Effectiveness of Covid-19 Vaccine in Preventing Infection and Disease Severity:A Case-control Study from An Eastern State of India

P2-G5

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Effectiveness of corona virus disease-19 (COVID-19) vaccines used in India is unexplored and need to be substantiated. The present case-control study was planned to elicit the effectiveness of COVID-19 vaccines in preventing infection and disease severity in the general population of Bihar, India. This case-control study was conducted among people aged ≥45 years during April to June 2021. The cases were the COVID-19 patients admitted or visited All India Institute of Medical Sciences (AIIMS), Patna, Bihar, India, and were contacted directly. The controls were the individuals tested negative for severe acute respiratory syndrome coronavirus-2 (SARS CoV-2) at the Virology laboratory, AIIMS-Patna and contacted telephonically for collection of relevant information. The vaccine effectiveness (VE) was calculated by using the formula (VE = 1 - odds ratio). The adjusted VE for partial and full vaccination were estimated to be 52.0% (95% confidence interval (CI) 39.0-63.0%) and 83.0% (95% CI 73.0-89.0%) respectively for preventing SARS CoV-2 infection. The sub-group analyses of the cases have shown that the length of hospital stays (LOS) (partially vaccinated: 9 days vs. unvaccinated: 12 days; P = 0.028) and the severity of the disease (fully vaccinated: 30.3% vs. partially vaccinated: 51.3% and unvaccinated: 54.1%; P = 0.035) were significantly low among vaccinated compared to unvaccinated individuals. To conclude, four out of every five fully vaccinated individuals are estimated to be protected from contracting SARS CoV-2 infection. Vaccination lowered LOS and chances of development of severe disease.

BACKGROUND

- Vaccination is one of the safest and cost-effective public health interventions for infectious disease prevention and control, especially in a pandemic situation.
- India started the world's largest vaccination drive with the use of Covaxin and Covishield on 16 January 2021.
- Both the COVID-19 vaccines in India demonstrated good clinical efficacy and received approval from the Drug Controller of India (DGCI) for emergency use.
- However, the real-world effectiveness of these vaccines has been largely unexplored and not documented in Indian settings.
- The current study was conducted to estimate the vaccine effectiveness (VE) of COVID-19 vaccines in preventing infection and disease severity in an Eastern State of India.

METHODS

Study Design: Unmatched Case-Control Study

Study Population:

    Cases - COVID-19 patients aged ≥45 years, admitted to or visiting AIIMS, Patna during the study period

    Controls - Individuals aged ≥45 years who tested negative for SARS-CoV-2 at AIIMS-Patna Virology laboratory

Inclusion Criteria:

