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GENERAL GYNECOLOGY

The effect of SARS-CoV-2 BNT162b2 vaccine on the symptoms of women with endometriosis

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Abstract

Purpose As the use of the messenger RNA (mRNA) BNT162b2 (Pfizer-BioNTech) Coronavirus disease 2019 vaccine has grown, reports on menstrual changes have arisen. We aimed to examine menstrual bleeding patterns and endometriosis-associated symptoms after receiving the mRNA BNT162b2 SARS-CoV-2 vaccine in women with endometriosis, as compared to the control group.

Methods This is a questionnaire-based cross-sectional study including a total of 174 women. The study group included 86 women with a confirmed diagnosis of endometriosis and the control group included 88 women with no diagnosis or suspected diagnosis of endometriosis. Each woman completed a questionnaire on menstrual bleeding patterns and endometriosis-associated symptoms before and after receiving two doses of the BNT162b2 vaccine. Primary outcomes were changes in amount or length of menstrual bleeding, rates of intermenstrual bleeding and worsening in dysmenorrhea in the endometriosis patient group, as compared to the control group. Secondary outcomes included changes in all endometriosis-associated symptoms.

Results In our cohort, women with endometriosis were more likely to experience changes in bleeding patterns (women with endometriosis: 39.5%, control group: 31.0%, $p=0.02$), and a significant worsening in endometriosis-associated symptoms with an almost 4.3-fold worsening in dysmenorrhea [95% CI 1.9–9.9, $p<0.01$] and 5.5-fold odds for any worsening in symptoms in endometriosis patients, as compared to the control group [95% CI 2.7–11.1, $p<0.01$].

Conclusion In our cohort, endometriosis was shown to be a significant risk factor for worsening of menstrual symptoms, after receiving the SARS-CoV-2 BNT162b2 mRNA vaccine. Further research is needed to confirm these findings.

Keywords Endometriosis · SARS-CoV-2 · Menstrual changes

What does this study add to the clinical work

With the wide use of the messenger RNA SARS-CoV-2 BNT162b2 vaccine, we believe it is important to research and understand any possible adverse effects. In our cohort, a previous diagnosis of endometriosis was shown to be a significant risk factor to worsening of menstrual symptoms, after receiving the vaccine. This knowledge may aid clinicians and patients and calls for further research to further characterize the groups who may suffer from menstrual changes following the vaccine and on possible ways to attenuate any possible negative effect of the vaccine which is necessary for public health.

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Introduction

In an effort to halt the spread of the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) pandemic, there has been a wide use of the messenger RNA (mRNA) BNT162b2 (Pfizer-BioNTech) Coronavirus disease 2019 (COVID-19) vaccine worldwide. Indeed, pivotal clinical trials have shown that the mRNA vaccine is effective in preventing symptomatic and asymptomatic SARS-CoV-2 infections [1].

Endometriosis is a major cause of pelvic pain and infertility and affects approximately 10% of reproductive age women [2]. Endometriosis is characterized by ectopic endometrial tissue outside the uterus and is associated with pain symptoms, especially during menses, and with higher rates of irregular bleeding and infertility [3, 4]. While a definitive diagnosis of endometriosis can be made only by means of surgery, deep lesions and endometriomas could also be detected with magnetic resonance imaging (MRI) or with an ultrasound scan [2].

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Following wide usage of the vaccine, menstrual cycle changes attributed to vaccination have been reported [5] and these reports became an item of interest of health organizations and clinicians around the world [6]. Of note, in some studies menstrual changes were very minimal [7]. In addition to these reports, clinicians taking care of women with endometriosis have anecdotally reported worsening of endometriosis symptoms after vaccination.

Hence, we aimed to examine whether the mRNA BNT162b2 (Pfizer-BioNTech) SARS-CoV-2 vaccine affects the menstrual bleeding pattern and symptoms of women with endometriosis.

