# Monitoring Adverse Events of Sinovac COVID-19 Vaccine (*CoronaVac*™) in a Tertiary Government Hospital in Pangasinan

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**Background.** COVID-19 pandemic led to a dramatic loss of human life worldwide and presented an unprecedented challenge to public health. One of the solutions in addressing the problem was mass vaccination in order to attain herd immunity. However, most people were hesitant to be vaccinated particularly due to their fear of the adverse events; hence the goal of this study was to determine the possible adverse events (AEs) experienced during administration of *CoronaVac*™ COVID-19 Vaccine.

**Objective.** The objective of the study was to monitor the occurrence of adverse events within one hour, two to 24 hours, and 25 to 72 hours after administration of the first and second dose of *CoronaVac*™ COVID-19 Vaccine in a tertiary government hospital in Pangasinan.

**Methodology.** This cross-sectional study was done from February to April 2021 at Region 1 Medical Center. Employees who received the two doses of *Sinovac-CoronaVac*™ vaccine and gave their informed consent were included in the study. Participants were monitored closely for adverse events within 30 minutes following administration of the vaccine and were instructed to report any local and systemic AEs to the Hospital Epidemiology Center Office. Individuals were also followed up through telephone to investigate the occurrence of any complaints after 24 to 72 hours.

**Results.** A total of 353 participants who received the complete doses of *CoronaVac*™ were included in the study. The incidence of AEs was higher after the first dose compared with the second dose. After the first dose of *CoronaVac*™ 12.5% reported AEs after the 1st hour, 14.2% two to 24 hours after the vaccine, and 1.4% on the 25$^{th}$ hour up to the 72$^{nd}$ hour. Pain on injection site was the most common adverse event during the first hour (8.2%). On the 2$^{nd}$ hour up to 24 hours, headache, and myalgia (14.2%) were more evident. Headache was reported in 1.1% of the participants after 25-72 hours of vaccination. After the second dose, only one participant reported multiple AEs such as fatigue, headache, rash and retroorbital pain (1, 0.7%).

**Conclusion.** In this study, 28.1% of the participants experienced adverse events after the first dose of *CoronaVac*™ vaccine. AEs were higher after the first dose (28.1%) compared with the second dose (0.3%). Injection site pain was the most common adverse event during the first hour, then headache and myalgia during the 2$^{nd}$ hour up to 24 hours, and headache on the 25$^{th}$ – 72$^{nd}$ hour after vaccination. Only one participant reported several AEs after the 2$^{nd}$ dose of the vaccine

**Keywords:** *CoronaVac*™, COVID-19 vaccination, Adverse Events

## Introduction

Since the 1918 Spanish flu, the world has never encountered a health situation in which different countries have been affected in a global scale. The novel virus was first isolated on January 7, 2020, and its genome sequenced on January 12, 2020.[1] On March 11, 2020, the World Health Organization declared the beginning of a pandemic brought about by 2019-nCoV, also known as Coronavirus Disease (COVID-19).[2] Due to its genetic similarity to a previously known coronavirus, Severe Acute Respiratory Syndrome Coronavirus (SARS-COV), the International Committee on Taxonomy of Viruses then renamed it to SARS-CoV-2.[1] Based on phylogenetic analysis, SARS-COV-2 was said to have originated from animals, particularly bats, with the pangolin as its intermediate vector. In China, pangolin meat is considered a delicacy wherein its ingestion may

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have caused the transmission of the virus to humans.[3,4]

Globally, according to the World Health Organization, there were about 399.6 million confirmed cases of COVID-19, and has caused 5.7 million deaths as of February 9, 2021.[2]

Since the beginning of the pandemic, a worldwide race began on the development of the very first vaccine that can be used against COVID-19. According to the World Health Organization, as of February 8, 2022, there were 142 COVID-19 vaccines in clinical development, while another 195 vaccines were in pre-clinical development.[5]

As of February 2022, 61.6% of the global population have been vaccinated.[6] In the Philippines, 10 vaccines were granted Emergency Use Authorization (EUA) by the Philippine FDA and can be used for the country's national immunization program. These were: *Pfizer/BioNTech (BNT162b2), Oxford/AstraZeneca (AZD1222), Sinovac CoronaVac™, Gamaleya Sputnik V™, Bharat BioTech Covaxin™, Janssen (Ad26.COV2.S), Moderna (mRNA-1273), Sinopharm (Beijing) BBIBP -CorV (Vero Cells), Sinopharm (Wuhan) - Inactivated (Vero Cells), and Gamaleya (Sputnik Light™.*[7]

