REVIEW

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The COVID-19 vaccine during pregnancy phase: A literature review

Vinsensius Tommy Wijaya Japola[1*], Willam Alexander Setiawan[1]

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[1]Department of Obstetrics and Gynecology, Faculty of Medicine, Universitas Udayana/Sanglah General Hospital, Denpasar, Bali, Indonesia;

*Correspondence:
Vinsensius Tommy Wijaya Japola;
Department of Obstetrics and Gynecology, Faculty of Medicine, Universitas Udayana/Sanglah General Hospital, Denpasar, Bali, Indonesia;
Tommyjapola@gmail.com

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ABSTRACT

Physiological change makes pregnant women more vulnerable to COVID-19 infection. It raises morbidity and mortality rates in pregnant women in comparison to the general population. Several morbidities have been reported such as earlier miscarriage, vaginal bleeding during pregnancy, edema in all extremities and also the face, hypertension during the gestational phase, foul-smelling vaginal discharge, and dysuria due to urinary tract infection, etc, with the effectiveness, of reducing morbidity and mortality, vaccines play a key role, especially for this group. However, concerns arise about the safe pregnancy and the fetus This paper addressed the most recent knowledge of the COVID-19 vaccine in pregnancy, as well as the vaccine's pathophysiology. and the current study about safeness.

Keywords: Covid-19 vaccine, pregnancy, review, safeness of vaccine.
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INTRODUCTION

Nowadays severe infection by coronavirus 2 is known to be COVID-19 infection. It becomes a global public health burden. A pregnant population is a high-risk group due to physiological changes.[1,2] It was documented in United State COVID-19 was found in 9 percent of pregnant women (8207 people). In Istanbul, 7% of 296 pregnant women tested positive for the COVID-19 virus.[3]

Due to their physiological changes, pregnant women tend to fall into critical conditions. There were several complications due to its infection that has been documented such as an increase the preterm labor, placenta dysfunction, spontaneous or missed abortion, and many others.[4] Knowing the morbidity-related to pregnancy is also needed, it can cause a significant negative impact on the fetus and may result in fatal outcomes There were several morbidities related to the pregnancy such as earlier miscarriage, vaginal bleeding during pregnancy, oedema in all extremities, and also face, hypertension during the gestational phase, foul-smelling vaginal discharge, and dysuria due to urinary tract infection.[5] Thus, this review article concern discussed COVID-19 infection in pregnancy.

PREGNANCY AND MORTALITY RATE AMONG POSTPARTUM WOMEN INFECTED BY COVID-19 INFECTION

There were 1.3% of pregnant women infected by the COVID-19 from 11.758 samples with a mortality rate was 0.19% of pregnant women in a high-income country. A high mortality rate was reported in middle-income compared with high-income countries. It is about 8.51%.[2,6] Severe cases of COVID-19 infection were reported at 13%. About 4% of them were admitted to ICU, and 0.4% required extracorporeal membrane oxygenation. Thus the number was higher in pregnant women rather than in the nonpregnant population. As a result of this data, prevention and prophylaxis are critical to preventing morbidity and mortality in pregnant women due to COVID-19.[1]

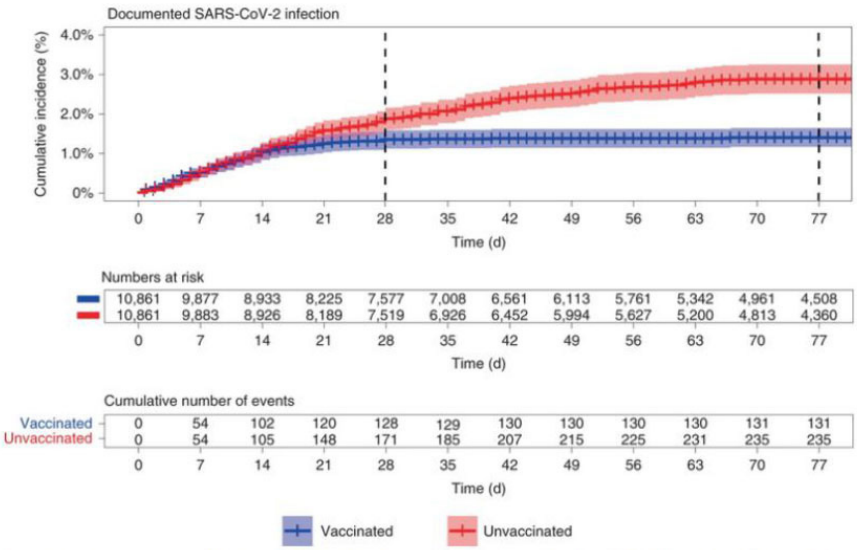
VACCINES FOR PREGNANT WOMEN

COVID-19 vaccine is established for pregnant women for preventing the worst infection by this virus in this population. High efficacy has been established in clinical trial research. The efficacy of mRNA vaccines, either Pfizer-BioNTech or Moderna vaccines were 95% and 94.1% respectively. Both vaccines could prevent

