ORIGINAL ARTICLE

# Adverse events following BNT162b2 mRNA COVID-19 vaccination among healthcare workers: A single-centre experience in Malaysia

**Li-Lian Gan, MSc[1], Zahidah Binti Abdul Razak, MD[2], Nur Hazirah Mohd Hazman Teh, MD[2], Nabilah Huda Binti Kamaluzaman, MD[2], Nur Aisyah Binti Zulkeplee, MBBS[2], Ili Najihah Binti Muhammad Amin, MBBCh[1], David Chun-Ern Ng, MRCPCH[3,4]**

[1]Clinical Research Centre, Hospital Tuanku Ja'afar Seremban, Negeri Sembilan, Ministry of Health Malaysia, [2]Occupational Safety and Health Unit, Hospital Tuanku Ja'afar Seremban, Negeri Sembilan, Ministry of Health Malaysia, [3]Department of Paediatrics, Hospital Tuanku Ja'afar Seremban, Negeri Sembilan, Ministry of Health Malaysia, [4]Negeri Sembilan Disaster Management Committee for COVID-19, Ministry of Health Malaysia

## ABSTRACT

**Introduction: The COVID-19 pandemic is a global health crisis that has resulted in a massive disease burden worldwide. Mass vaccination plays an important role in controlling the spread and severity of COVID-19 infections worldwide.**

**Materials and Methods: A cross-sectional study was conducted in Hospital Tuanku Ja'afar Seremban between 1 March 2021 and 4 May 2021 to describe the adverse events (AE) following BNT162b2 (Pfizer-BioNTech) vaccination. Healthcare personnel who received at least one dose of the vaccine were invited to complete an online questionnaire.**

**Results: Of 2282 analysed samples, AE were experienced in up to 64.5% (n=1472) of the study participants. Most AE were encountered after the second dose (56.5%, n=832). Pain at the injection site (41.5%, n=944), fever (35.1%, n=798) and lethargy (34.8%, n=792) were the most commonly reported AE. Severe AEFI were reported in a minority (2.9%, n=68). There were no documented anaphylaxis, vaccine-induced thrombosis, or myocarditis. The proportion of female recipients and recipients with a history of allergy were higher in the AE group compared to the non-AE group.**

**Conclusion: Our study reinforces the safety of the BNT162b2 mRNA vaccine in the local population. The main adverse events were mild, although they occurred in most patients.**

**KEYWORDS:**
*COVID-19, SARS-CoV-2, vaccines, adverse events*

## INTRODUCTION

The emergence of coronavirus disease 2019 (COVID-19) – caused by a novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) – has led to an unprecedented global health crisis. Since the World Health Organization (WHO) declared COVID-19 a pandemic on 11th March 2020, the virus has claimed more than 5.4 million deaths worldwide.[1] The rapidly spreading pandemic has stretched healthcare systems to the limit and forced many countries to implement harsh restrictions to curb the spread of the virus.

The development of safe and effective COVID-19 vaccines brought hope to control the pandemic. Malaysia started its COVID-19 vaccination program in February 2021.[1] The vaccination program was rolled out in three phases, starting with the frontliners such as healthcare workers (HCWs), police, and military personnel as a priority group. All HCWs were offered the BNT162b2 mRNA vaccine (Comirnaty), which was the vaccine available at that time.

The swift development of effective vaccines against COVID-19 was an unprecedented scientific achievement. However, several adverse events following immunisation have been reported. Adverse events following immunisation (AEFI) can range from mild to severe, where possible local reactions include pain, swelling, and redness at the injection site. In contrast, systemic events may include fever, fatigue, headache, chills, nausea, vomiting, diarrhoea, myalgia, arthralgia, lymphadenopathy, arrhythmias, syncope, and paraesthesia.[2,3]

If poorly dealt with, the experience of AEFI can result in vaccine misconceptions and contribute to vaccine hesitancy. There have been no studies about AEFI associated with COVID-19 vaccination in the local population. Thus, we aim to evaluate the incidence and severity of AEFI associated with the BNT162b2 mRNA vaccine and identify variables associated with the development of AEFI among healthcare workers.