A total of 128 million doses were already given as of February 2022 equivalent to 46 percent of the whole population of the Philippines. As of March 2023, according to a Social Weather Station (SWS) survey, 87% of the entire adult population of the country are already vaccinated, however 63% of the remaining 13% of the population refused to be vaccinated despite the vaccine's availability.[6]

One of the problems being faced by the country's COVID-19 vaccination program is the hesitancy of Filipinos to be vaccinated. This could be due to fear or anxiety of the people to experience unwanted adverse event after receiving the vaccine. The data derived from this study would hopefully assist the vaccination team during vaccination roll out in the dissemination of appropriate information, specifically with CoronaVac since it is one of the vaccines made readily available for health care workers nationwide.

Patients given the Sinovac COVID-19 Vaccine CoronaVac™ were studied since it was one of the first vaccines that became readily available at the Region I Medical Center. Another vaccine, *AstraZeneca*, was also available but was reserved for the elderly (60 years old and above), and was not included in the study.

*Objectives*

*General Objective*. To study the occurrence of adverse events within 1 hour, 2-24 hours and 25-72 hours after the first and second administration of Sinovac COVID-19 Vaccine CoronaVac™ in a tertiary hospital in Pangasinan.

*Specific Objectives*.

1. To identify the different adverse events of CoronaVac within 1 hour, 2-24 hours and 25-72 hours after inoculation.
2. To identify the frequency of adverse events.
3. To determine the possible association between risk factors for adverse events such as age, sex, and number of doses received.

*Significance of the Study*. During the height of this pandemic, numerous vaccines had become readily available worldwide. Aside from acquiring and distributing vaccines, its safety is also an important part of a nation's response to COVID-19. Thus, the aim of this study is to determine the possible side effects experienced with *CoronaVac™*.

*Definition of Terms*

*Coronavac(TM)* - Sinovac; Approved COVID-19 vaccine administered to Region I Medical Center employees

*Adverse Events*- Any untoward occurrence or incident that may occur after immunization; occurrence need not have a clear causal relationship with the administration of COVID-19 vaccine

*Region I Medical Center Employees*- Personnel employed and vaccinated in Region I Medical Center from February to April 2021

## Methodology

*Study Design*. This is a cross-sectional study done at a tertiary government hospital in Pangasinan. A Health Declaration Screening Form by the Philippine National COVID-19 Vaccine Deployment and Vaccination Program was utilized for screening the participants prior to vaccination and where adverse events were reported by Region I Medical Center employees vaccinated with *CoronaVac™*.

*Participants*. Informed consent was obtained for vaccine recipients to participate in the survey. A total of one-thousand six hundred (1600) employees from Region I Medical Center gave their consent to receive the COVID-19 vaccine. A target sample size of 310 was computed using the following formula:

$$n = (z)^2\, p\, (1 - p)/\, d^2$$

Confidence interval of 95% with a 5% margin of error was used. Population proportion of adverse events was estimated at 50%.

A total of 353 employees who received the two doses of Sinovac-*CoronaVac™* vaccine and gave their consent to participate in the study were randomly picked. Randomization was used to address possible confounding variables that may arise during the study.

The participant was observed for AEs within 30 minutes following administration of *CoronaVac™* at the vaccination area. The participants reported their local adverse events (e.g., pain or swelling at injection site), or systemic adverse events (e.g. fever or rashes) at the Hospital Epidemiology Center Office. After the first and second dose of vaccination, individuals were followed up through telephone to investigate the occurrence of adverse events, possibly related to the *Coronavac™*

