Scientific Foundation SPIROSKI, Skopje, Republic of Macedonia
Open Access Macedonian Journal of Medical Sciences. 2023 Jan 03; 11(B):134-140.
https://doi.org/10.3889/oamjms.2023.11237
eISSN: 1857-9655
Category: *B - Clinical Sciences*
Section: *Gynecology and Obstetrics*

Mother's Pregnancy Trimester Does Not Affect the Differences of IgG SARS-COV-2 Antibody Levels in Pregnant Women after mRNA and Inactivated Coronavirus Disease 2019 Vaccination

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Edited by: Mirko Spiroski
Citation: Anwar AD, Adriansyah PNA, Channel IC, Nugrahani AD, Febriani F, Surachman A, Santoso DPJ, Pramatirta AY, Handono B. Mother's Pregnancy Trimester Does Not Affect the Differences of IgG SARS-COV-2 Antibody Levels in Pregnant Women after Mrna and Inactivated Coronavirus Disease 2019 Vaccination. Open Access Maced J Med Sci. 2023 Jan 03; 11(B):134-140. https://doi.org/10.3889/oamjms.2023.11237
Keywords: COVID-19; IgG SARS-CoV-2; Inactivated vaccine; mRNA vaccine; Pregnancy trimester
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Received: 09-Nov-2022
Revised: 12-Nov-2022
Accepted: 26-Nov-2022

Funding: This research did not receive any financial support
Competing Interests: The authors have declared that no competing interests exist

Abstract

BACKGROUND: Since pregnancy increases the risk of coronavirus disease 2019 (COVID-19) and its morbidity in pregnant women, it is necessary and recommended to prevent COVID-19 in pregnant women by vaccination such as by messenger RNA (mRNA) and inactivated vaccines. SARS-CoV-2 antibodies produced from vaccination have different results according to the type of vaccine given. The previous studies showed that IgG SARS-CoV-2 antibody levels were influenced by various factors such as gestational weeks at the time when vaccines were given. Moreover, there have been no previous studies on the effect of gestational age on quantitative IgG levels after the second dose of the vaccine especially in Indonesia during this pandemic due to some restrictions on daily activities.

AIM: The aim of this study is to see the effect of giving the COVID-19 vaccine based on maternal gestational age (in trimester units) on maternal immunity (IgG SARS-CoV-2) in Dr. Hasan Sadikin General Hospital Bandung, Bandung Kiwari Hospital and Dr. Slamet Hospital, Garut.

METHODS: This was a retrospective and cohort study by taking secondary data using consecutive sampling from the previous tests on the levels of SARS-CoV-2 IgG antibodies after two doses of inactivated vaccine and mRNA. Healthy pregnant women 14–34 weeks at the Department of Obstetrics and Gynecology, Dr. Hasan Sadikin (RSHS) Bandung, Bandung Kiwari Hospital, and Dr. Slamet Hospital for the period October 2021 to January 2022 were the target population of this study. Based on inclusion and exclusion criteria, 103 samples met the criteria. Examination of Maternal SARS-CoV-2 IgG Antibody Levels procedures was carried out using *Chemiluminescent Microparticle Immunoassay*. Statistical analysis was done using IBM SPSS 28.00 and $p < 0.05$ was considered statistically significant.

RESULTS: There was no significant difference ($p = 0.236$, $p > 0.05$) between the mean maternal age in the mRNA and inactivated vaccine groups. The mRNA and inactivated vaccine groups also had no significant difference in the gestational age category (0.70). There was a significant difference ($p = 0.0001$) between the levels of SARS-CoV-2 IgG antibodies after the vaccine in the mRNA and inactivated vaccine groups. There was no significant difference in the levels of SARS-CoV-2 IgG antibodies in the gestational age group after the mRNA vaccine ($p = 0.426$) and after the inactivated vaccine ($p = 0.293$). There was a significant difference ($p < 0.05$) in the subgroup analysis in each gestational age group (second trimester and third trimester) between SARS-CoV-2 IgG antibody levels after the mRNA vaccine compared to inactivated vaccine.

