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# Adverse Events After the Third Dose of COVID-19 Vaccine: A Case Study of Healthcare Workers at Buntharik Hospital, Thailand

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**ABSTRACT**

**Introduction:** COVID-19 vaccine is currently being developed then the information regarding the unfavorable adverse events of vaccines is not clearly known.

**Objective:** The purpose of this study was to estimate the prevalence of and to determine factor adverse events after receiving the third dose of COVID-19 vaccine among healthcare workers who were working at Buntharik hospital in Ubon Ratchathani Province.

**Methods:** A cross-sectional study was conducted for data collection among healthcare workers who received the third dose of the AstraZeneca vaccine in July 2021. Data were collected from LINE group which was specific design to monitor the adverse events following immunization (AEFI) among people who received the 3rddose of the COVID-19 vaccine. Independent t-test and logistic regression were used to detect mean differences and factors associated between variables at the significance level of $\alpha$=0.05.

**Results:** A total of 74 participants were recruited into the study; 21.6% of vaccine-related adverse events without any severe symptoms were reported. More than half were females (62.2%), an average age was 37.2±10.5 years, and 18.8% were presented with chronic illness at the time of immunization. Fever was reported as the highest adverse event after getting the 3rddose (81.3%), myalgia (75.0%), and pain and edema at the injection site (56.3%). Two variables were found to be associated with having adverse events after getting the 3rddose of COVID-19 vaccination. Those who had body mass index (BMI) ≥23 kg/m2 had a 5.3 time (95%CI=1.34-20.95) greater chance to have adverse events than those who were normal BMI. Those who received the 3rddose after the 2ndfor 56 days had a 3.4 time (95%CI=1.02-11.49) greater chance to have an adverse event than those who received their 3rddose after 28-41days of the 2nddose.

**Conclusion:** Individuals' BMI and time interval between the 2nddose and 3rddose are presented as factors associated with presenting adverse event who receive COVID-19 vaccine. All people who are planning to receive COVID-19 vaccine should be informed in concerning their BMI and time between the doses to avoid adverse events.

**Keywords:** *Adverse events following immunization, COVID-19 vaccines, Risk factors, Thailand*

## Introduction

An important public health concern is the COVID-19 outbreak, which was caused by the coronavirus 2019. It has spread to various countries throughout the world. As of October 24, 2022, there had been 624,235,272 cases and 6,555,270 fatalities globally [1]. There have been 2,466,462 cumulative cases in Thailand and 11,224 total deaths as of October 23, 2022 [2].

COVID-19 vaccination is one of the critical measures that can help reduce the fatality rate and severity of COVID-19. According to the World Health Organization (WHO), the vaccine's development started in March 2020, and its extensive distribution abroad started in December 2020. As of February 2021, the COVID-19 vaccination program has begun in Thailand [3]. The WHO has approved six COVID-19 vaccines, which are divided into three groups: inactivated virus

vaccines, viral vector vaccines, and mRNA vaccines [3, 4].

The 2019 coronavirus, an Indian Delta strain, grew and succeeded as the major strain in Thailand through July 2021. Despite receiving two doses of the Sinovac vaccine, the majority of frontline healthcare workers tested negative for neutralizing antibodies to the delta strain. The National Communicable Disease Committee decided to vaccinate frontline healthcare workers who have received two doses of the Sinovac vaccine with a third dose of the AstraZeneca vaccine or mRNA after one to three months, unless the rate of COVID-19 infection among those who have received the vaccine increases and there were reported of fatalities. This policy has been implemented to prevent the infection and maintain operational competency throughout the outbreak. Early studies suggest that immunization with the AstraZeneca vaccine after the Sinovac vaccine could be able to boost individuals' immunity. The general public has wide concern on the immune stimulation from the later doses. Additionally, people hoped that more effective vaccines would be developed [5].

AstraZeneca vaccine is a new brand that has been hastily developed and produced to prevent and control of COVID-19. As a result, many organizations in several countries offer stimulation doses to their population including Thailand. The Ministry of Public Health in Thailand has created a mechanism to track adverse events following immunization. Monitoring the vaccine's safety and keeping public trust were the main goals [6].

However, information of the side effects or advise events after receiving the 3rddose of the COVID-19 vaccination were not clearly reported both locally [7, 8, 9] and internationally [8-10]. A few information was reported among healthy individuals with several exclusion criteria for selecting the study participants. In addition, there were a few reported by a study conducted with appropriate having a control group to identify the adverse events.

According to the executive summary of the report on the prevention and control measures for COVID-19 at Buntharik hospital between July-August 2021, a total of 149 healthcare workers were identified as a high-risk group for the COVID-19 infection. While the serious epidemic of the disease was reported in their living area. Healthcare workers who were working at Buntharik hospital were being monitored by a specific mechanism to ensure their safety after getting the COVID-19 vaccine including the 3rddose of the AstraZeneca vaccine. This specific design surveillance system was used to monitor adverse events following immunization (AEFI) among people who received the 3rddose of the COVID-19 vaccine at Buntharik hospital. The study aimed to estimate the prevalence of adverse events after receiving the 3rddose of AstraZeneca and to determine the factors associated with adverse events after receiving the 3rddose of AstraZeneca.