Materials and methods

Study design

This is a questionnaire-based cross-sectional study, carried out at a tertiary medical center between July 2021 and November 2021. Included were women aged 18–45 years who received at least two doses of the BNT162b2 mRNA SARS-CoV-2 vaccine (Pfizer-BioNTech) with a mean of 29.8 ± 43.2 days between the two doses. The study group included women with a definitive diagnosis of endometriosis who were recruited through records of our hospital's Endometriosis Clinic. We approached patients consecutively, from September 2018 onward. A definitive endometriosis diagnosis was defined by laparoscopic confirmation of endometriosis or by deep lesions or endometriomas diagnosed by an endometriosis ultrasound specialist, no surgeries were performed during the time of the study. The control group included women without a diagnosis of endometriosis and who were never evaluated for the presence of endometriosis. To avoid selection bias in which women with symptoms would be more likely to participate in the survey, the control group was mostly comprised of medical staff (nurses, doctors, and medical students). We avoided publication of the study through social networks. Excluded from the study were women who had been previously diagnosed with a COVID-19 infection. We also excluded patients with other gynecological or immunological disorders and pregnant and lactating women.

The study was approved by our hospital's Research and ethics committee. All participants gave their consent to participate in the study.

Interventions

All women completed a survey including the following: (1) demographics and general medical and obstetric and gynecological history; (2) menstrual and non-menstrual endometriosis-associated pain symptoms including: dysmenorrhea, dyspareunia, dyschezia, dysuria, abdominal pain between periods, chronic pelvic pain and back pain. All symptoms were assessed with a Numeric Rating Scale (NRS) in a scale of 0–3 (0 = no pain, 1 = mild pain, 2 = moderate pain, 3 = severe pain) [8]; (3) other endometriosis-associated symptoms (EAS) including urinary symptoms, abdominal bloating, diarrhea, nausea and vomiting, assessed also with a NRS; and (4) menstrual bleeding pattern, including amount of bleeding and length of period and any irregular bleeding pre or post vaccination.

Of note, to avoid recall bias, two types of questions were asked: (1) "was there an improvement, worsening or no change" in the specific symptom; (2) assessment by NRS of each pain symptom. In cases in which the 2 questions contradicted each other, the patient was excluded from the analysis for the specific pain symptom. All reports were retrospective and referred to the above symptoms in three specific time spans- before receiving the first dose, between the first and second doses and in the 3–6 months following the second dose of the SARS-CoV-2mRNA vaccine.

We also collected details on endometriosis stage and type of disease (superficial, deep, ovarian) from the patients' medical files.

Outcomes

Primary outcomes were: (1) changes in bleeding pattern during menstruation (changes in amount or flow of bleeding) and change in length of menstrual bleeding (number of total bleeding days); (2) intermenstrual bleeding; (3) worsening in dysmenorrhea.

Secondary outcomes included all other EAS.

Statistical analysis

Based on a power level of 80% and a 2-tailed $P < 0.05$ and on the assumption that a 20% absolute difference between women with endometriosis and the control group would be clinically significant, the required sample size of each group to perform a fully powered study was calculated to be 62 in each group. We however aimed for 85 eligible women in each group.

Baseline characteristics were first compared between women with and without endometriosis with chi-square and *t* test, as appropriate. Rates of change in bleeding pattern and worsening of dysmenorrhea were compared between groups. Worsening dysmenorrhea was defined as a positive answer to the question: "Has your menstrual pain got worse after the vaccine" and worsening or no change in the NRS. Change in bleeding pattern was defined as change in length of menstrual cycle or change in the amount of bleeding.

EAS were then compared between the study groups with the Wilcoxon-Rank test.

