

Transient Menstrual Cycle changes Post Precautionary Dose Covid Vaccine in Indian Population

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Abstract

Introduction: Increased reporting of menstrual disturbances Post Precautionary dose Covid Vaccine among peer group and inadequate answers to questions pertaining to changes in menstruation after precautionary dose vaccine was the rationale for conducting this study. The aim was to assess the influence of COVID-19 precautionary vaccine on menstruation. **Methodology:** Study was performed using Menstruation -vac Questionnaire. 198 participants of which 114 were included in the age group of 19-45 years. Participants with prior menstrual irregularities were excluded from the study. **Results:** The prevalence of changes in menstrual cycles post precautionary dose vaccination was in 30.70%. In our study the prevalence of changes in menstrual cycles post- precautionary dose vaccination was found to be 15.8%, 15.8%, 10.5%, 7.9%, 7% & 5.3% in 1st, 2nd, 3rd, 4th, 5th and 6th cycle respectively. **Conclusion:** Menstrual changes post-vaccination were insignificant; however a trend towards transient changes was observed returning to near normalcy after the 4th cycle post precautionary dose.

Keywords: Menstruation, Coronavirus disease 2019, Precautionary dose Covid – 19 vaccine.

Introduction

Over the past more than two years, the COVID-19 pandemic has taken the world by storm, affecting every aspect of human life.⁽¹⁾ The unprecedented development of the COVID-19 vaccine marks itself as a savior during the days of the COVID-19 pandemic.⁽⁴⁾ As a response, numerous vaccines were developed and approved in less than a year from when the virus was first identified. Nevertheless, this rapid worldwide use of the vaccines led the Centres for Disease Control and Prevention (CDC) to utilize a real-time Vaccine Adverse Event Reporting System called V-Safe to track potential side effects of the vaccine. ⁽¹⁾ In addition, many studies reported a

variety of vaccine-related side effects, ranging from mild symptoms like fever, chills, headache, fatigue, and arm pain ^(1,2) to severe side effects such as thrombosis and anaphylaxis⁽¹⁾. However, the progression of vaccination rollouts accompanied feeds from various media articles and social media platforms that the COVID-19 vaccine was affecting the menstrual status in women, which included delay or early menstruation, heavier bleeding patterns, painful sessions, and breakthrough bleeding.⁽⁴⁾ Changes to periods and unexpected vaginal bleeding are not listed, but primary care clinicians and those working in reproductive health are increasingly approached by people who have experienced

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these events shortly after vaccination.⁽²⁾ A range of menstrual cycle changes after Covid-19 vaccination have been reported, including longer and shorter cycles, missed cycles, heavier and lighter menstrual flow, and intermenstrual spotting⁽³⁾. Many people began sharing that they experienced unexpected menstrual bleeding after SARS-CoV-2 inoculation. This emerging phenomenon was undeniable yet understudied.⁽⁵⁾ While battling the life-threatening complications of COVID-19, its effect on the menstrual cycle and infertility has been somewhat ignored.⁽⁶⁾ Emergency authorization for use of numerous vaccines for Covid - 19 were given considering the mortality benefit, however adverse effects especially (minor) could have been overlooked.

Menstrual cyclicity is an overt sign of health and fertility⁽⁸⁾. Menstrual outcomes were not included in COVID-19 vaccine trials, limiting the ability of the manufacturers, public health agencies and clinicians to respond to questions about the impact of the vaccine on menstrual health.⁽¹⁷⁾ Henceforth questions related to menstruation should be given due importance.

Covishield is a non-replicating adenovirus vaccine, while Covaxin is a viral inactivating vaccination. In preclinical investigations, both Covishield and Covaxin showed encouraging outcomes.⁽¹¹⁾

Methodology

Descriptive study was performed on women in the menstruating age group, 19 to 45 years. The authors circulated an easy-to understand questionnaire titled "Menstruation - Vac Questionnaire" to women of reproductive age who had taken the Covid precautionary dose vaccine. The Questionnaire contained questions on demographic data, COVID-19 infection details (if infected), vaccination details, menstrual cycles changes post covid precautionary dose vaccine, past menstrual history, and a brief medical history. Prior approval by Institution Ethical Committee was taken as well as written consent from the participants. Mc Nemar statistical test was applied. A $p < 0.05$ was considered statistically significant.

