VIA MEDICA

ORIGINAL PAPER / GYNECOLOGY

Ginekologia Polska
2024, vol. 95, no. 3, 200–205

ISSN 0017–0011, e-ISSN 2543–6767

DOI 10.5603/gpl.94997

Effect of mRNA COVID-19 vaccine on ovarian reserve of women of reproductive age

Serkan Kumbasar[1], Suleyman Salman[1], Gizem Nur Çakmak[1], Fatma Ketenci Gencer[1], Leal Selin Sicakyüz[1], Ayşe Nur Kumbasar[2]

[1]Department of Obstetrics and Gynecology, Gaziosmanpaşa Taksim Training and Research Hospital, Istanbul, Türkiye
[2]University of Health Sciences, Umraniye Training and Research Hospital, Istanbul, Türkiye

ABSTRACT

Objectives: To evaluate the effect of messenger ribonucleic acid (mRNA) vaccines developed for severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) on the ovarian reserve of women of reproductive age.

Material and methods: This prospective study was conducted between July and December 2022 in a tertiary care hospital affiliated with a university. A total of 117 patients were included in the study. The patients were divided into two groups. The first group (n = 62) consisted of women of reproductive age who received two doses of Pfizer-BioNTech COVID-19 vaccine administered 21 days apart. The control group (n = 55) included women with the same demographic characteristics who did not plan to be vaccinated. Hormonal values and basal antral follicle count were compared between two groups.

Results: The mean age of the study group was 26.3 ± 3.6 years, and the mean age of the control group was 25.4 ± 6.2 years (p = 0.332). In the vaccinated group, mean follicular stimulating hormone (FSH) on day 2 was 5.29 ± 2.28; luteinizing hormone (LH): 5.18 ± 1.3; E2: 46.43 ± 24.51; anti-Mullerian hormone (AMH): 4.17 ± 2.1; antral follicle count: 16.23 ± ± 8.04; right ovarian volume: 6.4 ± 1.7; left ovarian volume: 6.2 ± 2.1. FSH measured at D2 in the control group was 5.68 ± ± 1.89; LH: 5.22 ± 2.2; E2: 48.41 ± 27.12; AMH: 4.30 ± 1.74; number of antral follicles: 15.64 ± 9.04; right ovarian volume: 6.1 ± 1.8; left ovarian volume: 6.3 ± 1.4. There were no statistically significant differences for FSH, LH, E2, AMH, ovarian volume, and number of antral follicles on the second day of menstruation between the groups.

Conclusions: According to the results of the present study, the mRNA SARS-CoV-2 vaccine does not affect the ovarian reserve of patients.

Keywords: SARS-CoV-2 mRNA vaccine; AMH; ovarian reserve; COVID-19; fertility

Ginekologia Polska 2024; 95, 3: 200–205

INTRODUCTION

Upon the increase in the number of pneumonia cases in Wuhan, Hubei province of China in December 2019, it was determined that the causative agent of the outbreak was a type of RNA virus from the beta coronavirus group of coronaviruses. This virus spread rapidly, causing an outbreak across China, and then spreading to all continents of the world except Antarctica, causing a pandemic [1].

The severity of coronavirus disease 2019 (COVID-19) ranges from mild symptoms to severe illness requiring long-term respiratory support in intensive care, depending on the immune system's response to the disease. Therefore, the COVID-19 pandemic put enormous pressure on scientists to develop a safe and effective vaccine. The genetic sequence of the virus was determined at the beginning of the pandemic, and vaccine studies against the virus were started by many countries [2].

Cell entry by severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) is similar to that of SARS-CoV-1; the viral spike protein is first cut and shaped by a cell protease (TMPRSS2) on the host cell surface, and afterwards the shaped spike protein is recognized by the ACE-2 receptor and can enter the cell [3]. Angiotensin converting enzyme 2 (ACE-2) has been determined in many different organs,

Corresponding author:
Serkan Kumbasar
Department of Obstetrics and Gynecology, Gaziosmanpaşa Taksim Training and Research Hospital, Istanbul, Türkiye
e-mail: doktor1977@hotmail.com

Received: 4.04.2023 Accepted: 23.08.2023 Early publication date: 18.10.2023

including the respiratory tract, heart, kidney, ovaries, uterus, vagina, placenta, testis, and gastrointestinal tract [4]. Since ACE-2 is known to be expressed in the ovarian tissues of women of reproductive age, it is thought that SARS-CoV-2 infection may cause ovarian damage and impairment of ovarian function, leading to decreased oocyte quality, which may result in infertility or miscarriage [5].