**Table I. Demographic and Clinical Profile of Participants**

| Characteristics | Age group | | Total (N = 353) |
|---|---|---|---|
| | 18-50 (N = 337) | 51-59 (N = 16) | |
| Sex | | | |
| Female | 200 (59.3%) | 12 (75%) | 212 (60.1%) |
| Male | 137 (40.7%) | 4 (25%) | 141 (39.9%) |
| Comorbidities | | | |
| Hypertension | 26 (7.7%) | 6 (37.5%) | 32 (9.1%) |
| Bronchial asthma | 11 (3.3%) | 1 (6.3%) | 12 (3.4%) |
| Diabetes mellitus | 7 (2.1%) | 3 (18.8%) | 10 (2.8%) |
| PCOS | 3 (.9%) | - | 3 (.8%) |
| RHD | 2 (.6%) | - | 2 (.6%) |
| Hypothyroidism | 2 (.6%) | - | 2 (.6%) |
| Allergic rhinitis | 1 (.3%) | - | 1 (.3%) |
| COPD | 1 (.3%) | - | 1 (.3%) |
| Epilepsy | 1 (.3%) | - | 1 (.3%) |
| BPPV | - | 1 (6.3%) | 1 (.3%) |
| COVID, recovered | - | 1 (6.3%) | 1 (.3%) |
| None | 291 (86.4%) | 7 (43.8%) | 298 (84.4%) |
| Vices | | | |
| Alcohol | 72 (21.4%) | 3 (18.8%) | 75 (21.2%) |
| Smoking | 13 (3.9%) | 1 (6.3%) | 14 (4%) |
| None | 263 (78%) | 13 (81.3%) | 276 (78.2%) |

**Table II. Adverse Events in the First Hour, 2-24 Hours, and 25-72 hours after *Coronavac*™ First Dose**

| Adverse events | One hour after vaccination | 2h-24h after vaccination | 25h-72h after vaccination | *p*- value |
|---|---|---|---|---|
| Overall | 44 (12.5%) | 50 (14.2%) | 5 (1.4%) | <0.001* |
| Pain on injection site | 29 (8.2%) | 5 (1.4%) | - | <0.001* |
| Headache | 11 (3.1%) | 15 (4.2%) | 4 (1.1%) | 0.045* |
| Dizziness | 4 (1.1%) | 1 (0.3%) | - | 0.074 |
| Rash/Itch/ Redness | 3 (0.8%) | 3 (0.8%) | - | 0.223 |
| Increased blood pressure | 3 (0.8) | - | - | 0.05* |
| Myalgia | 2 (0.6%) | 15 (4.2%) | 1 (0.3%) | <0.001* |
| Chest pain | 1 (0.3%) | 1 (0.3%) | - | 0.607 |
| Colds | 1 (0.3%) | 1 (0.3%) | - | 0.607 |
| Fatigue | 1 (0.3%) | 4 (1.1%) | - | 0.074 |
| Difficulty of breathing | 1 (0.3%) | - | - | 0.368 |
| Hot flushes | 1 (0.3%) | - | - | 0.368 |
| Joint pains | 1 (0.3%) | - | - | 0.368 |
| Palpitation | 1 (0.3%) | - | - | 0.368 |
| Fever | - | 6 (1.7%) | 1 (0.3%) | 0.012* |
| Drowsiness | - | 4 (1.1%) | 1 (0.3%) | 0.074 |
| Abdominal pain | - | 3 (0.8%) | - | 0.05* |
| Cough | - | 2 (0.6%) | - | 0.135 |
| Diarrhea | - | 1 (0.3%) | - | 0.368 |
| Easy fatigability | - | 1 (0.3%) | - | 0.368 |
| Hot tempered | - | 1 (0.3%) | - | 0.368 |
| Increased appetite | - | 1 (0.3%) | - | 0.368 |
| Incomplete sleeping pattern | - | 1 (0.3%) | - | 0.368 |
| Irritable | - | 1 (0.3%) | - | 0.368 |
| Lethargy | - | 1 (0.3%) | - | 0.368 |
| Nausea | - | 1 (0.3%) | - | 0.368 |
| Sore throat | - | 1 (0.3%) | - | 0.368 |
| Body malaise | - | - | 1 (0.3%) | 0.368 |

**Significant at p<0.05 level*

vaccine. Bias was minimized by calling the respondents at their most flexible time. Any adverse events were also validated by the principal investigator and the AEFI team.

*Study Setting and Study Period.* Data collection was carried out from February 1 to April 30, 2021 at Region I Medical Center.