## Methodology

### *Study design, study setting, and study population*

A cross-sectional was conducted to collect data to response the study objectives. Healthcare workers who were working at the Buntharik hospital in Ubon Ratchathani Province and received the third dose of the COVID-19 vaccine in July 2021 were met the study criteria. Healthcare workers who had and did not have experience on having adverse events after receiving the 3rddose of AstraZeneca were classified for the analysis. The sample size was calculated and required 57 people for the analysis from a total of 136 healthcare workers who met the criteria.

### *Data collection*

The hospital index (HI) computer was used to identify healthcare workers who met the study criteria. Since all healthcare workers who are working in the hospitals had joined the LINE group and asked to report signs and symptoms after getting the 3rddose of the vaccine. Then, all the records were available from the report channel. The LINE group has been formally used for this particular purpose. Medical records were also investigated among the selected cases after getting their approval for access to the information.

### *Data analysis*

Data were coded and entered into SPSS for Windows 16.0 for analysis. Frequency and percentage of adverse events following vaccination against the 3rddose of the COVID-19 vaccine were described. Intendent t-test and logistic regression were used to detect the means difference and estimate the odds ratio of the associations between variables at the significant level of $\alpha$=0.05.

### *Ethical consideration*

The project and its procedures had been approved by the Human Research Ethics Committee of the Ubon Ratchathani Provincial Public Health Office (SSJ.UB 2564-078).

## Results

A total of 74 cases were recruited into the study: the majority were female (62.2%), average age was 38.49±9.54 years. More than half (67.6%) were detected overweight (BMI ≥23 kg/m2), and 78.4% had no underlying disease. Time between the 2ndand the 3rddoses of the COVID-19 vaccination was 56.62±8.17 days.

The prevalence of adverse effects after receiving the 3rddose was 21.6%. The most common symptoms within 7 days were fever (81.3%), followed by myalgia (75.0%), and pain and edema of the injection site (56.3%) (Table 1)

**Table 1** Demographic data and adverse events following immunization for the 3rddose of COVID-19 (n=74)

| Demographic data | n | % |
|---|---|---|
| **Sex** | | |
| Female | 46 | 62.2 |
| **Age** (mean=38.49, SD=9.54) | | |
| 20 - 39 years | 40 | 54.1 |
| 40 - 60 years | 34 | 45.9 |
| **Underlying disease** | | |
| No | 58 | 78.4 |
| **BMI** (mean of body weight = 64.20, SD = 14.64) | | |
| < 18.5 kg/m$^2$ | 4 | 5.4 |
| 18.5-22.9 kg/m$^2$ | 20 | 27.0 |
| ≥ 23 kg/m$^2$ | 50 | 67.6 |
| **Days between the 2nd and the 3rd doses** (mean = 56.62, SD = 8.17) | | |
| 28 - 41 | 5 | 6.8 |
| 42 – 56 | 18 | 24.3 |
| ≥ 57 | 51 | 68.9 |
| **Adverse events*** | | |
| Fever | 13 | 81.3 |
| Myalgia | 12 | 75.0 |
| Pain and edema of the injection site | 9 | 56.3 |
| Malaise | 6 | 37.5 |
| Chills | 3 | 18.8 |
| Muscle weakness | 2 | 12.5 |
| Headache | 2 | 12.5 |
| Insomnia | 1 | 6.3 |
| Diarrhea | 1 | 6.3 |
| Limb numbness | 1 | 6.3 |
| Dizziness | 1 | 6.3 |
| Palpitation | 1 | 6.3 |
| Back pain | 1 | 6.3 |
| Total | 16 | 21.6 |

***Note*:** * More than one symptom can be answered.

There were 16 cases who reported having AEFI, and 74 cases reported having not had AEFI. The characteristics of those who had and who did not have AEFI were not statistical differences (Table 2).

**Table 2** Comparisons between healthcare workers who had AEFI and who did not.

| Characteristic | Without AEFI | With AEFI | p- value* |
|---|---|---|---|
| **Age** (years) Mean ± standard deviation | 38.84±9.32 | 37.18±10.50 | 0.540 |
| **Weight** (kg) Mean ± standard deviation | 63.60±13.80 | 66.37±17.65 | 0.500 |
| **BMI** (kg/m$^2$) Mean ± standard deviation | 24.81±4.89 | 24.57±4.89 | 0.860 |
| **Time between the 2nddose and 3rddose of COVID-19 vaccination** (days) Mean ± standard deviation | 57.37±8.06 | 53.87±8.21 | 0.130 |

