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Long Term Safety Analysis of BBV152 Coronavirus Vaccine in Adolescents and Adults: Findings From a One-Year Prospective Study in North India

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Abstract

Introduction: Evidence on long term safety of COVID-19 vaccines is scarce. Here in continuation of our previously published results on short term safety, we provide data on long term safety of the BBV152 vaccine in adolescents and adults.

Methodology: This was a prospective observational study conducted from January 2022 to August 2023. Adolescents and adults receiving BBV152 vaccine were interviewed telephonically about long-term adverse events of special interest (AESIs) after one year of vaccination. Risk factors of AESIs and AESIs persistent for at least one month were identified.

Results: Out of 1024 individuals enrolled, 635 adolescents and 291 adults could be contacted on one year follow-up. Viral upper respiratory tract infections (URTIs) were reported by 304 (47.9%) adolescents and 124 (42.6%) adults in this period. New onset skin and subcutaneous disorders (10.5%), general disorders (10.2%) and nervous system disorders (4.7%) were the common AESIs in adolescents. General disorders (8.9%), musculoskeletal disorders (5.8%) and nervous system disorders (5.5%) were the common AESIs in adults. Menstrual abnormalities were noticed in 4.6% females. Ocular abnormalities and hypothyroidism were observed in 2.7% and 0.6% participants respectively. Serious AESIs including stroke and Guillain-Barre syndrome were identified in around 1% participants. Among adolescents, females, those with history of allergy and post-vaccination typhoid were respectively at 1.6-, 2.8- and 2.8-times higher risk of AESIs. Majority of the AESIs were persisting at one year follow-up. Females, adolescents with pre-vaccination COVID-19, those with co-morbidities, and post-vaccination typhoid had respectively 1.6-, 2-, 2.7- and 3.2-times higher odds of persistent AESIs. Adults with co-morbidities had more than two 2 times higher odds of AESIs and persistent AESIs.

Conclusion: The patterns of AESIs developing after BBV152 differed from those reported with other COVID-19 vaccines as well as between adolescents and adults. With the majority of AESIs persisting for a significant period, extended surveillance of COVID-19 vaccinated individuals is warranted to understand the course and outcomes of late

onset AESIs. Relationship of AESIs with sex, co-morbidities, pre-vaccination COVID-19 and non-COVID illnesses should be explored in future studies.

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1. Introduction

To limit the impact of COVID-19, various vaccines based on novel and pre-existing technologies were granted approval for mass roll out. The COVID-19 vaccination program worldwide was started in the months of December 2020 and early January 2021. The viral vectored and mRNA based COVID-19 vaccines were the vaccines distributed on large scale across the globe. Vaccines based on inactivated SARS-CoV-2 included SinoVac-CoronaVac (China), Sinopharm-BBIBP-CorV (China) and Bharat BioTech-BBV152 (India). BBV152 was the second most distributed vaccine in India after the adenoviral-vectored AZD1222 (COVISHIELD). Considering the assumed benefits of vaccinating all, the approval of some of the COVID-19 vaccines was later extended to adolescents and children. The mRNA-based vaccines were the first ones to get the nod for administration in adolescents and children globally. [1] In India, the BBV152 was the only vaccine which was initially granted permission for mass roll out in adolescents of 15-18 years.[2] The short-term safety of COVID-19 vaccines approved for adolescents was shown to be favorable in controlled settings. [3][4][5] In this context, we provided the first short-term safety data of BBV152 in adolescents and the comparative safety profile in adults. [6] Despite nearly 2 years having elapsed since the approval of COVID-19 vaccines in adolescents, no long-term data on safety of these

vaccines has been released in the public domain. Here, in an extension of our previously published study, we provide data on long term safety of the BBV152 vaccine in adolescents and adults.

2. Methodology

2.1. Study design and setting

This was a one year long prospective observational study which started in January 2022 in a tertiary university hospital of North India. The study aimed to provide short-term and long-term safety data of BBV152 vaccine in adolescents and adults. Participants were initially contacted telephonically after 14 days of receiving the vaccine and the interim safety analysis in the form of adverse events following immunization (AEFIs) was published by us in 2022. [6]Here we provide the long-term safety data of BBV152 in the form of adverse events of special interest (AESIs) assessed at one year of follow up in the same study group.