*Inclusion Criteria.* Region I Medical Center employees,

**Table III. Adverse events in the First hour, 2-24 Hours, and 25-72 Hours of *Coronavac*™ Second Dose**

| Adverse events | 1 hour after vaccination | 2h-24h after vaccination | 5h-72h after vaccination | *p*- value |
|---|---|---|---|---|
| Overall | - | 1 (0.3%) | - | 0.368 |
| Fatigue | - | 1 (0.3%) | - | 0.368 |
| Headache | - | 1 (0.3%) | - | 0.368 |
| Rash/Itch/Redness | - | 1 (0.3%) | - | 0.368 |
| Retroorbital pain | - | 1 (0.3%) | - | 0.368 |

**Significant at p<0.05 level*

**Table IV. Adverse Events within the First hour of First Dose of Coronavac™ According to Sex and Age**

| Adverse Events | Total (N=353) | Sex | | | Age group | | |
|---|---|---|---|---|---|---|---|
| | | Female (N=212) | Male (N=141) | *p*- value | 18-50 (N=337) | 51-59 (N=16) | *p*- value |
| No adverse reaction | 309 (87.5%) | 178 (84%) | 131 (92.9%) | 0.013* | 294 (87.2%) | 15 (93.8%) | 0.704 |
| With adverse reaction | 44 (12.5%) | 34 (16%) | 10 (7.1%) | | 43 (12.8%) | 1 (6.3%) | |
| Pain on injection site | 29 (8.2%) | 20 (9.4%) | 9 (6.4%) | 0.331 | 29 (8.6%) | - | 0.381 |
| Headache | 11 (3.1%) | 11 (5.2%) | | 0.004* | 11 (3.3%) | - | 1 |
| Dizziness | 4 (1.1%) | 4 (1.9%) | | 0.153 | 4 (1.2%) | - | 1 |
| Increased BP | 3 0.8%) | 2 (0.9%) | 1 (0.7%) | 1 | 2 (0.6%) | 1 (6.3%) | 0.130 |
| Rash/Itch/ Redness | 3 (0.8%) | 3 (1.4%) | - | 0.278 | 3 (0.9%) | - | 1 |
| Myalgia | 2 (0.6%) | 2 (0.9%) | - | 0.519 | 2 (0.6%) | - | 1 |
| Chest pain | 1 (0.3%) | 1 (0.5%) | - | 1 | 1 (0.3%) | - | 1 |
| Colds | 1 (0.3) | 1 (0.5%) | - | 1 | 1 (0.3%) | - | 1 |
| Difficulty of breathing | 1 (0.3%) | 1 (0.5%) | - | 1 | 1 (0.3%) | - | 1 |
| Fatigue | 1 (0.3%) | 1 (0.5%) | - | 1 | 1 (0.3%) | - | 1 |
| Hot flushes | 1 (0.3%) | 1 (0.5%) | - | 1 | 1 (0.3%) | - | 1 |
| Joint pains | 1 (0.3%) | 1 (0.5%) | - | 1 | 1 (0.3%) | - | 1 |
| Palpitation | 1 (0.3%) | 1 (0.5%) | - | 1 | 1 (0.3%) | - | 1 |

**Significant at p<0.05 level*

ages 18 to 59 years old, who received two shots of *Coronavac*™ and willingly gave their informed consent were included in the study.

*Exclusion Criteria*. Patients not included in the study include: 1) those with previous history of severe allergic reactions to any vaccines, 2) symptoms like fever, colds, cough or flu- like symptoms in the past 3 days, 3) bleeding disorder or currently on blood thinner, 4) previously treated for COVID-19 in the past 90 days, 5) pregnant, 6) breastfeeding, 7) history of exposure to a confirmed or suspected COVID-19 case in the past two weeks, 8) received any vaccine in the past 2-4 weeks and 9) immunocompromised individuals or are currently on treatment for 6 months that affects the immune system.

*Ethical Considerations*. This study was approved by the Ethics Review board of Region I Medical Center. The study was conducted in accordance with the ethical standards of the institution and with Helsinki declaration and its later amendments. Written informed consent was obtained from all participants included in the study.

