Research Article

First long-term safety analysis of the ChAdOx1-nCoV-19 corona virus vaccine: results from a prospective observational study in priority vaccinated groups in North India

Upinder Kaur[1], Zeba Fatima[2], Kalika Maheshwari[2], Vikas Sahni[2], Amol Dehade[1], Anju KL[3], Ashish Kumar Yadav[4], Sangeeta Kansal[5], Vaibhav Jaisawal[3], Sankha Shubhra Chakrabarti[2]

1. Department of Pharmacology, Institute of Medical Sciences, Banaras Hindu University, India; 2. Banaras Hindu University, India; 3. Department of Kaumarbhritya-Balroga (Ayurvedic Paediatrics), Institute of Medical Sciences, Banaras Hindu University, India; 4. Center for Biostatistics, Institute of Medical Sciences, Banaras Hindu University, India; 5. Department of Community Medicine, Institute of Medical Sciences, Banaras Hindu University, India

Introduction: Various vaccines for protection against COVID-19 were provided emergency approval in late 2020 to early 2021. Despite more than 1.5 years of public use, no long-term safety data has been released by any vaccine manufacturer. The main aim of this study is to provide the one-year safety results of the ChAdOx1-nCoV-19/AZD1222 vaccine. Risk factors of development of adverse events of special interest (AESIs) as well as persistent AESIs have been determined.

Methodology: This was a prospective observational study conducted from February 2021 to April 2022 in a tertiary hospital of North India and its two associated centers. Health care workers, other frontline workers, and the elderly vaccinated with the ChAdOx1-nCoV-19 corona virus vaccine constituted the study population. Individuals were contacted telephonically at pre-decided intervals for one year and health issues of significant concern were recorded. Regression analysis was conducted to determine risk factors of AESI occurrence and determinants of persistent AESIs.

Results: Of 1650 individuals enrolled, 1520 could be assessed for outcomes of interest. COVID-19 at any time post vaccination occurred in 44.1% participants. Dengue occurred in 8% participants and was of 'serious' category (FDA) in 19.7% of those affected. Majority of the AESIs belonged to the MedDRA system organ class (SOC) of musculoskeletal disorders (3.7%) followed by general disorders and administration site conditions (2.1%) and infections (2%). Arthropathy in the form of

knee joint involvement was the commonest individual AESI (1.7%). New onset hypertension, thyroid function abnormalities and diabetes occurred respectively in 0.9%, 0.4% and 0.3% participants. Five deaths and eleven 'serious' adverse events were reported. Among participants receiving booster dose of the COVID-19 vaccine (n=184), 9.8% developed adverse events of concern, of which urticaria and new onset arthropathy were common. Regression analysis showed females, individuals with pre-vaccination history of COVID-19, diabetes, hypothyroidism and arthropathy had a 1.78-, 1.55-, 1.82-, 2.47- and 3.9-times higher odds of AESI development. Females and individuals with hypothyroidism were also at 1.66- and 2.23-times higher risk of persistent AESIs. Receiving any dose of the ChAdOx1 vaccine after history of COVID-19 in the past was associated with a 1.94-times higher risk of persistence of AESIs in comparison with participants developing COVID-19 after their vaccine dose. Compared to individuals with no history of COVID-19, individuals receiving vaccine after COVID-19 were at 2.85 times higher risk of persistence of AESIs. No association of AESI was observed with any post vaccination COVID-19.

Conclusion: COVID-19 occurred in close to half of the participants receiving ChAdOx1-nCoV-19 vaccine, over the follow-up period, and mostly within 3 months of complete vaccination. Vigilance is warranted for AESIs such as musculoskeletal disorders and severity of non-COVID-19 infections such as dengue. Individuals receiving COVID-19 vaccine after any natural SARS-CoV-2 infection were at increased risk of development as well as persistence of AESIs. Future studies with larger sample size and involving unvaccinated arm are required to give a concise and comparative data of vaccine safety. Sex- and hormonal differences in the occurrence of atypical adverse events should be explored as potential areas of future research. These data may be helpful in the development of safer and effective vaccines for future outbreaks.

