

Assessment of Menstrual Pattern in Women Post-COVID-19 Vaccination: An Observational Study

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Abstract

Purpose: Women all over the world are receiving COVID-19 vaccines. Commonly reported side-effects include sore arm, fever, fatigue, and myalgia. Recent literature has suggested about possible menstrual abnormalities due to these vaccines. This study aims to assess the incidence of heavy bleeding and menstrual irregularity in the month subsequent to COVID-19 vaccination.

Methods: An online questionnaire was distributed to reproductive-age women (18 - 45 years) who had received at least one dose of COVID-19 vaccine. They were asked to fill out a questionnaire after attaining informed consent. After exclusion of 96 responses, a final sample of 100 was obtained. Descriptive tables were generated and scoring and categorisation were done.

Results: Mean age of the participants was 22 years, majority of them being students (74%). Participants were vaccinated with Covishield (73%), Covaxin (26%), or Sputnik-V (1%). 5% described their bleeding as heavy, 31% reported blood clots during menstruation and 3 women had periods that lasted for more than one week. Moderate to severe dysmenorrhoea was present in 36%. Six per cent individuals could not predict the start date of their period at all, suggesting menstrual irregularity. Dose of vaccine whether first or second and type of vaccine did not have any association with heavy bleeding ($P = 0.587$ and $P = 0.158$ respectively) or menstrual irregularity ($P = 0.133$ and $P = 0.336$ respectively).

Conclusion: Heavy bleeding and menstrual irregularity were commonly present following COVID-19 vaccination. Participants reported blood clots very commonly. Larger studies with extended follow-up are needed to fully understand post-vaccination menstrual changes.

Key words: Heavy menstrual bleeding, COVID-19 vaccination, menstrual irregularity, covishield, covaxin.

Introduction

COVID-19 infection struck India during the month of February, 2020. More than 40 million people have been affected as of now¹. Occurrence of the pandemic led to rapid development of different vaccine types. Vaccination drive started in India in January, 2021 and presently adults are offered Astra Zeneca's Covishield, Bharat Biotech's Covaxin, or Sputnik-V. In contrast to Covaxin, which is an inactivated vaccine, Covishield and Sputnik-V are adenoviral vector vaccines. Covishield and Covaxin are available in two doses, separated by 12 - 16 weeks and 4 weeks, respectively, whilst sputnik-V is available in two doses separated by 21 days. Some commonly reported side-effects that women might experience after receiving the COVID-19 vaccine are injection site tenderness/pain, headache, fatigue, fever, myalgia, nausea, and vomiting, etc.². At the end of December 2021, the UK's Medicines and Healthcare Products Related Agency (MHRA) recorded more than 40,000 incidents of menstruation disturbances across all COVID-19 vaccination brands available in the UK, including Covishield³. These reported

menstrual changes were transient in nature³. COVID-19 infection itself can cause menstrual cycle changes, possibly due to an immune-mediated mechanism and inflammation of the endometrial lining^{4,6}.

In a published case-control study in the UK, menstrual cycle changes were found in 20% of women up to 4 months after receiving their first vaccine dose. The odds of reporting any menstrual changes were increased for smokers and individuals with positive COVID-19 status⁶. In a study from the Middle East and North Africa region, 66.3% of women experienced menstrual abnormalities after vaccination, and the majority of them had symptoms after the first dose¹⁰. A study among Japanese women found that age-adjusted odds of attending hospital were increased for abnormal amount of menstrual bleeding; irregular menstruation, and persistent occurrence of abnormal amounts of menstrual bleeding following HPV vaccine administration¹¹. So far, the Indian government has not listed menstrual cycle changes or unexpected vaginal bleeding¹². No study, done in India, is yet available in the literature.

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The objectives of this study were: 1) to assess the incidence of heavy bleeding and menstrual irregularity post-COVID-19 vaccination, and 2) to investigate the factors associated with menstrual abnormalities post-COVID-19 vaccination.

As per CDC, heavy menstrual bleeding is defined as menstrual bleeding that is heavy or lasting for more than 7 days or passing blood clots of the size of a quarter coin or larger¹³.