DISCUSSIONS: The mRNA vaccine is based on the principle that mRNA is an intermediate messenger to be translated to an antigen after delivery to the host cell via various routes. However, inactivated vaccines contain viruses whose genetic material has been destroyed by heat, chemicals, or radiation, so they cannot infect cells and replicate but can still trigger an immune response. The administration of the vaccine in the second and third trimesters of pregnancy has the same results in increasing levels of SARS-CoV-2 IgG antibodies after mRNA and inactivated vaccination in this study.

CONCLUSIONS: mRNA vaccination in pregnant women is better than inactivated vaccines based on the levels of IgG SARS-CoV-2 antibodies after vaccination. The maternal trimester of pregnancy was not a factor influencing the levels of SARS-CoV-2 IgG antibodies after either mRNA or inactivated COVID-19 vaccinations in this study.

Introduction

Coronavirus disease 2019 (COVID-19) is a pandemic causing an increase in deaths worldwide. The side effects of this pandemic are destroying various sectors of society and causing social and economic problems throughout the country. Emergency handling in the management of COVID-19 is carried out by all countries, including developing safe and effective vaccines for use [1]. Data from the World Health Organization (WHO) on May 18, 2022, showed as many as 520,102,852 confirmed cases with a total death of 6,268,956 people. On February 16, 2022, the WHO data stated that there were 4.9 million confirmed cases of COVID-19 in Indonesia, with a total death of 145,622 cases [2], [3].

Data from the Centers for Disease Control on May 16, 2022, in the United States, showed that as many as 208,937 pregnant women were affected by COVID-19 and more than 297 cases of death. Data from the *Perkumpulan Obstetri dan Ginekologi Indonesia* (POGI) show that from April 2020 to April 2021, 536 pregnant women with COVID-19 were found. In January–July 2021, there were 205 cases of pregnant women with COVID-19 at Hasan Sadikin Hospital. The number of cases of pregnant women who died from COVID-19 was 14 cases [4].

There is currently no specific treatment for COVID-19. The effective eradication to date is to increase global COVID-19 vaccination coverage. Since the end of 2020, the COVID-19 vaccine has begun to be developed. Research shows that vaccines can reduce mortality from COVID-19 and can overcome the pandemic. To date, 10 billion vaccinations have been carried out worldwide, and most do not cause complications [5].

Research shows an increased risk of pregnant women with COVID-19 compared to non-pregnant women of reproductive age. Changes in immunological responses and physiological adaptations cause pregnant women to be a vulnerable group infected with COVID-19. Several examples of cases in the previous treatment of coronavirus (SARS-CoV and MERS-CoV) and several cases of COVID-19, it is believed that pregnant women with comorbidities have a higher risk of suffering from severe symptoms, morbidity, and mortality than the general population [3]. Pregnant women with COVID-19 increase the risk of intensive care and invasive ventilation [6]. Therefore, it is necessary to prevent COVID-19 in pregnant women, one of which is vaccination. Recommendations for giving the SARS-CoV-2 vaccine to pregnant and lactating women have been approved by the WHO and POGI, although data and research are still limited to date [1], [7]. In the United States, during February 2022, 198,000 pregnant women received the COVID-19 vaccine. Most pregnant women received messenger RNA (mRNA) vaccines (Pfizer–BioNTech BNT162b2 and Moderna mRNA-1273) [8].

mRNA and inactivated vaccines have been mass-developed and used worldwide, including in Indonesia. The WHO recommends the use of both vaccines for pregnant women. Indonesia, through the Ministry of Health (Kemenkes) and POGI, has also issued recommendations for the use of these two vaccines in pregnant women [9], [10].

Research shows that inactivated vaccines have an efficacy of 65.3% in Indonesia [11]. The effectiveness of the inactivated SARS-CoV-2 vaccine in pregnant women is expected to be comparable to that of non-pregnant women in the same age group. CoronaVac inactivated vaccine has also been shown to produce an antibody response in the form of RBD-specific binding antibody at 28 days after vaccination [12]. Further studies are needed to evaluate the safety and immunogenicity of administering inactivated vaccines to pregnant women [7], [13].