## MATERIALS AND METHODS

We performed an online cross-sectional survey, where the target population comprised 3500 healthcare personnel working in Hospital Tuanku Ja'afar Seremban who received at least one dose of the Pfizer-BioNTech (BNT162b2) COVID-19 vaccine during the Phase 1 vaccination program from 1 March 2021 to 4 May 2021. Participants were approached and invited to join a self-administered survey via a Google

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*Corresponding Author: Li-Lian Gan*
*Email: lilian.gan@gmail.com*

**Table I: Baseline characteristics of the study population**

| Baseline characteristics of patients | n (%) |
|---|---|
| Sex | |
| • Female | 1744 (76.4) |
| • Male | 538 (23.6) |
| Ethnicity | |
| • Malay | 1898 (83.2) |
| • Chinese | 86 (3.8) |
| • Indians | 264 (11.6) |
| • Others | 34 (1.5) |
| Professional category | |
| • Medical doctors | 34 (1.5) |
| • Nurses and paramedics | 1132 (49.6) |
| • Pharmacists | 91 (4.0) |
| • Allied health personnel | 173 (7.6) |
| • Supportive staff | 445 (19.5) |
| • Administrative staff | 134 (5.9) |
| Comorbidities* | |
| • None | 1806 (79.1) |
| • Hypertension | 163 (7.1) |
| • Bronchial asthma | 123 (5.4) |
| • Diabetes mellitus | 114 (5.0) |
| • Cardiac disease | 40 (1.8) |
| • Haemato-oncological disorders | 36 (1.6) |
| • Neurological disorders | 28 (1.2) |
| • Immunodeficiency disorders | 13 (0.6) |
| • Tuberculosis | 10 (0.4) |
| • Liver disease | 6 (0.3) |
| • Chronic kidney disease | 6 (0.3) |
| Allergy history | |
| • Yes | 434 (19.0) |
| • No | 1848 (81.0) |
| Previous COVID-19 infection | |
| • Yes | 114 (5.0) |
| • No | 2168 (95.0) |
| Pregnancy | |
| • First trimester | 17 (0.7) |
| • Second trimester | 24 (1.1) |
| • Third trimester | 16 (0.7) |

* denotes that a subject may have more than one comorbidity.

**Table II: Comparison of reported adverse events after both BNT162b2 vaccine injections**

| Reported adverse events | Cumulative, n (%) | First dose, n (%) | Second dose, n (%) | OR[a] | 95% CI | p-value |
|---|---|---|---|---|---|---|
| Fever | 1006 (44.1) | 208 (9.1) | 798 (35.0) | 5.36 | 4.54–6.33 | <0.01 |
| Chills and rigors | 705 (30.9) | 120 (5.3) | 585 (25.6) | 6.21 | 5.05–7.63 | <0.01 |
| Lethargy | 1135 (49.7) | 343 (15.0) | 792 (34.7) | 3.00 | 2.60–3.47 | <0.01 |
| Pain at injection site | 1468 (64.3) | 524 (23.0) | 944 (41.4) | 2.36 | 2.08–2.69 | <0.01 |
| Swelling at injection site | 683 (29.9) | 243 (10.6) | 440 (19.3) | 2.00 | 1.69–2.37 | <0.01 |
| Headache | 770 (33.7) | 218 (9.6) | 552 (24.2) | 3.02 | 2.55–3.58 | <0.01 |
| Dizziness | 727 (31.9) | 239 (10.5) | 488 (21.4) | 2.33 | 1.97–2.75 | <0.01 |
| Myalgia and joint pain | 937 (41.1) | 265 (11.6) | 672 (29.4) | 3.18 | 2.72–3.72 | <0.01 |
| Vomiting | 75 (3.3) | 27 (1.2) | 48 (2.1) | 1.79 | 1.12–2.89 | <0.05 |
| Nausea | 186 (8.2) | 63 (2.8) | 123 (5.4) | 2.01 | 1.47–2.73 | <0.01 |
| Diarrhoea | 64 (2.8) | 15 (0.7) | 49 (2.1) | 3.32 | 1.85–5.93 | <0.01 |
| Cough | 72 (3.2) | 24 (1.1) | 48 (2.1) | 2.02 | 1.23–3.31 | <0.01 |
| Runny nose | 117 (5.1) | 38 (1.7) | 79 (3.5) | 2.12 | 1.43–3.13 | <0.01 |
| Sore throat | 132 (5.8) | 38 (1.7) | 94 (4.1) | 2.54 | 1.73–3.71 | <0.01 |
| Rashes | 103 (4.5) | 38 (1.7) | 65 (2.8) | 1.73 | 1.16–2.59 | <0.01 |
| Palpitations | 172 (7.5) | 62 (2.7) | 110 (4.8) | 1.81 | 1.32–2.49 | <0.01 |
| Shortness of breath | 40 (1.8) | 16 (0.7) | 24 (1.1) | 1.51 | 0.80–2.84 | 0.20 |
| Anaphylaxis | 13 (0.6) | 4 (0.2) | 9 (0.4) | 2.25 | 0.69–7.33 | 0.16 |