Informed consent was explained in English and Filipino as to whichever the participant is more comfortable to understand. All the information gathered were strictly held confidential by the investigators of the study. There are no risks of physical injury nor economic risk associated with participation in this study. Inclusion in this study is purely voluntary with no monetary benefit. The principal investigator did not receive any compensation for this study and solely shouldered all expenses.

*Statistical Analysis*. Statistical tests were analyzed using the Statistical Package for the Social Sciences (SPSS) version 26. Descriptive statistics was used to summarize the demographic and clinical characteristics of the respondents, wherein categorical variables were presented as frequencies and percentages. For inferential statistics, Fisher's exact test was utilized to determine differences or associations between categorical variables. A Cochran's Q test was also performed to determine differences between adverse reactions within one hour, 24 hours and three days of first and second dose. P-values less than 0.05 were considered statistically significant.

## Results

A total of 353 Region I Medical Center employees who received the complete doses of *Coronavac*™ vaccine participated in the study. *Table I* shows the demographic and clinical profile of the participants. Majority of the subjects were females (60.1%) and less than 50 years old (95.47%). Most have no co-morbidities (84.4%), and among those with co-morbidities, hypertension was the most common at 9.1%.

Table *II* summarizes the adverse events recorded after the first hour, 2-24 hours and 25-72 hours after the first dose of *Coronavac*™. The occurrence of AEs events was significantly different across the three periods being monitored after the first dose of *Coronavac*™ (12.5%) vs.

**Table V. Adverse Events Within 2-24 Hours of First Dose of *Coronavac*™ According to Sex and Age Group**

| Adverse events | Total (N=353) | Sex | | *p*- value | Age | | *p*- value |
|---|---|---|---|---|---|---|---|
| | | Female (N=212) | Male (N=141) | | 18-50 (N=337) | 51-59 (N=16) | |
| No adverse reaction | 303 (85.8%) | 29 (13.7%) | 120 (85.1%) | 0.757 | 288 (85.5%) | 15 (93.8%) | 0.711 |
| With adverse reaction | 50 (14.2%) | 7 (3.3%) | 21 (14.9%) | | 49 (14.5%) | 1 (6.3%) | |
| Headache | 15 (4.2%) | 8 (3.8%) | 8 (5.7%) | 0.293 | 15 (4.5%) | - | 1 |
| Myalgia | 15 (4.2%) | 3 (1.4%) | 7 (5%) | 0.600 | 15 (4.5%) | - | 1 |
| Fever | 6 (1.7%) | 4 (1.9%) | 3 (2.1%) | 0.686 | 6 (1.8%) | - | 1 |
| Pain on injection site | 5 (1.4%) | 3 (1.4%) | 1 (0.7%) | 0.652 | 5 (1.5%) | - | 1 |
| Drowsiness | 4 (1.1%) | 2 (0.9%) | 1 (0.7%) | 1 | 4 (1.2%) | - | 1 |
| Fatigue | 4 (1.1%) | 3 (1.4%) | 2 (1.4%) | 1 | 4 (1.2%) | - | 1 |
| Abdominal pain | 3 (0.8%) | 2 (0.9%) | - | 0.278 | 3 (0.9%) | - | 1 |
| Rash/Itch/ Redness | 3 (0.8%) | - | 1 (0.7%) | 1 | 3 (0.9%) | - | 1 |
| Cough | 2 (0.6%) | 1 (0.5%) | 2 (1.4%) | 0.159 | 2 (0.6%) | - | 1 |
| Colds | 1 (0.3%) | 1 (0.5%) | - | 1 | - | 1 (6.3%) | 0.045* |
| Chest pain | 1 (0.3%) | 1 (0.5%) | - | 1 | 1 (0.3%) | - | 1 |
| Dizziness | 1 (0.3%) | 1 (0.5%) | - | 1 | 1 (0.3%) | - | 1 |
| Nausea | 1 (0.3%) | 1 (0.5%) | - | 1 | 1 (0.3%) | - | 1 |
| Increased appetite | 1 (0.3%) | - | - | 0.399 | 1 (0.3%) | - | 1 |
| Lethargy | 1 (0.3%) | - | 1 (0.7%) | 0.399 | 1 (0.3%) | - | 1 |
| Incomplete sleeping pattern | 1 (0.3%) | - | 1 (0.7%) | 1 | 1 (0.3%) | - | 1 |
| Diarrhea | 1 (0.3%) | - | 1 (0.7%) | 0.399 | 1 (0.3%) | - | 1 |
| Sore throat | 1 (0.3%) | - | 1 (0.7%) | 0.399 | 1 (0.3%) | - | 1 |
| Easy fatigability | 1 (0.3%) | - | 1 (0.7%) | 0.399 | 1 (0.3%) | - | 1 |
| Hot tempered | 1 (0.3%) | - | 1 (0.7%) | 0.399 | 1 (0.3%) | - | 1 |
| Irritable | 1 (0.3%) | | | | 1 (0.3%) | - | 1 |