The mRNA vaccines widely used in Indonesia are mRNA-1273 (Moderna) and mRNA-BNT162b2 (Pfizer-BioNTech). The WHO issued the Emergency Use Listing for mRNA-1273 on April 30, 2021, and mRNA-BNT162b2 in December 2020. The mRNA-BNT162b2 and mRNA-1273 vaccines have been shown to have 95% and 94.1% efficacy, respectively [14]. The mRNA-1273 vaccine has been shown to produce an antibody response in the form of S protein and a T cell response, namely, CD4+ T cells [12]. The Current WHO data show that the benefits of administering mRNA vaccines outweigh the risks. With more and more types of vaccines available, priority groups can be vaccinated while considering national epidemiological data and other relevant considerations [14].

SARS-CoV-2 antibodies produced from vaccination have different results according to the type of vaccine given. A cohort study by Steensels *et al*. found that the increase in humoral immunogenicity after vaccination was significantly higher in the mRNA-1273 vaccine group (Moderna) compared to the BNT162b2 vaccine (Pfizer-BioNTech) [15], [16]. In research on vaccine clinical trials, pregnant women and lactating women are excluded from the study, so further research is needed on administering vaccines to pregnant women [10].

SARS-CoV-2 antibody levels are influenced by various factors. Kugelman *et al*.'s study found that maternal gestational age was associated with levels of SARS-CoV-2 antibodies produced after vaccination. However, research on things that affect SARS-CoV-2 antibody levels after vaccine administration to pregnant women is still very limited, especially in Indonesia and during this pandemic due to some restrictions on daily activities [17].

The WHO states, Herd immunity is one way to deal with this pandemic becoming endemic. Herd immunity can be achieved if vaccine efficacy is 90% and vaccination coverage is 66% of the total population [18]. Indonesia, with its different geography, has difficulty increasing the coverage and distribution of this SARS-CoV-2 vaccination.

The literature search does not mention the best type of vaccine, but we can measure the immune response that occurs after the vaccine. One of the immune responses that arise is the level of antibodies produced after vaccination. Research on COVID-19 and COVID-19 vaccination in pregnant women at Hasan Sadikin Hospital is still not widely known. Moreover, there have been no previous studies on the effect of gestational age on quantitative IgG levels after the second dose of the vaccine. Based on this, the researchers wanted to conduct research on COVID-19 vaccination in pregnant women at Dr. Hasan Sadikin General Hospital and see the effect of giving the COVID-19 vaccine based on maternal gestational

age in trimester units on maternal immunity, which is represented in maternal IgG levels.

Methods

Research design

This was an observational study with a retrospective and cohort method by taking secondary data from the vaccine polyclinic and tracing the results of the previous tests on the levels of SARS-CoV-2 IgG antibodies after two doses of inactivated vaccine and mRNA. The secondary data were analyzed according to the type of variables that had been determined. Comparison between groups (group comparison) was done in a comparable period and is independent. Researchers collected data on risk factors, especially the gestational age at the time of vaccination. This type of research aimed to study the dynamics of the relationship between risk factors for pregnant women and antibody levels after receiving two doses of mRNA and inactivated vaccination. Risk factors and antibodies were observed and followed retrospectively over a period of time.

Research subjects

The subjects of this study were taken from secondary data of pregnant women in the second and third trimesters who were given inactivated and mRNA vaccination at the vaccine clinic of Dr. Hasan Sadikin General Hospital Bandung, Bandung Kiwari Hospital and Dr. Slamet Hospital, Garut during the period October 2021 to January 2022 that met the criteria of inclusion and exclusion. Healthy pregnant women 14–34 weeks at the Department of Obstetrics and Gynecology, Dr. Hasan Sadikin (RSHS) Bandung, Bandung Kiwari Hospital, and Dr. Slamet Hospital for the period October 2021 to January 2022 were the target population of this study. Those populations that completely received two doses of the SARS-CoV-2 vaccine, denied a positive history of COVID-19 in the past 3 months and a history of close contact with a family who were confirmed positive for COVID-19 in the past 3 months, with a singleton alive fetus, as well as had a precise address and telephone number that could be contacted were included in this study. However, subjects that had incomplete secondary data on SARS-CoV-2 IgG antibody levels after two-dose vaccination and uncontrolled comorbid history (chronic hypertension, diabetes mellitus or gestational diabetes, and immunosuppression) were excluded from the study.