Table 1 Baseline characteristics of study participants

	Women with endometriosis ($N=86$)	Control group ($N=88$)	p-value
Age (years) mean (SD)	29.95 (5.4)	27.96 (4.2)	0.07
Body mass index mean (SD)	24.6 (15.6)	23.1 (4.4)	0.39
Parity *N* (%)			
0	63 (73.3)	77 (87.5)	0.051
1	11 (12.8)	4 (4.5)	
≥2	12 (14)	7 (8.0)	
Comorbidities *N* (%)			
None	69 (80.0)	81 (92.0)	0.053
Mood disorders	3 (3.4)	0 (0.0)	
Gastrointestinal	6 (6.9)	2 (2.3)	
Other	8 (9.3)	5 (5.7)	
Hormonal treatment *N* (%)			
None	39 (45.3)	54 (61.3)	0.048
Estrogen-progesterone combined medications	23 (26.7)	28 (31.8)	
Dienogest	10 (11.6)	0 (0)	
Gonadotropin releasing hormone agonist/antagonist	3 (3.5)	0 (0)	
Levonorgestrel-releasing intrauterine system	11 (12.8)	6 (6.8)	
History of infertility *N* (%)	36 (41.9)	2 (2.3)	<0.01

We then created the following composite variables: (1) urinary symptoms including dysuria and Urinary Tract Infection (UTI) symptoms; (2) gastrointestinal symptoms including dyschezia, abdominal bloating, diarrhea, nausea and vomiting; and (3) any symptom. Binary variables of worsening symptoms following the vaccine (worsening symptoms/ non-worsening symptoms) were then created for each pain symptoms and for each composite variable. Rates of symptoms worsening were first compared through Chi-Square test. We then carried out a logistic regression and calculated the adjusted odds ratios (aOR) and 95% Confidence Interval (95%CI) for each pain symptom and composite variable. A linear regression was also performed to assess continuously the change in symptoms following the vaccine. All regression models included in addition to presence or absence of endometriosis the following covariates: Body Mass Index (BMI), age, background disease, hormonal treatment and parity. The statistical software package SPSS 25.0 (SPSS Inc., Chicago, IL, USA) was used for all data analyses. A p-value <0.05 was considered statistically significant.

Results

Recruited were 100 patients in each group. Fourteen patients from the study group, and 12 from the control group have not completed the questionnaire and were excluded. Thus, the final cohort included 174 participants. Of them, 49.4% ($n=86$) had a definitive diagnosis of endometriosis, and 50.6% ($n=88$) had not suffered from endometriosis and were never evaluated for the presence of endometriosis and comprised the control group. Baseline characteristics of study participants are presented in Table 1.

Age and BMI did not differ between the two groups. Women with endometriosis were more likely to suffer from comorbidities such as mood disorders and gastrointestinal diseases. More women with endometriosis used hormonal treatments, as compared to the control group.

Primary outcomes

Figure 1 depicts the study primary outcomes: in our cohort, 31% ($n=54$) of women reported a change in their menstrual bleeding pattern following the vaccine. This change was more common in women with endometriosis, as compared to the control group (39 vs. 22.7%, $p=0.02$). A total of 45 (26.5%) women experienced worsening of dysmenorrhea, with a higher percentage of worsening in the endometriosis group (38.6 vs. 14.9% in the control group, $p<0.01$).

Of all women, 32.2% ($n=56$) reported intermenstrual bleeding after receiving the vaccine. Of them, 19.0% ($n=33$) reported intermenstrual bleeding after receiving the first dose and 27.6% ($n=48$) after the second dose. There was no significant difference in reported cases of intermenstrual bleeding between the study and control groups (37.2 vs. 27.3% respectively, $p=0.16$).

