
# Adverse Events Following Immunization with Inactivated SARS-Cov-2 (Vero Cell) Covid-19 Vaccine: Active Safety Surveillance Findings from Ethiopia.

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Contents

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## Abbreviation and/or Acronyms

AEFI: Adverse events Following Immunization

WHO: World Health Organization

SARS-CoV-2: Respiratory Syndrome Coronavirus 2

EUA: Emergency Use Authorization

EFDA: Ethiopian Food and Drug Authority

NIP: National Immunization Program

## Abstract

**Background**: The recent Coronavirus pandemic is a highly contagious, pathogenic viral infection that has spread globally at an unprecedented rate. It is associated with significant morbidity and mortality. The WHO declared it as a global pandemic on March 11, 2020. Since then, healthcare authorities all around the globe have launched awareness-raising and preparedness programs. Moreover, several vaccines were developed and introduced to prevent the occurrence and spread of the pandemic. As no vaccine is free of adverse events, this study was designed to investigate the incidence of adverse events following immunization (AEFI) with inactivated SARS-Cov-2 COVID-19 vaccine and its associated factors in Ethiopian population.

**Methods**: Active COVID-19 vaccine safety surveillance through an observational prospective single-arm cohort study was used. A total of 10,000 adults (age≥18 years) who took SARS-Cov-2 COVID-19 vaccine at selected health facilities and willing to participate were included in the study. Data was collected by trained data collectors. Data was collected through direct observation at the vaccination site for 30 minutes after vaccination and then by phone calls on days 2, 4 and 7 for the 1$^{st}$ week and then weekly, on the 2$^{nd}$, 3$^{rd}$ and 4$^{th}$ weeks. Participants were asked whether they encountered any AEFI or not. Data analysis was done using SPSS version 25 software. $P < 0.05$ is considered to be significant.

**Results**: The mean age of study participants was 34.2±12.2 years and majority were females (53.4%). The overall incidence of AEFI was 26.2%. Of these, 25.9% experienced AEFI after 30 minutes of taking the vaccine, while 0.6% experienced AEFI within 30 minutes. A total of 3839 AEFI manifestations were reported. Among participants who reported AEFI, 58.3% experienced two or more AEFIs. The frequently reported AEFIs include injection site pain (26.1%), headache (23.1%), fever (16.3%), arthralgia/joint pain (7.5%), fatigue (6.5%), chills (4.9%), and nausea and/or vomiting (2.9%). Majority of the AEFIs were minor and self-resolved with a week of vaccination. Age, being on medication and history of substance use were variables significantly associated with the occurrence of AEFIs following vaccination.

**Conclusions**: More than 25% of the study participants who took inactivated SARS-Cov-2 COVID-19 vaccine reported experiencing one or more adverse events. Majority of the AEFIs occurred after 30 minutes of vaccine administration. The top five AEFIs reported

were injection site pain, headache, fever, arthralgia/joint pain and fatigue. Age, being on medication and history of substance use were variables significantly associated with the occurrence of AEFIs.

**Keywords**: Inactivated SARS-Cov-2, COVID-19 Vaccine, Vero Cell, Ethiopia

## 1. Background

The coronavirus disease 2019 (COVID-19) pandemic is a global outbreak of coronavirus. It is an infectious disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). SARS-CoV-2 was declared as pandemic by the World Health Organization in December 2019 (1). Until the end of November, 2023, there have been 772,011,164 confirmed cases of COVID-19 and 6,979,786 deaths reported to WHO. In Africa, there have been a total of 12,844,465 confirmed cases, 258,847 deaths and 496,369 active cases. Ethiopia has reported about 501,060 Covid-19 cases, 7574 deaths, and 5315 active Covid-19 cases (2). Vaccination is considered an effective long-term solution to eliminate SARS-CoV-2 because it greatly reduces the chance of infection, severity, and fatalities of the disease (3). Major international biopharmaceutical companies have developed several COVID-19 vaccines. As of August, 2023 around 20 candidate COVID-19 vaccines got WHO emergency use authorization and Sinopharm Covid-19 vaccine received WHO emergency use authorization in July 2021(4).

The inactivated Sinopharm, also known as the BBIBP-CorV vaccine, which was manufactured by Beijing Institute of Biological Products Co., Ltd, China, is an inactivated vaccine that delivers SARS-CoV-2 antigens to the body through two injections, separated by 21 or 28 days. The intramuscular injection of an inactivated COVID-19 vaccine uses the virus' dead antigens to produce antibodies that boost the immune system to combat subsequent COVID-19 viral attacks (5). In Ethiopia, Emergency Use Authorization (EUA) was granted by Ethiopian Food and Drug Authority (EFDA) for Covishield COVID-19 vaccine, Pfizer-Biotech COVID-19 vaccine, inactivated SARS-Cov-2 COVID-19 vaccine, Janssen COVID-19 vaccine and Moderna COVID-19 vaccine.

The study conducted in Pakistan on the safety of Sinopharm COVID-19 vaccine showed that fever (51.3%), burning sensation at the injection site (40.7%) and pain at the injection site (38.0%) were the top three most frequently reported adverse effect following the first dose of the vaccine (6). In addition, a similar study from Patan hospital, Nepal found that incidence of Adverse Event Following Immunization (AEFI) with first dose of Sinopharm COVID-19 vaccine is 19% and pain at the injection site, lethargy, headache, muscle ache, and fever were among the frequently reported AEFIs (7). In both studies, all the AEFIs were considered to be mild to moderate in severity, and most of them started within 24 h of vaccination and resolved within 72 hrs (6, 7).

Another study also showed that systemic symptoms were the most commonly reported events after vaccination with Sinopharm COVID-19 vaccine, and injection site pain (19.3%) was the most prevalent AEFI (8).