2.2. Study participants

Adolescents of 15-18 years of age and adults of 19 years and above receiving any dose of BBV152 vaccine constituted the study population.

2.3. Safety analysis and outcome measures

All participants were interviewed telephonically about the occurrence of AESIs. The format used for collecting information on AESIs was guided by the list of AESIs provided by the CEPI-SPEAC-Brighton Collaboration, atypical adverse events published in PubMed/Medline and our own experience on COVID-19 vaccine related atypical adverse events reported in our center. [7][8]

All symptoms were labelled using the low-level terms (LLT) and system organ class (SOC) as per the MedDRA® terminology. [9] Severity of AESIs was rated using the Food and Drug Administration (FDA)-AEFI severity assessment scale.[10] Depending upon improvement, outcomes of AESIs were rated as ‘improved’ if no symptoms were present at the time of follow-up or the participant was off therapy required initially for the management of AESIs and ‘partially improved’ if symptoms were persisting at one year follow up or were controlled only on medication. Additionally, we enquired about “persistent AESIs” pre-defined as “any symptoms persisting for a minimum period of 4 weeks at the time of one year follow up”. [7]

The final list of AESIs selected for the present study is provided as**Supplementary Table 1**. Briefly, we enquired about the occurrence of infections such as upper respiratory tract infections, laboratory confirmed COVID-19 and dengue, among others. Additionally, detailed information was sought on new-onset rheumatologic disorders, cardiac disorders such as heart failure, myocardial infarction or myocarditis, metabolic disorders such as diabetes, endocrinal disorders such as thyroid abnormalities, nervous system disorders such as headaches, attention deficits, stroke and weakness in

limbs, hematologic disorders such as anemia and thrombocytopenia, skin disorders such as alopecia, reproductive disorders such as menstrual disturbances and flares of underlying diseases such as diabetes, hypertension and arthropathy. The causality association of 'serious' AESIs was performed using the 2005 WHO scale of causality assessment of AEFIs. [11]

2.4. Sample size

The sample size estimation of our one-year follow-up study was based on primary outcomes of rates of adverse events following immunization (AEFIs) following BBV152 vaccine. Details are provided in the published interim analysis. [6]

2.5. Statistical analysis

Dichotomous data was analyzed as frequencies and percentages and depending upon the normality, mean or median values were chosen for quantitative variables. Chi square test was separately applied to assess association of independent variables such as demographic factors, co-morbidities, pre-vaccination COVID-19 and non-COVID-19 illnesses with the two dependent variables, namely "AESIs" and "persistent AESIs". The variables with P value <0.05 in bivariate analysis and those presumed to be clinically significant were incorporated in the final regression model to determine the risk factors. Separate regression analyses were performed for the two dependent variables- "AESIs" and "persistent AESIs", and for adolescents and adults separately. Hence, altogether four different regression analyses were performed. SPSS version 16 was used to perform the statistical tests.

3. Results

A total of 1024 participants (698 adolescents and 326 adults) receiving BBV152 were enrolled in the study in January 2022. The initial short term AEFIs noticed within 14 days of receiving the vaccine have already been published.[6] Data on long term safety at one year of follow-up could be procured from 635 adolescents and 291 adults. Information about the total number of vaccine doses was not known for 58 adolescents and 66 adults. Thus, association between number of doses and AESIs could be analyzed for 577 adolescents and 225 adults. Four deaths were reported in adults. 635 adolescents and 287 adults were subsequently assessed for persistent AESIs at one year. The details of participants recruited and analyzed are depicted in **Figure 1.** Details of infections and AESIs reported in adolescents and adults are described subsequently.