Sangeeta Kansal and Vaibhav Jaisawal contributed equally to this work.

Corresponding authors: Sankha Shubhra Chakrabarti, sankha.chakrabarti1@bhu.ac.in; Sangeeta Kansal, sangeetakansalbhu@gmail.com; Vaibhav Jaisawal, drvaibhav29@gmail.com

1. Introduction

In the fight against COVID-19, various vaccines based on novel and pre-existing platforms were developed at an unprecedented scale and granted emergency use authorization (EUA) in late December 2020- early January 2021. Among these mRNA based COVID-19 vaccines and adeno viral vectored

vaccines coding for the Spike protein of SARS-CoV-2 were largely employed in the United states and European nations. In India, ChAdOx1-nCoV-19 (COVISHIELD, Serum Institute of India) based on the chimpanzee adeno viral platform of Oxford-AstraZeneca's vaccine and the inactivated SARS-CoV-2 based vaccine, COVAXIN (Bharat Biotech) were the first ones to receive approval from the drug regulatory body for step-wise mass roll out. The controlled setting results of more than desired protection rates against COVID-19 and an acceptable short term safety profile were the basis of approval of these vaccines for public use. The performance of vaccines in real world often vary from controlled settings and comprehensive assessment of vaccine safety and performance can be ascertained through active monitoring of vaccinated individuals in the post approval phase. The claims of excellent protection rates against symptomatic COVID-19 have been challenged in the post marketing period. In addition, an upsurge of conditions such as autoimmune diseases, atypical thrombotic events, and cardiac complications in the post vaccination period, is alerting researchers to conduct a thorough assessment of the safety profile of COVID-19 vaccines.[1][2][3] Despite more than 18 months of emergency approval and close to 5 billion people vaccinated worldwide, long term safety-specific data of most COVID-19 vaccines has not been provided in the public domain by any vaccine manufacturer.[4] Here, in continuation to our first real world safety study on the ChAdOx1-nCoV-19 vaccine, we provide the first long term safety data in vaccinated individuals over one year of follow up.

2. Methods

2.1. Study Design and participants

This was a prospective observational study conducted from February 2021 to April 2022 in a tertiary hospital of North India. In accordance with the Indian government's policies of mass roll out of COVID-19 vaccination, health care workers, other frontline workers, and the elderly were the groups vaccinated on priority basis in the first phase. Accordingly, the present study predominantly recruited health care and other frontline workers in the initial phase followed by elderly during the last few days of enrollment. The details of the enrollment procedure have been already published.[5] The enrolled participants were contacted at pre-planned time periods, with final follow-up at 12 months following vaccination. A support telephone number was provided to participants to report any atypical health issue or COVID-19 related complaint. The preliminary findings of the study pertaining to adverse

events following immunization (AEFIs) and occurrence of breakthrough COVID-19 during the first six months of study have already been published.[5][6]

2.2. *Safety analysis*

Adverse events following immunization (AEFIs) was the primary outcome, and COVID-19 specific details as well as long term safety analysis in terms of adverse events of special interest (AESIs) were the secondary outcomes of interest. The format for AESIs used in the study was based on the guiding document on AESIs by the CEPI-SPEAC-Brighton Collaboration as well as the studies available in PubMed/Medline on atypical adverse events following COVID-19 vaccination of any type from the period of January 2021 to January 2022.[7] In addition, atypical adverse events notified by the study participants to the study staff at any time during the study period were also incorporated in the AESI format for final follow up at one year. Apart from this, any health issue persisting for at least one month during the final follow up at one year was also recorded. The MedDRA terminology was used for labelling system organ class (SOC) of AESIs and severity categorization of each AESI was done using the Food and Drug Administration (FDA) scale of severity of vaccine related adverse events.