Ethics

All methods were carried out in accordance with relevant guidelines and regulations after obtaining approval and recommendations from the Ethics Committee Review Board of Hasan Sadikin General Hospital – Faculty of Medicine, Universitas Padjadjaran with reference number LB.02.01/X.6.5 / 349/2021. Written informed consent was obtained from all patients. Patients were provided with written and verbal information about the study. The sample used in this study was secondary data from pregnant women who received two doses of vaccination at the Obstetrics and Gynecology department at the Hasan Sadikin Hospital in Bandung and the satellite/network hospital. Since data collection is done through secondary data, no complaints may arise.

Sampling methods

The sampling technique in this study was consecutive sampling. Researchers will select all subjects recorded in secondary data, apply the selection criteria, and then include them in the study until the required number of subjects is met, starting from October 2021 to January 2022. Consecutive sampling is the best and easiest type of non-probability sampling. Most clinical studies use this technique for subject selection. The research data were taken from secondary data of pregnant women in the second and third trimesters who were given mRNA and inactivated vaccination at the vaccine clinic of Dr. RSUP. Hasan Sadikin (RSHS) Bandung, RSUD Bandung Kiwari, and RSUD dr Slamet from October 2021 to January 2022. Based on the above formula, the minimum sample size in this study is 30 samples [19].

Laboratory examination

SARS-CoV-2 IgG is an immunoserological test for the qualitative and quantitative determination of IgG antibodies against SARS-CoV-2 in human serum. The study was carried out in the following manner: The samples taken by the main researcher were allowed to settle for 2 h at room temperature or stand for 1 night at 40°C before being centrifuged for 15 min at 1000×*g* at 2°C–8°C. The mother's blood serum was taken to check the levels of IgG SARS-CoV-2 antibodies. If the examination was not carried out immediately, the serum must be stored at a temperature of 15°C–25°C (2 days), 2°C–8°C (7 days), or −20°C (1 month). Research samples were sent on the same day from 07.00 to 21.00 (GMT+7). Outside those hours, the samples were stored by the main researcher in a refrigerator at a temperature of 2°C–8°C on a temporary sample storage device determined and given by the laboratory to the main researcher.

Examination of maternal SARS-CoV-2 IgG Antibody Levels procedures was carried out using *Chemiluminescent Microparticle Immunoassay* in the following manner: (1) Samples, paramagnetic microparticles coated with SARS-CoV-2 antigen, and assay diluent were combined and incubated. The IgG antibody against SARS-CoV-2 present in the sample

binds to the microparticles coated with the SARS-CoV-2 antigen. (2) Then, the mixture was washed, and the acridinium-labeled human anti-IgG conjugate was added to form the reaction mixture and incubated. (3) After the wash cycle, Pre-Trigger and Trigger Solution are added. The reaction results are measured in relative light units (RLU). There is a direct relationship between the amount of IgG antibody against SARS-CoV-2 in the sample and the RLU detected by the optical system. As an interpretation, IgG-SARS-CoV-2 level <50 AU/mL was considered non-reactive and IgG-SARS-CoV-2 level ≥50 AU/mL was considered reactive.

Results

The study was conducted with secondary data from pregnant women who received two complete doses of vaccination from October 2021 to January 2022 and obtained a total sample of 103 pregnant women who met the study inclusion criteria. A total of 47 pregnant women received the Sinovac vaccine (inactivated vaccine) 1st and 2nd doses, and 56 pregnant women received the Pfizer (mRNA) vaccine doses 1 and 2. 60.7%) in the mRNA group, 33 pregnant women (70%) in the inactivated group. Based on the two groups, data on the characteristics and levels of IgG SARS-CoV-2 were obtained for the two research groups.

Based on the Mann–Whitney test, there was no significant difference (p = 0.236, p > 0.05) between the mean maternal age in the mRNA and inactivated vaccine groups. The mRNA and inactivated vaccine groups also had no significant difference in the gestational age category (0.70) based on the independent *t*-test and BMI (p = 0.865) based on the Chi-square test. From the comparative analysis of the characteristics of the two groups above, it can be concluded that the two groups are the same or there is no difference in characteristics at the time of the initial examination. This shows that the two groups are the same or homogeneous, meaning that they are worthy of comparison and further hypothesis testing (Table 1).

