**Letter to Editor**

**COVID-19 vaccination in pregnancy**

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Dear Editor,

Vaccination has been the most effective strategy against Covid-19 disease caused by SARS-CoV-2. In view of the disruptive nature of the pandemic, vaccines have understandably been approved after shortened assessment trajectories. Pregnant women face more than double the risk of needing admission to an intensive care unit, intensive ventilation, extracorporeal membrane oxygenation and death.1

Early studies on vaccination in pregnant women showed no increased risk of pregnancy complications, but the studies were retrospective and limited to Pfizer-BioNTech.2,3 Here, we compare pregnancy and neonatal outcomes in Vietnamese women vaccinated against COVID-19 with Astra Zeneca and Pfizer-BioNTech.

**Methods** Between August 2021 and November 2021, 954 pregnant women were offered vaccination against COVID-19 at around 30-31 weeks of gestation at My Duc Hospital, Ho Chi Minh City, Vietnam. The choice for Astra Zeneca or Pfizer-BioNTech vaccines depended on the availability of the vaccines at the time of vaccination. We prospectively investigated the side effects in the vaccinated pregnant women within 1 week after vaccination and followed their pregnancies till deliveries.

**Results** There were441 pregnant vaccinated with Astra Zeneca and 513 with Pfizer-BioNTech. Women receiving Pfizer-BioNTech were slightly older, more often multiparous, more often had conceived spontaneously, and more often (80.7% versus 60.1%) had received two doses. There were more side-effects reported after Astra Zeneca, but they were all mild (Table 2).

There were more women with preeclampsia and gestational diabetes mellitus after vaccination with Pfizer-BioNTech as compared to Astra Zeneca (both 1.0% versus 0.2%), but differences were not statistically significant (Table 3). The rate of birthweight <2500 gram was 2.5% after Astra Zeneca and 5.3% after Pfizer (RR 2.1; 95% CI 1.05, 4.18, P-value 0.046). Table 4 shows that this is due to a higher rate of growth restriction and not due to more preterm birth.

**Conclusion**

In this prospective cohort study, we showed that COVID-19 vaccines are generally safe and well-tolerated among pregnant women. Pfizer-BioNTech vaccine was associated with higher rate of low birthweight as compared with Astra Zeneca vaccine. More longitudinal follow-up, including follow-up of large numbers of women vaccinated earlier in pregnancy is necessary to inform maternal, pregnancy, and infant outcomes.

Yours sincerely,

Lan N Vuong, on behalf of co-authors.

**Contributions:**

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

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**Table 1**. Baseline characteristics of pregnant women vaccinated against COVID-19

|  |  |  |  |
| --- | --- | --- | --- |
| **Baseline demographics** | **Astra Zeneca**  **N=441** | **Pfizer BioNTech**  **N=513** | **p-value** |
| Maternal age – years | 30.0±4.4 | 30.8±4.5 | <0.001 |
| Previous pregnancies – n (%) |  |  | <0.001 |
| 0 | 240 (54.4) | 206 (40.2) |  |
| 1 | 92 (20.9) | 158 (30.8) |  |
| 2 | 87 (19.7) | 119 (23.2) |  |
| ≥ 3 | 22 (5.0) | 30 (5.8) |  |
| Type of pregnancy – n (%) |  |  | 0.009 |
| Spontaneous | 385 (87.3) | 475 (92.6) |  |
| In Vitro Fertilization | 56 (12.7) | 38 (7.4) |  |
| Number of vaccine doses – n (%) |  |  | <0.001 |
| Only 1 dose | 176 (39.9) | 99 (19.3) |  |
| 2 doses | 265 (60.1) | 414 (80.7) |  |
| Gestational age at vaccination – weeks | 31.9±4.5 | 32.4±4.0 | 0.067 |
| High blood pressure at vaccination | 0 (0.0) | 3 (0.6) | . |
| Diabetes at vaccination | 58 (13.2) | 62 (12.1) | 0.691 |

Data were presented as mean ± SD or n (%)