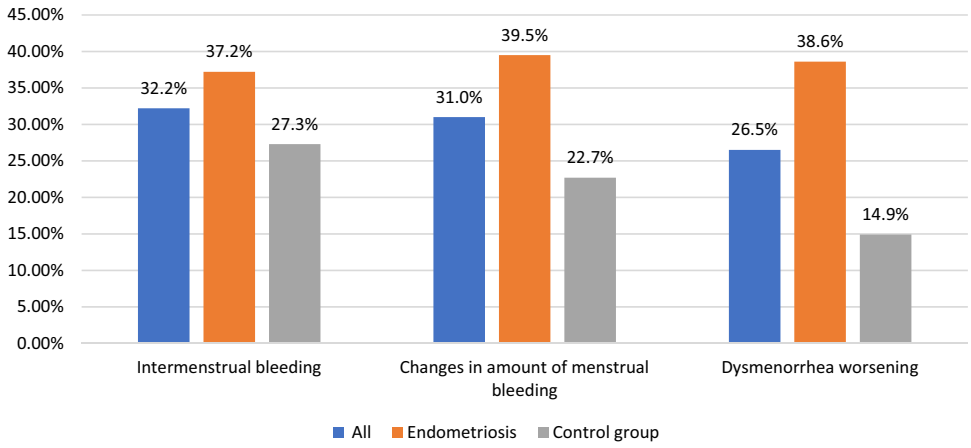

Fig. 1 Rates of menstrual changes following the mRNA BNT162b2 vaccine*. Intermenstrual bleeding, $P=0.16$; changes in amount of menstrual bleeding, $P=0.02$; worsening dysmenorrhea, $P<0.01$. *3–6 months after receiving at least two vaccine doses

Secondary outcomes

Table 2 presents the *p*-value of the change in a wide range of EAS before and after the vaccination in both groups (according to the NRS). We found that women with endometriosis experienced significant worsening in dysuria ($p=0.04$), abdominal pain between periods ($p=0.03$) and abdominal bloating ($p=0.01$) after receiving the vaccine. Improvement in back pain during period was found in women without endometriosis ($p=0.02$) after receiving the vaccine.

A comparison of rates of worsening of our composite outcomes and of other major pain symptoms between women with and without endometriosis is shown in Fig. 2. Women with endometriosis were more likely to experience worsening in gastrointestinal symptoms (41.9 vs 12.5%, $p<0.01$) and worsening of urinary symptoms (32.6 vs. 4.5%, $p<0.01$). Any worsening following the vaccine was demonstrated in 45.4% ($n=79$) of the entire cohort and in 65.1 and 26.1% in the study and control groups, respectively ($P>0.01$).

Of the women with endometriosis, 50% ($n=43$) had deep endometriosis, 53.5% ($n=46$) had ovarian involvement and 33.7% ($n=26$) had superficial disease only. No difference was observed in any worsening between these 3 groups (74.4, 50.0 and 58.6% for women with deep, ovarian and superficial endometriosis, respectively, $p=0.17$). No difference between groups was observed also for the specific pain symptoms.

Regression analysis

Table 3 shows a multivariable logistic regression of rates of worsening in EAS. The adjusted odds for worsening dysmenorrhea were 4.3-fold higher for patients with endometriosis, as compared to the control group. the same trend was seen in worsening in urinary symptoms, GI symptoms, abdominal pain between periods, chronic pelvic pain and back pain with adjusted odds of 12.4, 5.2, 4.9, 8.0, 7.4 in women with endometriosis as compared to the control group. When we examined the composite outcome of worsening in any symptom, we showed 5.5-fold increased odds in women with endometriosis.

We have also carried out a linear regression assessing the change in each endometriosis-associated symptom as a continuous variable with the same confounders. This analysis yielded similar results with endometriosis being a risk factor for worsening of all symptoms.

Table 2 Reported changes in endometriosis-associated symptoms before and after receiving the mRNA BNT162b2 vaccine

	Women with endometriosis	Control group
Dyspareunia	0.54[a]	0.34[a]
Dysuria	0.04[a]	0.65[a]
UTI like symptoms	0.55[a]	1.00[a]
Dyschezia	0.08[a]	0.41[a]
Abdominal pain between periods	0.03[a]	0.18[a]
Chronic pelvic pain	0.10[a]	1.00[a]
Back pain	0.59[a]	0.02[a]
Abdominal bloating	0.01[a]	0.06[a]
Diarrhea	0.83[a]	0.75[a]
Nausea/vomiting	0.08[a]	0.78[a]

UTI urinary tract infection

[a]*P*-value of the difference between before and after receiving at least 2 doses of vaccination (Wilcoxon-Rank test)

