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Review

Covid-19 vaccine and its consequences in pregnancy: Brief review

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ABSTRACT

Pregnancy is linked to a higher incidence of severe Covid-19. It's critical to find safe vaccinations that elicit protective pregnant and fetal immune responses. This review summarises the rate of COVID-19 infection, maternal antibodies responsiveness, placenta antibody transmission, and adverse events after COVID-19 vaccination in pregnancy studied in epidemiological studies evaluating mRNA vaccines. Potential COVID-19 infection in pregnant women can be prevented using mRNA-based vaccinations. Gestation, childbirth, and perinatal mortality were proven unaffected by COVID-19 vaccination. Injection-site discomfort, tiredness, and migraine are the most prevalent side effects, but these are temporary. After the first dosage of vaccinations, fast antibody responses were demonstrated. The adaptive immunity is found to be more significant after booster vaccination, and is linked to improved placental antigen transmission. Two vaccination doses are associated with more robust maternal and fetal antibody levels. Longer delays between the first immunization dosage and birth are linked to greater fetal IgG antibody levels with reduction in antigen transmission proportion. The mRNA vacciness are effective in reducing the severity of COVID-19 infection and these vaccinations are regarded to be safe options for pregnant women and their unborn fetus.

1. Introduction

COVID-19 infection in pregnancy leads to expansion of the respiratory tract and increases the susceptibility of expectant mother for acquiring respiratory diseases [1]. A pro-inflammatory stage is more evident during the first trimester where embryonic and placental implantation occur, as well as within the third trimester for adaptation towards delivery [2]. In particular, cytokine outbursts production is linked to acute COVID-19. This pro-inflammatory stage of gestation throughout the first and third trimesters rendered pregnant women to be more susceptible for more severe presentations of COVID-19 infection. Although the majority of pregnant mothers experienced mild to moderate symptoms with COVID-19 infection, the illness is more severe in this group compared to non-pregnant females, with a higher risk of hospitalization. Most of the hospitalized expectant mothers with COVID-19 infection were asymptomatic, allowing the virus to spread unnoticed [3]. This demonstrates the importance of effective measure that halt the viral transmission from one person to another.

One of the most effective public health measures to counter the spread of communicable diseases is through vaccination. The main goal of nationwide vaccination programs is to accomplish the desired herd immunity, but only if high vaccination rate is achieved [4]. mRNA vaccine, Moderna and Pfizer–BioNTech, are proven to be effective in preventing and reducing the severity of COVID-19 infections. However, the evidence on mRNA vaccines' safety profile and effectiveness during pregnancy are gradually emerging [5].

This brief review intends to summarise the rate of COVID-19 infection, maternal antibodies responsiveness, placenta antibody transmission, and adverse events after COVID-19 vaccination in pregnancy. The data involved the outcomes of epidemiological studies that evaluated two different mRNA vaccines; Pfizer–BioNTech vaccine and Moderna vaccine. The outcomes from this review should help to enhance the understanding on COVID-19 vaccination during pregnancy for assisting healthcare professionals on counselling expectant mothers.

1.1. COVID-19 infection after vaccination

After 14 days of receiving the Pfizer–BioNTech vaccine, 0.18% (4/2136) of expectant mothers had COVID-19 infection, while 0.51% (11/2136) acquired COVID-19 infection within 2 weeks of vaccination.

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Around 0.5% (9/1822) of pregnant women who received Moderna vaccine developed COVID-19 infection within 14 days of vaccination and 0.5% (9/1822) after 2 weeks of receiving this vaccine [6]. More than halved of these pregnant women who were diagnosed with COVID-19 within 14 days of vaccination were traced to acquire the virus before receiving their first dose of vaccine. mRNA vaccines substantially decreased the probability of acquiring COVID-19 infections in expectant mothers.

1.2. Antibody reaction in mothers

Antibodies responses are rapidly developed following vaccination, but such desired effect is not seen with natural infection as the latter tends to produce more gradual responses. This concept is applied for acquiring improved reactions with booster vaccine administration. In pregnancy, following vaccination, the rise in the concentration of IgG and IgM antibodies against COVID-19 were observed considerably [7]. In majority, IgG seroconversion was found to predominate in these pregnant women, but IgM seroconversion was seen, albeit in a much smaller proportion.