Even if, pre-marketing studies have found an acceptable safety profile of the Sinopharm Covid-19 vaccine, it is recognized that at the time of authorisation, information on the safety of the vaccine is relatively limited (9). Thus, post-marketing surveillance is critical to monitor the safety of the vaccine and helps to identify delayed onset AEFIs; population specific AEFIs and very rare AEFIs. Therefore, this prospective observational study was aimed to assess the safety of inactivated SARS-Cov-2 (Vero Cell) COVID-19 Vaccine and its associated factors in Ethiopia population.

### 1.1. Significance of the study

Vaccines approved for use in national immunization program (NIP), are considered safe and efficacious based on demonstrable evidence from randomized controlled clinical trials. They are, however, not completely free of risks, despite rigorous safety evaluation during clinical development, and occasional adverse events will occur following vaccination at the population level. Given vaccines are often recommended for otherwise healthy individuals, the key to success of NIPs is public trust in vaccine safety. Thus, systematic vaccine safety surveillance is indispensable for ensuring safety of vaccines and public trust across countries with various Pharmacovigilance capacities. WHO also recommends that, once plan for immunization with COVID-19 vaccines are set-up, pharmacovigilance systems should start simultaneously, and specific COVID-19 vaccine safety surveillance should be implemented.

Pre-marketing studies have found an acceptable safety profile of the Sinopharm vaccine; however, most of the adverse reactions are revealed when the vaccine is administered to a larger population, post-licensure. It is recognized that at the time of authorization, information on the safety of a medicinal product is relatively limited. This is due to many factors including the relatively small numbers of subjects in clinical trials compared with the intended treatment population, restricted population in terms of age, gender and ethnicity, restricted co-morbidity, restricted co-medication, restricted conditions of use, relatively short duration of exposure and follow up, and the statistical problems associated with looking at multiple outcomes. Furthermore, despite the Sinopharm vaccine being widely used in some nations, post-licensure safety data is limited. Post-

marketing surveillance is critical step in safety monitoring and helps to identify delayed onset AEFIs; population specific AEFIs; very rare AEFIs and other safety data which were not identified in clinical trial phases. In Ethiopia, once this vaccine got approval, no safety data was available. The present prospective observational study was, therefore, aimed to investigate the safety profile of the Sinopharm vaccine in Ethiopian population.

## 2. Objectives

### 2.1. General objective

To assess the safety of inactivated SARS-Cov-2 (Vero Cell) COVID-19 Vaccine and its associated factors in Ethiopia.

### 2.2. Specific objectives

- To determine the incidence of AEFIs
- To characterize the pattern of AEFI cases
- To determine factors affecting the occurrence of AEFIs
- To identify and assess signals if any

# 3. Methods

## 3.1. Study Setting and Period

The study was conducted in six regions (Afar, Amhara, Oromia, South-West Ethiopia, Sidama and South Ethiopia) and two city administrations (Addis Ababa, Dire Dawa) of Ethiopia from May 2021 to July 2022.

## 3.2. Study Design

Active COVID-19 vaccine safety surveillance through an observational prospective single-arm cohort study was conducted in Ethiopia.

## 3.3. Study Population

This study included 10,000 individuals aged ≥ 18 years who received inactivated SARS-Cov-2 (Vero Cell) COVID-19 vaccine at selected health facilities from six regions and two city administrations of Ethiopia.

## 3.4. Inclusion and Exclusion Criteria

Inclusion Criteria

- Individuals vaccinated with first dose of SARS-Cov-2 (Vero Cell) COVID-19 vaccine and willing to participate and give verbal/written informed consent.

Exclusion Criteria

- Individuals vaccinated with first dose of SARS-Cov-2 (Vero Cell) COVID-19 vaccine but not willing to participate.
- Individuals vaccinated with first dose of SARS-Cov-2 (Vero Cell) COVID-19 vaccine but unable to comply with study procedures (not accessible through phone call).

## 3.5. Sampling Technique and Size

Sample size of the study was determined based on the WHO protocol for Cohort event monitoring for safety signal detection after vaccination with COVID-19 vaccines. Accordingly, cohorts of 10,000 participants gives 95% chance of identifying uncommon or rare events with the incidence rate of 1:3000, based on WHO recommendation for identifying rare adverse effects of vaccine (10).

### 3.6. Data Collection Tool and Procedure

A total of 125 data collectors composed of 56 nurses, 55 pharmacists, 9 public health officers, 3 physicians and 2 laboratory technicians were participated in data collection. Data collectors were trained on vaccine safety and on how to collect data, which included questions about types, nature, dates, duration, and outcomes of AEFIs. A standard data collection tool that contains socio-demographic, clinical and other medication-related variables was used. Informed written/verbal consent was taken before enrolling participants for the study. Data was collected at the time of enrolment, at time of vaccination, and during follow-up following vaccination with first dose of SARS-Cov-2 (Vero Cell) COVID-19 vaccine. Data was collected through direct observation at the vaccination site for 30 minutes and after 30 minutes, by phone calls on days 2, 4, and 7 for the 1st week and then weekly on the $2^{nd}$, $3^{rd}$ and $4^{th}$ weeks of follow up period. Participants were asked whether they encountered any of AEFIs or not and the outcomes of AEFIs.

Data quality control

The questionnaire was pre-tested for completeness and validity among 5% of sample size at sites not included in the study. Based on the finding of this pre-test, the tool was revised. The data collection process was supervised by a team of clinical trial and pharmacovigilance experts from the Product Safety Directorate of Ethiopia Food and Drug Authority (EFDA).

### 3.7. Data Analysis

The collected data were entered into a pre-prepared Microsoft Excel spreadsheet template, pre-processed and cleaned, then exported to SPSS version 25, and coded for analysis. Data are presented as counts with proportions for categorical variables and using an appropriate measure of central tendency and dispersion for continuous variables. The results were presented in tables, charts and figures. The association of dependent and independent variables was initially determined by binary logistic regression and variables with P value $< 0.25$ are eligible for multivariable analysis to assess the association. In multivariable analysis, P value $<0.05$ considered to be significant and the strength of association was presented using Adjusted Odd Ratio (AOR) with its 95% confidence intervals (CI).