Outcomes	No of studies	Women (No with event/No in group (%))		Odds ratio (95% CI)	I^2 (%)
		Pregnant women with covid-19	Comparison group		
Comparison group: non-pregnant women of reproductive age with covid-19					
All cause mortality	4	16/8282 (0.2)	208/83 327 (0.2)	0.81 (0.49 to 1.33)	0
ICU admission	4	121/8276 (1.5)	758/83 330 (0.9)	1.62 (1.33 to 1.96)	0
Invasive ventilation	4	43/8276 (0.5)	226/83 330 (0.3)	1.88 (1.36 to 2.60)	0
ECMO	1	0/31 (0)	0/80 (0)	2.56 (0.05 to 131.60)	NE
Oxygen through nasal cannula	2	8/48 (16.7)	49/106 (46.2)	0.21 (0.04 to 1.13)	65.7
ARDS	1	0/17 (0)	0/26 (0)	1.51 (0.03 to 79.93)	NE
Major organ failure	1	0/17 (0)	0/26 (0)	1.51 (0.03 to 79.93)	NE
Comparison group: pregnant women without covid-19					
Maternal outcomes:					
All cause mortality	1*	5/427 (1.2)	0/694 (0)	18.08 (1.00 to 327.83)	NE
ICU admission	1*	40/427 (9.4)	1/694 (0.1)	71.63 (9.81 to 523.06)	NE
Preterm birth <37 weeks	2	7/44 (15.9)	18/295 (6.1)	3.01 (1.16 to 7.85)	0.9
Caesarean section	3*	184/491 (37.5)	577/1676 (34.4)	2.02 (0.67 to 6.10)	87.5
Perinatal outcomes:					
Stillbirth	1*	3/427 (0.7)	2/694 (0.3)	2.45 (0.41 to 14.71)	NE
Neonatal death	1*	2/427 (0.5)	1/694 (0.1)	3.26 (0.30 to 36.07)	NE
Admission to neonatal unit	1*	64/427 (15.0)	37/694 (5.3)	3.13 (2.05 to 4.79)	NE
Abnormal Apgar score at 5 minutes	1	0/30 (0)	12/740 (1.6)	0.96 (0.06 to 16.51)	NE
Fetal distress	1	3/34 (8.8)	12/242 (5.0)	1.86 (0.50 to 6.94)	NE

ICU=intensive care unit; ECMO=extracorporeal membrane oxygenation; ARDS=acute respiratory distress syndrome; NE=not estimable.
The denominator is number of pregnancies for all outcomes.
*Historical comparative cohort in UK Obstetric Surveillance System study.

Figure 1. Coronavirus disease outcomes in pregnant and lately pregnant women in 2019.[1]



Cumulative incidence curves of the documented infection outcome in pregnant women, CHS, 20 December 2020 through to 3 June 2021. The main line is the point estimate of the cumulative incidence and the shaded areas are the 95% CIs. The vertical lines at days 28 and 77 demarcate the period when an individual was considered 'fully vaccinated' in the manuscript (7 through to 56 d after receipt of the second dose). The curve represents the numbers at risk at each time point, along with the cumulative number of events. Each individual was included only once in each study group but individuals could move from the unvaccinated to the vaccinated group after receipt of the vaccine.

Figure 2. The incremental incidence of SARS-CoV-2 infection in pregnant women who had been vaccinated and matched controls.[7]

Pregnancy Complications†	Background Rate	V-safe Pregnancy Registry Overall
Gestational diabetes	7-14%	10%
Preeclampsia or gestational hypertension	10-15%	15%
Eclampsia	0.27%	0%
Intrauterine growth restriction	3-7%	1%
Neonatal Outcomes*	**Background Rate**	**V-safe Pregnancy Registry Overall**
Preterm birth	8-15%	9.4%
Congenital anomalies	3%	2.2%
Small for gestational age	3.5%	3.2%
Neonatal death	0.38%	0%

Figure 3. V-Safe gestational registry outcomes of interest in pregnant COVID-19 vaccinated women.[9]

the illness effectively after laboratory testing.[7] Meanwhile, inactivated vaccine (CoronaVac) is less effective than the mRNA vaccine. It was only 65.9 percent for COVID-19 prevention, 87.5 percent for inpatient hospital prevention, 90.3 percent for Intensive care unit admission prevention, and 86.3 percent for mortality prevention.[8] Therefore, the American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine on July 30, 2021, have been allowed several vaccines for pregnant women based on the previous studies that have been done.[9,10]