Discussion

In this study we have shown that in our cohort, women with endometriosis were more likely to experience menstrual changes after completing the two-dose series of the BNT162b2 SARS-CoV-2 mRNA vaccine. Changes included change in bleeding pattern and a significant worsening in

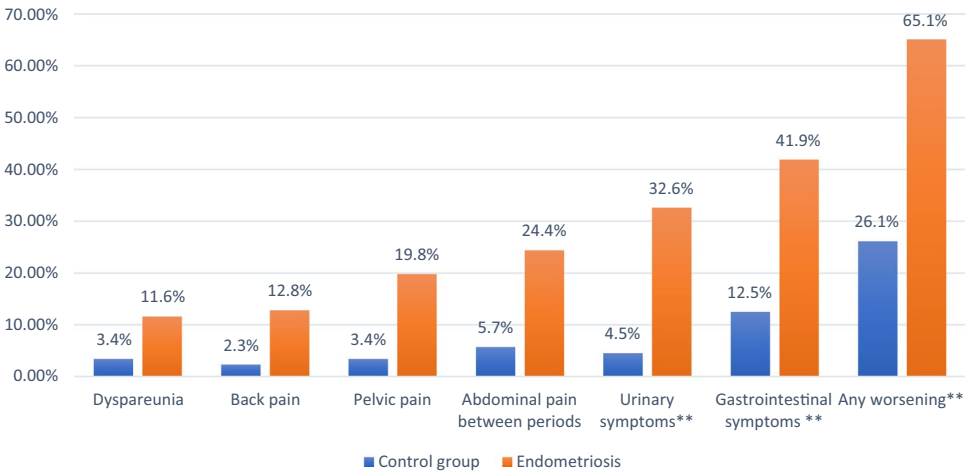

Fig. 2 Worsening in endometriosis-associated symptoms following the mRNA BNT162b2 vaccine***. *p-value for dyspareunia = 0.04, p-value for all other domains < 0.01. **Composite outcomes. ***3–6 months after receiving at least two vaccine doses

Table 3 The risk of worsening in endometriosis-associated symptoms after receiving the mRNA BNT162b2 vaccine—a multivariable logistic regression[a]

	Dysmenorrhea	Dyspareunia	Urinary tract symptoms[b]	Gastrointestinal symptoms[b]	Abdominal pain between periods	Pelvic pain	Back pain	Any worsening[b]
Presence of endometriosis								
aO[a] (CI 95%)	4.3 (1.9–9.9)	3.1 (0.8–12.3)	12.4 (3.9–38.9)	5.2 (2.3–11.8)	4.9 (1.7–14.2)	8.0 (2.1–29.8)	7.4 (1.5–37.0)	5.5 (2.7–11.1)
p-value	< 0.01	0.11	< 0.01	< 0.01	< 0.01	< 0.01	0.01	< 0.01

[a]Adjusted for: age, body mass index, background disease, hormonal treatment and parity

[b]Composite outcomes

endometriosis-associated symptoms with a 4.3-fold worsening in dysmenorrhea and 5.5-fold risk for any worsening in symptoms in endometriosis patients, as compared to the control group.

To the best of our knowledge, there are no previous studies who reported specifically on the impact of the vaccine on EAS. However, recent studies have shown changes in menstrual patterns in the general population after COVID-19 infection and after receiving the vaccine. A recent study by Li et al., demonstrated changes in the menstrual cycle pattern of reproductive-aged women with a COVID-19 infection, including changes in amount of bleeding, length of period and longer menstrual cycle, with a positive association between disease severity and menstrual changes [9]. A recent study on women with endometriosis showed that women with endometriosis are not more susceptible to the COVID-19 infection but the manifestations are different with more likelihood to suffer from rare symptoms [10].