The spike protein of the virus has been considered to be suitable for use as a presenting antigen in mRNA vaccines because the spike protein on the virus surface binds strongly to the ACE-2 receptor in the host cell and can enter the host cell [6]. The basic working principle of mRNA vaccines is based on the delivery of mRNA artificially synthesized to encode antigenic immunogens to the cytoplasm of the host cell within lipid nanoparticles [7]. Afterwards, the translation of the ribosome of the host cell with the transcript entering the cell takes place. Finally, the immunogenic proteins formed are expressed and presented at the cell membrane or released. It drives the production of viral S-protein in the host cells [8]. It has been investigated whether such a mechanism could negatively affect the integrity of the ovary [9, 10]

Although there have been studies on the effect of COVID-19 infection on ovarian reserve, the effect of mRNA vaccines developed for the COVID-19 pandemic on ovarian reserve is still unknown. Misinterpretation of the vaccine's biodistribution data has led to claims that the lipid nanoparticles contained in the mRNA vaccine are concentrated in the ovary and that the spike protein produced there will cause infertility. This type of misinformation about the COVID vaccine has contributed to vaccine hesitancy and strengthened the hand of anti-vaccination groups [11]. The safety of the vaccine was publicly questioned by various anti-vaccine groups [12]. Concerns that mRNA vaccines would negatively affect fertility in the future spread rapidly through social media, influencing individuals' decision-making and vaccination rates [13]. Women of reproductive age and their parents have been reluctant to get vaccinated because of concerns about reduced fertility in the future due to this non-evidence-based information. It is important to reduce concerns about vaccination and increase vaccination rates, especially in the young age group, which is a leading population in the spread of the disease in developing countries.

The aim of this study is to determine the effect of mRNA vaccines that were developed for the COVID-19 pandemic on ovarian reserve and thus to help inform the reproductive age group experiencing this common concern. For this purpose, we investigated the effects of the mRNA vaccine on ovarian reserve by looking at values such as antral follicle count, basal follicular stimulating hormone (FSH), E2, luteinizing hormone (LH) level, anti-Mullerian hormone (AMH), and ovarian volume in the vaccinated and non-vaccinated groups.

MATERIAL AND METHODS

This prospective cross-sectional study was initiated with ethical approval from the Ethics Committee of Gaziosmanpaşa Training and Research Hospital (date: 27/07/2022, NO: 100). All procedures done in the study complied with the ethical standards of the 1964 Declaration of Helsinki. Informed consent was obtained from the patients.

Including the 62 vaccinated and the 55 non-vaccinated groups, a total of 117 patients were included in the study. The study group included patients between the ages of 18 and 35 who were admitted to the gynecology outpatient clinic, who did not have COVID-19, had regular menstruation, had no current pregnancy, and had received the mRNA vaccine for SARS-CoV-2 in two doses (BioNTech) 21 days apart. The control group consisted of individuals who were not vaccinated, who did not have COVID-19, and who did not plan to be vaccinated.

Patients who were pregnant at the time of the study, had a history of infertility, comorbidities (hypo/hyperthyroidism, PCOS), genetic disorders (Turner syndrome, *etc.*), systemic chronic diseases (diabetes, kidney, heart, GIS, *etc.*), previous ovarian surgery, the presence of an ovarian mass (endometrioma), or use of any medication that could affect ovarian reserve were all excluded.

