes, Hypertension, Ischemic heart disease, Dyslipidaemia, Past H/O Covid-19, Covishield/Covaxin.

Table 7
Multiple regression to identify the independent predictors for non-responders (log-transformed anti-spike antibody levels were used as outcome variable) after first and second dose of either vaccine.

After first dose								
Model	Unstandardized Coefficients		Standardized Coefficients		t	Sig.	95.0% Confidence Interval for B	
	B	Std. Error	Beta				Lower Bound	Upper Bound
FINALSTEP	(Constant)	2.749	0.267		10.29	<0.001	2.224	3.273
	Age	0.156	0.088	0.108	1.766	0.078	-0.018	0.329
	Sex (ref = male)	0.110	0.046	0.088	2.377	0.018	0.019	0.200
	BMI	0.011	0.024	0.018	0.471	0.638	-0.035	0.058
	Blood group	-0.001	0.015	-0.004	-0.096	0.924	-0.031	0.028
	Comorbidities	-0.101	0.035	-0.153	-2.882	0.004	-0.171	-0.032
	Diabetes mellitus (DM)	0.006	0.097	0.003	0.065	0.948	-0.184	0.196
	DM Duration	0.113	0.087	0.068	1.309	0.191	-0.057	0.284
	Hypertension (HTN)	-0.013	0.083	-0.008	-0.155	0.877	-0.176	0.150
	HTN Duration	-0.127	0.069	-0.145	-1.858	0.064	-0.262	0.007
	Ischemic heart disease (IHD)	-0.122	0.174	-0.030	-0.697	0.486	-0.464	0.221
	Dyslipidaemia	1.156	0.000	-0.041	-0.901	0.368	0.000	0.000
	Vaccine Type (ref = Covishield)	-0.539	0.062	-0.333	-8.684	0.001	-0.661	-0.417
	Pre-vaccination	-0.752	0.073	-0.381	-10.33	0.001	-0.895	-0.609
After second dose								
FINALSTEP	(Constant)	3.231	0.185		17.45	<0.001	2.868	3.595
	Age	0.038	0.067	0.037	0.571	0.568	-0.094	0.171
	Sex (ref = male)	0.085	0.036	0.093	2.370	0.018	0.015	0.155
	BMI	-0.001	0.025	-0.001	-0.031	0.975	-0.049	0.048
	Blood group	0.000	0.012	0.001	0.026	0.980	-0.023	0.023
	Comorbidities	-0.133	0.052	-0.106	-2.573	0.010	-0.235	-0.031
	IHD	0.072	0.134	0.025	0.535	0.593	-0.192	0.336
	Dyslipidaemia	1.156E-005	0.000	-0.041	-0.901	0.368	0.000	0.000
	Vaccine Type (ref = Covishield)	-0.387	0.047	-0.327	-8.244	<0.001	-0.479	-0.295
	Pre-vaccination	-0.450	0.056	-0.316	-8.103	<0.001	-0.559	-0.341

a. Dependent Variable: Log (Antibody Titre), a-coefficient, β coefficients of the significant predictors were reported in the result section after back transformation by taking an antilog to facilitate information of the data with 95% Confidence Interval values describing the unstandardized coefficient.

Table 8
Comparison of seropositivity rate, geometric mean titre (95% CI) and median (IQR) anti-spike antibody after the first (21-days or more but before second dose) and second dose (day 21–36) in total, SARS-CoV-2 naïve, and recovered participants.

Characteristics	Total cohorts			SARS-CoV-2 naïve participant #			Past history of SARS-CoV-2 infection		
	Covishield, n/N	Covaxin, n/N	Odds ratio, [95% CI], P value	Covishield, n/N	Covaxin, n/N	Odds ratio, [95% CI], P value	Covishield, n/N	Covaxin, n/N	Odds ratio, [95% CI], P value
First dose	N = 552	N = 492	N = 60						
Seropositivity rate (%)	396/456, (86.8)	341/399, (85.5)	8.48 [5.22–13.79] *	55/57 (96.5)	3/3 (100)	3.17 [0.13–79.60] **	55/57 (96.5)	3/3 (100)	3.17 [0.13–79.60] **
Geometric Mean (95% CI) anti-spike antibody titre in AU/mL	62.37 (62.05–62.69)	16.84 (15.80–17.88)	*	51.13 (50.82–51.44)	15.38 (14.37–16.39)	*	250.55 (249.80–251.30)	239.75 (239.26–240.03)	P = 0.85
Median (IQR) anti-spike antibody titre in AU/mL	61.5 (30.0–119.5)	6.0 (4.0–99.7)	*	55.0 (28.0–94.0)	5.0 (4.0–85.5)	*	400.0 (298.0–400.0)	260.0 (214.0–260.0)	P = 0.42
Second dose	N = 515	N = 457	N = 58						
Seropositivity rate (%)	417/425, (98.1)	362/370, (97.8)	13.03 [5.46–31.09] *	69/87, (79.3)	69/87, (79.3)	11.80 [4.94–28.22] *	55/55 (100)	3/3 (100)	\$
Geometric Mean (95% CI) anti-spike antibody titre in AU/mL	129.30 (129.07–129.53)	48.26 (47.46–48.92)	*	113.95 (113.71–114.19)	45.28 (44.55–46.00)	*	302.90 (301.58–303.42)	256.25 (254.72–256.68)	P = 0.97
Median (IQR) anti-spike antibody titre in AU/mL	127.0 (80.5–268.5)	53.0 (22.3–131.0)	*	115.0 (75.8–199.3)	51.0 (20.0–125.0)	*	400.0 (278.0–400.0)	308.0 (233.0–308.0)	P = 0.64

May include asymptomatic and undiagnosed COVID-19.
\$ No statistics computed as seropositivity rate is constant.
* P < 0.001.
** P = 0.48.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.vaccine.2021.09.055>.

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