ORIGINAL RESEARCH

Effect Of Covid 19 Vaccine On Menstrual Cycle In Reproductive Age Group: An Observational Cross Sectional Study

[1]Dr. Maryada Jain, [2]Dr. Shubhra Agarwal, [3]Dr. Ratna Tejaswi Papola, [4]Dr. Priyanka Pachauri

[1]Junior resident (JR III), [2]Professor, [3]Junior resident (JR III), [4]Assistant Professor, Department of Obstetrics and Gynaecology, Teerthankar Mahaveer Medical College and Research Centre, Delhi Road, Moradabad, Uttar Pradesh, India

Corresponding author
Dr. Maryada Jain
JRIII, Department of Obstetrics and Gynaecology, Teerthankar Mahaveer Medical College and Research Center, Delhi Road, Moradabad, UP, India
Email: maryadajain94@gmail.com

ABSTRACT
Covid 19 has been responsible for one of the deadliest pandemics in human history, resulting in widespread human suffering and loss of life. Minor alterations in the menstrual cycle have caused females to worry about the covid 19 vaccination because they are seen as a threat to the health and fertility that regular menstruation represents. Understanding the correlation between the covid-19 vaccine & changes in menstural cycle is crucial for sustaining community confidence in vaccination programmes.
Aim: To analyse menstrual cycle patterns in reproductive age group women who have received covid 19 vaccination.
Materials & methods: It was an observational cross-sectional study of 382 women wherein before & after getting the immunisation, women were surveyed through web-based questionnaire to assess changes in menstrual cycle parameters such as menstrual cycle length, its duration, flow volume. Menstrual cycle patterns were evaluated before vaccination, between first and second dose, between second and third dose and post booster dose.
Results: Out of 382 women, majority of women were between the age group of 26-35 years.. Seventy-five percent of women got the covishield vaccine, and seventy percent of those were Hindu. Only 16% of women saw transient, minor changes in menstrual cycle characteristics such as flow volume and frequency of cycles.
Conclusion: Immunisation against COVID-19 did not significantly alter the characteristics of the menstrual cycle. Therefore, more research is needed to assuage worries about the impact of covid immunisation on the menstrual phase.
Keywords: COVID-19, Immunisation, Menstruation, Vaccination

INTRODUCTION
Worldwide, the 2019 corona virus disease (Covid 19) has resulted in massive amounts of sickness and death. [1] More than 2.5 million deaths are attributable to COVID 19 worldwide. [2]
Covid vaccination has emerged as a method for primary prevention, but it has been met with resistance because to myths about its effect on menstrual cycle and fertility[3]. The purpose of

this research is to compare pre- and post-vaccine cyclical parameters such as length and duration as well as flow.

Stress can also cause ovulation disturbances in women who menstruate regularly, which can lead to a skipped period or a temporary shift in the length of their cycles[4].This normal variability may be perceived as concerning, especially in the context of a new exposure such as covid 19 vaccination[4].

Concerns about the COVID-19 vaccine's potential side effects have dissuaded some women from getting vaccinated. These considerations must be accounted for in distinct study methodologies if healthcare providers and their patients are to have access to reliable data regarding vaccinations. [4] The pandemic has been known to be a source of tension that may have an effect on ovarian and menstrual cycle parameters, and this is on top of worries about vaccination. [5,6]

COVID19 instances continue to rise, and women may be less inclined to get vaccinated out of concern that the disease may disrupt their periods.

Surveillance schemes in UK has received increasing numbers of reports from people who have noticed a change to their period following covid 19 vaccination. There is a severe lack of information about covid vaccine and its effect on menstruation. When it comes to India, there just isn't enough data to do thorough investigations.

Maintaining community faith in the vaccination programme & allowing individuals to prepare for potential changes in their cycles necessitates further investigation into the probable connection between COVID-19 vaccination and menstrual alterations.

The aim of this research was to analyse menstrual cycle patterns in reproductive age group women prior to, during, and after vaccination.

MATERIALS & METHODS

Current research work was a cross-sectional observational study conducted for a period of 9 months (August 2021-April 2022) in the Obstetrics and Gynecology Department at TeerthankerMahaveer Medical College and Research Centre.

STUDY POPULATION

Women between the ages of 18 and 45 (the reproductive age range) who had already received their first dose of the covid vaccination (Covishield/Covaxin) and were willing to be followed for a second dose and booster were involved in the research. Not included in the research were women who did not receive the covid 19 vaccine, women who were menopausal, women who received any vaccine other than Covishield/Covaxin, women who were lost to follow up, women taking medications that disrupted their menstrual cycle, women using hormonal contraception, and women who contracted covid between vaccinations.

SAMPLE SIZE

$$n = \frac{Z^2_{\alpha/2}\, p(\%)q(\%)}{d(\%)^2}$$

where p is the observed prevalence

$q = 100 - p$

d is the margin of error

$Z_{\alpha/2}$ is the ordinate of standard normal distribution at α% level of significance

$p = 53\%$

$q = 78\%$

$d = 0.1\%$

$Z_{2.5\%}$ = 1.96 at α = 5% level of significance
n= 382.77
Hence the sample size required in the present study was 383.