In the study group, blood was collected from the antecubital vein for the measurement of FSH, LH, estradiol and AMH in serum on the 3rd day of the menstrual cycle and at least three months after mRNA vaccination. Blood samples for FSH, LH, and estradiol measurements were analyzed by chemiluminescence (Advia Centaur XP, Siemens AG, Munich, Germany) without delay. Blood samples for AMH measurement were centrifuged within 30 minutes (10 minutes at 3000 rpm) and stored at –20°C. AMH was measured by the enzyme immunoassay method [Elabscience, USA, detection limit: 0.09 ng/mL; coefficient of variation (CV): < 10%]. On the same day, the number of antral follicles (2–10 mm) and ovarian volume were determined by transvaginal ultrasonographic evaluation. In the control group, FSH, LH, E2, and AMH levels were measured on the 3rd day of the menstrual cycle; ovarian size and number of antral follicles were evaluated by TVUSG. Ultrasonography was performed by a single operator. The total number of antral follicles measuring 2–10 mm in both ovaries was recorded. Ovarian volume was calculated automatically (length*width*depth*0.52 = = volume) by USG by accepting the two widest diameters of the ovary (length and width) and the diameter (depth) obtained by turning the probe 90 degrees in two dimensions. A basal serum E2 value of < 80 pg/mL and an FSH value of 5–10 mIU/mL on the 2nd–3rd day of menstruation indicate adequate ovarian reserve. FSH values between 10–15 mIU/mL indicate limited reserve, while FSH levels above this level and

Table 1. Comparison of socio-demographic characteristics of the cases

	Group 1 (the vaccinated group) n = 62	Group 2 (unvaccinated group) n = 55	p^a value
Age	26.3 ± 3.6	25.4 ± 6.2	0.3325
Gravidity	2.2 ± 1	2.4 ± 1	0.2825
Parity	1.4 ±1	1.3±1	0.5903
Body mass index (BMI)	23.4 ± 3.1	22.8 ± 2.2	0.2353
Smoking	15 (24.1%)	11 (20%)	0.5957
Menstruation frequency [days]	27.4 ± 4.6	26.2 ± 3.8	0.1296
Menstruation length [days]	4.9 ± 2.1	4.3 ± 2.3	0.1430
Educational status			
Primary school	24 (38.7)	25 (45.4)	
High school	27 (43.5)	26 (47.2)	p^b: 0.234862.
University	11 (17.7)	4 (7.2)	X^2: 2.8975.
Employment			
Not working (housewife)	50 (80.6%)	48 (87.2%)	p^b: 0.4721
Working	12 (19.3%)	7 (12.7)	X^2: 0.517
Marital status			
Married	47 (75.8%)	49 (89%)	p^b: 0.103
Single	15 (24.1%)	6 (10.9%)	X^2: 2.649

P^a a independent samples t-test; Continuous variables are expressed as mean ± standard deviation; P^b Yates corrected chi-square test or Pearson chi-square test were used

E2 values > 80 pg/mL are associated with poor reproductive outcomes [14].

The total number of antral follicles in bilateral ovaries is a useful measurement as an indicator of ovarian reserve and also AMH is considered the best biochemical marker of ovarian function in many clinical situations [15, 16]. We aimed to recruit women of reproductive age with and without vaccination to investigate the effects of vaccination on ovarian reserve by comparing ovarian reserve markers between the two groups.

Statistical analysis

The statistical evaluation of the data in this study was performed using the Statistical Package for the Social Sciences, version 15.0 (SPSS Inc., Chicago, IL, USA). The results were given as a mean standard deviation or as a number (percentage). Normally distributed variables between the groups were analyzed using the independent samples t-test, and non-normally distributed variables were analyzed using the Mann–Whitney U test. Nominal and categorical variables were evaluated with appropriate chi-square tests depending on the expected values. A value of $p < 0.05$ was considered statistically significant.

RESULTS

The study consisted of a total of 117 women. Group-1 included 62 people who received two doses of the mRNA (BioNTech) vaccine 21 days apart. Group-2 included 55 unvaccinated individuals. The demographic characteristics of the cases are shown in Table 1. No significant differences were found between the groups in terms of age, gravidity, parity, body mass index, smoking, educational status, marital status, employment status, or length and frequency of menstrual periods (Tab. 1). The groups were homogeneous in terms of specified characteristics.