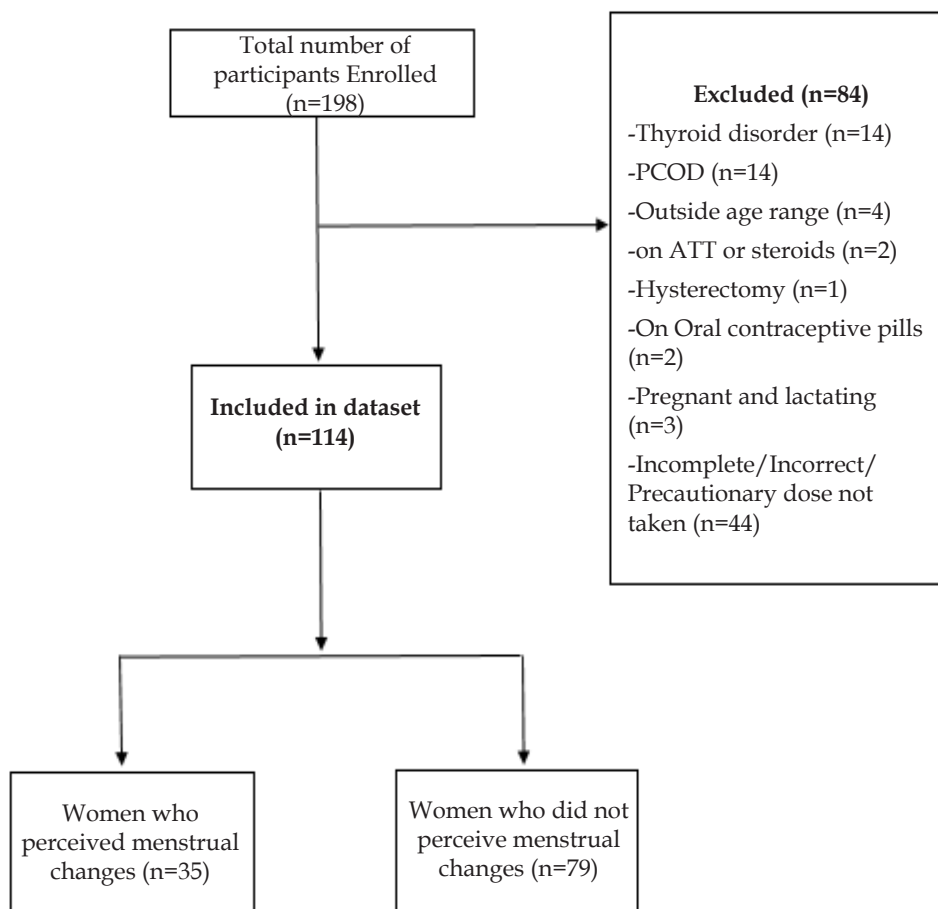


Figure 1: Flowchart

Results

Retrospective data was collected. A significant number of participants were physiotherapists, physiotherapy students and health care workers who maintained records of their menstrual data using mobile applications.

Table 1 summarizes the demographic data of the participants. A total of 198 subjects were taken and 114 subjects met the inclusion criteria. Subjects selected were of the age group 19 to 45 years, mean age- 27.1 years, BMI - 23.3. Of the selected subjects 10.5% reported to have tested positive for Covid infection twice, 35.1% reported to have tested positive once and 54.4% reported that they never tested positive for Covid infection.

Out of the 114 women who were selected for the study, 35 (30.7%) women complained of menstrual irregularities after the precautionary vaccination.

Table 1: Demographic Data

Age 19-45 YEARS (n=190)	MEAN±SD 27.1±7
BMI (n=190)	23.3 ± 4.2
Height (m) (n=190)	1.6 ± 0.1
Weight (kgs) (n=190)	59.2 ±11
Status of Infection	N (%)
Twice	12 (10.53)
Once	40 (35.08)
Never	62 (54.39)
Vaccine type	N (%)
COVISHIELD	107 (93.86)
COVAXIN	7 (6.14)

Changes in the menstrual cycle length and days of menstruation were taken into consideration. The percentage changes in menstrual cycle from 1st to 6th cycle post precautionary dose vaccine depicted in Table 2.

