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Effect of COVID-19 mRNA vaccine on serum AMH, TSH, FSH and LH concentrations

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Abstract

The aim of our study is to evaluate the effect of COVID-19 vaccination on serum anti-Müllerian hormone (AMH) level and female reproductive system. The study included 111 women who applied to the infertility clinic between December 2020 and September 2022 and received two doses of COVID-19 mRNA vaccine (BNT162b2, - Pfizer-BioNTech). Serum hormone levels (anti-Müllerian hormone (AMH), Thyroid Stimulating Hormone (TSH), Follicle Stimulating Hormone (FSH), and Luteinizing Hormone (LH) hormones) of women before and after vaccination were evaluated and compared. Serum AMH level was 1.90±2.48 (mean ± SD) before vaccination and 1.87±2.16 (mean ± SD) after vaccination (p = 0.052). Although there was a minimal decrease in AMH levels, no statistically significant difference was detected. TSH, FSH and LH serum levels were similar before and after vaccination and no statistical difference was detected. Our study indicates that the COVID-19 mRNA vaccine does not have a negative effect on serum AMH, TSH, FSH and LH levels.

Keywords: anti-müllerian hormone , coronavirus disease-19, mRNA vaccine, infertility, ovarian reserve

1. Introduction

Coronavirus disease 19 (COVID-19), which has become a worldwide epidemic, has caused serious losses. The spike protein found in the SARS-CoV-2 capsule exerts its effect by binding to the angiotensin-converting enzyme 2 (ACE2) receptor on the host cell. This interaction affects the respiratory tract and lungs. The same interaction may occur in the ovary, uterus and placenta, thus suggesting that COVID-19 may have a negative impact on female reproduction (1-3). Vaccination is one of the most effective and low-cost methods to prevent the epidemic (4, 5). The thought that vaccination may have negative effects causes rejection of vaccination. In particular, the possibility of affecting fertility negatively affects individuals (6, 7). The SARS CoV 2 virus and the messenger ribonucleic acid (mRNA) vaccine use the S protein when entering the cell. Therefore, it is thought that both the virus and the vaccine may be harmful to the ovary (2).

Serum anti-Müllerian hormone (AMH) levels are used to evaluate ovarian reserve. AMH is a glycoprotein produced in the granulosa cells of the preantral and small antral follicles of the ovaries (8). Follicle-stimulating hormone (FSH) and Luteinizing hormone (LH) must also be present in serum at certain levels for regular menstrual cycles and fertility.

In our study, the Anti-Müllerian Hormone (AMH), Thyroid Stimulating Hormone (TSH), Follicle Stimulating Hormone (FSH) and Luteinizing Hormone (LH) hormones of female patients who applied to the infertility clinic due to suspicion of infertility were examined before and after the COVID-19 vaccine administration. We aimed to evaluate whether vaccination has a negative effect on fertility.

2. Materials and Methods

This study was conducted on women who applied to the Infertility polyclinic at Gazi Yaşargil Education and Research Hospital, Department of Obstetrics and Gynecology, with suspicion of infertility. The study included 111 women who applied to the infertility clinic between December 2020 and September 2022 and received two doses of COVID-19 mRNA vaccine (BNT162b2 -Pfizer-BioNTech). Demographic and clinical characteristics of the women, such as age, BMI (Body Mass Index), duration of marriage and infertility period, were evaluated. Anti-Müllerian Hormone (AMH), Thyroid Stimulating Hormone (TSH), Follicle Stimulating Hormone (FSH) and Luteinizing Hormone (LH) levels were measured in the serum of women before and after COVID-19 vaccine administration. Serum hormone levels were measured on the 3rd day of the menstrual cycle. Women in the reproductive period, aged 18-42, were included in the study. The concentrations of AMH, TSH, FSH and LH hormones measured in serum before and after vaccine administration were evaluated and compared retrospectively. It was determined whether women received the COVID-19 mRNA vaccine or not with the online portal developed by the Ministry of Health of the Republic of Turkey. Women who had not completed at least two doses of the vaccine, those with a positive Reverse Transcription-Polymerase Chain Reaction

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(RT-PCR) test, and those with a body mass index of 30 and above were not included in the study. Post-vaccination serum hormone levels of women were measured 6-9 months after vaccination.

Ethics committee approval for the study was received from Gazi Yaşargil Training and Research Hospital Clinical Research ethics committee number 115.

2.1. Statistical analysis

Statistical evaluation was performed using the jamovi project (2022, Version 2.3). Data are expressed as mean + standard deviation and median (min-max). Categorical data were expressed as frequency and percentage. Normality of data distribution was tested with Shapiro Wilk tests. Wilcoxon tests were used to compare pre-post data. P<0.05 was considered significant as the significance level.

3. Results

A total of 111 women who applied to the infertility clinic were included in the study. Demographic characteristics and clinical features of the patients were evaluated (Table 1). The median age of the women was 36 (20-42) and median BMI was 24,97(18,52-28,04). Mean marriage duration was 7.55±4.35 (mean±SD) and mean infetility period was 4.79±3.86 (mean±SD).