***Note*** * tested by independent t-test

In the analysis by logistic regression, two variables were found to be associated with having AEFI after receiving the 3rddose of COVID-19 vaccine among healthcare workers who were working at Buntharik hospital in Ubon Ratchathani Province. Those who were BMI ≥ 23.0 had a 5.30 time (95%CI = 1.34 - 20.95) greater chance of having AEFI than those who were BMI <18.5. Those who had time between the 2nd and 3rddose of ≥ 57 days had a 3.40 time (95%CI = 1.02-11.49) greater chance of having AEFI than those who had 28-41 days.

| Factor | Without AEFI n (%) | With AEFI n (%) | OR | 95%CI |
|---|---|---|---|---|
| **Sex** | | | | |
| Male | 20 (71.4) | 8 (28.6) | 1.00 | |
| Female | 38 (82.6) | 8 (17.4) | 1.90 | 0.62-5.82 |
| **Age (years)** | | | | |
| < 30 | 12 (70.6) | 5 (29.4) | 1.11 | 0.21-6.00 |
| 30 - 40 | 17 (77.3) | 5 (22.7) | 0.78 | 0.15-4.12 |
| 41 - 50 | 21 (87.5) | 3 (12.5) | 0.38 | 0.63-2.29 |
| > 50 | 8 (72.7) | 3(27.3) | 1.00 | |
| **Underling disease** | | | | |
| No | 46 (77.6) | 13 (22.4) | 1.00 | |
| Yes | 12 (80.0) | 3 (20.0) | 1.50 | 0.30-7.76 |

| Factor | Without AEFI n (%) | With AEFI n (%) | OR | 95%CI |
|---|---|---|---|---|
| **BMI ($kg/m^2$)** | | | | |
| <18.5 | 3 (75.0) | 1 (25.0) | 1.00 | |
| 18.6-22.9 | 17 (85.0) | 3 (15.0) | 0.50 | 0.09-2.24 |
| ≥ 23.0 | 38 (76.0) | 12 (24.0) | 5.30 | 1.34-20.95* |
| **Number of days between the 2nd dose and 3rd dose of COVID-19** | | | | |
| 28-41 | 4 (80.0) | 1 (20.0) | 1.00 | |
| 42-56 | 11 (61.1) | 7 (38.9) | 0.56 | 0.14-2.24 |
| ≥ 57 | 43 (84.3) | 8 (15.7) | 3.40 | 1.02-11.49* |

* Statistical significance at $\alpha = 0.05$

## Discussion

A study at Royal Thai Air Force Hospital (Sikan), who received the 3rddose COVID-19 vaccine were reported in greater rate of AEFI compared to our study: 21.6% were reported on having AEFI which was classified in 65% within seven days, and 7.0% at one month, respectively. A study conducted in Indonesia by Hidayat R et al. [10] among 311 medical professionals also reported that there were many signs of AEFI reported among those who received the 3rddose of COVID-19 vaccine, but some were different. However, it is possible that the findings of this study would not be exactly the same due to differences of the vaccine productions and study population. Data collected and source of data in the study might impact the findings as well.

In our study, fever, myalgia, and pain and edema at the injection site were the most frequent adverse effects reported after the 3rddose. This coincides with the study conducted by the Royal Thai Air Force Hospital (Sikan) reported that fever, myalgia, and redness at the injection site were the most frequent adverse responses after the third dose of the COVID-19 vaccination [7]. Hidayat R et al. [10] reported that fever (50.8%), myalgia (51.4%), swelling, and redness (77.2%) were found as the major AEFI and a large proportion were reported in mild to moderate levels [10].The findings were also reported that the AEFI were presented within 2-3 days, and non-steroidal anti-inflammatory drugs (NSAIDs) were effectively used to reduce the pain [10]. These findings were also confirmed by Pinpathomrat N, et al. [8] and Kanokudom S, et al. [11].

In our study, we found that those people who had BMI ≥ 23 $kg/m^2$, and had been vaccinated for 56 days for the 3rddose after the 2nddose could present AEFI. Hidayat R et al. [10] also reported that those people having BMI more than 25 was one of the key factors to experience AEFI.

For the association between the time between the 2nddose and 3rddose and having AEFI which was detected in our study was the first report. There was no report previously in the issue. To wait to long time in our study before assessing AEFI, we need to make sure that our staff would not suffer from the AEFI.

Some limitations were found in this study. First, some participants would not favor all relevant signs and symptoms to the system, even if they were provided a very feasible channel. Second, some participants may not be happy to present their problem because they might not get another dose under the serious condition of the pandemic. Last, the study conducted among the healthcare workers who had strong knowledge in the field which were very much different from the general population, then, the findings might not be able to generalize to other populations.

Future research should also focus on other traits of the population such as the elderly, children, and people who are suffering with chronic diseases. A stronger study design to be implemented is recommended to ensure the accuracy of the findings, and could be applied in real life effectively.

## Conclusion

Monitoring the AEFI among people who received the 3rddose of COVID-19 vaccine especially AstraZeneca should be implemented particularly those who having high BMI and long days between the 2nddose and the 3rddose. Several signs and symptoms from the mild to severe could be reported to those who receive the 3rddose. Specific design channel for implementing the

## Competing interests

The authors had no competing interests to declare.

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