Previous studies have shown contradicting evidence on the effect of the SARS-CoV-2 mRNA vaccine on menstrual changes. While in a retrospective study by Male et al. no significant changes were demonstrated [11], significant changes were shown in two other studies. Lee et al. have shown relatively high rates of heavier bleeding and of breakthrough bleeding concluding that while not dangerous, changes to menstrual bleeding are not uncommon [12]. Similarly, a large study by Alvergne et al., demonstrated a 20% rate of menstrual disturbance, ranging from menstrual bleeding cessation to heavy menstrual bleeding [13]. Of note, previous studies on vaccines for other viral diseases, such as Hepatitis B virus also noted menstrual changes after receiving the vaccine [14].

Suggested theories on the demonstrated association between the mRNA BNT162b2 vaccine and worsening of EAS may be related to the immunological and inflammatory responses caused by the vaccine [5]. Recent studies have speculated that immunologic factors influence the menstrual cycle and cause changes in reproductive organs such as the cervical mucus and the uterine cells [15], and therefore could cause changes in the menstrual cycle.

Previous research on different types of mRNA vaccines have shown that their mechanism of action includes an inflammatory response and activation of the immune system [16, 17]. Similarly, Ugur Sahin et al. and Bettini E et al. [18, 19] have shown that the SARS-CoV-2 mRNA vaccine instigates an immune response that could possibly affect the hormonal and reproductive system.

Endometriosis is associated with chronic inflammation with the inflammatory response being a major contributor to disease progress and development of ectopic lesions [4, 20, 21], as well as to pain symptoms and infertility [4, 21]. It may be possible that the inflammatory response of the mRNA vaccine explains, at least in part, the worsening of endometriosis symptoms.

Lending support to our finding of almost 40% of change in the bleeding pattern amongst women with endometriosis, a recent study [11] that examined the effect of the COVID-19 mRNA vaccine on bleeding patterns in the general population, reported similar rates of abnormal bleeding in a subgroup of women with endometriosis.

While dysmenorrhea is the most common EAS [2–4], gastrointestinal and urinary symptoms are major complaints of endometriosis patients [22]. In our cohort, we found a strong association between the mRNA BNT162b2 vaccine and worsening in these symptoms in the endometriosis group with a 5.4-fold worsening in gastrointestinal and 11.3 in urinary symptoms, as compared to women without endometriosis.

Whether the mechanism for the worsening in symptoms is solely related to the inflammatory effect of the vaccine, remains to be studied.

One of the major concerns is whether there is an association between the reported menstrual changes and long-term fertility. While this was yet to be investigated specifically in endometriosis patients, previous studies have ruled out any negative effect of the vaccine on female fertility [23, 24]. Moreover, Li K et al. showed in their study that menstrual changes after SARS-CoV-2 infection were temporary and that women who experienced menstrual changes returned to their normal cycle within a few months [9]. It is thus likely that the changes demonstrated in our and other studies following the vaccine would also be temporary. This should be further evaluated in long-term studies.

Even though we found a correlation between the SARS-CoV-2 mRNA vaccine and worsening in EAS it should be emphasized that COVID-19 is an extremely contagious virus that could lead to a wide range of severe symptoms [25] and mortality even in healthy young people [26] and that the vaccine is the one proven way to prevent morbidity and mortality [1, 27].

Strengths and limitations

The main limitation of this study is its retrospective nature. This carries an inherent selection bias due to voluntary recruitment of participants. To address this limitation, we recruited patients from our endometriosis clinic and from the hospital's staff and avoided publication of our survey through social networks. Possible recall bias is another limitation of this study. However, this bias may be attenuated by asking on a wide range of time rather than a specific month.

While the control group included only women who were never considered or evaluated for endometriosis, we did not convey a symptom specific survey for this group, nor did this group undergo dedicated imaging or laparoscopy. Therefore, we cannot exclude the possibility that some of the women from the control group also had endometriosis. Also, we did not collect information about changes in hormonal therapy in the time span of the survey.

We have not formally documented reasons for exclusion of patients and recognize this as a limitation of the study. Although we met our sample size calculation, our sample size was moderate in size. Therefore, larger studies are needed to confirm our findings.