The mean FSH value was 5.29 ± 2.28 mIU/mL, the mean E2 value was 46.43 ± 24.51 pg/mL, the mean LH value was 5.18 ± 1.3 mIU/ML, the mean basal antral follicle number was 16.23 ± 8.04, mean right ovarian volume 6.4 ± 1.7 cm, mean left ovarian volume 6.2 ± 2.1 cm, and AMH value was 4.17 ± 2.1 ng/mL in the vaccinated group. In Group-2 who were unvaccinated, the mean FSH value was 5.68 ± 1.89 mIU/mL, mean LH value was 5.22 ± 2.2 mIU/mL, mean E2 value was 48.41 ± 27.12.pg/mL, mean basal antral follicle count was 15.64 ± 9.04, mean right ovarian volume was 6.1 ± 1.8 cm, mean left ovarian volume was 6.3 ± 1.4 cm, and mean AMH value was 4.30 ± 1.74.ng/mL. There were no statistically significant differences between the groups in terms of ovarian reserve parameters ($p > 0.005$) (Tab. 2).

DISCUSSION

The pandemic caused by SARS-CoV-2, a novel coronavirus, is the most important health challenge of the 21st century. The humanitarian and economic impact of the COVID-19 pandemic has made it mandatory to develop next-generation vaccine technology platforms [17]. Before

Table 2. Comparison of ovarian reserve markers between the two groups

	Group 1 (the vaccinated group) n = 62	Group 2 (unvaccinated group) n = 55	p[a] value
Day 3 FSH levels (mIU/mL)[a]	5.29 ± 2.28	5.68 ± 1.89	0.3195
Day 3 LH levels (mIU/mL)[a]	5.18 ± 1.3	5.22 ± 2.2	0.9037
Day 3 estradiol levels (pg/mL)[a]	46.43 ± 24.51	48.41 ± 27.12	0.6790
AMH levels (ng/mL)	4.17 ± 2.1	4.30 ± 1.74	0.7181
Basal antral follicle count	16.23 ± 8.04	15.64 ± 9.04	0.7093
Ovarian volume			
Right ovarian volume	6.4 ± 1.7	6.1 ± 1.8	0.3560
Left ovarian volume	6.2 ± 2.1	6.3 ± 1.4	0.7655

[a]Baseline FSH and LH estradiol levels measured in hormone panel test at day three of menstrual period; AMH — anti-Mullerian hormone; FSH — follicular stimulating hormone; LH — luteinizing hormone; p[a] — Independent samples t-test; Continuous variables are expressed as mean ± standard deviation

the COVID-19 pandemic, it took an average of 10 to 15 years to develop a vaccine [18]. This period was shortened after the COVID-19 virus was isolated and the entire genome of the virus was made available to researchers. Next-generation mRNA vaccines which have been intensively researched based on genetic bases over the last two decades, could be produced cheaply in a short time for SARS-CoV-2 [19].

False and misleading claims, such as that these lipid particles containing mRNA spread throughout the body and accumulate particularly in the ovaries, have been advanced and discussed publicly by opponents of vaccination. Such unsubstantiated claims have caused a certain amount of fertility-related concern among the public. The biodistribution and persistence of LNP-mRNA vaccine formulations for COVID-19 and other diseases have been studied in rodents and primates. Animal studies have shown that the highest concentration of lipid nanoparticle mRNA remains at the injection site. This was followed by the liver (up to 21.5%) and much less in the spleen (≤ 1.1%), adrenal glands (≤ 0.1%), and ovaries (≤ 0.1%). Mean concentrations and tissue distribution patterns did not differ between genders [20, 21].

Bowman et al. [22] published in May 2021 the results of their study on the effects of mRNA vaccines on the reproductive function of female mice. They found no changes in mating, fertility, or the size and volume of the uterus and ovary in female mice after vaccination.