2.3. *Ethical permission*

The study started after obtaining permission from the Institute Ethics Committee. Written informed consent was taken from each enrolled participant.

2.4. *Outcome measures*

The institute was affected by the pandemic of COVID-19 during the second wave in India (February 2021- June 2021, with peak in April 2021) and the third wave of pandemic (December 2021- March 2022). Data pertaining to COVID-19 during this period as well as during the intermediate time period was enquired telephonically in accordance with the study protocol. The booster dose of COVID-19 vaccine was initiated in the study center in the month of January 2022. Information about the same was also enquired as deemed suitable at the time of 1-year follow-up. COVID-19 was categorized as ‘Confirm’ and ‘Suspect’ and severity of COVID-19 was rated as per the investigators’ assessment and in accordance with the recommendations of MoHFW guidelines on COVID-19. As defined previously, we also labelled cases as ‘RT-PCR negative suspects’ with symptomatology resembling Covid-19 who tested negative on single RT-PCR based test and in whom RT-PCR test was not repeated.[5][6] In view

of a dengue epidemic which affected the region in the months of July-October 2021, the history of laboratory confirmed dengue was also enquired for separately during the final follow-up. Any dengue that required hospitalization with or without the need of intravenous fluids and with or without platelet transfusion was categorized as 'serious'. Among adverse events of special interest (AESIs), we included new onset rheumatologic disorders, new onset endocrinal disorders such as thyroid abnormalities, new onset diabetes, cardiac disorders such as heart failure, myocardial infarction or myocarditis, nervous system disorders such as headaches and weakness in limbs, blood disorders such as thrombocytopenia, reproductive system disorders such as menstrual abnormalities and flares of underlying diseases such as diabetes, hypertension and arthropathy among others. Apart from this, any health issue persisting for at least one month at the time of the final follow up was recorded. To validate the findings of our previously published study highlighting the importance of timing of COVID-19 vaccine with respect to COVID-19 on persistent adverse events, individuals were categorized into three groups as defined subsequently.[8]

Group A: Individuals with no history of COVID-19 till last follow up

Group B: Individuals who received any dose of vaccine (First, second or booster) after any episode of COVID-19

Group C: Individuals with history of COVID-19 after vaccine but who did not receive any vaccine thereafter

Individuals whose booster dose information was not available, and which was likely to change the categorization of patients in these groups were excluded from the analysis of risk of persistent adverse outcomes or persistent AESIs.

2.5. Sample size: The sample size for the present study was based on the primary outcome of rates of AEFIs following COVID-19 vaccination. Details of study methodology, sample size and preliminary results of safety analysis have already been published.[5]

2.6. Statistical analysis: Data was recorded as frequencies and percentages for categorical variables such as occurrence of COVID-19 and dengue and development of AESIs. Descriptive analysis of each AESI was performed. Bivariate analysis was done for the association between occurrence of AESIs and co-variates such as demographics, pre-existing co-morbidities, history of COVID-19 in 2020 (before vaccination) and history of COVID-19 in 2021 or 2022 (after vaccination). Chi square test was also applied for ascertaining relationship between individuals at risk of persistent AESIs and co-variates

including COVID-19 and timing of vaccine with respect to COVID-19. Variables with P value <0.05 or those deemed as clinically relevant were incorporated in binary logistic regression analysis. SPSS version 16 was used for performing statistical analysis.

2.7. Role of funding source

None

3. Results

A total of 1650 individuals were enrolled in the study. Baseline characteristics of the participants are provided in **Table 1**. After excluding 125 participants who were lost to follow up at the time of final follow up and 5 who died before June 2021, the remaining 1520 participants were assessed for occurrence of AESIs (**Figure 1**). Of these 1520, the booster dose information that was likely to change the categorization of patients into three groups as defined earlier, was missing for 48. After removing these 48, remaining 1472 persons were analyzed for risk of persisting adverse outcomes (health events persisting for a minimum period of 4 weeks at the time of final follow up).