To assess the effect of the vaccine on patients with endometriosis, we avoided recruitment of patients with suspected of clinically diagnosed endometriosis and rather included only women with a definitive diagnosis of endometriosis and without other gynecological conditions that may affect menstruation. While this is one of the strengths of the study, it should be noted that in addition to the possible vaccination effect, the natural history of the disease itself may also contribute to the worsening of symptoms in the endometriosis group, as compared to the control group.

This is one of the first studies assessing the effect of the Covid-19 vaccine on menstrual changes. We focused specifically on patients with endometriosis and gave attention to a wide range of symptoms related to endometriosis. However, as some of these symptoms affect only a portion of endometriosis patients, larger studies are needed to confirm our findings.

Conclusions

In our cohort, endometriosis was shown to be a significant risk factor to worsening of menstrual symptoms, after receiving the SARS-CoV-2 mRNA vaccine. More research is needed to further characterize the groups who may suffer from menstrual changes following the vaccine and on possible ways to attenuate any possible negative effect of the vaccine which is necessary for public health.

Author contributions All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by AG, SL, NL and UPD. The first draft of the manuscript was written by AG, SL and UPD and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

Ethical approval Human Research and Ethics Committee approval for this project was obtained from the hospital's Research and Ethics Committee (number 0286–21).

Consent to participate Informed consent was obtained from all individual participants included in the study.

