**Letter to Editor**

**COVID-19 vaccination in pregnancy: experience in Vietnam**

**Short title:** COVID-19 vaccination in pregnancy

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Vaccination has been the most effective strategy against coronavirus 2019 disease (COVID-19). However, given the disruptive nature of the pandemic, vaccines have understandably been approved using expedited assessment processes.

Studies on vaccination in pregnant women have shown no increased risk of pregnancy complications, but these had a retrospective design or were limited to mRNA vaccines.1,2 Furthermore, data on the comparative tolerability of different vaccines in this important patient group is lacking. Based on our experience, we compared pregnancy and neonatal outcomes in Vietnamese women vaccinated against COVID-19 with the Astra Zeneca versus Pfizer-BioNTech vaccines.

Between August and November 2021, 954 pregnant women at approximately 30–31 weeks’ gestation were offered COVID-19 vaccination at My Duc Hospital, Ho Chi Minh City, Vietnam. The vaccine used (Astra Zeneca or Pfizer-BioNTech) was based availability at the time of vaccination. We prospectively investigated side effects occurring within 1 week after vaccination, and followed pregnant women until their babies were delivered.

A total of 513 women were vaccinated with the Pfizer-BioNTech vaccine and 441 with the Astra Zeneca vaccine (mean age 30.8±4.5 vs. 30.0±4.4 years [p<0.001], first pregnancy 40.2% vs. 54.5% [p<0.001], spontaneous pregnancy 92.6% vs. 87.3% [p=0.009], gestation at vaccination 32.4±4.0 vs. 31.9±4.5 weeks [p=0.067], and two vaccine doses received 80.7% vs. 60.1% [p<0.001], respectively).

All side effects were mild, but the total number was lower after the Pfizer-BioNTech versus Astra Zeneca vaccine (Table 1). The proportion of women with preeclampsia and gestational diabetes mellitus was slightly, but not significantly, higher in those received the Pfizer-BioNTech versus AstraZeneca vaccine (both 1.0% versus 0.2%; p=0.225), and the proportion who had infants with birthweight <2500 g was significantly higher in women who received the Pfizer-BioNTech versus AstraZeneca vaccine (5.3% vs. 2.5%; relative risk 2.1, 95% confidence interval 1.05–4.18; p=0.046). This appeared to be due to a higher rate of growth restricted infants rather than a higher rate of preterm birth (data not shown).

This prospective cohort study showed that COVID-19 vaccines are generally safe and well-tolerated in pregnant women. A recent report of data from a large number of US-based women concluded that there was no overall increased risk for small for gestational age at birth or preterm delivery in vaccinated versus unvaccinated individuals.2 In our study, we did not compare rates of adverse events between vaccinated an unvaccinated women, but instead compared groups who received one of two different COVID-19 vaccines. Although our data should be considered preliminary due to the relatively small sample size, and lack of randomization and an untreated control group, we found that a higher proportion of women vaccinated with the Pfizer BioNTech vaccine had low birthweight infants compared to those vaccinated with the AstraZeneca product; this requires additional research. Additionally, more longitudinal follow-up, including evaluation of large numbers of women vaccinated earlier in pregnancy, is necessary to fully understand the maternal, pregnancy, and infant impacts of COVID-19 vaccination during pregnancy.

**Contributions:**

Conceptualisation: Lan N Vuong, Ben WJ Mol, Tuong M Ho

Data curation: Lan N Vuong, Minh N Chau, Duy L Nguyen, Toan D Pham

Investigation: Lan N Vuong, Minh N Chau, Tuong M Ho

Methodology: Lan N Vuong, Toan D Pham, Ben WJ Mol, Tuong M Ho

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Supervision: Tuong M Ho

Writing (original draft): Lan N Vuong, Ben WJ Mol

Writing (review & editing): all authors.