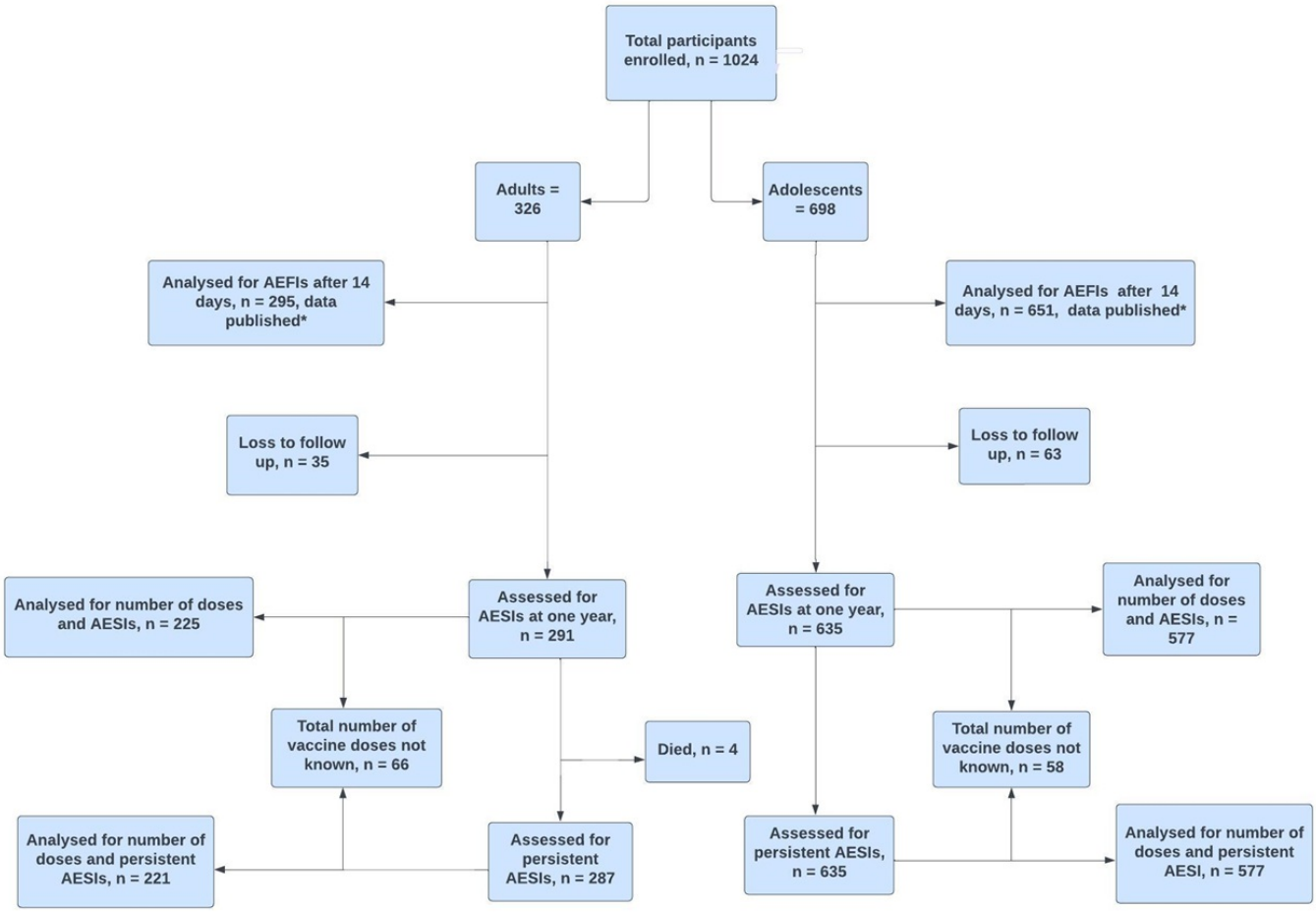

Figure 1. STROBE flow diagram of study.

3.1. Infections

3.1.1. Infections in adolescents

A total of 304 adolescents (47.9%) reported viral upper respiratory tract infections (URTIs) and all except one were moderate in severity. Majority of these infections were reported after June 2022. Among these 304, recurrent viral URTIs were complained by 26. Since laboratory tests for COVID-19 were not being opted for by patients during this period, no case of viral URTI could be labelled as COVID-19. Laboratory confirmed and symptomatic dengue occurred in 22 (3.5%). Eight cases (36.4%) of dengue were ‘severe’ or ‘serious’ cases and three among them required hospitalization. Laboratory confirmed typhoid was the third most common infection reported in 17 (2.7%) and was ‘severe’ in four cases. Details are provided in **Table 1.**

3.1.2. Infections in adults

Among 291 adults, viral URTIs were reported by 124 (42.6%) and majority were moderate in severity. Similar to adolescents, laboratory test for COVID-19 was not done in the cases of URTIs. Laboratory confirmed typhoid and symptomatic dengue were observed in seven and six cases respectively. Severity wise, one case of viral URTI was