### 3.8. Ethical Consideration

An ethical clearance letter was obtained from the School of Pharmacy, Addis Ababa University Ethical Review Committee. Prior to data collection, informed written/verbal consent was obtained from each participant. Each participant was informed about the risk and benefits of participating in the study and confidentiality of personal information. Participants were informed that they can withdraw from the study at any time for any reason.

## 4. Results

### 4.1. Sociodemographic and Clinical Characteristics of Study Participants

A total of 10,000 adults were enrolled for the study and complete response was obtained from 9129 participants with a response rate of 91.3%. Majority of the study participants were from Addis Ababa (4290, 47%) and Dire Dawa (1681, 18.4%) followed by Amhara (1003, 11.0%) region (Table 1)

Table 1: Number of study participants included in this study among regions and city administration (N=9129).

| Region/city administration | Frequency | Percentage |
|---|---|---|
| Addis Ababa | 4290 | 47.0 |
| Afar | 441 | 4.8 |
| Amhara | 1003 | 11.0 |
| Dire Dawa | 1681 | 18.4 |
| Oromia | 527 | 5.8 |
| Sidama | 242 | 2.7 |
| South Ethiopia | 247 | 2.7 |
| South West Ethiopia | 698 | 7.6 |

The mean age of the study participants was 34.2 ±12.2 (range: 18-98) years. Most of them (3778, 41.4%) were in the age group of 18-29 years. More than half of the study participants (4877, 53.4%) were females. Only about 1.0% (88) of study participants had a history of substance abuse (Table 2)

Table 2: Sociodemographic characteristics of study participants (N=9129).

| Variables | Category | Frequency | Percentage |
|---|---|---|---|
| Age in years | 18-29 | 3778 | 41.4 |
| | 30-39 | 2657 | 29.1 |
| | 40-49 | 1526 | 16.7 |
| | 50-59 | 788 | 8.6 |

| | | | |
|---|---|---|---|
| | 60 and above | 380 | 4.2 |
| Sex | Female | 4252 | 46.6 |
| | Male | 4877 | 53.4 |
| Do you have a history of any substance abuse? | No | 9041 | 99 |
| | Yes | 88 | 1 |

Regarding medication usage, 1.6% (143) study participants were on at least one medication at the vaccination date. Of these study participants, around 0.46% (42) took two or more drugs. Antihypertensive drugs (58, 40.6%) and antidiabetic drugs (51, 35.7%) were the most commonly used medications while drugs for asthma and/or chronic obstructive pulmonary disorders (8, 5.6%) and antiepileptic drugs (4, 2.8%) were the least encountered drugs (Table 3). Considering clinical conditions of the study participants at the time of vaccination, 1.4% (129) of study participants reported having one or more comorbidities/chronic health problems. The most frequently reported comorbidities were hypertension (47, 34.3%), diabetes (36, 26.3%), HIV/AIDS (17, 12.4%) and asthma and/or chronic obstructive pulmonary disorder (14, 10.2%). Very few of participants (46, 0.5%) reported having known allergies. Moreover, none the study participants reported receiving any vaccine within the past six months (Table 3)

Table 3: Medication and clinical characteristics of study participants (N=9129).

| Variables | Category | Frequency | Percentage |
|---|---|---|---|
| Presence of known allergies | Yes | 46 | 0.5 |
| | No | 9083 | 99.5 |
| Presence of comorbidity | Yes | 129 | 1.4 |
| | No | 9000 | 98.6 |
| Type of comorbidities (n=129) | Hypertension | 47 | 34.3 |
| | Diabetes | 36 | 26.28 |
| | HIV/AIDS | 17 | 12.41 |
| | Asthma and/or chronic obstructive pulmonary disorder | 14 | 10.22 |
| | Cholecystitis | 2 | 1.46 |
| | Hypothyroidism | 2 | 1.46 |
| | Multiple sclerosis | 2 | 1.46 |
| | Sinusitis | 2 | 1.46 |
| | Deep vein thrombosis | 2 | 1.46 |
| | Others* | 13 | 9.49 |
| Current medication at the time of vaccination | Yes | 143 | 1.6 |
| | No | 8986 | 98.4 |
| Type of medications (n=143) | Antihypertensive Drugs | 58 | 40.56 |
| | Antidiabetic Drugs | 51 | 35.66 |

| | | | |
|---|---|---|---|
| | ART Drugs | 11 | 7.69 |
| | Aspirin and Other Anti-inflammatory drugs | 10 | 6.99 |
| | Contraceptives | 8 | 5.59 |
| | Drugs for Ashma and COPD | 8 | 5.59 |
| | Antiepileptic drugs | 4 | 2.80 |
| | Others# | 17 | 11.89 |
| | Unspecified | 18 | 12.59 |

Others*: angioedema, back pain, cardiac problem, epilepsy, gastritis, gouty arthritis, neuritis, stroke, tuberculosis, central nervous disorder and urinary tract infection. Others#: warfarin, atorvastatin, RHZE, ciprofloxacin. Unspecified: study participants could not identify the name of the medication/s.

### 4.2. Incidence and characteristics of AEFI among study participants

Two thousand three hundred-ninety participants reported experiencing at least one AEFI following vaccination with inactivated SARS-Cov-2 (Vero Cell) COVID-19 vaccine and hence, the overall incidence of AEFI was 26.2%. Of these, 25.9% (2368) experienced AEFI after 30 minutes of taking the vaccine, while 0.6% (54) experienced AEFI within 30 minutes (Figure 1).