Table 2: Percentage of Change vs No Change in Menstrual Cycle from 1st to 6th cycle post precautionary dose vaccine

	1 st cycle	2 nd cycle	3 rd cycle	4 th cycle	5 th cycle	6 th cycle
No Changes Not Able to Recall (0)	84.20%	84.20%	89.50%	92.10%	93.00%	94.70%
Any Change (1)	15.80%	15.80%	10.50%	7.90%	7.00%	5.30%

Table 3: Depicting the percentage of menstrual changes reported 6 months post Covid-19 precautionary dose vaccine. (Changes of cycle length and/ or days of menstruation)

	FIRST CYCLE		SECOND CYCLE		THIRD CYCLE		FOURTH CYCLE		FIFTH CYCLE		SIXTH CYCLE	
	Change in Cycle Length	Change in Days of Menstruation	Change in Cycle Length	Change in Days of Menstruation	Change in Cycle Length	Change in Days of Menstruation	Change in Cycle Length	Change in Days of Menstruation	Change in Cycle Length	Change in Days of Menstruation	Change in Cycle Length	Change in Days of Menstruation
No change	72.8%	79.8%	72.8%	78.9%	74.6%	76.3%	78.9%	76.3%	79.8%	76.3%	78.1%	78.1%
Not able to recollect	6.1%	6.1%	8.8%	8.8%	9.6%	10.5%	10.5%	10.5%	10.5%	10.5%	11.4%	10.5%
Decrease	8.8%	7.9%	8.8%	5.3%	7.9%	6.1%	6.1%	7.9%	6.1%	7.9%	5.3%	7%
Increase	12.3%	6.1%	9.6%	7%	7.9%	7%	4.4%	5.3%	4.4%	5.3%	4.4%	4.4%

Table 4: Percentage changes after 1st and 2nd Dose after Covid Vaccine

% CHANGE AFTER 1 ST VACCINE	12.3%
% CHANGE AFTER 2 ND VACCINE	11.4%

Table 5: Comparison between 1st cycle to 6th cycle after Precautionary dose

COMPARISON	BETWEEN CYCLES CHANGE	Mc Nemar Test
1 ST Cycle - 2 nd Cycle	21.9%	0.687
1 ST Cycle - 3 rd Cycle	18.4%	0.238
1 ST Cycle - 4 th Cycle	15.8%	0.049 *
1 ST Cycle - 5 th Cycle	14.9%	0.03 *
1 ST Cycle - 6 th Cycle	14%	0.019 *
* p - value < 0.05 (significant)		

Discussion

During the exhausting pandemic of COVID-19, the gynecological care has somewhat taken a backseat with reduced reporting of menstrual abnormalities. (6) Unfortunately, clinical trials of the current COVID-19 vaccines did not collect menstrual cycle outcomes post-vaccination. Vaccines that were manufactured during the pandemic had questionable inclusion of menstruation in efficacy. (12)

The present study was conducted to evaluate the effect of precautionary dose COVID-19 vaccine on menstrual health in women aged between 19–45 years. At the conception of the study there were limited studies to know the impact of Covid vaccine/ precautionary dose vaccine on the menstrual cycle. In our study the prevalence of changes in menstrual cycles post- precautionary dose vaccination was found to be 15.8%, 15.8%, 10.5%, 7.9%, 7% & 5.3% in 1st, 2nd, 3rd, 4th, 5th and 6th cycle respectively. In the women who reported changes - on comparing the menstrual discrepancies between cycles, i.e. 1st cycle with 2nd cycle, 1st to the 3rd cycle and so on till the 6th cycle, it was found that from 4th cycle onwards - increased number of women returned to their normal cycle, suggesting that changes observed were in a small percentage and transient. Any change in menstrual pattern does bring about anxiety, stress and concern in women. Edelman A et al in their study also stated that any change, even if small and not clinically relevant, is important to the public, and even more so in the context of a new vaccine. Although small changes in menstrual characteristics might not be meaningful to clinicians and scientists, any perceived effect to a routine bodily function linked to fertility can cause alarm for those experiencing it, and can contribute to vaccine