[a]Odds ratios (OR) were calculated based on the number of adverse events following the second dose against the first dose.

**Table III: Comparison of the AE and non-AE groups**

| | AE occurred (n = 1472) | No AE (n = 810) | p-value[†] |
|---|---|---|---|
| Mean age (SD), years | 35.7 (7.2) | 36.7 (8.1) | <0.01 |
| Gender: | | | <0.01 |
| Female | 1181 (80.2%) | 563 (69.5%) | |
| Male | 291 (19.8%) | 247 (30.5%) | |
| Ethnicity: | | | 0.879 |
| Malay | 1223 (83.1%) | 675 (83.3%) | |
| Non-Malays | 249 (16.9%) | 135 (16.7%) | |
| Comorbidities | 316 (21.5%) | 160 (19.8%) | 0.335 |
| History of allergies | 336 (22.8%) | 98 (12.1%) | <0.01 |
| History of COVID-19 | 77 (5.2%) | 37 (4.6%) | 0.487 |
| Pregnancy | 43 (2.9%) | 14 (1.7%) | 0.081 |
| First dose vaccination on left arm | 1301 (88.4%) | 705 (87.0%) | 0.345 |
| Second dose vaccination on left arm | 1277 (86.7%) | 694 (85.7%) | 0.774 |
| Premedication: | | | |
| Paracetamol | 227 (15.4%) | 121 (14.9%) | 0.759 |
| NSAIDS | 7 (0.5%) | 3 (0.4%) | 0.716 |
| Antihistamines | 36 (2.4%) | 13 (1.6%) | 0.185 |
| Steroids | 10 (0.7%) | 5 (0.6%) | 0.861 |

[†] independent samples t-test for mean age, and chi-squared test computation for other groups.

form link. The questionnaire was composed of queries from the following domains: demographic details, baseline clinical characteristics, details on AEFI occurrences, and the clinical course after vaccination. Severe adverse events were defined as any adverse event requiring a visit to the emergency department (ED) or hospitalisation. The survey was done from June to August 2021, and 2755 responses were recorded. We removed 146 duplicate responses and further excluded 327 responses with suboptimal responses. The remaining 2282 responses were subsequently analysed.

Ethical approval for the use of an online survey form for the research in Hospital Tuanku Ja'afar Seremban was obtained from the Medical Research and Ethics Committee (MREC), and all users provided informed consent for non-commercial use of their data.

Descriptive statistics were used to analyse categorical variables collected in the study, where results were summarised and presented in frequencies and percentages. Data for continuous variables were presented as mean and standard deviation (SD). Chi-squared tests and Fisher exact tests were used to compare categorical variables as appropriate. A p-value of $< 0.05$ was considered statistically significant.

## RESULTS

A total of 2282 participants were included in the analysis. Table I summarises the baseline characteristics of all 2282 participants in this study. More than three-quarters of the study population were female respondents (n=1744, 76.4%). By ethnicity, Malays were the majority (83.2%), followed by Indians (11.6%), Chinese (3.8%), and others (1.5%). The mean age was 36.0 years (SD 7.6). Nurses and paramedics (n=1132, 49.6%) account for almost half the subjects in the study, followed by healthcare support staff (n=445, 19.5%), medical doctors (n=307, l3.5%), and other healthcare workers from the allied-health, pharmacy, and administrative departments. Comorbidities were present in 20.9% of participants, with hypertension, bronchial asthma, and diabetes mellitus being the three most common comorbidities. A total of 434 (19.0%) participants reported a history of allergy, and 114 (5%) HCWs documented a previous COVID-19 infection. Among the female participants, 57 (2.5%) were pregnant, with the majority in a gestational age beyond the second trimester.