'severe' and one case each of typhoid and dengue was 'serious'. Details are provided in **Table 1.**

3.2. AESIs in adolescents

Among 635 adolescents, AESIs were recorded in 214 (33.7%). General disorders (n=65, 10.2%) such as undiagnosed fever and weakness, skin and subcutaneous disorders (n=67, 10.5%) such as alopecia and nervous system disorders (n=30, 4.7%) such as headache and attention difficulty were the common three SOCs affected by AESIs in adolescents. Other common disorders included eye disorders (n=23, 3.6%) such as refractive error and musculoskeletal disorders (n=18, 2.8%). Around 5.7% (n=36) adolescents reported a flare of underlying disease. Cutaneous disturbances in the form of increased hair fall, eye disturbances such as increase in refractive error and nervous system disturbances such as aggravation of headache were the common flares. Details are provided in **Table 1**.

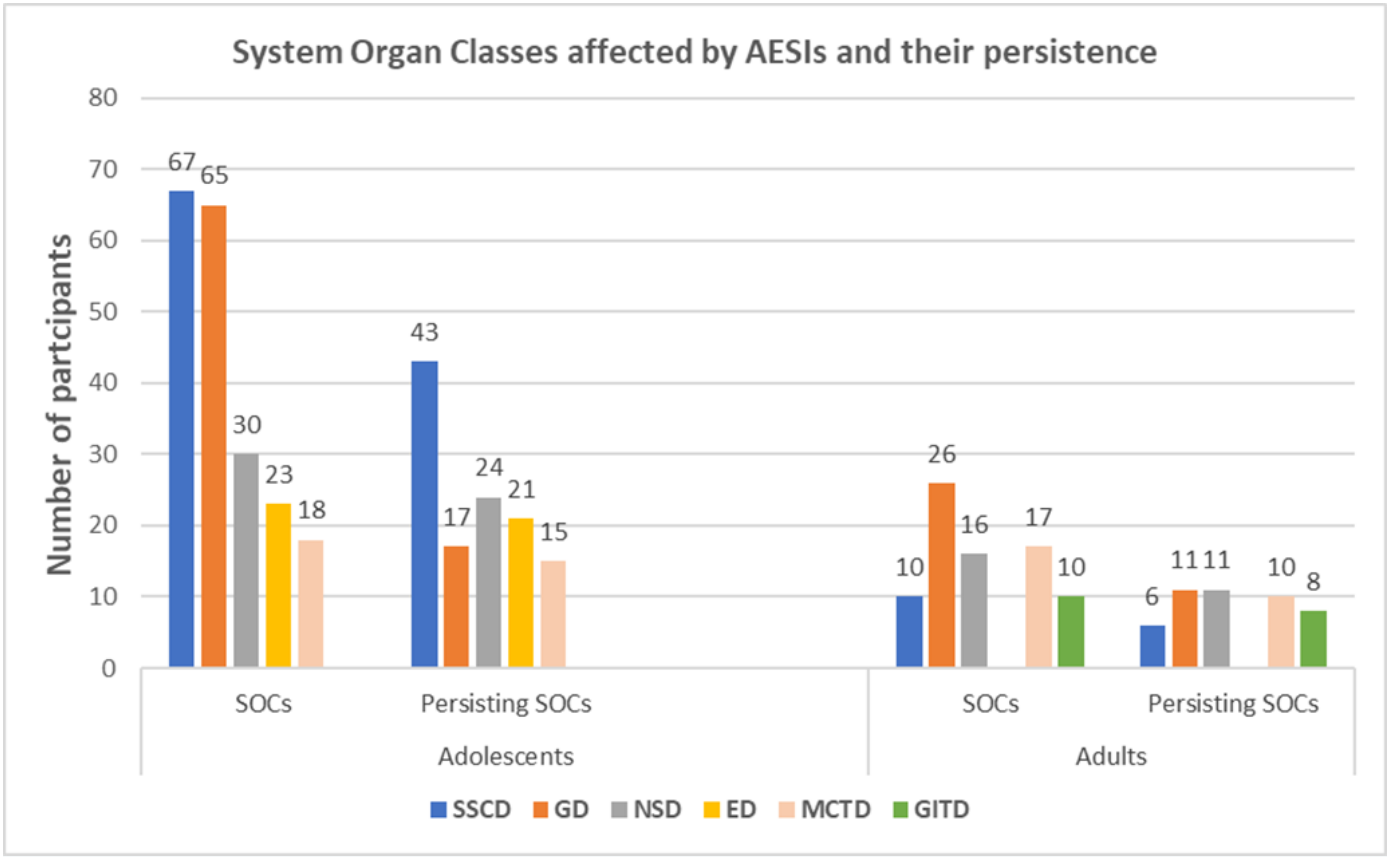

Figure 2. System Organ Classes (SOCs) affected by AESIs and their persistence in BBV152 vaccinated adolescents and adults. (Out of 635 adolescents and 291 adults; 287 adults for persistent AESIs)

Abbreviations- ED: Eye disorders, GD: general disorders, GITD: Gastrointestinal disorders, MCTD: musculoskeletal and connective tissue disorders, NSD: nervous system disorders, SSCD: skin and subcutaneous tissue disorders

3.2.1. Persistent AESIs in adolescents

Among 214 adolescents with AESIs, 142 (66.3%) had persistent AESIs. Alopecia (n=47), refractive errors (n=26),

headache (n=20), menstrual abnormalities (n=17) and increased symptoms of allergy (n=16) were the five common persistent AESIs. With respect to SOCs, all cases of psychiatric disorders, 91.3% of eye disorders, 88.2% of reproductive disorders, 83.3% each of musculoskeletal and immune system disorders, 80% of nervous system disorders and 64.2% of skin disorders were persisting till last follow-up. Details of persistent SOCs and the approximate time of persistence are mentioned in **Supplementary Table 2, Supplementary Table 3**and depicted **in Figure 2**.

3.2.2. Risk factors of AESIs and persistent AESIs in adolescents

