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Research Article

Comparative Evaluation of Short-term Clinical Safety and Efficacy of COVID-19 Vaccines - Covishield and Covaxin

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A B S T R A C T

Background: Many candidate vaccines against COVID-19 are competing for their clinical safety and efficacy but few have got approval from the competent authorities. However, people are still concerned about their use.

Objectives: To assess the clinical safety of COVID-19 vaccines, Covishield and Covaxin using the incidence of self-reported and solicited local and systemic adverse events and efficacy by collecting data on the occurrence of confirmed COVID-19 infection after vaccination and to compare the clinical safety and efficacy of both the vaccines.

Method: This study was conducted as an online survey using a self-administered questionnaire, among the individuals who were vaccinated in the months of February, March and April 2021. The participants were categorised into two groups, based on the type of vaccine they received as Covishield and Covaxin. The two groups did not differ in terms of age and gender.

Results: The proportion of participants who had adverse events after the first dose of vaccination was significantly high with Covishield (37.2%) compared to Covaxin (17.4%). But the proportion of participants who developed adverse events after the second dose was not significantly different between Covishield and Covaxin (16.1% with Covishield and 23.8% with Covaxin). The incidence of COVID-19 infection after vaccination was similar in both the groups (4.5% in Covishield group and 5.7% in Covaxin group, p = 0.5, Chi-square test).

Conclusion: The findings from this study gives real-world data that both Covishield and Covaxin are equally effective in preventing COVID-19 infection and have an acceptable safety profile.

Keywords: COVID-19, Covishield, Covaxin, Safety, Efficacy

Introduction

In India, two COVID-19 vaccines- Covishield and Covaxin were initially approved for restricted emergency use by the Drugs Controller General of India (DCGI) on January 3, 2021. The vaccination drive started in India on January 16, 2021 with the two vaccines and is actively going on at present. Later Sputnik-V, another COVID-19 vaccine, marketed by Dr Reddy's Laboratories, has been granted approval.

Bharat Biotech and Serum Institute of India, the two companies that market Covaxin and Covishield respectively released fact sheets of the vaccines to provide information for the healthcare workers and vaccine recipients. The fact sheets have details about the vaccines including dosing, contraindications, local and systemic adverse effects, based on the observations made in the clinical trials. As the vaccines were granted fast track approval, there were only limited data on the efficacy and the safety of vaccines at the time of approval.

The literature search could fetch only very minimal clinical information on the safety and efficacy of Covishield and Covaxin. The results of the phase III trial of Covaxin, released on July 3, 2021, showed that the vaccine demonstrated an overall efficacy of 77.8% against symptomatic COVID-19 infection. With regard to safety, it was observed that the adverse events were similar to the placebo group and serious adverse events were seen in less than 0.5% of the subjects.[1] The interim analysis of phase III trial of Covishield demonstrated an overall efficacy of 70.4% and a good safety profile.[2] A prospective observational study conducted in the UK evaluating the safety and effectiveness of Pfizer-BioNTech and Oxford-Astra Zeneca vaccines showed that the frequencies of adverse effects (both systemic and local) were lower than the data reported in the phase III trials of both vaccines.[3]

There were no significant data available in the literature or public domain regarding the clinical safety and effectiveness of the vaccines at the community level after the vaccines were marketed and beyond the controlled clinical trial environment for Covishield and Covaxin. This community-level information on vaccine safety and efficacy will be very useful for the doctors, paramedical staff and the general public as it will help to build confidence and reduce vaccine hesitancy among the public. Hence, this cross-sectional survey was planned to assess the clinical safety and efficacy of Covishield and Covaxin among the individuals who received any of these two vaccines.

Materials and Method

Study Design: Questionnaire based cross-sectional study.

Inclusion criteria

- Males and females, aged ≥18 years
- Subjects who had atleast one dose of COVID-19 vaccine (either Covishield or Covaxin)
- Subjects willing to give informed consent

Exclusion Criteria

- Subjects vaccinated with COVID-19 vaccines, other than Covishield and Covaxin
- Not willing to give informed consent

The study was conducted as a survey in the 4th week of April and 1st week of May 2021 among the individuals who received either Covishield or Covaxin. It was initiated after obtaining approval from the Institutional Human Ethics Committee (IHEC) and conducted using a self-administered questionnaire.