The study respondents were predominantly double-dose vaccine recipients, with only eight respondents (0.4%) receiving one dose. Reasons for opting out of the second dose were as follows: two respondents experienced severe AEFI following their first-dose injection, four respondents opted out due to pregnancy, whilst two other respondents did not complete vaccination due to job transfer.

In our study, AE (adverse event) was experienced in up to 64.5% (n=1472) of the study participants (Figure 1). Within this group, majority of the AE occurred after the second dose (56.5%, n = 832), while 31.6% (n=465) experienced AE with both doses. Despite the considerable number of AEs, a small number of participants (n=68, 3.0%) developed severe AE, warranting observation in the emergency department or hospitalisation. Most of the severe AEs (n=46, 67.6%) were experienced after the second dose of injection. The median duration of severe AEFI was 2 days (IQR=3). Severe AEFIs, such as life-threatening anaphylaxis, vaccine-induced thrombosis, myocarditis, or mortality, were not reported among our study participants.

The most frequently reported AEFI in this study was pain at the injection site (64.3%, n=1468), lethargy (49.7%, n=1135), and fever (44.1%, n= 1006). These AEFIs were more commonly reported after the second dose compared to the first dose, as well as other AEFIs such as chills and rigors, swelling at the injection site, headache, dizziness, myalgia and joint pain, vomiting, nausea, diarrhoea, cough, runny nose, sore throat, rashes, and palpitations (Table II).

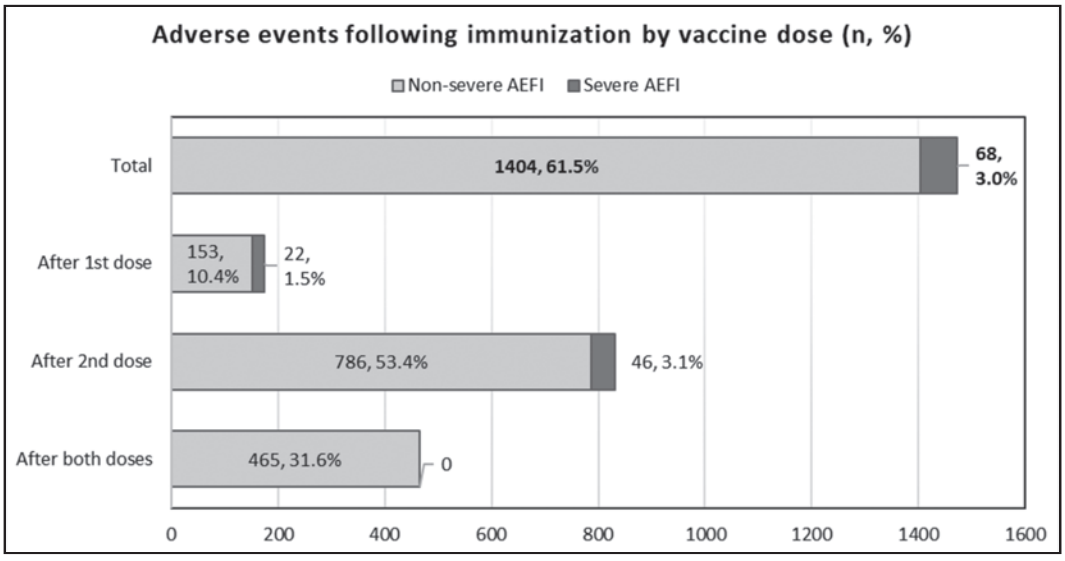


**Fig. 1:** Adverse events following COVID-19 vaccine immunisation.

The subjects who experienced AE were significantly younger than those who did not, with a mean age difference of 1.1 years (95% CI 0.4–1.8) (Table III). The proportion of females in the AE group (80.2%) was significantly higher than that in the non-AE group (69.5%). The site of vaccination, i.e., the left or right arm, did not affect the occurrence rates of AE during the first or second dose of vaccination. The proportion of vaccine recipients who received premedication with paracetamol, non-steroidal anti-inflammatory drugs (NSAIDs), antihistamines, or steroids did not differ significantly between both groups.