Jing et al. [4] reported in a review that COVID-19 does not only infect the female reproductive organs but can also infect the placenta via the ACE receptor. They suggested that COVID-19 can cause infertility and menstrual irregularities, as well as fetal distress in pregnant women. They therefore recommended that women with COVID-19 delay their pregnancies. The data on the impact of SARS-CoV-2 infection and SARS-CoV-2 mRNA vaccines on fertility and ovarian function in humans are limited. In a retrospective study published in 2021, no difference was found in the comparison of serum FSH and AMH levels in the follicular phase between 237 women after recovery of COVID-19 infection and the uninfected population [23] .

Mohr-Sasson et al. [24] investigated the effect of the mRNA COVID-19 vaccine on AMH, which is a marker of ovarian reserve in women of reproductive age. Their study group consisted of 129 women of reproductive age who received two mRNA vaccines 21 days apart. Subjects with ovarian failure, infertility treatment, pregnancy, previous mRNA vaccination, or COVID-19 infection were excluded from the study. Plasma AMH levels before vaccination and three months after the first vaccination were analyzed in different age groups. There was no significant difference in AMH levels before and after vaccination in all age groups. Also, Sason examined COVID-19 antibody levels in all vaccinated women at the end of three months and found no association between COVID-19 antibody levels and AMH levels. Therefore, Sason et al. stated in their study that SARS--CoV-2 mRNA vaccines were not associated with a decrease in ovarian reserve [24]. Similarly, Soysal et al. [25] studied the effect of mRNA vaccination on ovarian reserve. They compared AMH levels between the groups vaccinated with the mRNA vaccine and the unvaccinated group in their study. However, no significant difference was found between the AMH values of the vaccinated group and the control group after three months of vaccination in the study group. In our study, in addition to the ovarian reserve marker AMH, other ovarian reserve markers such as AFC (antral follicle count), basal FSH, basal LH, E2, and ovarian volume were compared between the mRNA vaccine group and the control group. A total of 117 cases were included in the study. The cases were selected from women of reproductive age without fertility problems. It was determined that there was no significant difference between the vaccinated and non-vaccinated groups according to parameters such as AFC, basal FSH, basal LH, E2, AMH, and ovarian volume.

There are also studies in the literature investigating the effect of the SARS-CoV-2 mRNA vaccine on IVF frequencies.

Bentov et al. [26] published in July 2021 the first study investigating the effects of mRNA vaccine in a cohort study of 32 patients with infertility and planned IVF. Group-1 (n = 9) included people who had received mRNA vaccine, group-2 (n = 9) included people who had COVID-19 infection, and group-3 (n = 14) included people who did not receive mRNA vaccine and did not have infection. As a conclusion of this study, it was observed that there was no deterioration in ovarian follicle quality and function in individuals with SARS--CoV-2 infection and mRNA vaccination [26]. Horowitz et al. compared AMH concentrations before and after vaccination in a group of 31 infertile patients undergoing IVF and found no significant difference [27]. Ortrento et al. [28] compared oocyte stimulation and embryologic characteristics before and after mRNA COVID-19 vaccination in an IVF patient group of 36 couples. In their study, they found no difference in the dose of gonadotropin used, peak estrogen and progesterone levels, number and quality of aspirated oocytes, fertilization rates, and embryo quality between IVF cycles in the same patient group before and after vaccination. In another study, they examined IVF treatment parameters and outcomes in 32 vaccinated and 22 non-vaccinated patients. Similar to the above results, no difference was found between the number of follicles formed, number of oocytes collected, oocyte quality, fertilization rates, and pregnancy rates in the vaccinated and non-vaccinated patient groups [29].

CONCLUSIONS

In this study, we aimed to estimate the effects of mRNA vaccines developed for COVID-19 on ovarian reserve and found that there was no significant difference between the vaccinated and unvaccinated groups in terms of ovarian reserve markers. The most important limitation of this study is the small number of cases, as in other published studies [24–29]. The second limitation of our study is the lack of long-term results of the mRNA vaccine on ovarian reserve functions. Additional studies with a larger number of cases and longer follow-up are required to determine the effect of the mRNA vaccine on ovarian reserve.

Article information and declarations

Acknowledgements

None.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Funding

None.

Conflict of interest

All authors declare no conflict of interest.