Bivariate analysis showed a statistically significant association of AESIs in adolescents with sex (p=0.006), history of allergy (p<0.001) and presence of any co-morbidity especially asthma (p=0.007). Though not statistically significant, a marginal association of AESIs was also observed with post-vaccination typhoid (p=0.09) (**Table 2a**). Since typhoid can influence occurrence of clinical symptoms such as musculoskeletal and subcutaneous disorders, it was incorporated in the regression model along with variables sharing a statistically significant association (p<0.05) with AESIs in bivariate analysis. After adjusting for confounders, females were observed to have a 1.57 times higher odds of AESIs compared to males (p=0.009) and history of allergy to any stimuli was associated with 2.81 times higher odds of AESIs (p=0.004) (**Table 2b).** A nearly similar odds (aOR 2.76) of AESIs was observed with post-vaccination typhoid (p=0.042).

For persistent AESIs, a statistically significant association was noted with sex (p=0.016) and presence of co-morbidity such as asthma (p=0.007). With marginal statistical significance, AESIs were also commoner in adolescents with history of allergy, pre-vaccination history of COVID-19 and post vaccination typhoid (p=0.07 for each). (**Table 3a**) All these factors were included in the regression analysis which showed 1.61 times higher risk of persistent AESIs in females (p=0.018) and 2.71 times higher risk in adolescents with co-morbidities (p=0.011). Pre-vaccination COVID-19 increased the odds of persistent AESIs by around 2 times (p=0.047) and a close to 3.2 times higher risk of persistent AESIs was observed with post-vaccination typhoid (p=0.023). (**Table 3b**) No association of persistent AESIs was observed with history of allergy.

3.3. AESIs in adults

Among 291 adults, AESIs were recorded in 83 (28.5%). General disorders were the most common SOC affected by AESIs (n=26,8.9%). This was followed by musculoskeletal disorders (n=17, 5.8%) and nervous system disorders (n=16, 5.5%). Other common disorders were gastrointestinal disturbances and skin and subcutaneous disorders, each seen in 10 (3.4%) cases. Flare of underlying disease was reported by ten adults (3.4%). Details are provided in **Table 1**.