The questionnaire was prepared with 20 questions in two languages - English and regional language (Tamil), as most of the participants were residents of Tamil Nadu, India. The questionnaire started with the consent of the participant, followed by the demographic details and vaccine details (type of vaccine, number of doses taken, and the date of first and second dose).

To assess the safety of vaccines, the local and systemic adverse events given in the fact sheets of Covishield[4] and Covaxin[5] were listed in the questionnaire. The local reactions included in the survey were pain, swelling, redness and itching at the injection site and systemic reactions included headache, fever, body ache, feeling tired, generally feeling unwell, nausea, vomiting, rashes, sore throat, running nose, cough, chills, dizziness, decreased appetite and excessive sweating. A semi-open question was placed at the end of the listed adverse events so that the participants could add any adverse event (AE) they had experienced, other than those mentioned in the list. The time of onset of occurrence of adverse events after vaccination was framed as a closed question with different time points ranging from 'within a day' to 'more than 2 weeks'.

To assess the efficacy of vaccine, a closed question with dichotomous option 'yes' or 'no' was framed to know whether the participant had acquired COVID-19 infection after vaccination.

The questionnaire was designed as Google Form. A pilot study was conducted with 20 vaccinated individuals including both healthcare and non-healthcare individuals to validate the questionnaire. Modifications were done to the questionnaire, based on the feedback or comments received from the participants. After validation, the questionnaire was sent as a web link to the people who were vaccinated for COVID-19 in February, March and April 2021. The list of people who were vaccinated was collected from the Institutional database of COVID-19 vaccination. In this survey, the safety and efficacy were evaluated for only a short duration ranging from 1 month to a maximum of 4 months post-vaccination.

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The Google Form link was sent to about 2000 participants including health care professionals and non-healthcare professionals. Among them, 914 participants expressed their willingness to participate in the survey and submitted their responses. The responses were transcribed in the excel sheet and analysed.

Based on the type of vaccine received, the participants were categorised into 2 groups- Covishield and Covaxin. The statistical analysis was done using graph pad prism software version 9.1.2. The numerical data were summarised as mean ± SD and compared using unpaired t-test between two groups while the categorical data were expressed as frequencies or percentages and the comparative analysis was done using chi-square test. P-value < 0.05 was considered significant.

Results

Out of 914 respondents, 793 (86.8%) received Covishield and the remaining 121 (13.2%) received Covaxin.

Demographic Details

The mean age of the participants in Covishield group was 51.6 ± 16.6 years and in Covaxin group it was 49.3 ± 15.2 years (p-value = 0.15, not significant, unpaired t-test).

The number of males and females did not significantly differ between the groups (p = 0.19, chi-square test). The proportion of males and females in each group is represented graphically in Figure 1.

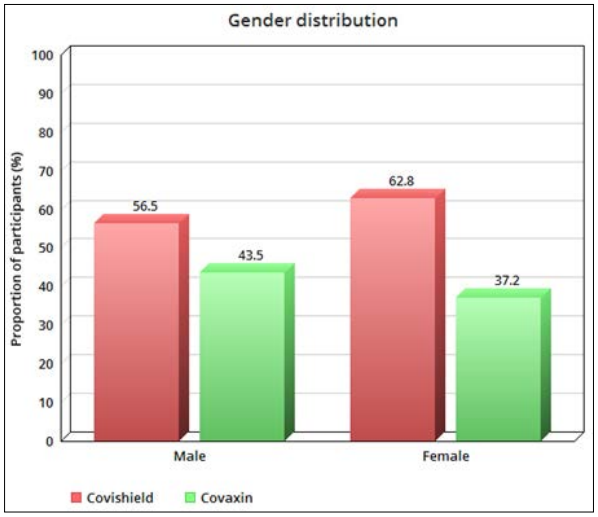

Figure 1.Gender distribution

The survey was conducted among health care workers and other professionals. The proportion of health care workers participated in the survey was low in both the groups when it is compared with other professionals and the pictorial representation of the same is shown in Figure 2.

Number of Doses of Vaccine Received

More than 60% of the participants received both doses of the vaccine in Covishield group and Covaxin group. 497 (62.7%) Covishield recipients and 80 (66.1%) Covaxin recipients got vaccinated with two doses while 296 (37.3%) participants in Covishield group and 41 (33.9%) participants in Covaxin group received only a single dose of vaccine at the time of survey.