Table 1: Characteristics of research subjects in the messenger RNA and inactivated vaccine groups

Variable	Group		p-value
	mRNA (n = 56)	Inactivated (n = 47)	
Maternal age			
Mean ± SD	29.05 ± 3.849	28.06 ± 5.844	0.236
Median	28.00	28.00	
Range (minimum–maximum)	21.00–39.00	17.00–41.00	
Gestational age (weeks)			
Mean ± SD	24.46 ± 5.24	24.87 ± 5.51	0.70
Median	24.00	24.00	
Range (minimum–maximum)	15.00–34.00	14.00–33.00	
BMI (kg/m^2), *n* (%)			
Low	6 (10.7)	4 (8.5)	0.865
Normal	34 (60.7)	24 (51.1)	
Overweight	13 (23.3)	13 (27.7)	
Obesity	3 (5.4)	6 (12.8)	

For numerical data, the *P* value was tested by unpaired *t*-test if the data were normally distributed with the alternative of Mann–Whitney test if the data were not normally distributed. Categorical data p value was calculated based on the Chi-square test with the alternative exact Fisher's test if the requirements of the Chi-square were not met. p < 0.05 was considered as statistically significant. mRNA: Messenger RNA, SD: Standard deviation, BMI: Body mass index.

There was a significant difference (p = 0.0001) between the levels of SARS-CoV-2 IgG antibodies after the vaccine in the mRNA and inactivated vaccine groups based on the Mann–Whitney test (Table 2).

Table 2: Comparison of severe acute respiratory syndrome coronavirus 2 immunoglobulin G antibody levels in pregnant women after second dose vaccination between the messenger RNA and inactivated groups

Variables	Group		p-value
SARS-CoV-2 IgG (AU/mL) antibody after vaccination	mRNA (n = 56)	Inactivated (n = 47)	
Mean ± SD	6 ± 13,355.43	2325.47 ± 6029.25	0.0001*
Median	18,434.90	977.40	
Range (minimum–maximum)	138.40–40,000.00	49.00–40,000.00	

For numerical data, the p value was tested by unpaired *t*-test if the data were normally distributed with the alternative of Mann–Whitney test if the data were not normally distributed. Categorical data p value was calculated based on the Chi-square test with the alternative exact Fisher's test if the requirements of the Chi-square were not met. p < 0.05 was considered as statistically significant. SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, IgG: Immunoglobulin G, mRNA: Messenger RNA, SD: Standard deviation.

Based on the Kruskal–Wallis test, there was no significant difference in the levels of SARS-CoV-2 IgG antibodies in the gestational age group after the mRNA vaccine (p = 0.426) and after the inactivated vaccine (p = 0.293). Therefore, the factor of gestational age (considered in trimester of pregnancy) did not affect the level of quantitative SARS-CoV-2 IgG antibodies after mRNA vaccination and was inactivated in this study (Table 3).

Table 3: Comparison of severe acute respiratory syndrome coronavirus 2 immunoglobulin G antibody levels after vaccine according to gestational age (in trimester) in each vaccine group

Gestational age	SARS-CoV-2 IgG antibody levels (AU/mL) after vaccination			
category (trimester)	mRNA (n = 56)	p-value	Inactivated (n = 47)	p-value
2nd trimester	n = 37	0.426	n = 28	0.293
Mean ± SD	18,649.11 ± 14,091.17		2966.86 ± 7529.31	
Median	19,702.60		1040.25	
Range (minimum – maximum)	138.40–40,000.00		50.00–40,000.00	
3rd trimester	n = 19		n = 19	
Mean ± SD	15,530.65 ± 1878.87		1380.27 ± 2506.06	
Median	16,680.50		966.10	
Range (minimum – maximum)	237.90–40,000.00		49.00–1131.50	

The p value is tested by the ANOVA test if the data are normally distributed, with the alternative of the Kruskal–Wallis test if the data are not normally distributed. The value of significance is based on the value of p < 0.05. SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, IgG: Immunoglobulin G, mRNA: Messenger RNA, SD: Standard deviation.