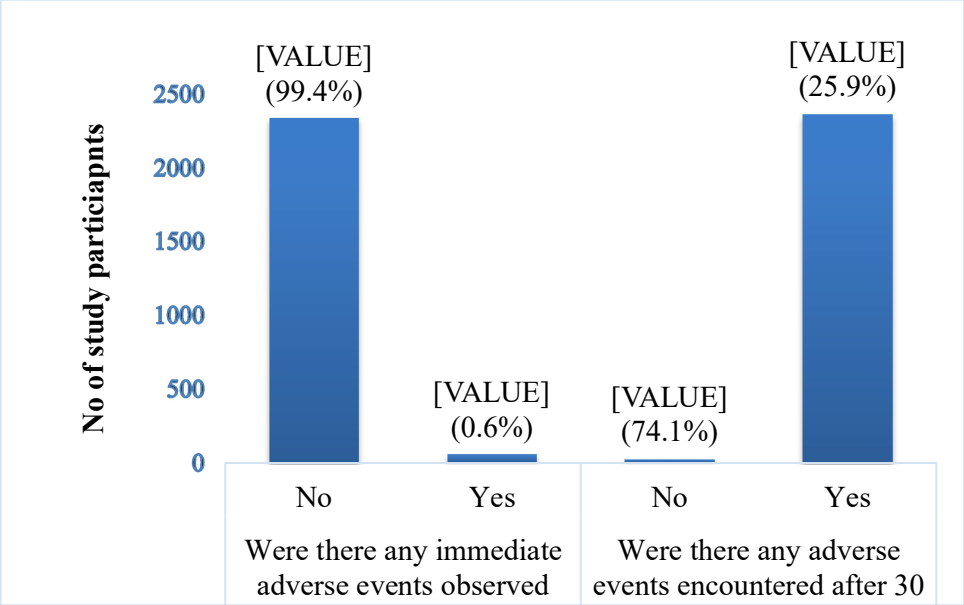


Figure 1: Percentage of study participants who reported experiencing at least one adverse event within in and after 30 minutes of getting inactivated SARS-Cov-2 (Vero Cell) COVID-19 vaccine.

### 4.3. Socio-demographic and clinical characteristics of participants with AEFI

The mean (±SD) age of the participants who reported experiencing at least one AEFI following vaccination with inactivated SARS-Cov-2 (Vero Cell) COVID-19 vaccine was

35.05 ±11.84 (range=18 to 88 years). More than one-third (869, 36.4%) of the participants who reported encountering at least one AEFI was reported in the age group of 18-29 years. Majority of the participants (1315, 55%) who reported at least one AEFI were females (Table 4)

Table 4: Sociodemographic characteristics of participants who reported AEFI (n=2390).

| Variables | Category | Frequency | Percent |
|---|---|---|---|
| Age in years | 18-29 | 869 | 36.4 |
| | 30-39 | 755 | 31.6 |
| | 40-49 | 446 | 18.7 |
| | 50-59 | 235 | 9.8 |
| | 60 and above | 85 | 3.6 |
| Sex | Male | 1075 | 45 |
| | Female | 1315 | 55 |

Regarding the presence of known allergies, 1.4% (34) of participants with AEFI reported that they had previous history of allergies. Similarly, 1.4% (34) participants with AEFI reported having history of substance use. Among participants with AEFI, 3.1% (73) reported that they had one or more comorbidities. The frequently reported comorbidities were hypertension (24, 32.9%), diabetes (19, 26.0%) and HIV/AIDS (8, 11.0%) (Table 5).

Table 5: History of allergy, substance use and comorbidity pattern among participants with AEFI (n=2390).

| Variables | Category | Frequency | Percentage |
|---|---|---|---|
| Presence of known allergies | Yes | 34 | 1.4 |
| | No | 2356 | 98.6 |
| History of substance abuse | Yes | 34 | 1.4 |
| | No | 2356 | 98.6 |
| Presence of comorbidity | Yes | 73 | 3.1 |
| | No | 2317 | 96.9 |
| Type of comorbidities (n=73) | Hypertension | 24 | 32.9 |
| | Diabetes | 19 | 26.0 |

| | | | |
|---|---|---|---|
| | HIV/AIDS | 8 | 11.0 |
| | Asthma and/or chronic obstructive pulmonary disorder | 6 | 8.2 |
| | Cholecystitis | 2 | 2.7 |
| | Hypothyroidism | 2 | 2.7 |
| | Multiple sclerosis | 2 | 2.7 |
| | Sinusitis | 2 | 2.7 |
| | Deep vein thrombosis | 2 | 2.7 |
| | Others* | 8 | 11.0 |

Others* include schizophrenia, angioedema, back pain, gastritis, gouty arthritis, stroke, tuberculosis, urinary tract infection.

From 2390 participants with AEFI, only 4% (n= 96) were on medication for their acute /or chronic health problems. The most commonly used medications were anti-diabetics and anti-hypertensive drugs (Figure 2)

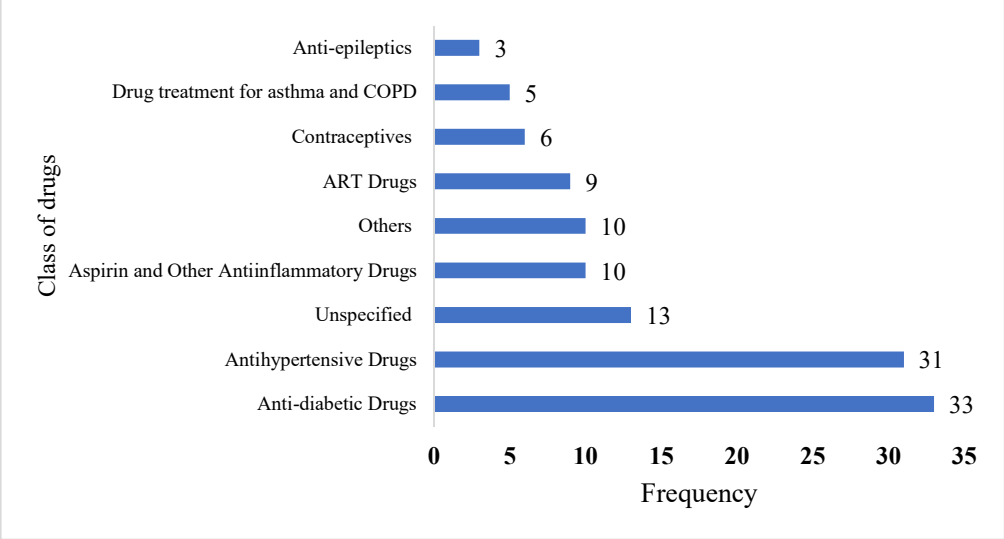


Figure 2: Medication use pattern among participants who reported AEFI (n=2390)