The IgG against spike (both S1 and S2) and RBD proteins are produced in response to COVID-19 vaccine, whereas IgG towards spike (both S1 and S2) RBD and neutralising proteins are generated after infected with COVID-19 [8]. In 72% of expectant mothers, COVID-19 vaccination has led to IgG and IgM antibodies production, in which 14% generated IgG only antibody with remaining 14% had immeasurable IgG or IgM antibody levels. After receiving the first dose of vaccine, the spike-IgG and RBD-IgG titers grew fast, but these levels are more significant with the second dose compared to the initial one.

S1-IgG and RBD-IgG levels are greater in expectant mothers after vaccinated [9]. On the other hand, infected pregnant women had greater titres of S2-IgG and neutralising-IgG antibodies. The spike-IgG level was 22.814.5AU in pregnant women who had flu-like symptoms compared to the spike-IgG level of 0.040.05 AU among expected mothers who were asymptomatic after COVID-19 vaccination. The median RBD-IgG levels were 27601 AU and 1321 AU respectively with neutralising-IgG antibody titres of 900 AU and 150 AU in the vaccinated and infected pregnant women correspondingly. On the other hand, among non-pregnant females, the median RBD-IgG titers were 38000 among those who were vaccinated but only 800 AU in infected individuals, with corresponding neutralising-IgG levels of 900 AU and 200 AU, respectively.

1.3. Transfer of antibodies

Following COVID-19 vaccination, the antibodies produced are transferred to the fetus. Maternal and fetal antibodies in blood were demonstrated to be almost comparable [10]. The blood plasma concentration of IgG antibodies was discovered at 1.31 U/mL among expectant mothers receiving the second dose of Pfizer–BioNTech vaccine and one dose of Moderna vaccine. The IgG antibodies were found in 98.5% of newborns born to mothers that had completed two doses of Pfizer–BioNTech vaccination. On contrary, 43.6% of newborns of mothers that had one dose of Pfizer–BioNTech vaccine demonstrated evidence of COVID-19 specific IgG antibodies in their blood [11].

Both RBD-IgG and neutralising-IgG antibodies were found in the fetal blood samples. The maternal and fetal (cord) blood plasma levels of RBD-IgG antibody were measured around 15000 AU and 20000 AU with neutralising-IgG antibody titre of 1000 AU and 300 AU correspondingly after COVID-19 vaccination [12].

Aside from the number of vaccine dosages, the time between the vaccination and birth was found to be associated to the levels of IgG antibodies titres and its transfer ratio [13]. A higher IgG transfer ratio is associated with longer duration of completed vaccination to childbirth. Transfer ratio, calculated by dividing the IgG antibody concentration in fetal cord blood with the IgG antibody concentration in maternal blood, of spike-IgG antibody was reported to be almost halved (transfer ratio of 0.45).

1.4. Adverse reactions

The safety of COVID-19 vaccination is the primary concern for both the expectant mothers and clinicians. According to a poll conducted in 16 countries, pregnant mothers were less inclined to accept vaccinations for themselves [14]. Despite the established report of COVID-19 vaccination delivering up to 90% effectiveness, approximately three-quarter of non-pregnant women agreed for vaccination, compared to around 50% of pregnant women. One significant predictor of vaccination uptake was the trust in the vaccination efficacy and safety. Surprisingly, vaccine safety was not considered as a significant contributing factor in both pregnant and non-pregnant women.

It should be noted that unpleasant responses and adverse events affect both expectant mothers and non-pregnant women [15]. In both the Moderna and Pfizer–BioNTech vaccinations, injection-site discomfort is the most prevalent complication in pregnant mothers. After the Pfizer–BioNTech vaccine, up to 84% and 89% of expectant mothers who received one and two doses respectively, have reported injection-site discomfort [16]. For the Moderna vaccination, 93% and 96% had injection-site discomfort after the first and subsequent doses, correspondingly. In another study, 88% of pregnant women complained of injection-site discomfort after the first dosage and 57% after the second dose. In contrast, following the first and second vaccination doses, 75% of non-pregnant females reported similar adverse event. Sore shoulders or discomfort were reported in 97% of expectant mothers and 90% of non-pregnant women after receiving the Moderna and Pfizer–BioNTech vaccinations.

The incidence of systemic adverse reactions increased following the second dose of vaccination in Moderna and Pfizer–BioNTech vaccinations [17]. Tiredness, migraines, shivers, malaise, rash, and vomiting were among the most commonly reported systemic side effects. In most cases, these were temporary and rarelt lasted beyond three days. Compared to the first dosage, the frequency for these systemic adverse reactions to occur was significantly higher following the second dosage. In terms of numbers, the Moderna vaccination group had more people who had these systemic side effects than the Pfizer-BioNTech category.