Age (years) **Median (Q1,Q3)**	35 (29,47)
Males/Females	1123/527
Body mass index (Kg/m^2) **Mean ± SD**	24.77 ± 3.59
Diabetes mellitus, n (%)	155 (9.4)
Hypertension, n (%)	189 (11.5)
Hypothyroidism, n (%)	62 (3.7)
Lung disease, n (%)	48 (2.9)
History of allergy, n (%)	154 (9.3)
History of COVID-19 in 2020, n (%)	222 (13.5)

Table 1. Baseline characteristics of participants (N=1650)

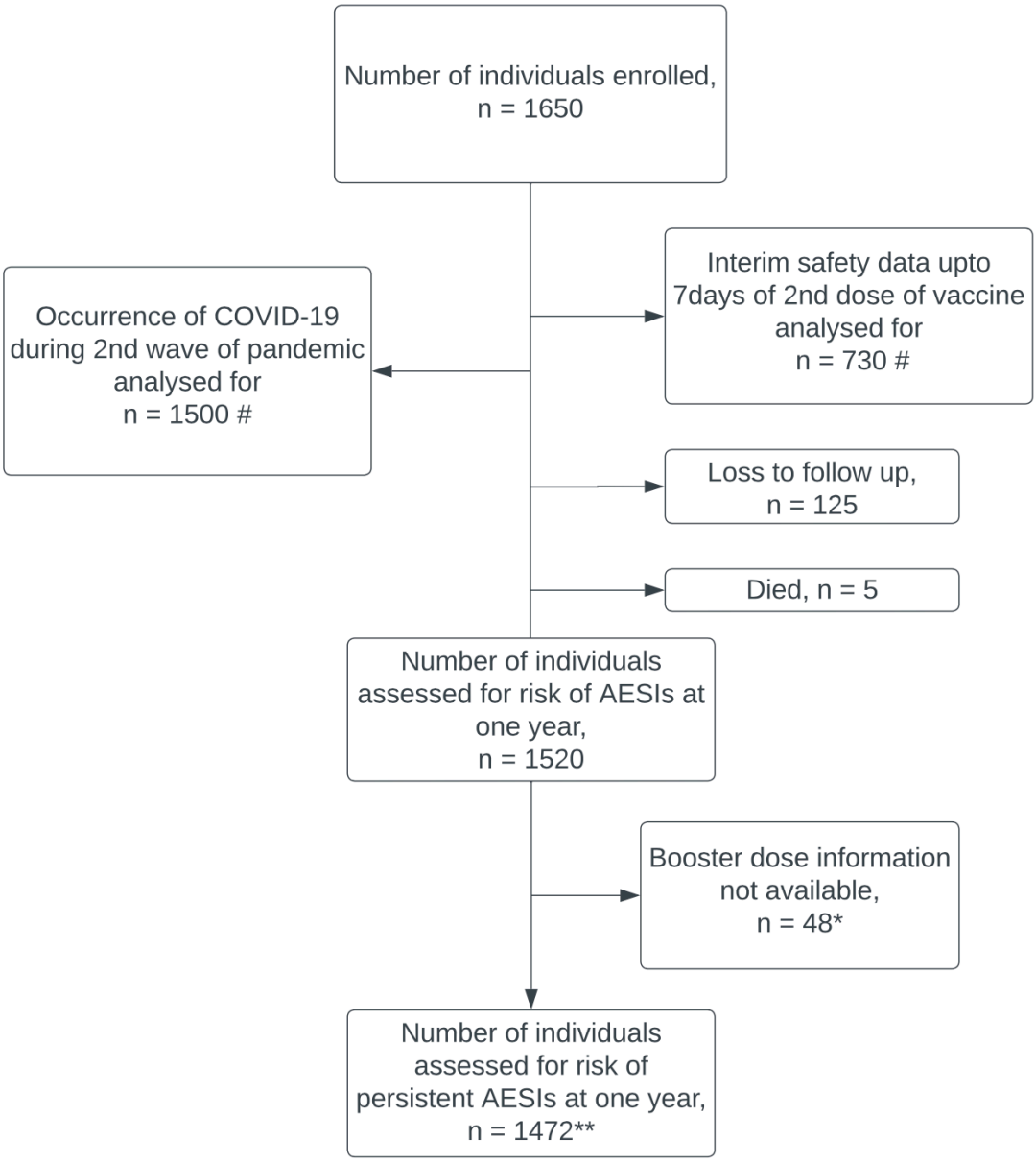

Figure 1. ***The STROBE flow diagram of the study.*** *Out of 1650 vaccinees enrolled, data for 730 (AEFIs) and 1500 (occurrence of COVID-19) have been already published (#). 125 participants were lost to follow-up and 5 participants died. 1520 participants were analyzed for risk of AESIs. Among these, booster dose information likely to change classification into groups A,B,C were unavailable for 48 participants (*). AESIs persistent for at least one month at one year follow-up were assessed in 1472 individuals.*

The occurrence of COVID-19 during second wave of pandemic has been already described and published.[6] **Supplementary Table 1** describes in detail the occurrence of COVID-19 during the third

wave of the pandemic, occurrence of dengue and system organ class (SOC)-wise distribution of all AESIs. COVID-19 during the third wave of the pandemic occurred in 259 (17.0%) and was of 'mild' severity in majority (95.4%). COVID-19 at any time post vaccination occurred in 671 out of 1520 (44.1%). Interestingly, occurrence of COVID-19 during the 3rd wave of the pandemic was statistically more common in vaccinated individuals with history of COVID-19 in 2nd wave of the pandemic also. Dengue occurred in 8% individuals and of those affected, serious form of dengue occurred in 19.7%. Musculoskeletal and connective tissue disorders (MCTDs) were commonly reported AESIs (57, 3.7% of all AESIs) predominated by complaints of