**Significant at p<0.05 level*

**Table VI. Adverse Events Within 25-72 Hours of First Dose of *Coronavac*™ According to Sex and Age Group**

| Adverse events | Total (N=353) | Sex | | | Age group | | |
|---|---|---|---|---|---|---|---|
| | | Female (N=212) | Male (N=141) | *p*- value | 18-50 (N=337) | 51-59 (N=16) | *p*- value |
| No adverse reaction | 348 (98.6%) | 210 (99.1%) | 138 (97.9%) | 0.392 | 332 (98.5%) | 16 (100%) | 1 |
| With adverse reaction | 5 (1.4%) | 2 (0.9%) | 3 (1.4%) | | 5 (1.5%) | - | |
| Headache | 4 (1.1%) | 2 (0.9%) | 2 (1.4%) | 1 | 4 (1.2%) | - | 1 |
| Body malaise | 1 (0.3%) | 1 (0.5%) | - | 1 | 1 (0.3%) | - | 1 |
| Drowsiness | 1 (0.3%) | 1 (0.5%) | - | 1 | 1 (0.3%) | - | 1 |
| Fever | 1 (0.3%) | - | 1 (0.7%) | 0.399 | 1 (0.3%) | - | 1 |
| Myalgia | 1 (0.3%) | - | 1 (0.7%) | 0.399 | 1 (0.3%) | - | 1 |

**Significant at p<0.05 level*

**Table VII. Adverse Events of Second Dose of *Coronavac*™ According to Sex and Age group**

| Adverse reaction | Total (N=353) | Sex | | | Age group | | |
|---|---|---|---|---|---|---|---|
| | | Female (N=212) | Male (N=141) | *p*- value | 18-50 (N=337) | 51-59 (N=16) | *p*- value |
| No adverse reaction | 352 (99.7%) | 212 (100%) | 140 (99.3%) | 0.399 | 336 (99.7%) | 16 (100%) | 1 |
| With adverse reaction | 1 (0.3%) | - | 1 (0.7%) | | 1 (0.3%) | - | |
| Fatigue | 1 (0.3%) | - | 1 (0.7%) | 0.399 | 1 (0.3%) | - | 1 |
| Headache | 1 (0.3%) | - | 1 (0.7%) | 0.399 | 1 (0.3%) | - | 1 |
| Rash/Itch/ Redness | 1 (0.3%) | - | 1 (0.7%) | 0.399 | 1 (0.3%) | - | 1 |
| Retroorbital pain | 1 (0.3%) | - | 1 (0.7%) | 0.399 | 1 (0.3%) | - | 1 |

**Significant at p<0.05 level*

14.2% vs. 1.4%, *p<0.001*). Within the first hour, the most common adverse event reported was pain at the injection site (29, 8.2%), followed by headache (11, 3.1%), then dizziness (4,1.1%).

On the second hour up to 24 hours after vaccination, headache and myalgia were the most common symptoms (15, 4.2%), followed by fever (6, 1.7%). As for the 25th hour up to the 72nd hour, headache (4, 1.1%) was the most common, followed by body malaise, drowsiness, fever and myalgia (1, 0.3%). Headache and myalgia were the only adverse reactions present in all three periods after receiving the first dose.

*Table III* shows AEs after receiving their 2nd dose. On the 2nd hour to the 24th hour after vaccination, only one participant experienced multiple AEs.