    Cases - All consecutive patients aged ≥45 years who tested positive for COVID-19 (RT-PCR or Rapid Antigen Test) and were admitted to AIIMS-Patna during the study period
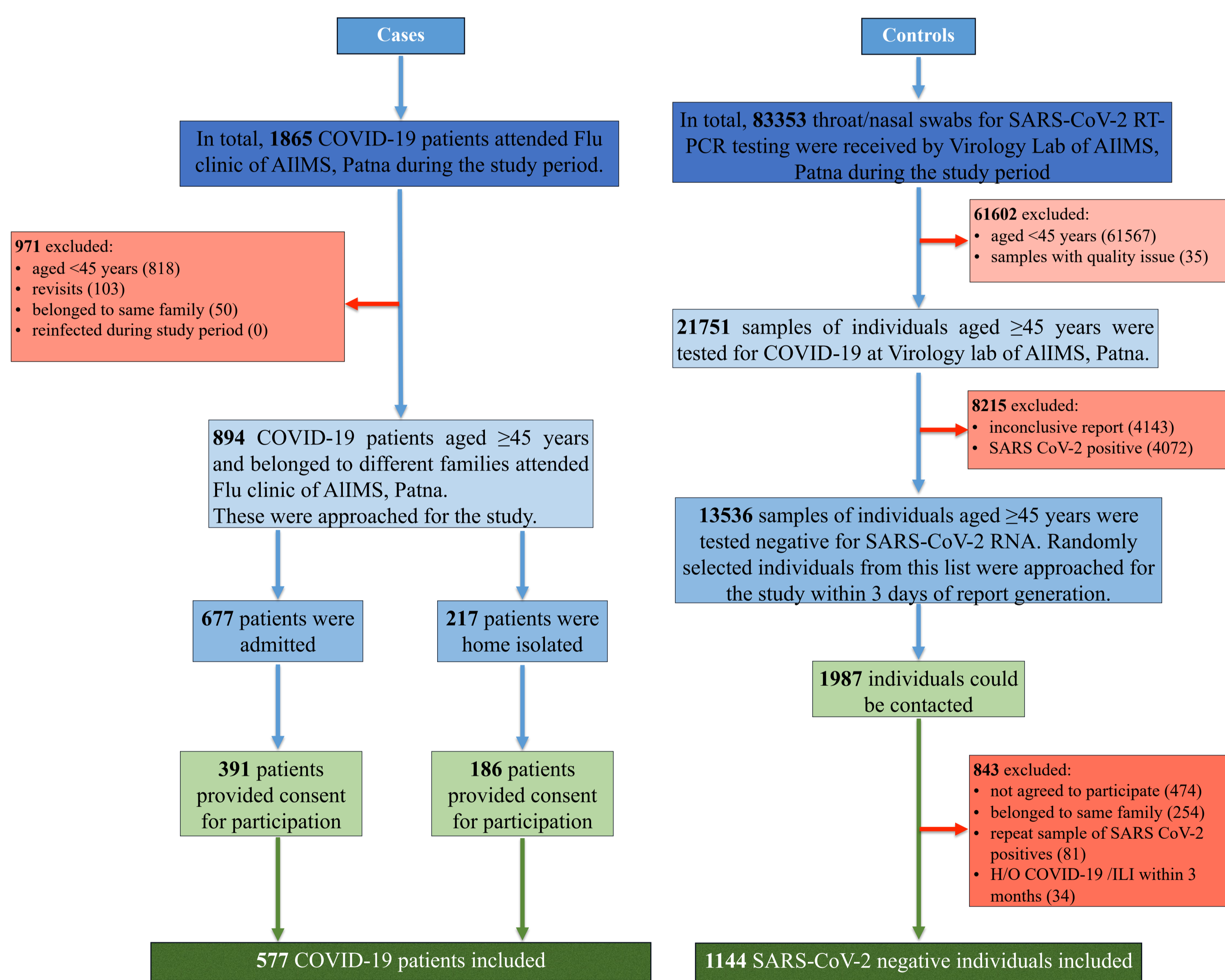
    Controls - Individuals aged ≥45 years who tested negative for SARS-CoV-2 at the AIIMS-Patna Virology laboratory

Exclusion criteria:

    Cases - Individuals who had reinfection during the study period or multiple eligible participants from the same family (only one member was included)

    Controls - Individuals with a history of COVID-19 or Influenza-like illness (ILI) in the preceding 3 months from the day of data collection

Sample size: calculated based on an odds ratio (OR) of 0.3 and an anticipated vaccine effectiveness of 70%. Considering the first-dose vaccination coverage in Bihar during April 2021 (3.7%), the control-to-case ratio of 2:1, 95% precision, and 80% power; the estimated minimum sample size was 507 cases and 1013 controls.

Cases (flowchart)

- In total, **1865** COVID-19 patients attended Flu clinic of AIIMS, Patna during the study period.
- **971** excluded:
  - aged <45 years (818)
  - revisits (103)
  - belonged to same family (50)
  - reinfected during study period (0)
- **894** COVID-19 patients aged ≥45 years and belonged to different families attended Flu clinic of AIIMS, Patna. These were approached for the study.
- **677** patients were admitted
- **217** patients were home isolated
- **391** patients provided consent for participation
- **186** patients provided consent for participation
- **577** COVID-19 patients included

Controls (flowchart)