### 4.4. Pattern of AEFIs among participants who reported AEFI

Among participants who reported AEFIs, 99.1%(2368) of them reported expering AEFIs after 30 minutes of vaccination, while very few of them (54, 2.3%) reported AEFIs within 30 minutes of vaccine administration. Of the participants who reported AEFI within 30 minutes, 59.3% (32) also reported AEFI after 30 minutes. On the other hand, 97.7% (2336) of participants with AEFI responded that they had AEFI only after 30 minutes of vaccination. Further, 1.3% (32) participants reported AEFI both within and after 30 minutes of vaccination (Figure 3).

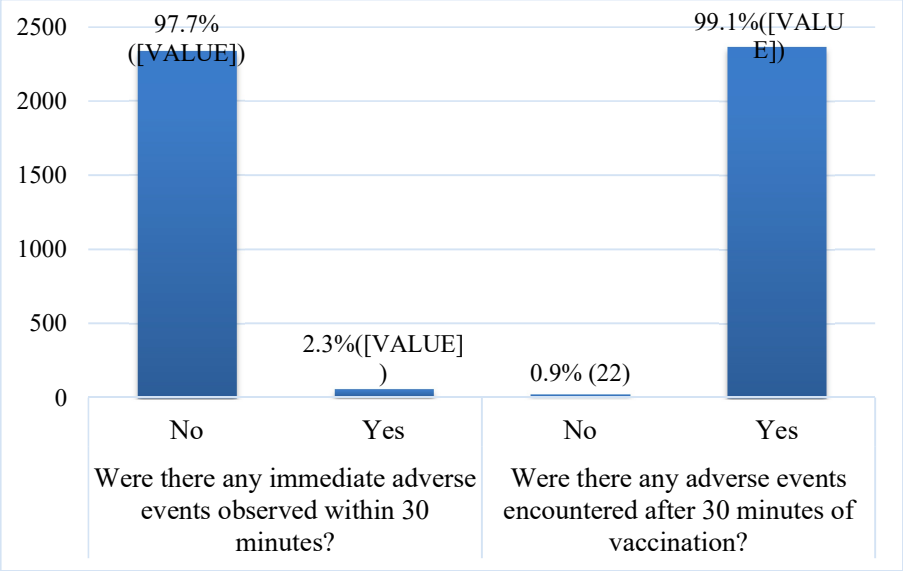


Figure 3: Pattern of AEFI occurrence among study participants who reported AEFI (n=2390).

As shown in Table 6 below, a total of 3839 AEFI manifestations were reported by 2390 study participants that indicated the occurrence of 1.6 AEFI manifestations per participant with AEFI. Among the participants who reported experiencing AEFI, 58.3% (1393) experienced two or more AEFI manifestations. Majority of the AEFIs were minor and self-resolved within a week of taking the vaccine. However, two cases of abortion were reported as serious AEFIs.

Table 6: Pattern of reported AEFIs among study participants with AEFI (n=3839).

| Reported AEFIs | Frequency | Percent of AEFI from total AEFIs |
|---|---|---|
| Injection site pain | 1002 | 26.10 |
| Headache | 889 | 23.16 |
| Fever | 624 | 16.25 |
| Arthralgia/Joint pain | 288 | 7.50 |
| Fatigue | 233 | 6.07 |
| Chills | 186 | 4.85 |
| Nausea and/or vomiting | 111 | 2.89 |
| Myalgia/Muscle pain | 81 | 2.11 |
| Back pain | 80 | 2.08 |
| Dizziness | 56 | 1.46 |
| Hyperhidrosis/Sweating | 52 | 1.35 |
| Cough | 29 | 0.76 |
| Flu-like symptoms | 23 | 0.60 |
| Sore throat | 18 | 0.47 |
| Decreased appetite | 18 | 0.47 |
| Diarrhoea | 15 | 0.39 |

| | | |
|---|---|---|
| Insomnia | 14 | 0.36 |
| Numbness of left hand | 15 | 0.39 |
| Hypersomnia/sleepiness | 13 | 0.34 |
| Malaise | 13 | 0.34 |
| Abdominal crampy pain | 11 | 0.29 |
| Delirium | 11 | 0.29 |
| Chest pain | 8 | 0.21 |
| Blurred vision | 7 | 0.18 |
| Mood changes | 5 | 0.13 |
| Others | 39 | 1.02 |

n: number of AEFIs reported.

The top ten frequently reported AEFI manifestations were injection site pain (26.1%, 1002), headache (23.1%, 889), fever (16.3%, 624), arthralgia/joint pain (7.5%, 288), fatigue (6.5%, 233), chills (4.9%,186), nausea and/or vomiting (2.9%, 111), myalgia/muscle pain (2.9%, 81), back pain (2.1%, 80) and dizziness (1.5%, 56) (Figure 4). Unfortunately, two abortion cases were reported.