*Table IV* shows the occurrence of AEs according to sex and

age group. AEs were more frequent among (16%) among females compared to males (7.1%). AEs were also more common among the younger age group of 18–50-years-old (43, 12.8%), with pain at injection site as still the most common (29, 8.6%). In the older age group of 51-59- year-old, only one participant reported an AE which was an increase in blood pressure (1, 6.3%). In summary, sex was associated with the occurrence of adverse events within one hour after the first dose (*p=0.013*). The only significant difference found among sex was headache (*p=0.004*).

*Table V* shows an increase in the number of participants who experienced an adverse event on the 2nd hour to 24th hour (50, 14.2%). In this time frame, AEs were more common among males (14.9%). For females, myalgia (8, 3.8%) was the most common AE while for males, headache (8, 5.7%) was more prominent. Like the findings after the 1st hour, AEs were still more common in the younger subgroup (14.5%). Overall, sex and age groups were not associated with the occurrence of AEs within 2 to 24 hours of *Coronavac*™.

On the 25$^{th}$ to 72$^{nd}$ hour after the first dose of vaccination, 5 (1.4%) participants experienced at least one adverse event, with headache as the most common (4, 1.1%). AEs were more reported by males (1.4%) in this time frame. The most common adverse event noted after 24 hours of vaccination for both female and male groups was headache (0.9%, 1.4%). As per age group, only the younger group reported at least one adverse event with headache (4, 1.2%) as still the most common symptom. Age and sex again had no association with the occurrence of adverse events 25 to 72 hours post vaccination.

Out of the 353 participants of the study, only one male (0.3%) from the 18-50 years old age group reported multiple adverse events within two to 24 hours after the second dose of *Coronavac*™. Adverse events reported were fatigue, headache, rashes, and retro-orbital pain. No other adverse events were reported after 24 hours of vaccination. Similarly, sex and age were not associated with occurrence of any AEs after the second dose of *Coronavac*™.

## Discussion

The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is an enveloped, positive single-strand RNA virus with crown-like spikes on their surfaces belonging to the Orthocoronavirinae family.[8] This SARS-COV-2 which causes coronavirus disease 2019 (COVID-19), produces a biphasic pattern of illness due to the combination of an early viral response phase and an inflammatory second phase.[9] The clinical presentations may vary from mild symptoms resembling that of influenza such as fever, cough, body malaise, myalgia, headache, plus taste and smell disturbances to severe life-threatening situation.[10]

As with any other drug, vaccines in some cases may produce adverse events due to hypersensitivity reactions. Adverse event following immunization is defined by the World Health Organization as any untoward medical occurrence following immunization which may not necessarily have a causal relationship to the vaccine given. It ranges from unwanted signs and symptoms, to abnormal laboratory findings.[11]

Adverse reactions or events experienced may be a local reaction including pain at the injection site, or systemic reactions such as headache, fever, or myalgia.[12] They may also be mild, moderate, or severe depending on the intensity of the symptoms experienced brought about by the vaccine. Aside from the immune response to the vaccine, it also includes other events such as vaccination errors and reactions correlated with anxiety and product quality defect. [13]

The discovery of vaccines has been an important breakthrough in saving millions of lives. This all began when Edward Jenner, an English physician, inoculated an 8-year-old boy with cowpox, which later protected the boy from smallpox, thus discovering the very first vaccine.[14] Vaccines mainly work by introducing an antigen to a person's body, which is present in pathogens, triggering an immune response which will be used by the body to fight off the actual pathogen if exposed to in the future.[15] Since the discovery and first use of vaccines, different types of vaccines are used today.

Since majority of the vaccines used were given emergency approval, the safety profile is based on published clinical trials, and little is known about their safety for the general population. One of the first COVID-19 vaccines that were made available especially for health care workers in the Philippines was *Coronavac*™. Despite the availability of this vaccine however, many Filipinos are hesitant to receive the vaccine due to fear of its possible side effect or adverse event.