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

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**Table 1.** Side effects within 1-week after vaccination against COVID-19 in pregnant women.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Side effects, n (%)** | **First dose** | | | **Second dose** | | |
| **AstraZeneca**  **(n=441)** | **Pfizer-BioNTech (n=513)** | **p-value** | **AstraZeneca**  **(n=265)** | **Pfizer-BioNTech (n=414)** | **p-value** |
| Pain/swelling at injection site | 354 (80.3) | 418 (81.5) | 0.696 | 38 (14.3) | 169 (40.8) | <0.001 |
| Redness at injection site | 11 (2.5) | 8 (1.6) | 0.425 | 1 (0.4) | 11 (2.7) | 0.034 |
| Itching at injection site | 70 (15.9) | 64 (12.5) | 0.158 | 5 (1.9) | 9 (2.2) | 1 |
| Self-reported fatigue | 261 (59.2) | 60 (11.7) | <0.001 | 15 (5.7) | 64 (15.5) | <0.001 |
| Sore throat/runny nose | 14 (3.2) | 3 (0.6) | 0.006 | 0 (0.0) | 0 (0.0) | - |
| Coughing | 6 (1.4) | 0 (0.0) | - | 0 (0.0) | 2 (0.5) | **-** |
| Headache | 183 (41.5) | 43 (8.4) | <0.001 | 7 (2.6) | 37 (9.0) | 0.002 |
| Muscle pain | 187 (42.4) | 49 (9.6) | <0.001 | 10 (3.8) | 38 (9.2) | 0.011 |
| Chilling | 159 (36.1) | 14 (2.7) | <0.001 | 5 (1.9) | 16 (3.9) | 0.219 |
| Fever (>38oC) | 113 (25.6) | 1 (0.2) | <0.001 | 13 (4.9) | 49 (11.9) | 0.003 |
| Nausea | 34 (7.7) | 5 (1.0) | <0.001 | 0 (0.0) | 5 (1.2) | - |
| Joint pain | 78 (17.7) | 8 (1.6) | <0.001 | 19 (7.2) | 14 (3.4) | 0.04 |
| Stomach ache | 7 (1.6) | 1 (0.2) | 0.028 | 2 (0.8) | 0 (0.0) | - |
| Diarrhea | 16 (3.6) | 2 (0.4) | 0.001 | 0 (0.0) | 2 (0.5) | - |
| Rash skin | 4 (0.9) | 1 (0.2) | 0.188 | 1 (0.4) | 0 (0.0) | - |
| Vaginal hemorrhage | 4 (0.9) | 1 (0.2) | 0.188 | 0 (0.0) | 0 (0.0) | - |
| Thrombocytopenia | 0 (0.0) | 0 (0.0) | - | 0 (0.0) | 0 (0.0) | - |
| Myocarditis | 0 (0.0) | 0 (0.0) |  | 0 (0.0) | 0 (0.0) | - |
| Anaphylactic shock | 0 (0.0) | 0 (0.0) |  | 0 (0.0) | 0 (0.0) | - |

**Table 2**. Pregnancy and neonatal outcomes in pregnant women vaccinated against COVID-19.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **AstraZeneca**  **(N=441)** | **Pfizer-BioNTech**  **(N=513)** | **Difference**  **(95% CI)** | **Relative risk**  **(95% CI)** | **p-value** |
| **Pregnancy outcomes** |  |  |  |  |  |
| Preeclampsia after vaccination, n (%) | 1 (0.2) | 5 (1.0) | 0.75 (–0.42, 1.92) | 4.3 (0.5, 36.65) | 0.225 |
| Diabetes after vaccination, n (%) | 1 (0.2) | 5 (1.0) | 0.75 (–0.42, 1.92) | 4.3 (0.5, 36.65) | 0.225 |
| Gestational age at birth, weeks | 38.4±1.6 | 38.6±1.3 | 0.1 (–0.1, 0.3) | - | 0.176 |
| Preterm delivery, n (%) |  |  |  |  |  |
| <28 weeks | 3 (0.7) | 0 (0.0) | - | - | - |
| <34 weeks | 6 (1.4) | 8 (1.6) | 0.2 (–1.52, 1.92) | 1.15 (0.4, 3.28) | 0.95 |
| <37 weeks | 28 (6.4) | 34 (6.6) | 0.28 (–3.07, 3.62) | 1.04 (0.64, 1.69) | 0.9 |
| Oligohydramnios, n (%) | 12 (2.7) | 15 (2.9) | 0.19 (–2.11, 2.49) | 1.07 (0.51, 2.26) | 0.95 |
| Polyhydramnios, n (%) | 14 (3.2) | 23 (4.5) | 1.31 (–1.33, 3.95) | 1.41 (0.74, 2.71) | 0.381 |
| ICU monitoring, n (%) | 0 (0) | 2 (0.4) | - | - | - |
| Stillbirth, n (%) | 2 (0.5) | 1 (0.2) | 0.43 (0.04, 4.72) | –0.26 (–1.2, 0.69) | 0.6 |
| Maternal death, n (%) | 0 (0.0) | 0 (0.0) | - | - | . |
| **Neonatal outcomes** |  |  |  |  |  |
| Birth weight, g | 3148.3±376.8 | 3132.1±403.5 | - | –16.1 (–65.9, 33.6) | 0.524 |
| Low birth weight (<2500 g), n (%) | 11 (2.5) | 27 (5.3) | 2.1 (1.05, 4.18) | 2.75 (0.12, 5.39) | 0.046 |
| High birth weight (>4000 g), n (%) | 6 (1.4) | 10 (2.0) | 1.42 (0.52, 3.88) | 0.58 (–1.25, 2.41) | 0.66 |
| Birthweight percentile | 50.0 [25.0; 75.0] | 50.0 [25.0; 75.0] | - | - | 0.445 |
| Birthweight <10th percentile, n (%) | 65 (14.7) | 85 (16.6) | 1.12 (0.84, 1.51) | 1.83 (–3, 6.66) | 0.493 |
| NICU, n (%) | 24 (5.5) | 23 (4.5) | 0.82 (0.47, 1.44) | –0.96 (–3.95, 2.03) | 0.594 |
| Birth defects, n (%) | 4 (0.9) | 4 (0.8) | 0.86 (0.22, 3.42) | –0.13 (–1.42, 1.17) | 0.95 |

Data are mean ± standard deviation, median [interquartile range], or number of patients (%).

CI, confidence interval; ICU, intensive care unit; NICU, neonatal intensive care unit.