hesitancy. Even small changes, when unanticipated, can have a large adverse impact on the quality of life of people who menstruate and who experience episodes of social embarrassment, anxiety related to uncontained bleeding or fertility planning or prevention, and worry about what bleeding changes mean for their overall health. (3) Moolamalla S, Bakshi K, Medarametla V in their study stated that the prevalence of unusual menstrual cycles post-vaccination/ infection was 21.7%. However, the cycles returned to normal within three cycles in 61.9 and 53.8% post-vaccination and infection respectively, suggesting that the changes were transient. (12) Ata B et al have also documented a transient effect on the menstrual cycle. (10) It emerged that symptoms such as delayed menstruation and abnormal uterine bleeding (metrorrhagia, menometrorrhagia, and menorrhagia) were generally reported within the first three weeks of vaccination, especially after the second dose, with a percentage of 23% and 77%, respectively. The COVID-19 vaccination originates an immune response and subsequent inflammation may transiently disturb the ovarian hormonal production over one or two cycles, with consequential anomalous menstrual bleeding. (13) Pourmasumi S et al states that the female reproductive system is an organ system affected by COVID-19 that has received less attention due to the lack of related deaths. The angiotensin-converting enzyme (ACE2) receptor has been reported to be the main receptor involved in the penetration of coronaviruses into cells. Postcell invasion, COVID-19 disrupts the renin-angiotensin system (RAS) by down-regulating ACE2 expression in host cells, leading to an exacerbated proinflammatory response by angiotensin-II. This receptor is present in the female reproductive system, particularly in the ovaries and uterus, where it affects

folliculogenesis, steroidogenesis, oocyte maturation, ovulation, and endometrial regeneration.⁽⁹⁾

Our research was only taking note of any changes observed in the menstrual cycles similar to research by Eldelman A which was also not designed to determine why these changes might happen; these changes are probably due to temporary vaccine-related activation of immune response, but more research is needed.⁽³⁾ However, in clinical experience, following the administration of all COVID-19 vaccines, both mRNA and adenoviruses vectorized adenoviruses, some adverse drug reactions of the menstrual cycle have been recorded. COVID-19 vaccination gives rise to an immune response^(14, 11), and the subsequent inflammation can transiently disrupt ovarian hormone production for one or two cycles, resulting in abnormal menstrual bleeding MHRA.⁽¹⁴⁾

Study by Lagana A S et al stated menstrual changes following vaccination are indeed not so unusual, given that such modifications were observed after vaccination for other microbes, like the Human Papilloma virus, or human hormones, such as human chorionic gonadotropin. Such disturbances could likely be ascribed to the inflammatory/immunological reaction ensuing from adjuvants comprised in the vaccines, at least in some cases. Menstrual irregularities after both the first and second doses of the vaccine were found to self-resolve in approximately half the cases within two months.⁽¹⁶⁾ Changes in menstruation were observed with HPV and flu vaccinations also.⁽¹⁵⁾ Similar changes in menstruation such as decreased cycle length and dysmenorrhea were found in 53% of the population that got vaccinated for Typhoid, as reported by a medical doctor at the Presbyterian Hospital, New York in 1913. However, the cycles were regularized within six months post-vaccination.⁽¹²⁾ Determining the scale of menstrual problems, their cause and the impact on those who menstruate and wider society will allow identification of new preventative and therapeutic strategies.⁽¹⁵⁾

Limitations: Our study has a few limitations. Small sample size. Recall bias may also be a problem since the study was self-reporting and questions asked required details of about six months. Our study does not cover aspects such as impact on quality of

life, pain etc., which gives a future scope of study. The only vaccines used in our study was Covishield and Covaxin, so specific conclusion about any other vaccine could not be drawn.

Conflict of Interest: None

Any Sponsors: None, self-funded by the group.

Ethical Committee Approval: Ethical clearance was given by our hospital HOLY FAMILY ETHICAL COMMITTEE in June 2023. All participants submitted signed informed consent and then only proceeded. No vulnerable patients were taken up during study

Conclusion

The number of women who reported change was small and the changes observed were transient but any number of changes in a women menstrual cycle does bring about anxiety, stress and discomfort in her quality of life.

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