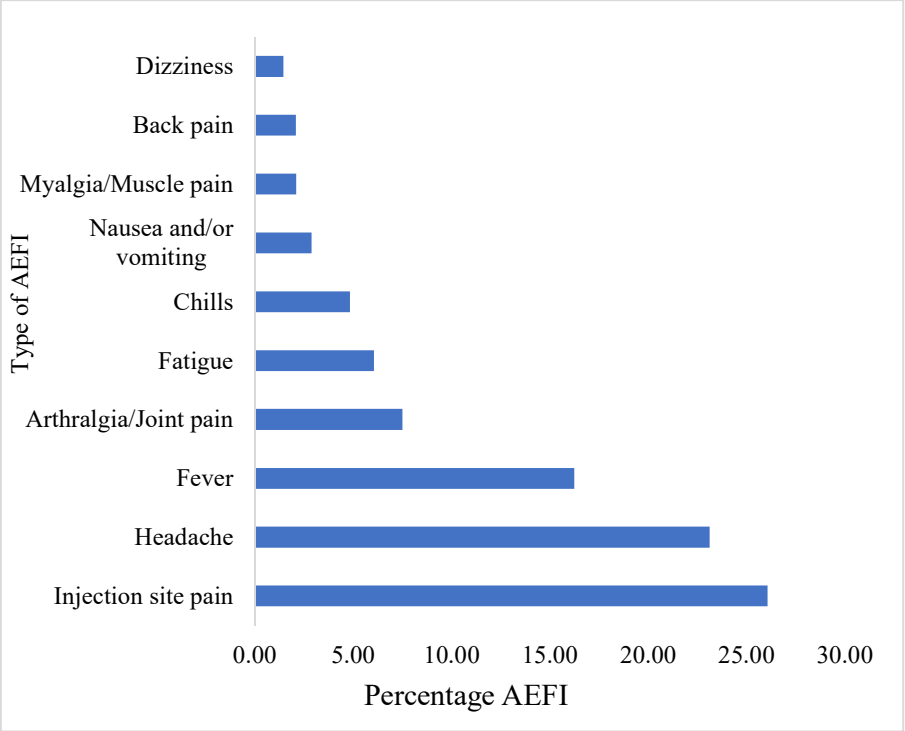


Figure 4: The top ten frequently reported AEFI manifestations.

### 4.5. AEFIs reported within and after 30 minutes of vaccination

Regarding AEFIs that occurred within 30 minutes of vaccination, a total of 70 AEFI manifestations were reported by 54 respondents, 1.3 AEFI manifestations per respondent. The three frequently reported AEFI manifestations were injection site pain (25, 35.7%), headache (24, 34.3%) and nausea and/or vomiting (15, 21.4%), respectively (Table 7).

Table 7: Pattern of AEFIs reported within 30 minutes of vaccination (n=70 AEFIs).

| AEFIs reported | Frequency | Percentage |
|---|---|---|
| Injection site pain | 25 | 35.71 |
| Headache | 24 | 34.29 |
| Nausea/ or vomiting | 15 | 21.43 |
| Fever | 2 | 2.86 |
| Arthralgia/joint pain | 1 | 1.43 |
| Fatigue | 1 | 1.43 |
| Numbness at the injection site | 1 | 1.43 |
| Swelling at the injection site | 1 | 1.43 |

Concerning AEFIs that happened after 30 minutes of vaccination, a total of 3771 AEFI manifestations were reported by 2368 respondents, 1.6 AEFI manifestations per respondent with AEFI. Injection site pain (976, 25.9%), headache (864, 22.9%), fever (622, 16.5%), fatigue (287, 7.6%) and chills (232, 6.2%) were the top five AEFI manifestations (Table 8).

Table 8: Pattern of AEFIs reported after 30 minutes of vaccination (N=3771 AEFIs).

| Reported AEFIs | Frequency | Percentage |
|---|---|---|
| Injection site pain | 976 | 25.88 |
| Headache | 864 | 22.91 |
| Fever | 622 | 16.49 |
| Arthralgia/Joint pain | 287 | 7.61 |
| Fatigue | 232 | 6.15 |
| Chills | 186 | 4.93 |
| Nausea and/or vomiting | 96 | 2.55 |
| Myalgia/Muscle pain | 81 | 2.15 |
| Back pain | 80 | 2.12 |
| Dizziness | 56 | 1.49 |
| Hyperhidrosis/Sweating | 52 | 1.38 |
| Cough | 29 | 0.77 |
| Flu-like symptoms | 23 | 0.61 |
| Sore throat | 18 | 0.48 |
| Decreased appetite | 18 | 0.48 |

| | | |
|---|---|---|
| Diarrhoea | 15 | 0.40 |
| Insomnia | 14 | 0.37 |
| Numbness of left hand | 14 | 0.37 |
| Hypersomnia/sleepiness | 13 | 0.34 |
| Malaise | 13 | 0.34 |
| Abdominal crampy pain | 11 | 0.29 |
| Delirium | 11 | 0.29 |
| Chest pain | 8 | 0.21 |
| Blurred vision | 7 | 0.19 |
| Itching/redness at the site of injection | 7 | 0.19 |
| Others | 38 | 1.01 |

### 4.6. Factors associated with the occurrence of AEFI

Univariate analysis showed that gender, age/age category, current medication, co-morbidity, and history of substance use were found to have some association with occurrence of AEFI with p-value which was less than 0.25 and thence hey were incorporated for multivariate binary logistic regressions. According to the multivariate analysis, only three variables (age, current medication and history of substance use) were significantly associated with occurrence of adverse event following immunization. A significant association was found between vaccinated individual who experienced AEFI and age category between 30-39 (AOR = 1.23; 95% CI: 1.025-1.472, p= 0.026). Vaccinated individuals with in the age category between 30-39, are at 1.23 times higher risk of developing AEFI as compared to their counterparts. The occurrence of AEFI is also higher in vaccinated participants who were on current medication (AOR = 5.19; 95% CI: 3,147 – 8.563, P = 0.000). Thus, those vaccinated individuals who were taking current medication were five-times at higher risk of developing AEFI than who were not on medication at the time of vaccination. Moreover, history of substance uses among vaccinated individual result in a significant association with the occurrence of AEFI (AOR = 1.600; 95% CI: 1.030 – 2.485, P = 0.036). The vaccinated individual who had a history of substance use are 1.6-times at higher risk of developing AEFI (Table 9).