References

1. Thompson MG, Burgess JL, Naleway AL, Tyner H, Yoon SK, Meece J et al (2021) Prevention and attenuation of Covid-19 with the BNT162b2 and mRNA-1273 vaccines. N Engl J Med 385(4):320–329. https://doi.org/10.1056/NEJMoa2107058
2. Giudice LC (2010) Clinical practice. Endometr N Engl J Med 362(25):2389–2398. https://doi.org/10.1056/NEJMcp1000274
3. Mahmood TA, Templeton AA, Thomson L, Fraser C (1991) Menstrual symptoms in women with pelvic endometriosis. Br J Obstet Gynaecol 98(6):558–563. https://doi.org/10.1111/j.1471-0528.1991.tb10370.x
4. Vercellini P, Viganò P, Somigliana E, Fedele L (2014) Endometriosis: pathogenesis and treatment. Nat Rev Endocrinol 10(5):261–275. https://doi.org/10.1038/nrendo.2013.255
5. Male V (2021) Menstrual changes after covid-19 vaccination. BMJ 374:n2211. https://doi.org/10.1136/bmj.n2211
6. COVID-19 Vaccines and the Menstrual cycle. https://covid19.nih.gov/news-and-stories/covid-19-vaccines-and-menstrual-cycle (2021). Accessed 12 Dec 2021
7. Edelman A, Boniface ER, Benhar E, Han L, Matteson KA, Favaro C et al (2019) Association between menstrual cycle length and coronavirus disease 2019 (COVID-19) vaccination: a US. cohort. Obstet Gynecol. https://doi.org/10.1097/AOG.0000000000004695
8. Taylor HS, Giudice LC, Lessey BA, Abrao MS, Kotarski J, Archer DF et al (2017) Treatment of endometriosis-associated pain with elagolix, an oral GnRH antagonist. N Engl J Med 377(1):28–40. https://doi.org/10.1056/NEJMoa1700089
9. Li K, Chen G, Hou H, Liao Q, Chen J, Bai H et al (2021) Analysis of sex hormones and menstruation in COVID-19 women of childbearing age. Reprod Biomed Online 42(1):260–267. https://doi.org/10.1016/j.rbmo.2020.09.020
10. Moazzami B, Chaichian S, Samie S, Zolbin MM, Jesmi F, Akhlaghdoust M et al (2021) Does endometriosis increase susceptibility to COVID-19 infections? a case-control study in women of reproductive age. BMC Womens Health 21(1):119. https://doi.org/10.1186/s12905-021-01270-z
11. Male V (2021) Menstrual changes after covid-19 vaccination, vol 374. BMJ (Clinical research ed.), England, p n2211
12. Lee KMN, Junkins EJ, Fatima UA, Cox ML, Kathryn BH (2021) Clancy characterizing menstrual bleeding changes occurring after SARS-CoV-2 vaccination medRxiv 2021. https://doi.org/10.1101/2021.10.11.21264863
13. Alvergne A, Kountourides G, Argentieri MA, Agyen L, Rogers N, Knight D et al (2021) COVID-19 vaccination and menstrual cycle changes: a United Kingdom (UK) retrospective case–control study. MedRXiv. https://www.medrxiv.org/content/10.1101/2021.11.23.21266709v1
14. Shingu T, Uchida T, Nishi M, Hayashida K, Kashiwagi S, Hayashi J et al (1982) Menstrual abnormalities after Hepatitis B vaccine. Kurume Med J 29(3):3. https://doi.org/10.2739/kurumemedj.29.123
15. Monin L, Whettlock EM, Male V (2020) Immune responses in the human female reproductive tract. Immunology 160(2):106–115. https://doi.org/10.1111/imm.13136
16. Edwards DK, Jasny E, Yoon H, Horscroft N, Schanen B, Geter T et al (2017) Adjuvant effects of a sequence-engineered mRNA vaccine: translational profiling demonstrates similar human and murine innate response. J Transl Med 15(1):1. https://doi.org/10.1186/s12967-016-1111-6
17. Pardi N, Hogan MJ, Naradikian MS, Parkhouse K, Cain DW, Jones L et al (2018) Nucleoside-modified mRNA vaccines induce potent T follicular helper and germinal center B cell responses. J Exp Med 215(6):1571–1588. https://doi.org/10.1084/jem.20171450
18. Sahin U, Muik A, Derhovanessian E, Vogler I, Kranz LM, Vormehr M et al (2020) COVID-19 vaccine BNT162b1 elicits human antibody and T. Nature 586(7830):594–599. https://doi.org/10.1038/s41586-020-2814-7
19. Bettini E, Locci M (2021) SARS-CoV-2 mRNA vaccines: immunological mechanism and beyond. Vaccines (Basel). https://doi.org/10.3390/vaccines9020147
20. Augoulea A, Alexandrou A, Creatsa M, Vrachnis N, Lambrinoudaki I (2012) Pathogenesis of endometriosis: the role of genetics, inflammation and oxidative stress. Arch Gynecol Obstet 286(1):99–103. https://doi.org/10.1007/s00404-012-2357-8
21. Berbic M, Fraser IS (2011) Regulatory T cells and other leukocytes in the pathogenesis of endometriosis. J Reprod Immunol 88(2):149–155. https://doi.org/10.1016/j.jri.2010.11.004
22. Parasar P, Ozcan P, Terry KL (2017) Endometriosis: epidemiology, diagnosis and clinical management. Curr Obstet Gynecol Rep 6(1):34–41. https://doi.org/10.1007/s13669-017-0187-1
23. Bentov Y, Beharier O, Moav-Zafrir A, Kabessa M, Godin M, Greenfield CS et al (2021) Ovarian follicular function is not altered by SARS-CoV-2 infection or BNT162b2 mRNA COVID-19 vaccination. Hum Reprod 36(9):2506–2513. https://doi.org/10.1093/humrep/deab182
24. Safrai M, Rottenstreich A, Herzberg S, Imbar T, Reubinoff B, Ben-Meir A (2021) Stopping the misinformation: BNT162b2 COVID-19 vaccine has no negative effect on women 's fertility. Cold Spring Harbor Laboratory Press
25. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX et al (2020) Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 382(18):1708–1720. https://doi.org/10.1056/NEJMoa2002032
26. Berlin DA, Gulick RM, Martinez FJ (2020) Severe Covid-19. N Engl J Med 383(25):2451–2460. https://doi.org/10.1056/NEJMcp2009575
27. Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S et al (2020) Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. N Engl J Med 383(27):2603–2615. https://doi.org/10.1056/NEJMoa2034577