**Table 2.** Side effects within 1-week post-vaccination in pregnant women

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Side effects – n (%)** | **Astra Zeneca** | | **Pfizer-BioNTech** | | **P1** | **P2** |
| **First dose**  **(N=441)** | **Second dose**  **(N=265)** | **First dose**  **(N=513)** | **Second dose**  **(N=414)** |
| Pain and swelling at injection site | 354 (80.3) | 38 (14.3) | 418 (81.5) | 169 (40.8) | 0.696 | <0.001 |
| Redness at injection site | 11 (2.5) | 1 (0.4) | 8 (1.6) | 11 (2.7) | 0.425 | 0.034 |
| Itching at injection site | 70 (15.9) | 5 (1.9) | 64 (12.5) | 9 (2.2) | 0.158 | 1 |
| Self-reported fatigue | 261 (59.2) | 15 (5.7) | 60 (11.7) | 64 (15.5) | <0.001 | <0.001 |
| Sore throat / Running nose | 14 (3.2) | 0 (0.0) | 3 (0.6) | 0 (0.0) | 0.006 | . |
| Coughing | 6 (1.4) | 0 (0.0) | 0 (0.0) | 2 (0.5) | . | . |
| Headache | 183 (41.5) | 7 (2.6) | 43 (8.4) | 37 (9.0) | <0.001 | 0.002 |
| Muscle pain | 187 (42.4) | 10 (3.8) | 49 (9.6) | 38 (9.2) | <0.001 | 0.011 |
| Chilling | 159 (36.1) | 5 (1.9) | 14 (2.7) | 16 (3.9) | <0.001 | 0.219 |
| Over 38oC fever | 113 (25.6) | 13 (4.9) | 1 (0.2) | 49 (11.9) | <0.001 | 0.003 |
| Nausea | 34 (7.7) | 0 (0.0) | 5 (1.0) | 5 (1.2) | <0.001 | . |
| Joint pain | 78 (17.7) | 19 (7.2) | 8 (1.6) | 14 (3.4) | <0.001 | 0.04 |
| Stomachache | 7 (1.6) | 2 (0.8) | 1 (0.2) | 0 (0.0) | 0.028 | . |
| Diarrhea | 16 (3.6) | 0 (0.0) | 2 (0.4) | 2 (0.5) | 0.001 | . |
| Rash skin | 4 (0.9) | 1 (0.4) | 1 (0.2) | 0 (0.0) | 0.188 | . |
| Vaginal hemorrhage | 4 (0.9) | 0 (0.0) | 1 (0.2) | 0 (0.0) | 0.188 | . |
| 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) | . | . |

Data were presented as mean ± SD or n (%)

P1: p-value for first dose of Astra Zeneca versus first dose of Pfizer-BioNTech

P2: p-value for second dose of Astra Zeneca versus second dose of Pfizer-BioNTech

**Table 3**. Pregnancy and neonatal outcomes in pregnant women vaccinated against COVID-19

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Astra Zeneca**  **(N=441)** | **Pfizer-BioNTech**  **(N=513)** | **RR**  **(95% CI)** | **AD**  **(95% CI)** | **p-value** |
| **Pregnancy outcomes** | | | | | |
| Preeclampsia after vaccination – n (%) | 1 (0.2) | 5 (1.0) | 4.3 (0.5, 36.65) | 0.75 (-0.42, 1.92) | 0.225 |
| Diabetes after vaccination – n (%) | 1 (0.2) | 5 (1.0) | 4.3 (0.5, 36.65) | 0.75 (-0.42, 1.92) | 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) | 1.15 (0.4, 3.28) | 0.2 (-1.52, 1.92) | 0.95 |
| < 37 weeks | 28 (6.4) | 34 (6.6) | 1.04 (0.64, 1.69) | 0.28 (-3.07, 3.62) | 0.9 |
| Oligohydramnios | 12 (2.7) | 15 (2.9) | 1.07 (0.51, 2.26) | 0.19 (-2.11, 2.49) | 0.95 |
| Polyhydramnios | 14 (3.2) | 23 (4.5) | 1.41 (0.74, 2.71) | 1.31 (-1.33, 3.95) | 0.381 |
| Being monitored at ICU | 0 (0) | 2 (0.4) | - | - | - |
| Stillbirth | 2 (0.5) | 1 (0.2) | -0.26 (-1.2, 0.69) | 0.43 (0.04, 4.72) | 0.6 |
| Maternal death | 0 (0.0) | 0 (0.0) | - | - | . |
| **Neonatal outcomes** | | | | | |
| Birth weight – grams | 3148.3±376.8 | 3132.1±403.5 | - | -16.1 (-65.9, 33.6) | 0.524 |
| Low birth weight (under 2500g) – n (%) | 11 (2.5) | 27 (5.3) | 2.1 (1.05, 4.18) | 2.75 (0.12, 5.39) | 0.046 |
| Heavy birth weight (over 4000g) – 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 (%) | 16 (3.6%) | 26 (5.1%) | 1.40 (0.76, 2.57) | 1.44 (-1.35, 4.23) | 0.356 |
| 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 were presented as mean ± SD or n (%); RR: relative risk, AD: absolute difference, CI: confident interval