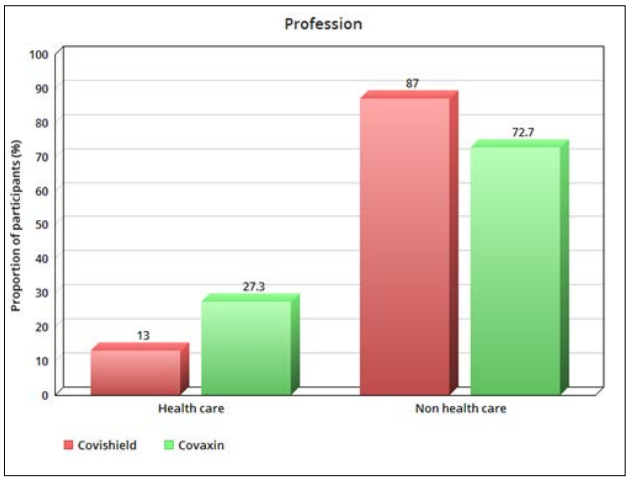

Figure 2.Profession

Adverse Effects after First Dose of Vaccine

The proportion of participants who experienced adverse effects after the first dose was significantly high in Covishield group (37.2% - 295 out of 793 recipients) while it was less (17.4% - 21 out of 121 recipients) in Covaxin group (p = 0.00003, chi-square test).

Pain at the injection site was the commonly reported local adverse effect in both the groups, 25.7% with Covishield and 11.6% with Covaxin. Among the systemic adverse effects, 29% in Covishield group and 12.4% in Covaxin group reported that they felt tired after the first dose of vaccine. The proportion of participants who had adverse events in both groups is shown in Table 1.

The study participants reported a few adverse events not listed in the questionnaire. For example, those who received Covishield, reported excessive sedation (0.2%), abdominal pain (0.1%) and boils in the skin (0.1%). Similarly, abdominal pain occurred in 0.8% of the individuals who received Covaxin.

When the incidence of individual adverse effects is compared between the groups, a few AEs such as pain at the injection site, headache, fever, body ache, tiredness, chills and generally feeling unwell are significantly high with Covishield as compared to Covaxin. The details are shown in Table 1.

More than 80% of the adverse effects occurred within 3 days after the first dose in both groups and the graphical representation of the time of onset of adverse effects is shown in Figure 3.

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Table 1.Adverse Effects after First Dose

Type	Total (914) N (%)	Covishield (793) N (%)	Covaxin (121) N (%)	p-value, Chi-square test
Pain at injection site	217 (23.7)	203 (25.7)	14 (11.6)	0.00009*
Swelling at injection site	45 (4.9)	43 (5.4)	2 (1.7)	0.74
Redness at injection site	29 (3.2)	26 (3.3)	3 (2.5)	0.64
Itching at injection site	11 (1.2)	11 (1.4)	0 (0)	-
Headache	117 (12.8)	111 (14)	6 (5)	0.005*
Fever	184 (20.1)	179 (22)	5 (4.1)	< 0.00001*
Body ache	203 (22.2)	192 (24.2)	11 (9.1)	0.0001*
Feeling tired	245 (26.8)	230 (29)	15 (12.4)	
Generally feeling unwell	152 (16.6)	145 (18.3)	7 (5.8)	0.0005*
Nausea	21 (2.3)	21 (2.6)	0 (0)	-
Vomiting	6 (0.7)	6 (0.8)	0 (0)	-
Rashes	8 (0.9)	7 (0.9)	1 (0.8)	0.95
Sore throat	9 (1)	9 (1.1)	0 (0)	-
Running nose	12 (1.3)	11 (1.4)	1 (0.8)	0.61
Cough	10 (1.1)	10 (1.3)	0 (0)	-
Chills	64 (7)	63 (7.9)	1 (0.8)	0.004*
Feeling dizzy	60 (6.6)	56 (7.1)	4 (3.3)	0.12
Decreased appetite	37 (4)	35 (4.4)	2 (1.7)	0.15
Excessive sweating	18 (2)	17 (2.1)	1 (0.8)	0.33
Any other AE	39 (4.3)	35 (4.4)	4 (3.3)	0.57