Different postulated mechanisms regarding pathophysiology of vaccine induced allergic responses results to mast cell activation and degranulation.[16] According to the Center for Disease Control and Prevention, immediate allergic reaction happens within four hours of getting vaccinated and may include symptoms such as hives, swelling, and wheezing (respiratory distress), while delayed allergic reaction can occur 48 to 96 hours post vaccination due to overstimulation of T cells and macrophages, resulting in cytokine damage.[17,18]

The Sinovac COVID-19 vaccine, also known as *Coronavac*™ is a two-dose vaccine created by Sinovac Life Sciences in Beijing, China against COVID-19.[24] *Coronavac*™ is an inactivated vaccine created from African green monkey kidney cells inoculated with SARS-CoV-2. It is a two-dose vaccine given in 14- or 28-days interval.[19] In a clinical trial for CoronaVac done in Suining County of Jiangsu Province, China, a total of 743 participants, aged 18-59 years were enrolled. The most common adverse event is still pain at injection site, with one participant experiencing hypersensitivity reaction.[19] Another vaccine is the AstraZeneca vaccine (AZD1222 (ChAdOx1), a non- replicating viral vector vaccine

developed by AstraZeneca and University of Oxford and given in two doses. At a clinical research facility in UK, healthy adults aged 18 years and older were given this vaccine. The most common adverse reaction noted was injection site pain and tenderness, occurring most frequently during the first 48 hours.[20]

Based on the data gathered, AEs vary depending on the duration post-vaccination. During the first hour, pain at the injection site was the most common reported event. In a cross-sectional study by Riad et al and Yanjun Zhang, the most common adverse event immediately reported was pain at the injection site. This is particularly true in any vaccine administered via injection.[21,22]

While on the 2nd hour up to 24 hours post vaccination, headache and myalgia were the most common symptoms followed by fever. For 25 hours to 72 hours, headache is still the most common, but this time followed by body malaise, drowsiness, fever, and myalgia.

Also, in the same study by Riad et al, fatigue (23.6%), headache, myalgia and joint pain were listed as the most common systemic effects of *Coronavac*™ among healthcare workers in Turkey.[21]

When adverse events are documented based on sex and age group, adverse events were more common in the female and younger age group, with pain at injection site still the most common documented adverse event. This is consistent with a study by Riad et al, where increased risk for side effects were noted among the younger age group.[21] In the older age group of 51-59-year-old, only one participant reported an adverse event which was an increase in blood pressure. However, it should be noted that the participants involved were mostly from the female and younger age group.

In a study by Supangat et al, it was mentioned that there was no correlation between the event of AEFI symptoms with sex.[28] A study by Shengli Xia et al also revealed that there was no significant difference of side effects among different groups.[23]

On the 2nd hour to 24th hour after vaccination, participants started to experience more adverse events. Adverse events in males were more common, with headache as the most common symptom, while for females, myalgia was experienced more. After 24 hours, only 5 participants reported an adverse event, with headache as still the most common regardless of sex or age group. Age and sex again had no association with the occurrence of adverse events 25 to 72 hours post vaccination.

Similarly, sex and age were not associated with occurrence of any AEs after the second dose of *Coronavac*™.

Compliance with a higher safety standard is essential since vaccines are mainly administered to healthy people. As vaccines undergo several trials and become readily available, the public should be informed of their safety upon administration to have a successful national vaccination effort.[24]

## Conclusion

The incidence of adverse events among the participants was higher after the first dose of *Coronavac*™ vaccine compared with the second dose. Pain on the injection site was the most common adverse event during the first hour, then headache and myalgia during the 2nd hour up to 24 hours, and headache on 25-72 hours after vaccination. However, on the second dose, the occurrence of adverse events was not significantly different across the three period since only one participant reported adverse event such as fatigue, headache rash and retroorbital pain.

In relation to sex, it was noted that adverse events were more common in females in the first 24 hours after the first dose of *Coronavac*™, then after 24 hours, adverse events were common in males. As to age group, adverse events were common in 18-50 years old. However, sex and age groups were not associated with the occurrence of adverse events of *Coronavac*™ vaccine.

In this study, *Coronavac*™ has an acceptable safety profile among individuals due to the low incidence of reported adverse events. These findings may provide reassurance to healthcare providers as well as vaccine recipients; and to promote confidence in the safety of *Coronavac*™.

## Limitations and Recommendations

Limitations of this study are as follows, only one brand of COVID-19 vaccine was used and our data came from a single center only. We therefore recommend to include other available COVID-19 vaccines on future studies and to include other hospital institutions or local government units who are actively participating in the country's vaccination program.

**Conflict of Interest.** The authors declare no conflict of interest.

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