arthropathy (54, 3.5%). Knee joint (n=26, 1.7%) and lower back (n=12, 0.8%) were the commonly affected sites of arthropathy. Outcome wise, majority of the vaccinees with new onset arthropathy reported persisting joint pain at one year of follow up (48, 3.2%) with median (Q1-Q3) duration of symptoms of 120 days (86.2,180). Next to MCTDs, were general disorders (32, 2.1%) and infections and infestations (31, 2%). New onset hypertension developed in thirteen (0.9%) individuals. Endocrinal disorders such as thyroid function abnormalities and newly diagnosed diabetes occurred in 6 (0.4%) and 5 (0.3%) individuals, respectively. Three miscarriages and two serious cardiac events were reported in the vaccinees. Altogether, serious AESIs occurred in 11 (**Supplementary Table 1**) and 5 persons died during the first four months of follow up.

In unadjusted analysis, AESIs occurred commonly in individuals of 40 years and above, females, individuals with diabetes, hypertension, arthropathy, heart disease and hypothyroidism. Pre-vaccination history of COVID-19 also shared a positive association with occurrence of AESIs though the statistical significance was marginal. No significant association was observed between AESIs, and history of post vaccination COVID-19.

3.1. Determinants of individuals at risk of AESIs

Results of binary logistic regression analysis (**Table 2a**) showed a 1.78-, 1.82- 2.47-, and 3.9-times higher odds of occurrence of AESIs in females, individuals with diabetes, hypothyroidism and arthropathy with respect to comparators. Vaccines received after having had an episode of COVID-19 in the year 2020 was associated with 1.55-times higher odds of AESI-development compared to individuals with no pre-vaccination history of COVID-19. Post vaccination COVID-19 (in the years 2021 and 2022) was not associated with any risk of AESI-development.