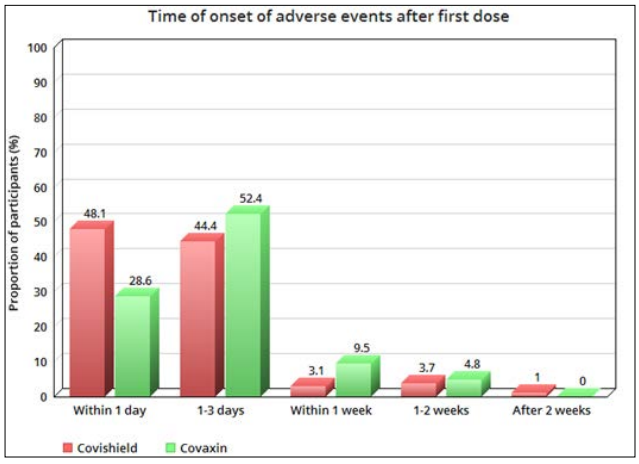

Figure 3.Time of onset of adverse effects after first dose

Adverse Effects after Second Dose of Vaccine

62.7% (497 out of 793) of participants in Covishield group and 66.1% (80 out of 121) in Covaxin group received their second dose of vaccine at the time of survey. Among them, 16.1% Covishield recipients (80 out of 497) and 23.8% Covaxin recipients (19 out of 80) reported adverse effects after the second dose and the difference was not statistically significant (p = 0.09, chi-square test).

The incidence of individual adverse events did not differ between the groups except for excessive sweating, which was observed in 2.5% of participants in Covaxin group as against 0.5% in Covishield group (p = 0.03, significant). The local adverse reaction observed commonly after the second dose was pain at the injection site and the systemic reaction was tiredness, which are similar to the first dose of both the vaccines. The proportion of participants who had the local and systemic adverse effects after the second dose is shown in Table 2.

One male participant, aged 72 years, reported that he developed Deep Vein Thrombosis (DVT) and 2 participants reported that they had boils in the scalp after the second dose of Covishield. Among the Covaxin recipients, 1 participant reported that he had loose stools after the second dose.

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Table 2.Adverse Effects after Second Dose

Type	Total (577) N (%)	Covishield (497) N (%)	Covaxin (80) N (%)	p-value, Chi-square test
Pain at injection site	56 (9.7)	47 (9.5)	9 (11)	0.6
Swelling at injection site	12 (2.1)	11 (2.2)	1 (1)	0.3
Redness at injection site	5 (0.9)	3 (0.6)	2 (3)	0.08
Itching at injection site	2 (0.3)	2 (0.4)	0 (0)	_
Headache	32 (5.5)	26 (5.2)	6 (8)	0.41
Fever	28 (4.9)	22 (4.4)	6 (8)	0.23
Body ache	54 (9.4)	44 (8.9)	10 (13)	0.29
Feeling tired	66 (11.4)	53 (10.7)	13 (16)	0.14
Generally feeling unwell	39 (6.8)	33 (6.6)	6 (8)	0.77
Nausea	3 (0.5)	3 (0.6)	0 (0)	_
Vomiting	0 (0)	0 (0)	0 (0)	_
Rashes	1 (0.2)	1 (0.2)	0 (0)	_
Sore throat	2 (0.3)	2 (0.4)	0 (0)	_
Running nose	6 (1)	5 (1)	1 (1.3)	0.83
Cough	4 (0.7)	3 (0.6)	1 (1.3)	0.51
Chills	3 (0.5)	3 (0.6)	0 (0)	_
Feeling dizzy	12 (2.1)	11 (2.2)	1 (1.3)	0.57
Decreased appetite	6 (1)	6 (1.2)	0 (0)	
Excessive sweating	2 (0.3)	2 (0.4)	2 (2.5)	0.03*
Any other AE	13 (2.3)	9 (1.8)	4 (5)	0.07

Similar to the first dose, most of the participants experienced the adverse effects within 3 days after the second dose (85% in Covishield group and 73.7% in Covaxin group). The details are shown in Figure 4.