Material and Methods

This descriptive, cross-sectional study was conducted among Indian women aged 18 - 45 years who were menstruating after attaining informed consent. It involved an anonymous questionnaire distributed online using a convenient sampling method. The research proposal was approved by The Institutional Ethics Committee for Human Research (IEC-HR), University College of Medical Sciences, Delhi (Proposal no. IECHR-2021-51-5-R2). Women who received at least one dose of the COVID-19 vaccine between July, 2021 and December, 2021 were included in the study. We excluded those women who refused participation, had any changes to periods in terms of pattern or flow in 3 months prior to vaccination, had a recently diagnosed medical/inflammatory disorder, had pregnancy or abortion prior to vaccination, and had recent changes in contraception.

Since at the time of sample size calculation, no study was available to find out the prevalence of heavy menstrual bleeding post-COVID-19 vaccination, prevalence was assumed to be 50%, with a 10% margin of error. On calculation initial sample size came out to be 96. Therefore, 100 women were recruited to study. Fig. 1 shows a flowchart of the study population selection.

Recruitment was done by the principal investigator, strict confidentiality was maintained and data was kept completely anonymised. An online questionnaire containing a semi-structured proforma was used to collect:-

1. Socio-demographic details such as age, occupation, income, religion, and marital status;
2. Clinical details such as parity, abortion, substance abuse, height and weight for calculation of BMI (based on revised consensus guidelines for Asian Indians and World Health Organisation (WHO) criteria)¹⁴.
3. Details about the COVID-19 received and dates of 1st and 2nd doses.

Categorisation of the socio-economic class was based on the BG Prasad scale updated for the year 2021, calculated using the total number of family members and total monthly income of the family in rupees¹⁵. The menstrual bleeding questionnaire was used to assess heavy bleeding, passage

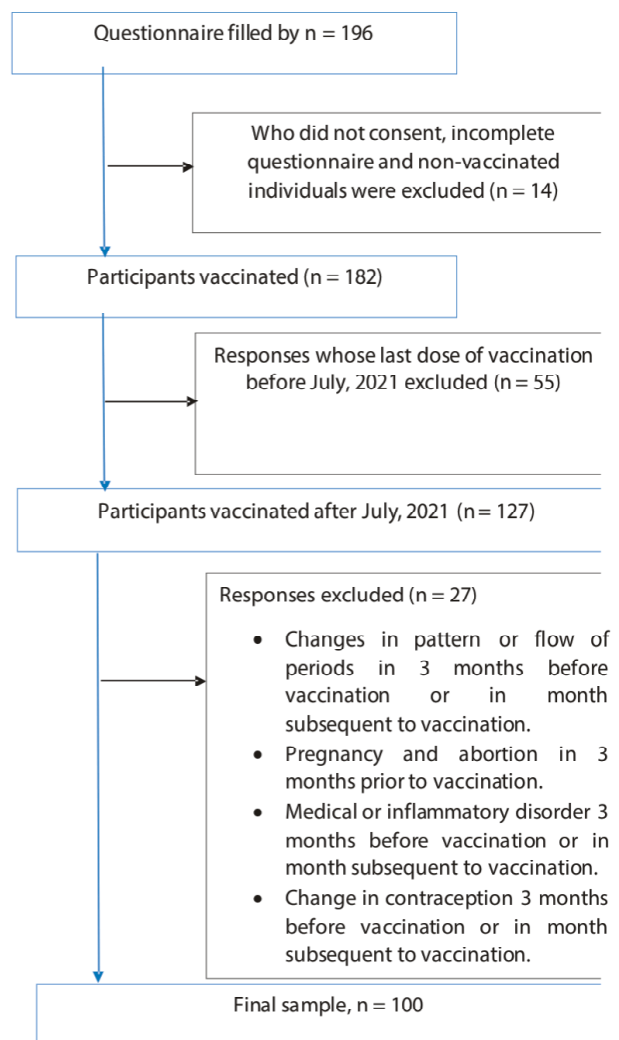


Fig. 1: Flowchart of study population selection.

of blood clots, menstrual pain, and irregularity in the one month post-vaccination¹⁶.