Table 1: Demographic characteristics and clinical features

Demographic Characteristics	Mean±SD;medyan(min-max); Number (%)
Age (year),	
mean ± SD;	34,29±5,99
Medyan (Min- Max)	36 (20-42)
BMI (kg/m2);	
mean ± SD;	24,31±2,50
Medyan (Min- Max)	24,97(18,52-28,04)
Duration of marriage;	
mean±SD	7,55±4,35
Medyan (Min- Max)	7 (1-21)
Infertility period;	
mean± SD;	4,79±3,86
Medyan (Min- Max)	3 (1-16)

Serum hormone levels of women before and after vaccination were evaluated and compared (Table 2). While the serum AMH level was 1.90±2.48 (Mean ± SD) before vaccination, it was 1.87±2.16 (Mean ± SD;) after vaccination (p= 0.052). Although there was a minimal decrease in AMH levels, no statistically significant difference was detected. TSH, FSH and LH serum levels were respectively before vaccination (1.79±1.06, 10.80±9.98, 8.75±7.03) (mean ± SD) and after vaccination (1.83±1.11, 11.34±9.37, 9.18±6.26) (mean ± SD) (p= 0.062, 0.252, 0.064) and no statistical difference was detected in these values.

Table 2. Comparison of hormone parameters before and after COVID-19 vaccination; (BNT162b2 -Pfizer-BioNTech)

Hormone parameters	Pre-vaccination (n: 111)	Post-vaccination (n: 111)	P Value
AMH (µg/l)			
Mean ± SD;	1,90±2,48	1,87±2,16	0.052
Median (Min- Max)	1,10 (0,01-12,23)	0,89 (0,01-10,35)	
TSH (mU/L)			
Mean ± SD;	1,79±1,06	1,83±1,11	0.062
Median (Min- Max)	1,53 (0,05-6,15)	1,65 (0,03-5,81)	
FSH (IU/L)			
Mean ± SD;	10,80±9,98	11,34±9,37	0.252
Median (Min- Max)	7,93 (1,90-+63,8)	8,44 (0,98-66,52)	
LH (IU/L)			
Mean ± SD;	8,75±7,03	9,18±6,26	0.064
Median (Min- Max)	6,68 (0,37-46,79)	7,78 (0,10-41,20)	

COVID-19, Coronavirus Disease 2019; AMH: Anti Müllerian Hormone; TSH: Thyroid stimulating hormone; FSH: Follicle-Stimulating Hormone LH: Luteinizing Hormone; ESD; Standart Deviation; Min-Max: Minimum-Maximum

4. Discussion

Our study showed that two doses of COVID-19 mRNA vaccine did not reduce serum AMH levels. Additionally, it was determined that the vaccine did not negatively affect serum TSH, FSH and LH levels. Recently, the possibility of a negative effect of the COVID-19 vaccine on fertility has been a matter of debate (9).

In a prospective study by Mohr-Sasson et al., AMH levels were evaluated in women vaccinated with two Pfizer-BioNTech vaccines. AMH levels before vaccination were 5.30 ± 4.29 versus 5.30 ± 4.50 ng/mL at the 3rd month after vaccination (10). In another study, Soysal et al. compared 30 patients with and without mRNA vaccination. They examined AMH in women on the 90th day after vaccination and found no significant difference (11). The results were similar in our study. No statistically significant decrease was detected in AMH levels (p=0.052). However, one of the strengths of our study compared to similar studies was that AMH levels were measured 6-9 months after vaccination. Kolotorova et al. examined AMH values after 3 doses of vaccination in 25 women. Although the study was conducted with a small number of women, it was conducted in a special group that received three doses of vaccine and no decrease in AMH levels was detected (12). Horowitz and colleagues prospectively evaluated 31 infertile women and found that the mean AMH values before and after vaccination did not change within 4 months (13). Mean AMH levels before and after vaccination at 4 months were 1.7 versus 1.6 ng/mL. The common aspect of our studies was that the patient groups consisted of infertile women. Since infertile patients are a very sensitive group, determining that the vaccine does not have a negative effect on

AMH levels in these patients is a very important result. In another study designed considering that the decrease in AMH might be related to age, subgroup analysis was performed for women aged <35 and ≥35 and it was found that it did not affect the decrease in ovarian reserve in different age groups (14). In the study of Yıldız et al. AMH levels were examined by creating subgroups according to age groups, and although a decrease in AMH levels was detected after 6 months in the > 35 age group compared to the others, it was not found to be statistically significant (15). Although, in our study, the fact that the analysis was not made according to age groups is one of the limitations of the study, but our results are similar.

It is known that fertility is not only related to AMH levels and that ACE receptors, which carry the S protein used in the mRNA vaccine into the cell, are also found in the endometrium (16). For this reason, menstrual cycle is thought to be one of the main parameters affecting fertility (17). In our study, serum TSH, FSH and LH levels, which may affect the menstrual cycle, were evaluated before and after vaccination, and no significant change was detected. However, unlike our study, Wang et al.'s study found that the vaccine caused minimal prolongation of menstrual cycle time (18) . In our opinion, it will be possible to reach conclusions in this field with more studies involving larger patient groups.

In conclusion, our study proves that the COVID-19 mRNA vaccine does not have a negative effect on serum AMH, TSH, FSH and LH levels. Therefore, vaccination can be safely administered to infertile patients with fertility concerns. However, multicenter, prospective studies with a large number of patients are needed to confirm our results.

Conflict of interest

The authors state no conflict of interest.

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None to declare.

Authors' contributions

Concept: M.F.A, S.M.Ö., Design: M.F.A, S.M.Ö., Data Collection or Processing: M.A., S.Y., K.B., Analysis or Interpretation: M.A., S.Y., K.B., Literature Search: M.F.A., Writing: M.F.A., K.B., S.M.Ö.

Ethical Statement

Ethics committee approval for the study was received from Gazi Yaşargil Training and Research Hospital Clinical Research ethics committee number 115.

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