2a [N=1520]				2b [N=1472]	
Tentative risk factors	**aOR (CI)**	**p-value**		**aOR (CI)**	**p-value**
Age (years) ≥40 <40 (Reference)	1.06 (0.74-1.50)	0.76		1.37 (0.91-2.06)	0.13
Sex Female Male (Reference)	**1.78** (1.30-2.45)	**<0.001**		**1.66 (1.15-2.40)**	**0.007**
Body Mass Index (Kg/m^2) ≥25 <25 (Reference)	-- --			1.3 (091-1.86)	0.14
Hypertension Yes No (Reference)	1.29 (0.79-2.11)	0.29		1.38 (0.80-2.37)	0.24
Heart Disease Yes No (Reference)	1.97 (0.78-4.97)	0.15		2.34 (0.90-6.02)	0.07
Diabetes Mellitus Yes No (Reference)	**1.82** (1.11-2.97)	**0.01**		1.5 (0.86-2.65)	0.15
Arthropathy Yes No (Reference)	**3.9** (1.01-15.08)	**0.04**		3.44 (0.82-14.39)	0.09
Hypothyroidism Yes No (Reference)	**2.47** (1.36-4.49)	**0.003**		**2.23 (1.15-4.32)**	**0.01**

2a [N=1520]				2b [N=1472]	
Pre-vaccination COVID-19 (in 2020) Yes No (Reference)	**1.55 (1.03-2.32)**	**0.03**		--	--
Post vaccination COVID-19 (In 2021 or 2022) before AESIs Yes No (Reference)	1.14 (0.84-1.55)	0.39		--	--
Timing of vaccine in relation to COVID-19					
1. Vaccine after COVID-19 (Group B) COVID-19 after Vaccine (Group C) (Reference)	-- --			**1.94** (1.24-3.0)	**0.003**
2. COVID-19 after Vaccine (Group C) No COVID-19 (Group A) (Reference)	-- --			1.47 (0.95-2.27)	0.08 **<0.001**
3. Vaccine after COVID-19 (Group B) No COVID-19 (Group A) (Reference)	-- --			**2.85** (1.87-4.36)	

Table 2. Regression analysis of adverse events of special interest (AESIs)

[2a: Regression analysis of individuals at risk of AESIs, 2b: Regression analysis of individuals at risk of persistent AESIs

aOR: adjusted Odds ratio, CI: confidence interval]

3.2. Determinants of individuals at risk of persistent AESIs

Of 210 individuals developing AESIs, 153 complained of persistent AESIs. Median (Q1,Q3) duration of persistence of AESIs was 120 days (60-195). Tests of proportion were first used to evaluate association between individuals with persistent AESIs and co-variates. In unadjusted analysis, statistically significant association of persistent AESIs was noticed with age, sex, presence of obesity, diabetes,

hypertension, heart disease, prior arthropathy and hypothyroidism. Timing of vaccine with respect to COVID-19 also shared a statistically significant association. After adjusting for co-variates, regression analysis highlighted a statistically significant 1.66- and 2.23-times higher odds of persistence of AESIs in females and individuals with hypothyroidism. With marginal statistical significance, a 2.34- and 3.44-times higher odds of persistence of AESIs was observed in individuals with pre-existing heart disease and arthropathy. An interesting association was observed with the timing of vaccine received with respect to COVID-19. Receiving any dose of the COVID-19 vaccine after any prior history of COVID-19 was associated with a 1.94- times higher odds of persistence of AESIs compared to COVID-19 occurring after receipt of any dose of COVID-19 vaccine. Compared to vaccinees who didn't develop any COVID-19, individuals receiving the COVID-19 vaccine after any COVID-19 of the past were observed to be at 2.85 higher odds of persistence of AESIs with statistical significance (**Table 2b**).

3.3. Adverse events after booster dose of COVID-19 vaccine

Till the last follow up, 184 participants had received the booster dose of COVID-19 vaccines. Of these 18 vaccinees reported significant adverse events, giving the adverse event rate of 9.8%. Skin and subcutaneous disorders in the form of urticaria and new onset arthropathy were the common adverse events in this subset.