## DISCUSSION

In this cross-sectional observational study, we evaluated the adverse effects following administration of BNT162b2 vaccines among healthcare workers in a tertiary, hospital-based setting. Our study showed that AEFIs following vaccination were common, but mostly mild and self-limiting. Only 3% of participants encountered severe AE requiring emergency department observation or hospitalisation. There were no documented vaccine-induced thrombotic thrombocytopenia or myocarditis among our study participants.

Our findings were consistent with previous studies documenting that AEs were more likely to occur following the second dose of BNT162b2 vaccine.[4,5] Prior studies reported that systemic AEs (such as fever, fatigue, and myalgia) were more likely to occur than local side effects (such as pain, redness, and swelling) following the second dose.[6,7] However, in our study, all local and systemic AEs were more frequently seen after the second dose. The reasons for this were unclear but could be related to a short inter-dose interval between the first and second vaccination. There are emerging data showing that a longer time interval between COVID-19 mRNA doses was associated with a reduced risk of AEFI such as myocarditis.[8]

Our results support previous findings that female recipients with a younger age were more likely to experience AEFI following the BNT162b2 vaccination.[9] Our findings of higher AEFI among females were consistent with the results of several other studies on the reactogenicity of the BNT162b2 vaccines.[6,10] The gender differences in AEFI occurrences have been previously observed with seasonal flu shots, which may be ascribed to various hormonal, genetic, and immunologic distinctions.[11]

Our study showed the AE group had a significantly higher proportion of participants with a history of allergy. This finding was also supported by Nittner et al.,[12] who reported that local and systemic reactions were more frequently seen in allergic individuals. Nevertheless, severe allergic reactions such as anaphylaxis were not seen in our study population, even among those with a prior allergy history. This could be due to the relatively rare occurrence of anaphylaxis,[13,14] which would not be captured in our study population of 2,282 people.

The proportion of those who had prior COVID-19 did not differ significantly between the AE and non-AE groups, although other studies showed an increased likelihood of developing AEFI among individuals with prior COVID-19 infections.[15–17] We did not find significant differences between those with underlying comorbidities, consistent with existing reports.[17–19] This suggests that the BNT162b2 vaccine can be safely administered to individuals with underlying comorbidities as the potential benefit outweighs the risk of developing adverse events. Our results showed no differences in the development of AEFI among pregnant mothers, consistent with the findings of several large-scale studies.[20–22]

We found no significant differences in the proportion of subjects who premedicated themselves with paracetamol, non-steroidal anti-inflammatory drugs (NSAIDs), antihistamines, or steroids in the AE and non-AE groups. This is compatible with studies demonstrating that premedication

does not prevent subsequent allergic reactions.[23,24] Instead, the use of premedication may mask acute cutaneous reactions and lead to delayed detection of severe allergic reactions.[23] There are also concerns from non-COVID-19 vaccine studies that the usage of prophylactic antipyretics may attenuate antibody responses to vaccine antigens.[25,26]

This study has several limitations. First, this is a single-centre study comprising of healthcare workers; thus, the results might not be generalisable to the greater population. Second, participation in the study was on a voluntary basis. This may lead to the possibility of bias in our results as vaccine recipients who had experienced AEFI were potentially more likely to participate in the study. Finally, at the time of study initiation, the Pfizer-BioNTech, BNT162b2 was the only vaccine available; hence, comparison with other vaccine types was not possible. Further studies involving different types of vaccines are required to allow fair comparison in terms of tolerability and effectiveness. Despite those limitations, our study provided a sufficiently broad overview of the types of AEFI, which were commonly experienced following BNT162b2 vaccination among healthcare workers.

## CONCLUSION

In conclusion, local and systemic AEFIs following the BNT162b2 vaccination were commonly experienced; however, most were self-limiting. These findings could come in handy to address vaccine hesitancy caused by concerns regarding severe AEFIs associated with the COVID-19 vaccines. Our study, conducted in the context of a local population, adds to the growing amount of literature on the safety of the COVID-19 mRNA vaccines.

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## CONFLICTS OF INTERESTS

The authors declare no conflict of interests.

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