3.3.1. Persistent AESIs in adults

Among 83 adults with AESIs, 54 (65.1%) had persistent AESIs. Joint pain (n=12), weakness (n=8), alopecia (n=8). headache (n=6) and dyspepsia (n=4) were the common five AESIs that were persistent in adults at one-year of follow up. Regarding SOCs, 80% of gastrointestinal disorders, 75% of cardiac disorders, 68.7% of nervous system disorders and 60% each of skin and reproductive disorders were persisting at one year of follow-up. Details are described in **Supplementary Table 2, Supplementary Table 3**and **Figure 2**.

3.3.2. Risk factors of AESIs and persistent AESIs in adults

With statistical significance, AESIs were more common in adults of age 45 years and above (p=0.035), those with co-morbidities such as hypertension (p=0.009) and those receiving three doses of BBV152 (p=0.001) (**Table 4a**). Upon adjusting for confounders, regression analysis showed a 2.23 times higher risk of AESIs in adults with co-morbidities (p=0.04). Individuals receiving three doses and the ones receiving a single dose of BBV152 were respectively at 4.03 times and 2.16 times higher risk of AESIs compared to those receiving two doses. Difference was not significant between individuals receiving one and three doses of BBV152 (**Table 4b**).

For persistent AESIs, the unadjusted analysis showed a significant association with age (p=0.056) and presence of co-morbidities (p=0.004) (**Table 5a**). In regression analysis, the effect of age was nullified and only presence of co-morbidities remained a significant determinant, increasing the odds of persistent AESIs by 2.26 times (p=0.025) (**Table 5b**). Among co-morbidities, the risk of persistent AESIs was attributed to hypertension. This was confirmed in a separate regression analysis based on age groups and hypertension as independent variables (Results not shown).

3.4. Serious AESIs in adolescents and adults

A total of nine adults and one adolescent developed serious AESIs. A case of haematemesis (upper gastrointestinal bleed) was reported in a 15-year female. Stroke events were reported in three adults and one adult in his 20's was hospitalized for Guillain-Barré syndrome (GBS). Using the WHO scale of causality assessment, the latter was attributed a 'probable' association with the vaccine. Details of all serious AESIs are given in **Supplementary Table 4.** Four deaths were reported in adults. History of COVID-19 before receiving the vaccine was present in two of these. Three deaths occurred in females with stroke as the main contributor in two. One among these had a history of diabetes and hypertension and was in her late 60's and the other in her late 50's had a history of diabetes. Cause of death in the third lady could not be identified but the lady in early 70's had diabetes and hypertension and had a history of multiple episodes of unconsciousness after receiving the vaccine whose etiology could not be identified. The fourth mortality was recorded in a diabetic male in his 40's with a history of post COVID-19 rhino cerebral mucormycosis before receiving the vaccine. The concerned participant succumbed to the illness around 2.5 months after receiving the vaccine. Three of these fatalities shared a 'possible' association with the vaccine while the fourth was 'unclassifiable'.

3.5. Symptoms with reduced frequency and severity

Though not included in the study format, some study participants self-reported the health benefits they observed after receiving the BVV152 vaccine. Around 6.3% (n=40) adolescents and 5.5% (n=16) adults mentioned reduced frequency or severity of health issues they had before vaccination. Among these, reduced frequency and/or severity of upper respiratory tract infections was the commonest health benefit observed, being reported by 37 adolescents and 13 adults. Details of the symptoms in which improvement was noticed after BBV152 are mentioned in **Supplementary Table 4**.

4. Discussion

In the absence of long-term safety data of COVID-19 vaccines, the main aim of the present study was to highlight the safety issues in recipients of the BBV152 vaccine, particularly among adolescents, at one year of follow-up. Nearly 50% of study participants complained of infections during the follow-up period, predominated by viral URTIs. Among AESIs, new onset skin and subcutaneous disorders, general disorders and nervous system disorders were the three most common disorders in adolescents after receiving the vaccine. More than 10% adolescents complained of skin conditions, mainly in the form of alopecia and a similar percentage had general disorders such as weakness. While majority of general disorders had recovered, skin disorders were present in majority during final follow up with a median time of persistence of 8.5 months. General disorders and musculoskeletal disorders were the common long term AESIs in adults. General disorders had recovered in more than 50% but symptoms of musculoskeletal disorders were persisting in majority for almost 6 months at final follow-up. Close to 5% adolescents and adults complained of nervous system disorders such as headache which were persisting in majority for around 9 months at final follow-up. Among other atypical and persistent AESIs, eye disorders such as new onset refractive error was reported in 3.6% adolescents and 5% adolescent females complained of new onset menstrual abnormalities. Hypothyroidism was reported by around 0.6% adolescents and adults, each.