4. Discussion

Vaccines against COVID-19 were granted emergency use authorization in late December 2020- early January 2021. Such approval was driven primarily by high efficacy rates against COVID-19 occurrence and a favorable short term safety profile of the vaccines in controlled settings. Post approval, however, the claims of high effectiveness of vaccines against COVID-19 has been challenged by some studies with new evidence reflecting a marginal to modest rate of protection.[8][9] Likewise, a negative vaccine efficacy rates has been reflected in exploratory outcomes of some controlled studies as well as in the findings of some real world studies.[8][10][11] The post approval phase also witnessed reports of atypical adverse events and adverse events of special interest (AESIs). These included cases of vaccine induced thrombosis and thrombocytopenia (VITT), new onset cardiac events, flares and new onset of autoimmune phenomena such as rheumatoid arthritis, diabetes mellitus, Guillain Barre syndrome and encephalitis.[2][3][12][13][14] Though passive reporting of AESIs is recommended by drug regulatory bodies to strengthen the safety profile of vaccines, spontaneous reporting rates are low mainly

because of scanty awareness on AESIs and a deficient knowledge of reporting, even among medical professionals. Actual estimates of AESIs can be represented by active surveillance methods of which prospective cohort-based study designs involving vaccinated individuals are one of the preferred approaches.

Nearly one third of our study participants developed COVID-19 during the 2nd wave and around 17% were affected during the 3rd wave of the pandemic. Close to 44% individuals developed COVID-19 at any time since vaccination and over one year of follow up. That occurrence of COVID-19 was common in participants with history of COVID-19 in the second wave suggests a need for understanding the genetic basis of predilection to SARS-CoV-2, as well as raises questions on the concept of longer hybrid immunity gained after natural infection in vaccinated individuals. The protective effect of primary or booster doses of COVID-19 vaccine against subsequent viral strains also needs a comprehensive assessment. Apart from COVID-19, dengue occurred in 8% participants. With nearly 20% of the affected individuals developing dengue of 'serious' category, future research involving an unvaccinated arm is needed for comparison and generating pathogenetic hypotheses.

Among AESIs, disorders involving the musculoskeletal system largely predominated by arthropathy occurred in close to 4% participants. Pain in the knee joint followed by new onset lower back pain were the commonly observed arthropathies. The joint problems were persistent in majority at the time of last follow up, with median duration of persistence of four months. Events belonging to the system organ class of 'General disorders and administration site conditions' and 'Infections and infestations' were the other commonly reported health issues. Persistent fatigability was the commonest event reported among the general disorders and typhoid and recurrent viral upper respiratory tract infections were commonly reported non COVID-19, non-dengue infections. Among other rare and atypical adverse events, new onset hypertension, thyroid function abnormalities, and new onset diabetes were reported. Considering a probable autoimmune etiology of most of these AESIs, further research is warranted into how the ChAdOx1 vaccine may act as a potential trigger.[15]

Eleven participants (0.7%) developed adverse events of 'serious' grade, some of which have been published in the preliminary analyses of the study, and as part of other ongoing work.[5][6][8] A total of 5 deaths were reported of which one occurred in an adult male because of sepsis and encephalopathy in an individual with diabetes (both doses received), and the remaining occurred in elderly. Of the latter, one death occurred due to aggravation of pre-existing congestive heart failure within hours of vaccination, followed weeks later by COVID-19 (single dose received), one because of

cardiac arrest in an individual with pre-existing diabetes and hypertension (both doses received), one because of cardiac arrest in an individual with underlying coronary artery disease after recovery from COVID-19 (single dose received) and one because of COVID-19 itself (single dose received).