There was a significant difference (p < 0.05) in the subgroup analysis in each gestational age group (second trimester and third trimester) between SARS-CoV-2 IgG antibody levels after the mRNA vaccine compared to inactivated vaccine based on the Mann–Whitney test (Table 4).

Discussion

The mRNA vaccine is based on the principle that mRNA is an intermediate messenger to be translated to an antigen after delivery to the host cell through various routes. The mRNA vaccine has the

Table 4: Comparison of severe acute respiratory syndrome coronavirus 2 immunoglobulin G antibody levels after messenger RNA vaccination versus inactivated according to gestational age (in trimester)

Gestational age category (trimester)	SARS-CoV-2 IgG antibody levels (AU/mL) after vaccination		p-value
	mRNA (n = 56)	Inactivated (n = 47)	
2nd trimester	n = 37	n = 28	
Mean ± SD	18,649.11 ± 14091.17	2966.86 ± 7529.31	0.0001*
Median	19,702.60	1040.25	
Range (minimum–maximum)	138.40–40,000.00	50.00–40,000	
3rd trimester	n = 19	n = 19	
Mean ± SD	15,530.65 ± 1878.87	1380.27 ± 2506.06	0.0001*
Median	16,680.50	966.10	
Range (minimum–maximum)	237.90–40,000.00	49.00–1131.50	

SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, IgG: Immunoglobulin G, mRNA: Messenger RNA, SD: Standard deviation.

active ingredient modRNA, which encodes the viral spike glycoprotein (S protein) of SARS-CoV-2, lipid (4-hydroxybutyl), (hexane-6,1-diyl), (ALC 3015), 2-[(polyethyleneglycol) -2000], salts such as potassium chloride and monobasic potassium phosphate, and finally sucrose. A spike protein around SARS-CoV 2 is used for migration into human cells. Thus, identifying the spike protein becomes a potential vaccine manufacturer and treatment target. Lipid nanoparticle (LNP)-based carriers effectively aid the delivery of mRNA into target cells and protect mRNA from RNase [20].

Vaccines that are injected through IM will contact muscle cells or antigen-presenting cells (APCs), such as dendritic cells or macrophages, through endocytosis. The mRNA molecule is removed from the LNP and translated to the S protein on the ribosome. Newly synthesized protein S is secreted into the extracellular space, internalized by endocytosis into APCs, and incorporated as part of the major histocompatibility complex (MHC) Class II antigen presentation complex to present antigens to immune cells, including T and B cells 132. S peptides are partially degraded by proteosomes inserted into the MHC Class I complex, then transported to the plasma membrane and presented as an antigen to immune cells [21].

The primary mechanism of immunization with mRNA vaccines is the humoral immune response through activating B cells. After naive B cells are activated by interacting with CD4+ T cells and CD40 ligation, the activated B cells will proliferate and differentiate into memory B cells or plasma cells that secrete antibodies in lymphoid organs. Newly activated high and low-affinity B cells will differentiate into short-lived plasma cells and quiescent memory B cells. After exposure to a secondary antigen, circulating antibodies produced from plasma cells will bind and neutralize the antigen, thereby preventing the antigen-carrying virus from infecting the target cell. Insufficient antibodies will activate good memory B cells to trigger a secondary immune response [21].

Inactivated vaccines contain viruses whose genetic material has been destroyed by heat, chemicals, or radiation, so they cannot infect cells and replicate but can still trigger an immune response. When the vaccine is given, the antigen is picked up by APCs and transported to the draining lymph nodes of the vaccinated person. The APC will place a piece of antigen, an epitope, on its surface along with a MHC molecule. These complexes can interact with and activate T cells, resulting in helper T cells stimulating an antibody-mediated or cell-mediated immune response and developing an antigen-specific adaptive response. This process creates an immunological memory against a specific pathogen and allows the immune system to respond more effectively and quickly after a subsequent encounter with a pathogen, by eliciting a secondary immune response to produce antibodies [22], [23].