Statistical analysis was performed using SPSS 22.0 (IBM, Armonk, NY, USA). Descriptive analysis was done to calculate the frequencies. Pearson's Chi-square or Fisher's exact test was used to compare qualitative variables. Quantitative variables such as BMI was compared by independent t-test. An exact 95% confidence interval was calculated for reported heavy bleeding and irregularity. Statistical significance was assumed at $p < 0.05$.

Results

The final sample size of vaccinated individuals was 100, of which the majority (73%) received Covishield, 26% received Covaxin, and the remaining (1%) received Sputnik-V. The majority received both doses of vaccine (77%). Among the participants, ages ranged from 18 - 45

years with a mean of 22 years. Most respondents were students (74%) and belonged to the upper socio-economic class (89%). Table I shows the baseline characteristics of the study population. The vast majority of participants were disease-free, although 4% of them had a chronic skin condition, and 2% each had thyroid disease, PCOS, and tuberculosis. 13% of the participants used the barrier method of contraception. Participants who were smokers were only 1%.

Table I: Baseline characteristics of study population.

Characteristics	Study population (n = 100)	
	Number	%
AGE (years)		
< 20	24	(24)
20 - 30	61	(61)
> 30	15	(15)
Religion		
Hindu	95	(95)
Muslim	2	(2)
Others	3	(3)
Occupation		
Housewife	14	(14)
Student	74	(74)
Professional	11	(11)
None	1	(1)
Marital status		
Unmarried	82	(82)
Married	18	(18)
Socio-economic status		
Upper class	73	(73)
Upper middle class	16	(16)
Middle class	9	(9)
Lower middle class	1	(1)
Lower class	1	(1)
Parity		
0	89	(89)
1	4	(4)
> = 2	7	(7)
Name of vaccine		
Covishield	73	(73)
Covaxin	26	(26)
Sputnik-V	1	(1)
Status		
Partially vaccinated (single dose)	23	(23)
Fully Vaccinated (double dose)	77	(77)

Five per cent of women experienced heavy bleeding (95% CI 1.6 - 11.2), 31% of women (95% CI 22.1 - 41) reported blood clots during menstruation and, 3 women had periods lasting for more than 1 week. Additionally, moderate-to-severe menstrual pain was experienced by 36% of women. The questionnaire also contained a question concerning the predictability of the start date of the period, which was used to assess menstrual irregularity. Six per cent of participants (95% CI 2.2 to 12.6) could not predict the start date of the periods at all; in 57%, it was somewhat predictable, and in the remaining 37%, it was completely predictable (Fig. 2).

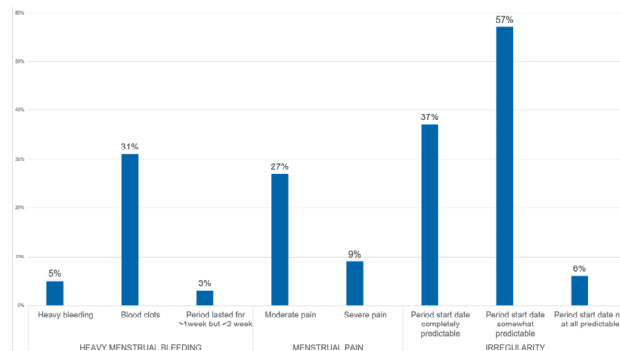


Fig. 2: Percentages of heavy menstrual bleeding, menstrual pain, and irregularity post-COVID-19 vaccination.

The univariable analysis showed that heavy bleeding and menstrual irregularity were reported after both the first and second dose of vaccination but it was not statistically associated with any particular dose. ($p = 0.587$ for reported heavy bleeding, $p = 0.217$ for blood clots, and $p = 0.133$ for irregularity) (Fig. 3). Heavy bleeding, the passage of blood clots, or menstrual irregularity did not have any association with the brand of vaccine administered, i.e., Covishield or Covaxin ($p = 0.158$ for heavy bleeding, $p = 0.575$ for blood clots, and $p = 0.336$ for menstrual irregularity). Both vaccine brands were associated with menstrual abnormalities, indicating that neither adenovirus vector nor inactivated virus strategy is specifically linked to these changes. For this analysis, a respondent who received Sputnik-V ($n = 1$) was excluded (Fig. 4).