REFERENCES

1. Wang C, Horby PW, Hayden FG, et al. A novel coronavirus outbreak of global health concern. Lancet. 2020; 395(10223): 470–473, doi: 10.1016/S0140-6736(20)30185-9, indexed in Pubmed: 31986257.
2. Polack FP, Thomas SJ, Kitchin N, et al. C4591001 Clinical Trial Group. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. N Engl J Med. 2020; 383(27): 2603–2615, doi: 10.1056/NEJMoa2034577, indexed in Pubmed: 33301246.
3. Tu YF, Chien CS, Yarmishyn AA, et al. A review of SARS-CoV-2 and the ongoing clinical trials. Int J Mol Sci. 2020; 21(7): 2657, doi: 10.3390/ijms21072657, indexed in Pubmed: 32290293.
4. Jing Y, Run-Qian Li, Hao-Ran W, et al. Potential influence of COVID-19/ACE2 on the female reproductive system. Mol Hum Reprod. 2020; 26(6): 367–373, doi: 10.1093/molehr/gaaa030, indexed in Pubmed: 32365180.
5. Sun J. The hypothesis that SARS-CoV-2 affects male reproductive ability by regulating autophagy. Med Hypotheses. 2020; 143: 110083, doi: 10.1016/j.mehy.2020.110083, indexed in Pubmed: 32679425.
6. Hamming I, Cooper ME, Haagmans BL, et al. The emerging role of ACE2 in physiology and disease. J Pathol. 2007; 212(1): 1–11, doi: 10.1002/path.2162, indexed in Pubmed: 17464936.
7. Kowalzik F, Schreiner D, Jensen C, et al. mRNA-based vaccines. Vaccines (Basel). 2021; 9(4): 390, doi: 10.3390/vaccines9040390, indexed in Pubmed: 33921028.
8. Schoenmaker L, Witzigmann D, Kulkarni JA, et al. mRNA-lipid nanoparticle COVID-19 vaccines: Structure and stability. Int J Pharm. 2021; 601: 120586, doi: 10.1016/j.ijpharm.2021.120586, indexed in Pubmed: 33839230.
9. Reis FM, Bouissou DR, Pereira VM, et al. Angiotensin-(1-7), its receptor Mas, and the angiotensin-converting enzyme type 2 are expressed in the human ovary. Fertil Steril. 2011; 95(1): 176–181, doi: 10.1016/j.fertnstert.2010.06.060, indexed in Pubmed: 20674894.
10. Hamming I, Cooper ME, Haagmans BL, et al. The emerging role of ACE2 in physiology and disease. J Pathol. 2007; 212(1): 1–11, doi: 10.1002/path.2162, indexed in Pubmed: 17464936.
11. Morris R, Morris A, IL N. Exposure of ovaries to COVID-19 vaccination does not impair fertility. Fertility and Sterility. 2021; 116(3): e473, doi: 10.1016/j.fertnstert.2021.08.027.
12. Rameneni T, Sayeed T, Kumar S. A perspective on COVID-19 vaccine hesitancy in India. National Journal of Community Medicine. 2022; 13(07): 491–493, doi: 10.55489/njcm.130720221612.
13. Lamptey E. Overcoming barriers to COVID-19 vaccination of pregnant women. Gynecology and Obstetrics Clinical Medicine. 2022; 2(1): 29–33, doi: 10.1016/j.gocm.2022.01.007.
14. Buyalos RP, Daneshmand S, Brzechffa PR. Basal estradiol and follicle-stimulating hormone predict fecundity in women of advanced reproductive age undergoing ovulation induction therapy. Fertil Steril. 1997; 68(2): 272–277, doi: 10.1016/s0015-0282(97)81514-2, indexed in Pubmed: 9240255.
15. Hsu A, Arny M, Knee AB, et al. Antral follicle count in clinical practice: analyzing clinical relevance. Fertil Steril. 2011; 95(2): 474–479, doi: 10.1016/j.fertnstert.2010.03.023, indexed in Pubmed: 20434151.
16. Moolhuijsen LME, Visser JA. Anti-Müllerian hormone and ovarian reserve: update on assessing ovarian function. J Clin Endocrinol Metab. 2020; 105(11): 3361–3373, doi: 10.1210/clinem/dgaa513, indexed in Pubmed: 32770239.
17. Thanh Le T, Andreadakis Z, Kumar A, et al. The COVID-19 vaccine development landscape. Nat Rev Drug Discov. 2020; 19(5): 305–306, doi: 10.1038/d41573-020-00073-5, indexed in Pubmed: 32273591.
18. Kis Z, Shattock R, Shah N, et al. Emerging technologies for low-cost, rapid vaccine manufacture. Biotechnol J. 2019; 14(1): e1800376, doi: 10.1002/biot.201800376, indexed in Pubmed: 30537361.
19. Anderson EJ, Rouphael NG, Widge AT, et al. mRNA-1273 Study Group. Safety and immunogenicity of SARS-CoV-2 mRNA-1273 vaccine in older adults. N Engl J Med. 2020; 383(25): 2427–2438, doi: 10.1056/NEJMoa2028436, indexed in Pubmed: 32991794.
20. European Medicines Agency. Assessment Report EMA/707383/2020 Corr.1*: Comirnaty COVID-19 MRNA Vaccine (NucleosideModified); Assessment Report; European Medicines Agency: Volume 31, pp. 1–140 Amsterdam, The Netherlands, 2021.