**Table 9:Univariate and multivariate logistic regression analysis of factors associated with adverse event following immunization of Sinopharm Covid-19 Vaccination among vaccinated individuals in Ethiopia from** May 2021 to July 2022 **(N = 9129).**

| Outcome variables | Sinopharm Covid-19 Vaccination | | Univariate analysis | | Multivariate analysis | |
|---|---|---|---|---|---|---|
| | AEFI, n (%) | Non-AEFI, n (%) | COR (95%CI) | P-value | AOR (95% CI) | P-value |
| Gender | | | | | | |
| Male | 1307(55.2) | 3570(52.8) | 1.000 | | 1.000 | 0.080 |
| Female | 1061(44.8) | 3191(47.2) | 0.908(.827-.998) | 0.045 | 0.918 (0.835-1.010) | |
| **Age** | | | | | | |
| 18-29 | 869(36.4) | 2909(43.2) | 1.000 | | 1.000 | |
| 30-39 | 755(31.6) | 1902(28.2) | 1.317 (1.175- 1.475) | 0.000 | 1.228(1.025-1.472) | 0.026* |
| 40-49 | 446(18.7) | 1080(16) | 1.384(1.210-1.583) | 0.000 | 1.195(0.878-1.625) | 0.257 |
| 50-59 | 235(9.8) | 553(8.2) | 1.399(1.179-1.660) | 0.000 | 1.114(0.716 - 1.735) | 0.632 |
| ≥60 | 85(3.6) | 295(4.4) | 0.943(0.943 - 0.730) | 0.649 | 0.629(0.327 - 1.211) | 0.166 |
| Current medication | | | | | | |
| No | 2294(96) | 6692(99.3) | 1.000 | | 1.000 | 0.000* |
| Yes | 96(4) | 47(0.7) | 5.000(3.550 - 7.044) | 0.000 | 5.191(3.147-8.563) | |
| Co-morbidity | | | | | | |
| No | 2317(96.9) | 6683(99.2) | 1.000 | | 1.000 | 0.906 |
| Yes | 73(3.1) | 56(0.8) | 3.247(2.291- 4.603) | 0.000 | 0.968(0.565- 1.660) | |
| History of substance use | | | | | | |
| No | 2357(98.6) | 6684(99.2) | 1.000 | | 1.000 | 0.036* |
| Yes | 33(1.4) | 55(0.8) | 1.723(1.116 - 2.660) | 0.014 | 1.600(1.030-2.485) | |

COR = crude odds ratio, AOR = adjusted odds ratio, CI = confidence interval, AEFI = Adverse Event Following Immunization, * = significant association ($p < 0.05$).

## 5. Discussion

This study was conducted to assess the safety of inactivated SARS-Cov-2 (Vero Cell) COVID-19 vaccine in Ethiopian population. Active COVID-19 vaccine safety surveillance through an observational prospective single-arm cohort study was conducted enrolling 10,000 adults and complete response was obtained from 9129 participants. Majority of the study participants were from Addis Ababa (4290, 47%) because of easy accessibility of this vaccine to the vaccinees during the study period, simplicity of monitoring and evaluation of data collection processes, as well as to minimize lost to follow-up that may result from poor network. Moreover, most of the study participants (3778, 41.4%) were in the age group of 18-29 years and their mean age was 34.2 ±12.2 years. More than half of the study participants (4877, 53.4%) were females. Besides, the finding of the study revealed that around 1.0% (88) of the study participants had a history of substance abuse. Moreover, the results of the study showed that 1.4% the study participants had one or more comorbidities; hypertension, diabetes and HIV/AIDS being the most prevalent chronic health problems reported. The finding of a previous study showed that, 27.8% of the participants had one or more chronic medical problems. Of these, diabetes and hypertension constitute the highest prevalence that is in line with our findings (11).

The overall incidence of inactivated SARS-Cov-2 (Vero Cell) COVID-19 vaccine-associated AEFI was 26.2% and most the AEFIs occurred within 7 days of vaccination. Similarly, a study conducted by Aryal et al., (2021) showed that out of the 4574 Sinopharm vaccine recipients, 868 (19%) individuals reported encountering AEFI after the first dose of the vaccine and most of the AEFIs resolved within 72-hours (7). In this study 25.9% of the study participants reported AEFIs after 30 minutes of vaccination, while 0.6% of them reported AEFIs within 30 minutes of vaccine administration. Participants in the age range of 18-29 years showed higher rates of AEFI reports, while the lowest incidence was reported among elderly patients (≥ 60 years). In addition, females (55%) had a higher AEFI incidence than males (45%).

Regarding participants with AEFIs, 99.1%, 2.3% and 1.3% of them reported AEFIs after, within, and after and within 30 minutes of vaccine administration, respectively. In addition, 1.4% of participants with AEFIs reported history of substance abuse, while 1.4% had history of allergies. Further, 4% and 3.1% of them had one or more comorbidities and currently on drugs, respectively. Hypertension, diabetes and HIV/AIDS were the frequent reported comorbidities.

In this study, a total of 3839 AEFI manifestations were reported in 2390 study participants resulting in 1.6 AEFI manifestations per participant. Similarity, in a previous study conducted to assess the safety of Sinopharm Covid-19 vaccine, a total of 1336 AEFIs (1.5 per participant) was reported in 868 (19%) first-dose vaccine recipients. This result is in-line with that of our findings (7). The most frequently reported AEFI manifestations include injection site pain (26.1%), headache (23.1%), fever (16.3%), arthralgia/joint pain (288, 7.5%) and fatigue (233, 6.5%). Majority of these AEFIs were mild and self-resolved within 7 days following vaccination. However, two abortion cases were reported as serious AEFIs following vaccination with this vaccine. One of these serious cases was carefully investigated and causality assessment was conducted. The case was classified as co-incidental and has no association with the vaccine. However, the other case was not further investigated because the patient was not willing to cooperate. Study conducted by Haider et al (2023) revealed that fever (51.3%) was the most frequently reported adverse effect followed by burning at the injection site (40.7%) and pain at the injection site (38.0%) (6). In addition, a study by Saeed et al.,(2021) showed that injection site pain, fatigue and headache were the three common adverse events reported after the first dose of vaccination with Sinopharm covid-19 vaccine (11). Similar findings were reported by Jin et al study (12). On the other hand, Mohebbi et al., (2023) reported that systematic symptoms, such as body pain, fever, shivering, fainting, nasal drip, sore throat, and muscular spasm, were found to be the most reported side efects (8).