**Table 4:** Birthweight against gestational age at delivery in pregnant women vaccinated against COVID-19.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **<34 weeks** | | **34-<37 weeks** | | **37-<38 weeks** | | **38-<39 weeks** | | **39-<40 weeks** | | **40-<41 weeks** | | **41 weeks** | | **Overall** | | **RR (95% CI)** |
|  | **AZ**  **(N = 6\*)** | **Pf**  **(N = 8)** | **AZ**  **(N = 22)** | **Pf**  **(N = 26)** | **AZ**  **(N = 53)** | **Pf**  **(N = 56\*\*)** | **AZ**  **(N = 175)** | **Pf**  **(N = 164)** | **AZ**  **(N = 145)** | **Pf (N = 203)** | **AZ**  **(N = 39)** | **Pf**  **(N = 55)** | **AZ**  **(N = 1)** | **Pf**  **(N = 1)** | **AZ**  **(N = 441)** | **Pf**  **(N = 513)** |
| **<p10 - n (%)** | 1 (16.7) | 1 (12.5) | 2 (9.1) | 6 (23.1) | 3 (5.7) | 2 (3.6) | 7 (4.0) | 5 (3.0) | 2 (1.4) | 12 (5.9) | 1 (2.6) | 0 (0) | 0 (0) | 0 (0) | 16 (3.6%) | 26 (5.1%) | 1.40 (0.76, 2.57) |
| **p10-p25 - n (%)** | 0 (0) | 0 (0) | 2 (9.1) | 2 (7.7) | 4 (7.5) | 7 (12.5) | 20 (11.4) | 16 (9.8) | 14 (9.7) | 26 (12.8) | 7 (17.9) | 8 (14.5) | 0 (0) | 0 (0) | 47 (10.7%) | 59 (11.5%) | 1.08 (0.75, 1.55) |
| **p25-p50 - n (%)** | 2 (33.3) | 2 (25.0) | 6 (27.3) | 10 (38.5) | 12 (22.6) | 13 (23.2) | 39 (22.3) | 38 (23.2) | 45 (31.0) | 53 (26.1) | 10 (25.6) | 11 (20.0) | 0 (0) | 1 (100) | 114 (25.9%) | 128 (25%) | 0.97 (0.78, 1.20) |
| **p50-75 - n (%)** | 1 (16.7) | 1 (12.5) | 5 (22.7) | 3 (11.5) | 13 (24.5) | 21 (37.5) | 38 (21.7) | 41 (25.0) | 43 (29.7) | 49 (24.1) | 14 (35.9) | 23 (41.8) | 1 (100) | 0 (0) | 115 (26.1%) | 138 (26.9%) | 1.03 (0.83, 1.28) |
| **p75-p90 - n (%)** | 0 (0) | 1 (12.5) | 2 (9.1) | 3 (11.5) | 8 (15.1) | 4 (7.1) | 50 (28.6) | 41 (25.0) | 27 (18.6) | 41 (20.2) | 6 (15.4) | 9 (16.4) | 0 (0) | 0 (0) | 93 (21.1%) | 99 (19.3%) | 0.92 (0.71, 1.18) |
| **>p90 - n (%)** | 0 (0) | 3 (37.5) | 5 (22.7) | 2 (7.7) | 13 (24.5) | 8 (14.3) | 21 (12.0) | 23 (14.0) | 14 (9.7) | 22 (10.8) | 1 (2.6) | 4 (7.3) | 0 (0) | 0 (0) | 54 (12.2%) | 62 (12.1%) | 0.99 (0.70, 1.39) |
| **Overall - n (%)** | 6\* (1.4) | 8 (1.6) | 22 (5.0) | 26 (5.1) | 53 (12) | 56\*\* (10.9) | 175 (39.7) | 164 (32.0) | 145 (32.9) | 203 (39.6) | 39 (8.8) | 55 (10.7) | 1 (0.2) | 1 (0.2) |  |  |  |
| **RR (95% CI)** | 1.15 (0.40, 3.28) | | 1.02 (0.58, 1.77) | | 0.91 (0.64, 1.29) | | 0.81 (0.68, 0.96) | | 1.20 (1.01, 1.43) | | 1.21 (0.82, 1.79) | | 0.86 (0.05, 13.7) | |  |  |  |

Data were presented as n (%); RR: relative risk, CI: confident interval, AZ: Astra Zeneca, Pf: Pfizer-BioNTech, p: Birth weight percentile

\*included 2 stillbirths (1 at 24 2/7 weeks and 1 at 26 6/7 weeks)

\*\*included 1 stillbirth (at 37 0/7 weeks)