The patterns and incidence of AESIs differs with respect to the type of vaccine and study population. In a predominantly adult based population receiving ChAdOx1-nCov-19 vaccine, general disorders, musculoskeletal disorders, and cardiac-vascular disorders were the common AESIs in our earlier follow-up study but the incidence reported was low, being 3.7%, 2.1% and 1.4% respectively. Reproductive system disturbances and ocular disturbances were rare and were documented in 0.7% and 0.26% participants. [7] Three out of five mortalities reported with ChAdOx1-nCoV-19 happened due to cardiac causes in contrast with the neurological events such as stroke reported in the present study. Another 18-month long study commented upon the late AESIs after protein subunit based PastoCovac vaccine in Iran. Cutaneous disturbances (3.3%), musculoskeletal disorders (1.1%) and neurological events (1.1%) were the common AESIs with PastoCovac given in heterogeneous regimen with AstraZeneca or Sinopharm vaccine. The rates were further low with standard regimen of PastoCovac vaccine in which neurological, musculoskeletal, and metabolic disturbances, were the common events, each witnessed in 0.3% individuals. [12] Apart from the type of vaccine and study population, the system affected and the incidence of AESIs is strongly influenced by reporting rates and awareness regarding AESIs.

Among adolescents, occurrence of AESIs and persistent AESIs was higher in females, those with co-morbidities, those with a history of allergy to any stimuli and those developing typhoid after receiving the vaccine. Some association of persistent AESIs was also observed with pre-vaccination history of COVID-19. The adjusted analysis showed females to have 1.6 times higher odds of AESIs. Adolescents with history of allergy and those developing typhoid after receiving the vaccine, each, were independently at 2.8 times higher risk of AESIs. With respect to persistence of AESIs, factors which emerged as independent risk factors were sex, presence of co-morbidities, pre-vaccination history of COVID-19 and post-vaccination development of typhoid. Females were at 1.6 times higher risk and adolescents with co-morbidities were at 2.7 times higher risk of persistent AESIs compared respectively to males and adolescents without co-morbidities. The pre-

vaccination history of COVID-19 and post vaccination occurrence of typhoid increased the odds of persistent ASESIs by 2 and 3.2 times respectively. In our previous work, pre-vaccination history of COVID-19 was shown as an independent risk factor for long COVID-19, AESIs and persistent AESIs in recipients of ChAdOx1-nCoV-19 vaccine. [7][13] Females were also the common victims of AESIs and persistent AESIs after ChAdOx1-nCoV-19, similar to the findings of the present study.

Among adults, those with co-morbidities such as hypertension were at more than 2 times higher risk of AESIs and persistent AESIs. Interestingly, adults receiving three doses of BBV152 were at four times higher risk of AESIs compared to adults receiving two doses of BBV152. The results need corroboration from larger studies owing to limited number of adults receiving the third dose of vaccine.

Four deaths (3 F, 1 M) were reported in adults. All of them had diabetes while hypertension and history of pre-vaccination COVID-19 were present in three and two individuals respectively. Stroke was the main contributor in two and one fatality was due to post COVID-19 rhino-cerebral mucormycosis which supposedly disseminated after vaccination as reported by the caregivers. The fourth death happened in a lady with multiple episodes of unconsciousness post vaccination, the etiology of which remained unidentified till death.

