

COVID-19 vaccination in pregnancy

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March 31, 2022

Letter to Editor

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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 were 441 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.

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Writing – Review & Editing: Lan N Vuong, Minh N Chau, Duy L Nguyen, Toan D Pham, Ben WJ Mol, Tuong M Ho.

Competing interests: No competing interests.

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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 First dose (N=441)	Astra Zeneca Second dose (N=265)	Pfizer-BioNTech First dose (N=513)	Pfizer-BioNTech Second dose (N=414)	P1	P2
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 38°C 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 $\pm$ 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) Pregnancy outcomes	Pfizer- BioNTech (N=513) Pregnancy outcomes	RR (95% CI) Pregnancy outcomes	AD (95% CI) Pregnancy outcomes	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 $\pm$ 1.6	38.6 $\pm$ 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	Neonatal outcomes	Neonatal outcomes	Neonatal outcomes	Neonatal outcomes	Neonatal outcomes
Birth weight – grams	3148.3 $\pm$ 376.8	3132.1 $\pm$ 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 < 10 th 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 were presented as mean $\pm$ 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 weeks	34- <37 weeks	34- <37 weeks	37- <38 weeks	37- <38 weeks	38- <39 weeks	38- <39 weeks	39- <40 weeks	39- <40 weeks	40- <41 weeks	40- <41 weeks	41 weeks	41 weeks	Overall
	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 = 44)
<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 (36.4)
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 (106.8)
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)	111 (250.0)
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)	111 (250.0)
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 (209.1)
>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 (120.9)
Overall6* - n (%)	1 (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)	446 (1000)
RR (95% CI)	1.15 (0.40, 3.28)	1.15 (0.40, 3.28)	1.02 (0.58, 1.77)	1.02 (0.58, 1.77)	0.91 (0.64, 1.29)	0.91 (0.64, 1.29)	0.81 (0.68, 0.96)	0.81 (0.68, 0.96)	1.20 (1.01, 1.43)	1.20 (1.01, 1.43)	1.21 (0.82, 1.79)	1.21 (0.82, 1.79)	0.86 (0.05, 13.7)	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)