Vaccination does not affect the gestation or delivery when compared to unvaccinated expectant mothers. There were no demonstrable significant differences on the frequency of gestational hypertension or thrombosis between vaccinated and unvaccinated pregnant women [18]. Looking from the delivery perspective, there were no significant negative impact on the incidence of premature birth, endometrial break, or unexpected ICU hospitalization among vaccinated expectant mothers [19].

2. Limitations of review

This review, albeit its attempt to compile as much evidence as possible, is not without limitations. Firstly, the gathering of evidence for the review was conducted in the absence of systematic literature search and methodological quality assessment. Therefore, the review lacks its ability to provide clear recommendations as one would have expected with systematic review or scoping review articles. Nevertheless, the evidence included remained as the few available studies that were conducted among pregnant females which provide required safety and effectiveness profile on the mRNA vaccines for combating COVID-19. Secondly, the review covered several key topics of concern on the use of this vaccine in this particular vulnarable group. Although the review is not solely focusing on a single safety profile or exploring on a specific angle of vaccine's efficacy, the presented brief data has strong inclined towards the use of vaccine. Thirdly, the included literature are primarily observational studies performed in specific regions of the world. A major pondering question is for clinicians to consider and expect similar

outcomes for recommending this vaccine to pregnancy women within countries having completely different genetic make-up and cultural beliefs. Even so, considering the grieve complications from COVID-19 infection in pregnancy, the evidence from this review could further heightened the needs for recommending this vaccine to expectant mothers.

3. Conclusion

As randomised controlled trials on COVID-19 vaccination in pregnancy is lacking, the resultant derived outcomes are purely observational from epidemiological studies evaluating mRNA vaccines. mRNA vaccines are proven to be beneficial in deterring COVID-19 in pregnant women and demonstrated the ability to induce antibody reactions in this vulnarable population and their unborn fetus. It is highly recommended for pregnant women to receive two doses of vaccination and achieve completion earlier aiming for higher levels of antibody titres and transfer ratio. The mRNA vaccine is primarily safe for expectant mothers and common adverse reactions are similar with non-pregnant individuals including fever and injection-site discomfort. There is no evidence that COVID-19 vaccination affects gestation, birth, or birth complications.

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Author contribution

Nang Kham Oo Leik: First Author, writing the paper.

Fatimah Ahmedy: Corresponding author, review and revise the paper for submission.

Rhanye Mac Guad: revising the structure of the write up.

Dg Marshitah Pg Baharudin: data/evidence collection.

Consent

Acquiring consent from patients is not relevant for this article.

Registration of Research Studies

Registration of research studies is not relevant for this article.

Guarantor

Nang Kham Oo Leik.

Declaration of competing interest

No potential conflict of interest relevant to this article was reported.

References

[1] K.J. Gray, E.A. Bordt, C. Atyeo, E. Deriso, B. Akinwunmi, N. Young, et al., Coronavirus disease 2019 vaccine response in pregnant and lactating women: a cohort study, Am. J. Obstet. Gynecol. 26 (2021), https://doi.org/10.1016/j.ajog.2021.03.023. S0002-9378(21)00187-3.

[2] J. Allotey, E. Stallings, M. Bonet, M. Yap, S. Chatterjee, T. Kew, et al., Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis, BMJ 370 (2020) m3320, https://doi.org/10.1136/bmj.m3320.

[3] L.D. Zambrano, S. Ellington, P. Strid, R.R. Galang, T. Oduyebo, V.T. Tong, et al., Update: characteristics of symptomatic women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status - United States, January 22-October 3, 2020, MMWR Morb. Mortal. Wkly. Rep. 69 (44) (2020) 1641–1647, https://doi.org/10.15585/mmwr.mm6944e3.

[4] H. Randolph, L. Barreiro, Herd immunity: understanding COVID-19, Immunity 52 (5) (2020) 737–741, https://doi.org/10.1016/j.immuni.2020.04.012.

[5] F. Polack, S. Thomas, N. Kitchin, J. Absalon, A. Gurtman, S. Lockhart, et al., Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine, N. Engl. J. Med. 383 (27) (2020) 2603–2615, https://doi.org/10.1056/NEJMoa2034577.