STUDY METHOD

All patients of reproductive age attending OBGY OPD who satisfied the inclusion and exclusion criteria were included, and those who wished to remain anonymous were requested to fill out a web-based form in which they reported their age, demographic and obstetric characteristics, and menstrual cycle information. Measurements of the menstrual cycle were taken at:

- 3 pre-vaccine menstrual cycles were noted (before 1st dose of vaccine)
- Between 1st dose and 2nd dose of vaccine
- Between 2nd dose and booster dose of vaccine
- After booster dose of vaccine (3 post vaccine menstrual cycle)

Menstrual cycle parameters included: regularity of the cycle, cycle length and flow of each menstrual cycle.
The average menstrual cycle lasts between 2 and 8 days.

CYCLE LENGTH

24-36 days
Cycle flow rate: 20-80ml (it was measured on the basis of pads used per day)[7]

STATISTICAL ANALYSIS

The mean, standard deviation, and 95% confidence interval (CI) for each variable related to the menstrual cycle were calculated using descriptive statistics with the help of SPSS software version 24. Chi square test was used to determine the significant difference and the level of p was set at <0.05.

RESULTS

Over the course of 9 months, 480 participants were registered, however only 382 were ultimately analysed. Twenty individuals could not be located for further investigation. Only 38 out of 480 women contracted COVID, and only 10 of those women went on to have children. 18 women on investigation were found to have coagulopathy and 12 women were reported to be taking anti coagulants and hence were excluded from the study.
Three pre vaccine menstrual cycles were evaluated followed by cycle between first and second dose, then a cycle between second and booster dose and three post booster menstrual cycles.
As shown in Table 1, the results of the survey were compiled. Patients typically ranged in age from 26 to 35 years old. Seventy-five percent of the female participants were vaccinated with covishield. Seventy percent of the vaccinated women identified as Hindu.The average interval between vaccinations was 28.8 days.

Variables	N (%)	P value
Age (years)		
18-25	114(29.84)	0.002
26-35	137(35.86)	
36-45	131(34.29)	
Vaccine		
Covishield	287(75.13)	0.033
Covaxin	95(24.87)	
Doses Received		

1 2 Booster	382(100) 343(89.80) 12(3.14)	0.008
All doses received (Religion) Hindu (n= 226) Muslim (n= 156)	159(70.3) 62(39.7)	0.052

Menstrual cycles before and after vaccination are shown in Table 2.

Variables(n=382)	Duration of menses (Mean ± SD)	Frequency of cycle (Mean ± SD)	Flow volume (no. of pads used/ day) (Mean ± SD)
Before 1st dose	5.3 ± 0.9	28.8 ± 2.4	3.1 ± 1.7
Between 1st dose and 2nd dose	6.5 ±1.2	24.9 ±2.6	4.3 ± 0.9
After 2nd dose	5.2 ± 0.9	28.8 ± 2.3	3.0 ± 1.5
After booster dose	5.2 ± 1.2	28.6 ± 2.2	2.6 ± 1.6

Before the 1st dose, after the 2nd dose, 3rd dose & after the booster dose, there were no statistically significant variations in cycle duration, regularity of menses, or flow during menses. [p = 0.09]. Menstrual cycle characteristics, such as flow during menses and cycle length between the first and second dose, varied in just 16% of women.

DISCUSSION

Women can monitor concerns with their reproductive hormones by keeping track of their menstrual cycles. [8] There has been speculation that pressure/tension during the pandemic may have affected menstrual cycle characteristics [5,6]. However, it is important to differentiate between objective assessment of change and subjective perception of change that is vulnerable to recollection and confirmation bias.

Women who kept daily and prospective records of their menstrual cycles before and after the COVID-19 vaccine showed that only 16% of responders had transient changes in menstrual bleeding and the characteristics of the menstrual cycle. There is no correlation between the vaccine brand and either the onset or duration of menstruation.

Edelman et al[9] in 2019 conducted a study on Association Between Menstrual Cycle Length and Coronavirus Disease concluded that vaccine was connected with a not more a day shift in cycle interval for dual vaccine-dose cycle with prevaccine cycles, that unvaccinated individuals did not notice a important alteration compared to 3 baseline cycles, and that menstrual cycle length change was not associated with vaccination which was consistent with our findings where only 16% women has minor changes in their menstrual cycle after second dose of vaccine and was temporary.