5. Limitations

The study enrols individuals vaccinated with BBV152. To understand the link of AESIs with COVID-19 vaccines, a control arm of unvaccinated individuals is needed to compare the rates of AESIs between the two groups. In the absence of data on background rates of the observed AESIs, no comments can be made on change in the incidence of the observed events in the post-vaccination period. Findings of our study are confined to BBV152 and should not be extrapolated to viral vectored or mRNA vaccines. The study primarily involved adolescents and the sample size of adults was relatively small. Larger adult based studies are needed to understand the long-term safety of BBV152 in adults. The study participants belonged to northern belt of India and ethnicity related differences in vaccine tolerability should be explored. The sample size was decided based on the primary outcomes of AEFIs and not based on AESIs as no study on incidence of AESIs was available when the present study was started. However, considering the high observed rates of overall AESIs the study sems to be well-powered for detecting AESIs. The final follow-up being at one year, the study is subject to recall bias at certain points. For example, the exact time of onset of AESIs was not available but the approximate time of persistence of AESIs was obtained. For the same reason, some of the AESIs not persisting during final follow-up but which occurred for significant period at any time in the past one year might have gone unreported. As the reporting rates of COVID-19 went down in India after May 2022, the routine testing for SARS-CoV-2 was not performed in individuals developing viral upper respiratory tract infection (URTI). The possibility of COVID-19 cannot be excluded in these individuals. Relationship of AESIs with typhoid and pre-vaccination COVID-19 need corroboration from larger studies owing to smaller representation of these subsets. The specific lab test used for diagnosis of typhoid was not enquired. Also, in the experience of study researchers (UK, SSC, KP, VJ and SK) findings concerned with seropositivity for typhoid should be interpreted cautiously as the test was commonly found to be co-positive in patients of COVID-19 during the

second and third wave of the pandemic. The possibility of sera of COVID-19 patients showing cross-reactivity in the ELISA tests designed for typhoid needs to be determined. More than 5% participants self-reported reduced Viral URTIs. The percentage might be falsely low as symptoms improving after vaccination were not a part of the designed proforma of the present study.

6. Conclusion

Nearly one-third of participants receiving the BBV152 vaccination reported AESIs. Female adolescents and those with history of allergy are at higher risk of AESIs after BBV152 vaccine. Vaccinated adolescents developing typhoid after BBV152 might also be at higher risk of AESIs, but the finding of seropositivity for typhoid needs to be viewed cautiously. Adolescent females and those with co-morbidities, are at higher risk of persistent AESIs also. Focussed monitoring for persistent AESIs is warranted for individuals with pre-vaccination history of COVID-19. Adults with co-morbidities especially hypertension are at higher risk of AESIs and persistent AESIs after BBV152 administration. The patterns of AESIs developing after BBV152 differ from those seen after ChAdOx1-nCoV-19 as well as among different age groups. Vigilance is advised in adolescents for alopecia, headache, and menstrual abnormalities and in adults for musculoskeletal and nervous system disorders. With majority of the AESIs persisting for a significant period, extended surveillance is suggested for COVID-19 vaccinated individuals to understand the course and outcomes of late onset AESIs. Relationship of AESIs with sex, co-morbidities, pre-vaccination COVID-19 and non-COVID illnesses should be explored in future studies.

Tables

This material is available from the Supplementary data section and can be downloaded from the following links:

- Table 1 here.
- Table 2 here.
- Table 3 here.
- Table 4 here.
- Table 5 here.
- Supplementary Tables here.

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Statements and Declarations

Competing interests: The authors have no conflicts of interest to declare.

Funding: No funding support.

Ethical approval: The study was conducted after permission from the Institute Ethics Committee of the Institute of Medical Sciences, Banaras Hindu University. No human experimentation was performed. All procedures were performed as per the Declaration of Helsinki and its subsequent modifications.

Consent to participate: Written informed consent was taken from each participant for participating in the study

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

Code availability: NA

Authors' contribution

- **Conceptualization**: [Upinder Kaur, Sankha Shubhra Chakrabarti, Sangeeta Kansal, Vaibhav Jaisawal, Kishor Patwardhan]
- **Methodology:** [Upinder Kaur, Sankha Shubhra Chakrabarti, Vaibhav Jaisawal]
- **Formal analysis and investigation**: [Upinder Kaur, Vaibhav Jaisawal, Aakanksha Jaiswal, Ayushi Jaiswal Kunal Singh, Aditi Pandey, Mayank Chauhan, Mahek Rai]
- **Writing - original draft preparation**: [Upinder Kaur, Aakanksha Jaiswal, Ayushi Jaiswal, Kunal Singh, Mahek Rai]
- **Writing - review and editing**: [Upinder Kaur, Sankha Shubhra Chakrabarti]
- **Funding acquisition:** [None], **Resources:** [None]
- **Supervision**: [Upinder Kaur, Vaibhav Jaisawal]

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