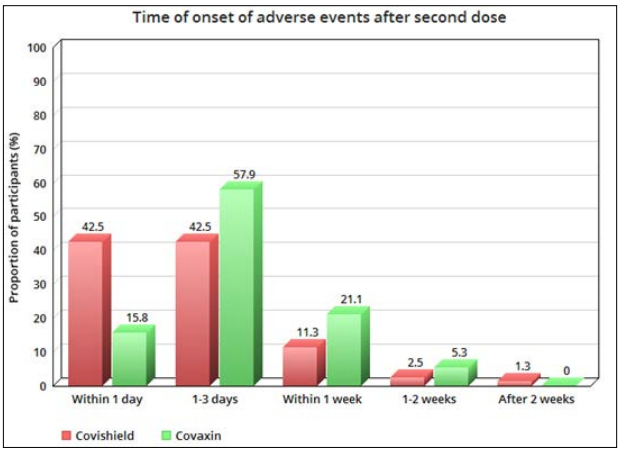

Figure 4.Time of onset of adverse effects after second dose

COVID-19 Infection after Vaccination

The incidence of COVID-19 infection in the Covishield group was 4.5% (36 out of 793) and 5.7% (7 out of 121) in Covaxin group after vaccination and the difference was not statistically significant (p = 0.5) (Figures 5 and 6).

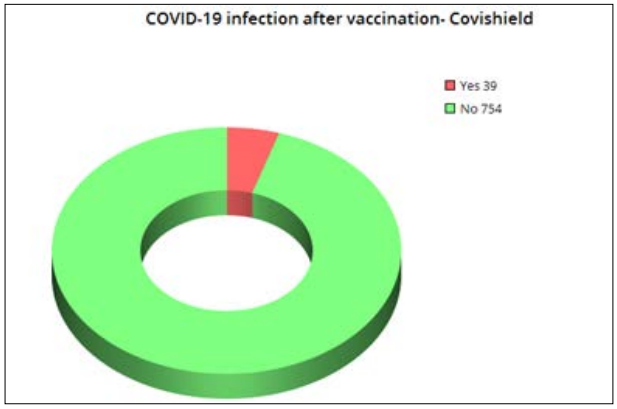

Figure 5.COVID-19 Infection after Vaccination – Covishield

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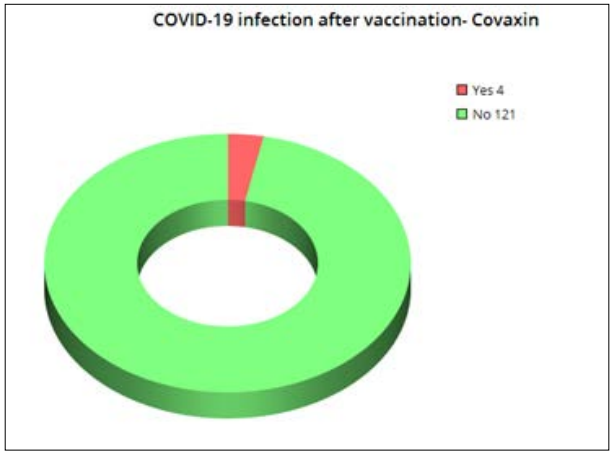

Figure 6.COVID-19 Infection after Vaccination – Covaxin

When the incidence rate was compared between those who received single-dose with those who received both the doses of Covaxin, it was noted that the incidence was significantly less with 2 doses (2 out of 80) when compared to a single dose (5 out of 41) (p = 0.08, Chi-square test, Chi-square value-2.93).

In Covishield group, no such difference was noted between those who received single dose and two doses of the vaccine (p = 0.98, chi-square test). 22 out of 497 participants who got a single dose and 14 out of 296 participants who got both doses of Covishield developed COVID-19 infection after vaccination. The details on the time of occurrence of COVID-19 infection after vaccination in both groups is given in Figure 7.

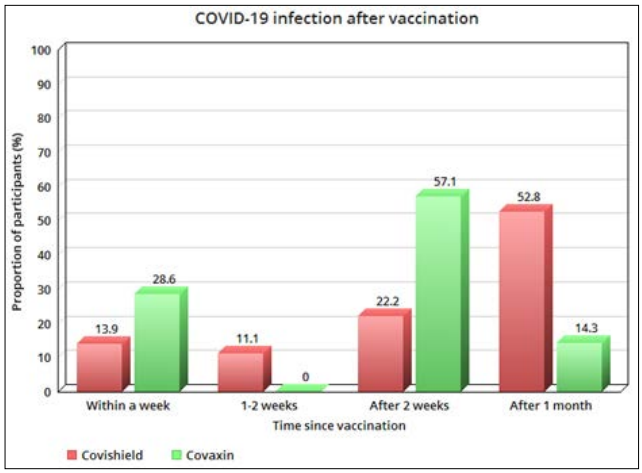

Figure 7.COVID-19 Infection after Vaccination

Discussion

This cross-sectional survey conducted to assess the clinical safety and efficacy of Covishield and Covaxin showed that there was no difference between Covishield and Covaxin in terms of incidence of confirmed COVID-19 after vaccination. 4.5% of Covishield recipients and 5.7% of Covaxin recipients acquired COVID-19 infection after vaccination. This indicates that the effectiveness of both the vaccines is similar in the community setting.