After adjusting for co-variates, regression analysis showed a close to 2-times higher odds of occurrence of AESIs in females and individuals with diabetes and a nearly 2.5-times higher odds of AESIs in individuals with hypothyroidism. In our previously published work, both these factors were projected as risk factors of adverse events following immunization (AEFIs) with ChAdOx1-nCoV-19 vaccine.[5] Understanding the hormonal and sex related differences in the occurrence of adverse events following COVID-19 vaccines is of interest considering common trends between AEFIs and AESIs. Another interesting positive association of AESIs was observed with the pre-vaccination history of COVID-19. As previously suggested by us, guidelines need to be revisited with regards to vaccinating those who have recovered from COVID-19.[8]

Adjusted analysis was also performed to determine individuals at risk of persistent AESIs. A close to 1.6-times and 2.2-times higher risk was observed in females and individuals with hypothyroidism. Though, pre-existing heart disease and arthropathy were also associated with higher risk of persistent AESIs, relevant conclusions cannot be drawn at present because of poor overall representation of these co-morbidities in the study sample. Validating the findings of another recently published study of ours, an interesting link was observed between individuals with persistent AESIs and timing of COVID-19 vaccine. Any dose of the vaccine received after recovery from COVID-19 was associated with higher odds of persistent AESIs compared to both COVID-19 occurring after vaccination, and not developing any COVID-19 till last follow up.

Close to 10% individuals receiving the booster dose developed adverse events of concern. Cutaneous conditions and new onset arthropathy were commonly reported. Though number of individuals receiving the booster dose till last follow up were small, detailed safety studies should be conducted to delineate the profile of booster doses.

4.1. Limitations

The study was based on vaccinated individuals and data on events such as third wave of COVID-19 and dengue need comparison with an unvaccinated population, which may be difficult to obtain. Individuals with co-morbidities represented a small sample and results may not be generalized to these groups. With this being a telephonic study, detailed evaluation of many AESIs was not possible.

Also, the study being observational with last two follow ups conducted at six-month intervals, information such as exact onset of AESIs without laboratory workup, is expected to be affected by recall bias. However, medical records were obtained electronically for majority of the diagnosed and serious cases of AESIs. Further, the safety related data is specific for ChAdOx1-nCoV-19 and cannot be generalized to mRNA vaccines and inactivated vaccines. Only a small number of individuals had received booster doses till the last contact and a larger population needs to be recruited to understand the safety profile of boosters. Further, among participants receiving booster doses, AESIs were reported commonly within 2-3 weeks of the booster dose. As such safety related information might be inadequate or underreported for individuals contacted within days of receiving the boosters.

5. Conclusion

COVID-19 occurred in close to 44% individuals post vaccination with the ChAdOx1-nCoV-19 vaccine. AESIs occurred commonly in females, individuals with hypothyroidism, diabetes, or pre-vaccination history of COVID-19. Females and individuals with hypothyroidism were also at high risk of persistent adverse events. Though the effect of COVID-19 on persistence of AESIs cannot be underestimated, vaccines received after any COVID-19 was associated with two times risk of persistence of adverse events compared to vaccine received before COVID-19. Among AESIs, caution is advised particularly for arthropathy, recurrent viral infections and severe forms of dengue. The sex related and hormonal differences in the occurrence of COVID-19 vaccine related adverse events should be explored in future. With considerable rates of breakthrough COVID-19 and non-modest rates of AESIs in vaccinated, blanket recommendations on mass roll out need strategic reconsideration. Females, individuals with co-morbidities such as hypothyroidism and those with a history of COVID-19 should be informed about the benefit of protection offered by vaccines against COVID-19 as well as risk of post vaccination adverse events, in order to guide individual decisions. An individualized vaccination strategy rather than mass roll out may be a better alternative towards public health safety.

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Conflicts of Interest: None

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Ethical Statement: The study was conducted after permission from the Institute Ethical Committee of the Institute of Medical Sciences, Banaras Hindu University. Written informed consent was taken from each participant. No human experimentation was performed. All procedures were performed as per the Declaration of Helsinki and its subsequent modifications.

Data Availability Statement: All data produced in the present study are available upon reasonable request to the authors, as per institutional and national legal norms and procedures.

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