With regard to the specific time periods for the occurrence of AEFIs, injection site pain (35.7%), headache (34.3%) and nausea/or vomiting (21.4%), respectively were the frequent AEFI manifestations within 30 minutes of vaccination, while injection site pain (25.9%), headache (22.9%) and fever (16.5%) were the frequently reported AEFI manifestations after 30 minutes. Age between 30-39 years, being on medication and history of substance use were variables associated with the occurrence of AEFI following this COVID-19 vaccine. This showed that the probability of developing AEFI was experienced among age between 30-39 years respondents by 1.23 higher risk than their counterparts. This finding was consistent to the findings of a study conducted elsewhere where younger age group vaccine recipients were observed to have a higher incidence of reported AEFI (13-15).

## 6. Conclusions

More than one in four participants who took inactivated SARS-Cov-2 (Vero Cell) COVID-19 vaccine reported one or more adverse events. Majority of the AEFIs occurred after 30 minutes of vaccine administration. The frequently reported AEFI manifestations were injection site pain, headache, fever and arthralgia/joint pain. Majority of the AEFIs were mild and self-resolved within 7-days. Age between 30-39 years, being on medication and history of substance use were variables significantly associated with the occurrence of AEFIs following vaccination with inactivated SARS-Cov-2 (Vero Cell) COVID-19 vaccine in Ethiopia.

## 7. References


1. Park SE. Epidemiology, virology, and clinical features of severe acute respiratory syndrome -coronavirus-2 (SARS-CoV-2; Coronavirus Disease-19). Clin Exp Pediatr. 2020; 63(4): 119–24.
2. Pshenichnaya NY, Lizinfeld IA, Zadorozhnyy AV. New Coronavirus Pandemic Worldwide: Some Lessons from Covid-19 Control. Meditsina Katastrof = Disaster Medicine.2022: 2:26-31 (In Russ.).
3. Fiolet T, Kherabi Y, MacDonald CJ, Ghosn J, Peiffer-Smadja N. Comparing COVID-19 vaccines for their characteristics, efficacy and effectiveness against SARS-CoV-2 and variants of concern: a narrative review Clin Microbiol Infect. 2022; 28(2):202-21.
4. Pagliusi S, Hayman B, Jarrett S. Vaccines for a healthy future: 21st DCVMN Annual General Meeting 2020 report. Vaccine. 2021; 39(18):2479-88.
5. Xia S, Duan K, Zhang Y, Zhao D, Zhang H, Xie et al.,. Effect of an Inactivated Vaccine Against SARS-CoV-2 on Safety and Immunogenicity Outcomes. JAMA. 2020; 324(10):951-60.
6. Haider T, Abidi SRZ, Fatima M, Zafar A, Siddiqui RQU, Khan W, Saeed T, Anwar A, Hashmi AA. The Prevalence of Side Effects of Sinopharm COVID-19 Vaccine: An Experience from Pakistan. Cureus. 2023; 26;15(4):e38180.
7. Aryal S, Devbhandari RP, Shrestha S, Shrestha A, Rajbhandari P, Shakya T, et al. Adverse events following Sinopharm (Vero Cell), the inactivated COVID-19. Journal of Patan Academy of Health Sciences. 2021; 8(2):18-24.
8. Mohebbi A, Eterafi M, Fouladi N, Golizadeh M, Panahizadeh R, Habibzadeh S, Karimi K, Safarzadeh E. Adverse Effects Reported and Insights Following Sinopharm COVID-19 Vaccination. Curr Microbiol. 2023; 20;80(12):377.
9. World Health Organization. Background document on the inactivated COVID-19 vaccine BIBP developed by China National Biotec Group (CNBG), Sinopharm. World Health Organization.2021; http://www.jstor.org/stable/resrep41174.
10. World Health Organization. Protocol template to be used as template for observational study protocols for sentinel surveillance of adverse events of special interest (AESIs) after vaccination with COVID-19 vaccines.2021; Geneva. Licence: CC BY-NC-SA 3.0 IGO.

11. Saeed BQ, Al-Shahrabi R, Alhaj SS, Alkokhardi ZM, Adrees AO. Side effects and perceptions following Sinopharm COVID-19 vaccination. Int J Infect Dis.2021; 111:219-26.
12. Jin Y, Zheng M, He S, Chen M, Cao C. Safety of Inactivated SARS-CoV-2 Vaccines Among Adults with Experience of Allergies to Food or Medicines. Int J Gen Med. 2023; 16:3105-13.
13. Gee J, Marquez P, Su J, Calvert GM, Liu R, Myers T, et al. First Month of COVID-19 Vaccine Safety Monitoring - United States, December 14, 2020-January 13, 2021. MMWR Morb Mortal Wkly Rep. 2021;70(8):283-288.
14. Jayadevan R, Shenoy R, Anithadevi TS. Survey of symptoms following COVID-19 vaccination in India. 2021; doi: 10.1101/2021.02.08.21251366. LicenseCC BY 4.0
15. Xiong X, Yuan J, Li M, Jiang B, Lu ZK. Age and Gender Disparities in Adverse Events Following COVID-19 Vaccination: Real-World Evidence Based on Big Data for Risk Management. Front Med (Lausanne).2021; 8:700014.