- In total, **83353** throat/nasal swabs for SARS-CoV-2 RT-PCR testing were received by Virology Lab of AIIMS, Patna during the study period.
- **61602** excluded:
  - aged <45 years (61567)
  - samples with quality issue (35)
- **21751** samples of individuals aged ≥45 years were tested for COVID-19 at Virology lab of AIIMS, Patna.
- **8215** excluded:
  - inconclusive report (4143)
  - SARS CoV-2 positive (4072)
- **13536** samples of individuals aged ≥45 years were tested negative for SARS-CoV-2 RNA. Randomly selected individuals from this list were approached for the study within 3 days of report generation.
- **1987** individuals could be contacted
- **843** excluded:
  - not agreed to participate (474)
  - belonged to same family (254)
  - repeat sample of SARS CoV-2 positives (81)
  - H/O COVID-19 /ILI within 3 months (34)
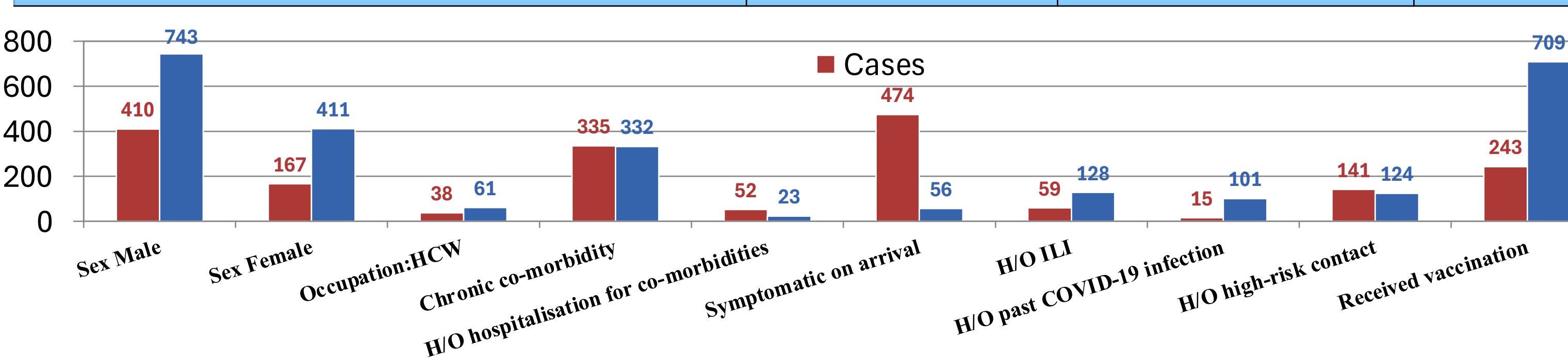- **1144** SARS-CoV-2 negative individuals included
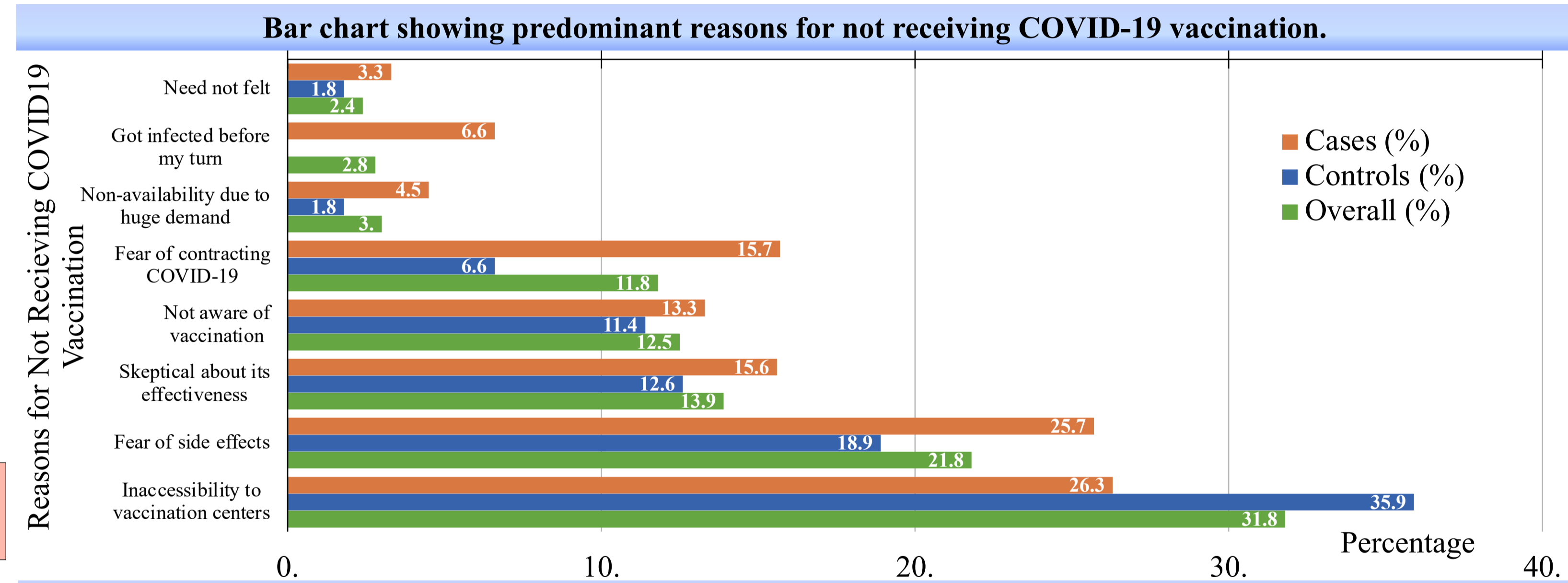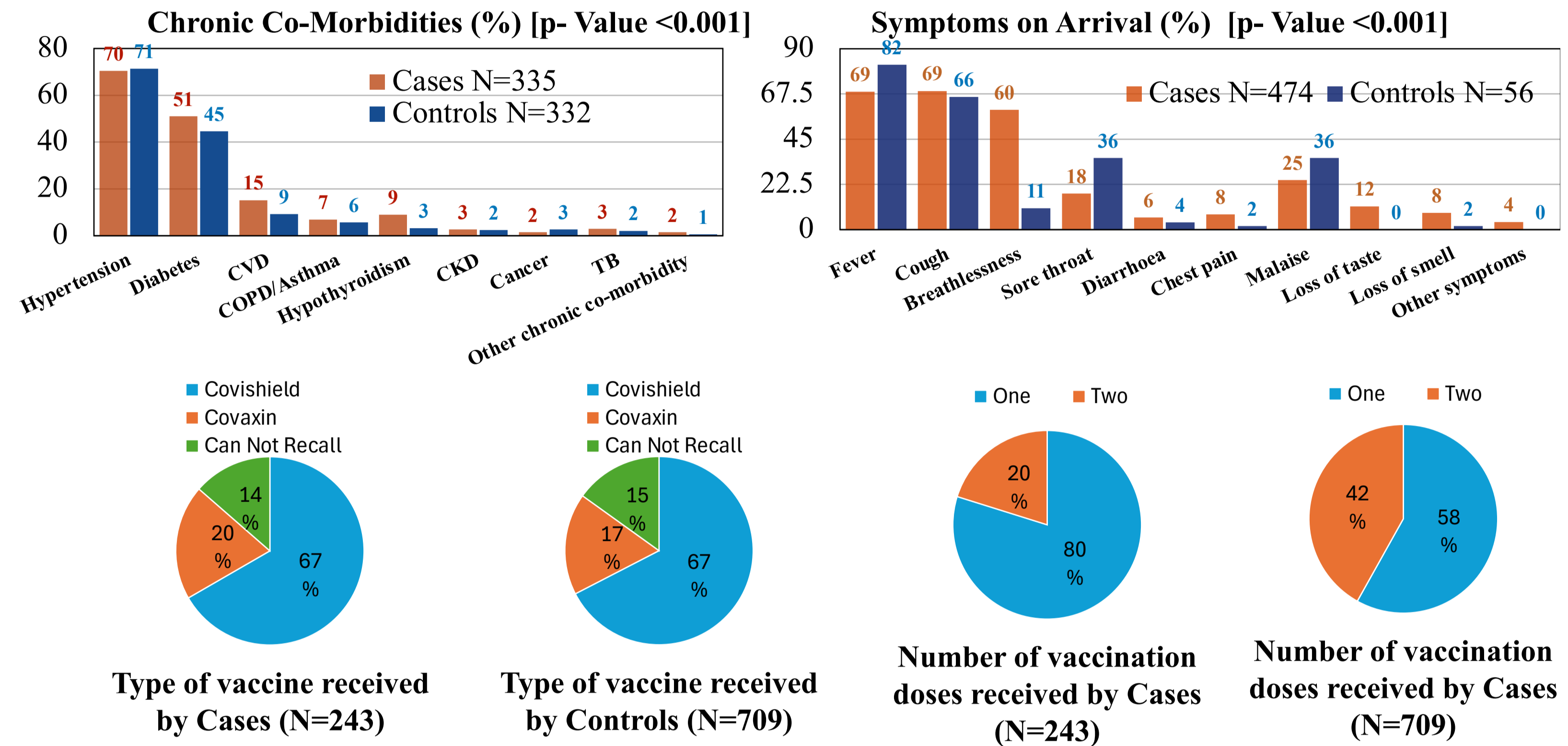
DATA ANALYSIS