With regard to clinical safety, we observed that tiredness was reported by the maximum number of Covishield recipients (29%), followed by pain at the injection site (25.7%), body ache (24.2%), fever (22%) and headache (14%) after the first dose. A similar trend of adverse events was observed after the second dose i.e., tiredness (10.7%), pain at the injection site (9.5%), body ache (8.9%), headache (5.2%) and fever (4.4%).

The commonly reported adverse events by Covaxin recipients after the first dose were feeling tired (12.4%), pain at injection site (11.6%), body ache (9.1%), headache (5%) and fever (4.1%). After the second dose, 16% of Covaxin recipients reported tiredness, 13% body ache, 11% pain at injection site and 8% reported fever, headache and generally feeling unwell. The incidence of adverse events declined with the second dose when compared to the first dose with Covishield but it was increased with second dose compared to the first dose with Covaxin.

The trend of having fewer AEs with the second dose has been observed in a study done in Korea with ChAdOx1 nCoV-19 vaccine which showed that the adverse events declined with the second dose (90.9%) of vaccine compared to the first dose (98.1%) (P < 0.001).[6]

Though the AEs are more with the second dose for Covaxin, it was in line with what was observed in the phase 2 study of Covaxin. The incidence of solicited local and systemic adverse events after the second dose was high when compared to the first dose and most of them were mild in nature.[1]

The reason for the increased incidence of AEs after the second dose of COVID vaccines is that the first dose induces an immune response, which involves an inflammatory process producing virus-specific antibodies against the antigens and other components present in the vaccine. When this is followed by the second dose of vaccine, the memory T cells and B cells would generate a more robust immune response and hence the reactogenicity might be more with the second dose compared to first dose and the same has been observed with Covaxin and mRNA COVID vaccines, where the second dose was associated with more AEs compared to the first dose.[7]

But, the reason for decreased AEs after the second dose of Covishield is not very clear and we could not get sufficient data from the literature supporting this phenomenon. But the clinical trials and other observational studies of

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Covishield showed a similar trend of AEs after the first and second doses, as observed in this study.

A similar online survey[8] conducted among the health care staff vaccinated with Covishield reported that 69.7% of them had adverse events following vaccination. In that survey, body ache was the commonest AE reported in 46.8% of subjects, followed by headache (30.3%) and fever (22%). 95% of them experienced the adverse events within 24 hours after vaccination[8]. In our study, among those who developed AE, about 80% of the adverse events occurred within 3 days after vaccination.

The adverse events reported by Covaxin were similar to Covishield. The number of Covishield recipients who experienced adverse events was significantly high compared to Covaxin after the first dose. But there was no significant difference observed between Covishield and Covaxin after the 2nd dose when AE data were statistically compared. One participant who received Covishield developed a serious adverse event (SAE), Deep Vein Thrombosis after the second dose whereas no such SAE was reported by Covaxin recipients.

Though the adverse events were more in number with Covishield as compared to Covaxin after the first dose, all of them were minor in nature. Hence, both vaccines have similar clinical acceptability and safety profile.

Limitations

- Though the questionnaire was sent to about 2000 vaccinated individuals, only 914 of them responded (45.7% response rate). If the responses were more in number, it could have added more value to the study.
- The effectiveness was assessed only based on confirmed COVID-19 status and there was no assessment of immunogenicity and asymptomatic COVID-19 left undiagnosed.
- As this was a self-administered questionnaire, the responses are subjective in nature and might vary from one individual to the other.

Conclusion

This survey provides preliminary real-world data about the short-term clinical safety and effectiveness of Covishield and Covaxin. Although the adverse effects were more with Covishield when compared to Covaxin, the difference was noted only after the first dose and there was no difference in the occurrence of adverse events after the second dose. The incidence of COVID-19 infection after vaccination did not significantly differ between Covishield and Covaxin. Hence, this study shows that both Covishield and Covaxin are equally effective in preventing COVID-19 infection and have an acceptable safety profile.

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Conflict of Interest: None

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