21. 'European Medicines Agency. Assessment Report EMA/15689/2021 Corr.1*: Covid-19 Vaccine Moderna; European Medicines Agency: Volume 11, p. 169'. Amsterdam, The Netherlands, 2021.
22. Bowman CJ, Bouressam M, Campion SN, et al. Lack of effects on female fertility and prenatal and postnatal offspring development in rats with BNT162b2, a mRNA-based COVID-19 vaccine. Reprod Toxicol. 2021; 103: 28–35, doi: 10.1016/j.reprotox.2021.05.007, indexed in Pubmed: 34058573.
23. Li K, Chen Ge, Hou H, et al. Analysis of sex hormones and menstruation in COVID-19 women of child-bearing age. Reprod Biomed Online. 2021; 42(1): 260–267, doi: 10.1016/j.rbmo.2020.09.020, indexed in Pubmed: 33288478.
24. Mohr-Sasson A, Haas J, Abuhasira S, et al. The effect of Covid-19 mRNA vaccine on serum anti-Müllerian hormone levels. Hum Reprod. 2022; 37(3): 534–541, doi: 10.1093/humrep/deab282, indexed in Pubmed: 34935913.
25. Soysal Ç, Yılmaz E. The effect of COVID-19 vaccine on ovarian reserve. Saudi Med J. 2022; 43(5): 486–490, doi: 10.15537/smj.2022.43.5.20220007, indexed in Pubmed: 35537728.
26. Bentov Y, Beharier O, Moav-Zafrir A, et al. Ovarian follicular function is not altered by SARS-CoV-2 infection or BNT162b2 mRNA COVID-19 vaccination. Hum Reprod. 2021; 36(9): 2506–2513, doi: 10.1093/humrep/deab182, indexed in Pubmed: 34364311.
27. Horowitz E, Mizrachi Y, Ganer Herman H, et al. The effect of SARS-CoV-2 mRNA vaccination on AMH concentrations in infertile women. Reprod Biomed Online. 2022; 45(4): 779–784, doi: 10.1016/j.rbmo.2022.06.015, indexed in Pubmed: 35985956.
28. Orvieto R, Noach-Hirsh M, Segev-Zahav A, et al. Does mRNA SARS-CoV-2 vaccine influence patients' performance during IVF-ET cycle? Reprod Biol Endocrinol. 2021; 19(1): 69, doi: 10.1186/s12958-021-00757-6, indexed in Pubmed: 33985514.
29. Odeh-Natour R, Shapira M, Estrada D, et al. Does mRNA SARS-CoV-2 vaccine in the follicular fluid impact follicle and oocyte performance in IVF treatments? Am J Reprod Immunol. 2022; 87(5): e13530, doi: 10.1111/aji.13530, indexed in Pubmed: 35220640.