- Quantitative variables were expressed as median (interquartile range (IQR)), and categorical variables as proportions and percentages.
- The Mann–Whitney U test and Kruskal–Wallis test were used for comparing medians, while Pearson's χ² test was used for categorical variable associations. Post-hoc Bonferroni's test was applied for ordinal variable analysis.
- The protective effect of vaccines was assessed using univariable and multivariable logistic regression, with odds ratios (OR) used to calculate vaccine effectiveness (VE). Adjustments were made for potential confounders like age, sex, co-morbidities, and COVID-appropriate behaviour.

RESULTS

Background characteristics of the study participants

Variable	Cases N = 577,	Controls N = 1154	P value
Age in years: median {IQR}	59 {52–67}	53 {48–60}	<0.001a
COVID-inappropriate behaviour score: **median {IQR}	2 {1–4}	2 {0–3}	<0.001a
Duration between first vaccine dose and COVID testing date in days: median {IQR}	27 {14–45}	40 {23–62}	<0.001a
Duration between second vaccine dose and COVID testing date in days: median {IQR}	23 {12–48}	24 {10–48}	<0.001a

Bar chart (Cases): Sex Male 410/743, Sex Female 167/411, Occupation:HCW 38/61, Chronic co-morbidity 335/332, H/O hospitalisation for co-morbidities 52/23, Symptomatic on arrival 474/56, H/O ILI 59/128, H/O past COVID-19 infection 15/101, H/O high-risk contact 141/124, Received vaccination 243/709

RESULTS CONTINUED

Chronic Co-Morbidities (%) [p- Value <0.001]

Cases N=335, Controls N=332. Hypertension 70/71, Diabetes 51/45, CVD 15/9, COPD/Asthma 7/6, Hypothyroidism 9/3, CKD 3/2, Cancer 2/3, TB 3/2, Other chronic co-morbidity 2/1

Symptoms on Arrival (%) [p- Value <0.001]

Cases N=474, Controls N=56. Fever 69/82, Cough 69/66, Breathlessness 60/11, Sore throat 18/36, Diarrhoea 6/4, Chest pain 8/2, Malaise 25/36, Loss of taste 12/0, Loss of smell 8/2, Other symptoms 4/0

Type of vaccine received by Cases (N=243)

Covishield 67%, Covaxin 20%, Can Not Recall 14%

Type of vaccine received by Controls (N=709)

Covishield 67%, Covaxin 17%, Can Not Recall 15%

Number of vaccination doses received by Cases (N=243)

One 80%, Two 20%

Number of vaccination doses received by Cases (N=709)

One 58%, Two 42%

Bar chart showing predominant reasons for not receiving COVID-19 vaccination.

Reasons for Not Receiving COVID19 Vaccination (Cases %, Controls %, Overall %):
- Need not felt: 3.3 / 1.8 / 2.1
- Got infected before my turn: 6.6 / 2.8 / —
- Non-availability due to huge demand: 4.5 / 1.8 / 3
- Fear of contracting COVID-19: 15.7 / 6.6 / 11.8
- Not aware of vaccination: 13.3 / 11.4 / 12.5
- Skeptical about its effectiveness: 15.6 / 12.6 / 13.9
- Fear of side effects: 25.7 / 18.9 / 21.3
- Inaccessibility to vaccination centers: 35.9 / 26.3 / 31.8