ANTIGENIC TARGET

A large surface spike of protein was found in the major antigenic target of the SARS-Cov-2 and MERS vaccine. The spike protein has emerged as the primary antigenic target for COVID-19 vaccine development during pregnancy. In general, it stimulates membrane fusion by binding to the angiotensin-converting enzyme 2 (ACE2) receptor on host cells. Study results that antibodies bound to the receptor-binding domain of the SARS-CoV-2 spike protein can prevent virus attachment and neutralization (P.0001).[11]

VACCINE EFFECTIVITY

The titer antibody of the vaccine among the nonpregnant population was equivalent to pregnant and lactating groups by the median was 5.74 (P=0.24).[11]

In the pregnancy and lactating phase after getting the second dose of the vaccine, established the median titer antibody of RBD-IgG was higher rather than before the vaccination. Furthermore, binding, neutralizing, and functional non-neutralizing antibody responses, as well as CD4 and CD8 T-cell responses, were performed under that condition.[12]

During a 77-day media follow-up, in the vaccination group, there were 131 infections, while the control group had 235 infections. were documented. After the first dose of the vaccine (around 14-20 days). The vaccine effectiveness was approximately 67% (95%CI = 40-84). The enhancement of titer after the first vaccination was performed. After re-evaluation on days 21-27 the titer was

71% (95%CI=33-94). The secondary dose also was done. It performed 96% (95%CI=89-100) in days 7-56. For the symptomatic patient, the estimation of the first dose vaccine (days 14-17) was 66% (95% CI = 32–86%). It increases after administering the second dose. The enhancement became 76% (95% CI=30–100) on days 21–27 and 97% (CI95%=91–100) on days 7–56. After 7–56 days of vaccination, vaccine effectiveness for COVID-19-related hospitalization was 89 percent (95 percent CI =43–100). Due to the small number of events, vaccine effectiveness for the other outcomes and periods could not be estimated meaningfully.[7]

A study related to the neonates that were born from the mother who was infected by the COVID-19 during pregnancy has been reported by Megan *et al*. In this study showed from 36 samples, all of the neonates were positive for anti-S IgG at high titers: 34 with a titer of > 250 U/mL and two with titers of 201 U/mL and 249 U/mL, respectively.[13]

VACCINE SAFETIES

There was no adequate evidence of adverse events for the fetus after the mother administered the COVID-19 vaccine. It also did not impact fetal development.[14] The study invivo did not find a harmful effect on the sample in pregnancy. Vaccine effectiveness for COVID-19-related hospitalization was 89 percent after 7–56 days of vaccination (CI95 % =43–100). Due to the small number of events, vaccine effectiveness for the other outcomes and periods could not be estimated meaningfully. Another supporting study has been declared by England public health that the state did not find any serious adverse events after administering the first dose vaccine of COVID-19 to 62.000 pregnant women. The same results were also reported by Scotland public health with 4000 pregnant women samples. Meanwhile, no long-term effects on babies born to women who received a COVID-19 vaccine during pregnancy have been studied, but because COVID-19 vaccines are made by not alive vaccines, it could not cause any infection, and other similar vaccines besides COVID-19 vaccine have been given during pregnancy phase for many years with no safety concerns. Another report stated that 133 women who received at least one dose of the COVID-19 vaccine during pregnancy had similar rates of adverse pregnancy outcomes (P>0.05 for all), including stillbirth (0.0 percent vs 0.3 percent), fetal anomalies (2.2 percent vs 2.7 percent), intrapartum pyrexia (3.7 percent vs 1.5 percent), and postpartum hemorrhage (9.8 percent (5.3 percent vs 5.4 percent) if it compared with the nonpregnant woman.[15]

Furthermore, no differences were discovered when pregnant women who participated in the v-safe pregnancy registry were compared to the baseline rates of adverse pregnancy outcomes (Figure 3). These systems will continue to collect evidence on this topic and will provide data for recommendations in the future.[9]

CONCLUSION

The vaccine has great benefits for the pregnant women population. Not only give protection for pregnant women but also the neonates who were just born from a vaccinated mother have antibodies to COVID-19. Studies also show there are no adverse effects to pregnancy and the fetus compared to the nonvaccine population. However, the long-term effect of this vaccine has not been known yet.

AUTHOR CONTRIBUTION

All authors have contributed substantially during the conception of the manuscript, gathering and analyzing related literature, drafting and revising the manuscript, giving final approval, and have agreed to be accountable.

CONFLICT OF INTEREST

None.

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