The mRNA vaccine has its own advantages and disadvantages compared to other vaccine types. *In vivo*, mRNA vaccines use the host cell machinery to translate mRNA to the appropriate antigen, thereby stimulating both humoral and cellular immune responses. The mRNA vaccine can stimulate a good immune system because of its ability to mimic the nature of the intact pathogen without causing complications that can be caused by the presence of the intact pathogen. mRNA vaccines are produced by *in vitro* reactions between recombinant enzymes, ribonucleotide triphosphates, and DNA templates, so the production of mRNA vaccines tends to be simpler and faster when compared to whole-pathogen vaccines and subunit vaccines. Nucleoside modification can significantly improve mRNA stability and translational capacity, and LNPs are efficient carriers for delivering mRNA *in vivo*. These advances increase the number of spike proteins produced in cells that allow rapid uptake and expression in host cells and ultimately lead to strong humoral and cellular adaptive immune mechanism [21], [22].

In this study, there was no significant difference between the levels of SARS-CoV-2 IgG antibodies in the gestational age group after the mRNA vaccine ($p = 0.426$) and after the inactivated vaccine ($p = 0.293$). It can be concluded that the administration of the vaccine in the second and third trimesters of pregnancy has the same results in increasing levels of SARS-CoV-2 IgG antibodies after mRNA and inactivated vaccination in this study (Table 1). There have been no previous studies on the effect of gestational age on quantitative IgG levels after the second dose of the vaccine. Still, a study by Yang *et al*. found that maternal anti-spike IgG levels detected at delivery were not affected by the timing of vaccination during pregnancy. However, vaccination in the early third trimester was associated with the highest IgG levels in maternal and umbilical cord blood because of the close time to delivery [24].

In addition to efficacy, vaccine side effects are also a consideration for giving the COVID-19 vaccine to pregnant women. No previous studies have compared the side effects of COVID-19 vaccination with mRNA vaccines to inactivated vaccines in pregnant women. Both types of vaccines are generally well tolerated. Both can cause mild-to-moderate local and systemic

adverse reactions within the first 1–2 days, which generally resolve within a few days. Severe reactions such as anaphylaxis are rare.

Vaccination guidelines for pregnant women in America are based on the Advisory Committee on Immunization Practices (ACIP). According to ACIP, there is no evidence of a safety risk to the fetus or mother caused by inactivated, inactivated, or toxoid vaccines. As for live vaccines, several things must be considered so that giving live vaccines during pregnancy is avoided unless there is a high risk to the fetus and mother if exposed to the disease [25].

In addition to protecting the mother, the vaccine can protect the baby from infection with SARS-CoV-2. Pregnant women who receive the COVID-19 mRNA vaccine, the body will form antibodies against COVID-19, as in people who are not pregnant. Antibodies that are formed after pregnant women get the COVID-19 vaccine are also found in the umbilical cord bloodstream. This means that giving the COVID-19 vaccine during pregnancy is likely to provide protection to the baby from COVID-19 infection [24], [25]. Newborns acquire passive immunity by transferring IgA, IgM, and IgG antibodies across the placenta or secreted in breast milk. After being received by the neonate during breastfeeding, these immunoglobulins will provide mucosal immune protection by inhibiting the adhesion and invasion of pathogens [25]. Further studies should focus on delineating the timing of vaccination that optimizes antibody transfer through breast milk for newborns. In this study, there was no significant difference ($p > 0.05$) for side effects (injection site pain, redness at the injection site, headache, myalgia, fatigue, chills, and fever) in the mRNA vaccine group and the inactivated vaccine group based on the Chi-square test.

Limitation

This study is an observational study without any intervention. The number of samples in this study was limited, and the research was conducted by taking secondary data in three different places, and probably will resulting in many confounding variables that could not be removed. Confounding variables should be removed by randomization, but in this observational study, randomization could not be done.

Conclusion

mRNA vaccination in pregnant women is better than inactivated vaccines based on the levels of IgG SARS-CoV-2 antibodies after vaccination. The maternal trimester of pregnancy was not a factor influencing the levels of SARS-CoV-2 IgG antibodies after either mRNA or inactivated COVID-19 vaccinations in this study.

Availability of Data and Materials Section

The authors declare that the personal data from any patients involved in this study will not be shared based on patients' confidentialities.

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