[6] E.D. Shanes, S. Otero, L.B. Mithal, C.A. Mupanomunda, E.S. Miller, J.A. Goldstein, Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccination in pregnancy: measures of immunity and placental histopathology, Obstet. Gynecol. (2021), https://doi.org/10.1097/AOG.0000000000004457, 10.1097/AOG.0000000000004457.

[7] M. Prabhu, E.A. Murphy, A.C. Sukhu, J. Yee, S. Singh, D. Eng, et al., Antibody Response to SARS-CoV-2 mRNA Vaccines in Pregnant Women and Their Neonates, bioRxiv, 2021 (preprint), 2021.04.05.438524.

[8] K.J. Gray, E.A. Bordt, C. Atyeo, E. Deriso, B. Akinwunmi, N. Young, et al., Coronavirus disease 2019 vaccine response in pregnant and lactating women: a cohort study, Am. J. Obstet. Gynecol. 26 (2021), https://doi.org/10.1016/j.ajog.2021.03.023. S0002-9378(21)00187-3.

[9] G. Mor, The unique immunological and microbial aspects of pregnancy, Nat. Rev. Immunol. 17 (2017) 469–482, https://doi.org/10.1038/nri.2017.64.

[10] L. Gill, C.W. Jones, Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibodies in neonatal cord blood after vaccination in pregnancy, Obstet. Gynecol. 137 (5) (2021) 894–896, https://doi.org/10.1097/AOG.0000000000004367.

[11] A. Rottenstreich, G. Zarbiv, E. Oiknine-Djian, R. Zigron, D.G. Wolf, S. Porat, Efficient maternofetal transplacental transfer of anti-SARS-CoV-2 spike antibodies after antenatal SARS-CoV-2 BNT162b2 mRNA vaccination 3 (2021) ciab266, https://doi.org/10.1093/cid/ciab266.

[12] O. Beharier, R. Plitman Mayo, T. Raz, K. Nahum Sacks, L. Schreiber, Y. Suissa-Cohen, et al., Efficient maternal to neonatal transfer of antibodies against SARS-CoV-2 and BNT162b2 mRNA COVID-19 vaccine, J. Clin. Invest. (2021) 150319, https://doi.org/10.1172/JCI150319.

[13] L.B. Mithal, S. Otero, E.D. Shanes, J.A. Goldstein, E.S. Miller, Cord blood antibodies following maternal coronavirus disease 2019 vaccination during pregnancy, Am. J. Obstet. Gynecol. 1 (2021), https://doi.org/10.1016/j.ajog.2021.03.035. S0002-9378(21)00215-5.

[14] M. Skjefte, M. Ngirbabul, O. Akeju, D. Escudero, S. Hernandez-Diaz, D. Wyszynski, et al., COVID-19 vaccine acceptance among pregnant women and mothers of young children: results of a survey in 16 countries, Eur. J. Epidemiol. 36 (2) (2021) 197–211, https://doi.org/10.1007/s10654-021-00728-6.

[15] F. Polack, S. Thomas, N. Kitchin, J. Absalon, A. Gurtman, S. Lockhart, et al., Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine, N. Engl. J. Med. 383 (27) (2020) 2603–2615, https://doi.org/10.1056/NEJMoa2034577.

[16] R.A.K. Kadali, R. Janagama, S.R. Peruru, S. Racherla, R. Tirumala, R.R. Madathala, et al., Adverse effects of COVID-19 messenger RNA vaccines among pregnant women: a cross-sectional study on healthcare workers with detailed self-reported symptoms, Am. J. Obstet. Gynecol. 10 (2021), https://doi.org/10.1016/j.ajog.2021.06.007. S0002-9378(21)00638-4.

[17] T.T. Shimabukuro, S.Y. Kim, T.R. Myers, P.L. Podo, T. Oduyebo, L. Panagiotakopoulos, et al., Preliminary findings of mRNA Covid-19 vaccine safety in pregnant persons, N. Engl. J. Med. 384 (24) (2021) 2273–2282, https://doi.org/10.1056/NEJMoa2104983.

[18] M.B. Cavalcante, C.T. Cavalcante, M. Sarno, R. Barini, J. Kwak-Kim, Maternal immune responses and obstetrical outcomes of pregnant women with COVID-19 and possible health risks of offspring, J. Reprod. Immunol. (2020 Nov 19) 103250.

[19] R.N. Theiler, M. Wick, R. Mehta, A. Weaver, A. Virk, M. Swift, Pregnancy and Birth Outcomes after SARS-CoV-2 Vaccination in Pregnancy, medRxiv, 2021 (preprint), 2021.05.17.21257337.