Alvergne A. et al. did a retrospective study on ‘Effect of covid 19 vaccination on menstrual periods in a retrospectively recruited cohort’ and observed that 20% of females experienced menstrual abnormalities after having a covid-19 vaccine which was in accordance with our study. Among the 33 variables evaluated in retrospective study by Alvergne A. et al , smoking and past SARS-Cov 2 contamination were identified as threat factors, while the use of contraceptive drugs having estradiol was identified as protective. [10]

Garg R et al., did a study on Indian population titled "Menstrual cycle modifications following Covid 19 infection: Does Coronavirus-induced stress lead to Hormonal shift." wherein only one-third of women had their monthly cycles disrupted by covid 19 infection, and the effect

was only brief. Anxiety and stress may be to blame for this effect, as they have been shown to have an impact on the hypothalamic-pituitary axis (HPA). [11]
Bouchard TP et al [12] found that 22% of vaccinated women experienced menstrual cycle abnormalities. Additional stressors present at the same time as the immunisation may account for the sense of changes in the menstrual cycle.
The study was unable to identify this cycle difference in our smaller sample, even among women who received both doses of the vaccination in a cycle. These results imply that some women who have been immunised and who also have COVID-19 infection may experience subtle changes that would require a larger sample size to detect but that are unlikely to be clinically meaningful.
Our research shows that one in six women experience menstrual cycle irregularities, the most common of which are shorter-than-usual intervals between periods or more frequent bleeding overall but was temporary. Within three to four months of experiencing symptom relief, nearly all of these individuals had returned to their normal menstrual cycles.

CONCLUSION

Menstruation is among the basic benchmark for the health of women in reproductive age group and any change in it is of great concern among women. Covid 19 vaccination affected menstrual cycle of only 16% of women which was temporary. Concerns about possible association between covid 19 vaccination and abnormal menstrual cycles may lead to vaccine hesitancy. Women of childbearing age need not worry about the vaccine interfering with their menstrual cycles due to the lack of variance in menstrual bleeding volume, ovulation symptoms, or menstrual cycle hormone changes.

LIMITATIONS

The limitations of the study were no such research has been done in northern India. The study's limited sample size is due to the fact that it exclusively recruited women who were patients or visitors at TMU hospital. Infertility due to the covid 19 vaccination was not studied. So, to understand the consequence of covid 19 vaccine on the phases of mensturation and debunk the myths surrounding covid 19 immunisation, more research work in this field is needed.

REFERENCES

1. Nersesjan V, Amiri M, Christensen HK, Benros ME, Kondziella D. Thirty-day mortality and morbidity in COVID-19 positive vs. COVID-19 negative individuals and vs. individuals tested for influenza A/B: a population-based study. Frontiers in medicine. 2020:891.
2. WHO Coronavirus Disease (COVID-19) Dashboard. Geneva: World Health Organization; 2021. Available from: https://covid19.who.int/. Accessed March 1, 2021.
3. Güner HR, Hasanoğlu İ, Aktaş F. COVID-19: Prevention and control measures in community. Turkish Journal of medical sciences. 2020;50(9):571-7.
4. American College of Obstetricians and Gynecologists. COVID-19 vaccination considerations for obstetric–gynecologic care. Updated December. 2021;3.
5. Ozimek N, Velez K, Anvari H, Butler L, Goldman KN, Woitowich NC. Impact of stress on menstrual cyclicity during the coronavirus disease 2019 pandemic: a survey study. Journal of Women's Health. 2022 Jan 1;31(1):84-90.
6. Phelan N, Behan LA, Owens L. The impact of the COVID-19 pandemic on women's reproductive health. Frontiers in endocrinology. 2021:191.
7. Munro MG, Critchley HO, Broder MS, Fraser IS; FIFO Workinng Group on Menstrual Disorder. FIGO classification system (PALM-COEIN) for causes of abnormal uterine

bleeding in nongavid women of reproductive agew. Int J Gynaecol Obset. 2011 Apr;113(1):3-13

8. Nguyen BT, Pang RD, Nelson AL, Pearson JT, BenharNoccioli E, Reissner HR, Kraker von Schwarzenfeld A, Acuna J. Detecting variations in ovulation and menstruation during the COVID-19 pandemic, using real-world mobile app data. PloS one. 2021 Oct 20;16(10):e0258314.
9. Edelman A, Boniface ER, Benhar E, Han L, Matteson KA, Favaro C, Pearson JT, Darney BG. Association between menstrual cycle length and coronavirus disease 2019 (COVID-19) vaccination: a US Cohort. Obstetrics &Gynecology. 2022 Apr 28;139(4):481-9.
10. Alvergne A, Kountourides G, Argentieri MA, Agyen L, Rogers N, Knight D, Sharp GC, Maybin JA, Olszewska Z. COVID-19 vaccination and menstrual cycle changes: A United Kingdom (UK) retrospective case-control study. MedRXiv. 2021 Jan 1.
11. Garg R, Lal P, Agrawal P, Agrawal N, Gupta P, Singh AP. Menstrual Cycle Changes after COVID-19 Infection: Does Coronavirus-induced Stress Lead to Hormonal Change?. Journal of South Asian Federation of Obstetrics and Gynaecology. 2022 Jul 27;14(3):248-52.
12. Bouchard TP, Schneider M, Schmidt M, Manhart M, Fehring RJ. Menstrual cycle parameters are not significantly different after COVID-19 vaccination. Journal of Women's Health. 2022 Aug 1;31(8):1097-102.