Vaccine effectiveness in preventing COVID-19 infection

Variables	Total N = 1731, N [%]	COVID-19 infection Yes, N = 577, N (%)	COVID-19 infection No, N = 1154, N (%)	Unadjusted odds ratio, OR (95% CI)	Unadjusted vaccine effectiveness % (95% CI)	Adjusted odds ratio, OR (95% CI)	Adjusted vaccine effectiveness % (95% CI)
Age in completed years: median {IQR}	55 {50–63}	59 {52–67}	53 {48–60}	1.05 (1.04–1.07)	–	1.05 (1.04–1.06)	–
Gender: males	1153 [66.6]	410 (35.6)	743 (64.4)	1.36 (1.09–1.69)	–	1.36 (1.06–1.73)	–
Occupation: HCW	99 [5.7]	38 (38.4)	61 (61.6)	1.26 (0.83–1.92)	–	1.87 (1.11–3.14)	–
Chronic co-morbidity: yes	667 [38.5]	335 (50.2)	332 (49.8)	3.43 (2.78–4.22)	–	2.51 (1.97–3.19)	–
H/O hospitalisation for co-morbidities: yes	75 [4.3]	52 (69.3)	23 (30.7)	4.87 (2.95–8.04)	–	3.11 (1.74–5.57)	–
H/O ILI: no	1544 [89.2]	518 (33.5)	1026 (66.5)	1.09 (0.79–1.52)	–	1.08 (0.72–1.62)	–
H/O past COVID-19 infection: no	1615 [93.3]	562 (34.8)	1053 (65.2)	3.59 (2.07–6.24)	–	5.33 (2.83–10.04)	–
COVID-inappropriate behaviour score: a median {IQR}	2 {0–4}	2 {1–4}	2 {0–3}	1.15 (1.09–1.20)	–	1.12 (1.05–1.18)	–
H/O high-risk contact with COVID-19 case or suspect: yes	265 [15.3]	141 (53.2)	124 (46.8)	2.69 (2.06–3.50)	–	3.86 (2.80–5.31)	–
Vaccination status							
Partially vaccinated	550 [31.8]	154 (28.0)	396 (72.0)	0.55 (0.44–0.70)	45.0 (30.0–56.0)	0.48 (0.37–0.61)	52.0 (39.0–63.0)
Fully vaccinated	234 [13.5]	33 (14.1)	201 (85.9)	0.23 (0.16–0.35)	77.0 (65.0–84.0)	0.17 (0.11–0.27)	83.0 (73.0–89.0)

a- It was calculated based on the use of mask while going outdoors, adherence to social distancing, avoidance of crowded places, handwashing before touching face in preceding 14 days of COVID testing.
{ }: interquartile range; [ ]: column percentage; (): row percentage. The vaccine effectiveness of the Covishield and Covaxin subgroups is being reported in Supplementary

Effect of COVID-19 vaccination on disease characteristics of the cases

Vaccination status	Total, N [%]	Sympt-omatic N (%)	Hospit-alised N (%)	LOS median {IQR}	Disease severity on arrival Mild N (%)	Moderate N (%)	Severe N (%)	Highest disease severity Mild N (%)	Moderate N (%)	Severe N (%)	Final outcome Death N (%)	Recovery N (%)
Un-vaccinated	390 [67.6]	320 (82.1)	260 (66.7)	12 {6–16}	169 (43.3)	55 (14.1)	166 (42.6)	136 (34.9)	43 (11.0)	211 (54.1)	110 (28.2)	280 (71.8)
Partially vaccinated	154 [26.7]	128 (83.1)	111 (72.1)	9 {5–13}	79 (51.3)	26 (16.9)	49 (31.8)	54 (35.1)	21 (13.6)	79 (51.3)	33 (21.4)	121 (78.6)
Fully vaccinated	33 [5.7]	26 (78.8)	20 (60.6)	10 {6–15}	20 (60.6)	7 (21.2)	6 (18.2)	14 (42.4)	9 (27.3)	10 (30.3)	6 (18.2)	27 (81.8)
P-value		0.837a	0.316a	0.034b,†	0.022a,‡			0.035a,§			0.156a	

LOS, length of hospital stay in days; IQR, interquartile range. a- χ2 test; b- Kruskal–Wallis test.
†In Bonferroni post-hoc test, difference in median LOS between partially vaccinated and unvaccinated (P = 0.028) was significantly different.
‡In post-hoc analysis, using adjusted standardised proportion of severe disease was significantly lower in fully vaccinated group compared to others while this was significantly higher in unvaccinated compared to others.
§In post-hoc analysis, using adjusted standardised proportion of severe disease was significantly lower in fully vaccinated compared to others.
[ ]: column percentage; (): row percentage; { }: interquartile range.

CONCLUSIONS

- One out of two and four out of five individuals were found to be protected against SARS-CoV-2 infection following partial and full vaccination, respectively.
- The vaccinated individuals had lesser LOS compared to unvaccinated ones.
- Additionally, the fully vaccinated individuals were less likely to develop severe disease.
- Studies with a larger sample size are recommended to elicit the VE of individual COVID-19 vaccines.

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