Participants who had a diagnosis of a medical disorder did not differ in experiencing menstrual abnormalities from those who were medically healthy. No association was found between reported blood clots in periods ($p = 0.678$) or irregularity ($p = 0.441$) and long-standing history of medical disorders such as Tuberculosis, thyroid disorder, chronic skin condition, or PCOS. BMI was not associated with heavy bleeding or menstrual irregularity. On an independent t-test, it was found that BMI values of women with heavy bleeding or menstrual irregularity and those who did not have heavy bleeding or menstrual irregularity

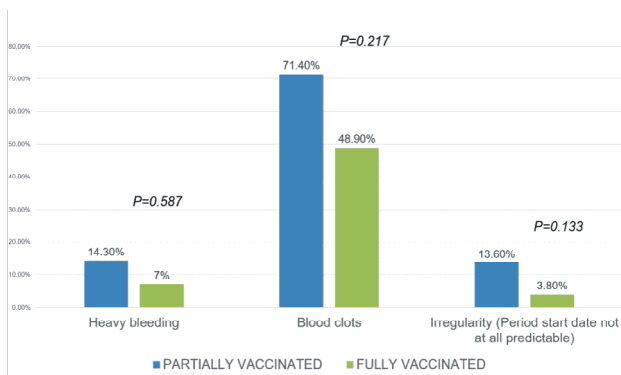


Fig. 3: Comparison of menstrual pattern (heavy bleeding, blood clots and irregularity) in single dose and doubled dose vaccinated individuals.

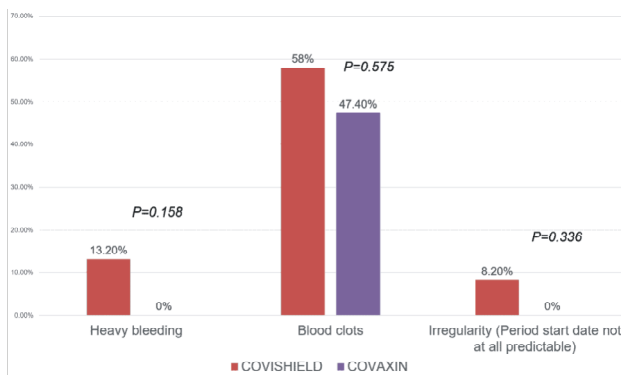


Fig. 4: Comparison of menstrual pattern (heavy bleeding, blood clots and irregularity) in Covishield and Covaxin.

were not statistically different ($p = 0.398$ for heavy bleeding and $p = 0.136$ for menstrual irregularity).

In response to a question concerning whether or not they would refrain from advising other women to get the vaccine in light of any menstrual abnormalities (if observed), we discovered that 4% of respondents had done so. This showed that there was some amount of vaccine hesitancy in the general population.

Discussion

This study, done among 100 women in India, found that among vaccinated women of reproductive age who had no change in the pattern or flow of their periods prior to vaccination, 5% reported heavy bleeding, one in 3 women passed blood clots during menses, and 6% were unable to predict the start of their periods one month after their last dose of vaccination.

We found that heavy bleeding and menstrual irregularity were reported after both the first and second dose of the vaccine. Here, menstruation was assessed for one month

after the last dose of the vaccine. There is a possibility that findings reported after the second dose might be a result of the first dose of the vaccine as seen in a UK-based case-control study where 20% reported any changes to their menstrual cycle up to 4 months after receiving their first injection⁶. In this sample, we did not find any association of heavy bleeding or menstrual irregularity with any particular brand of vaccine. A similar finding was observed in a study done in the UK by Male where the brand of vaccine was not associated with differences in timing or flow of the next period¹⁹. A study done in the Middle East and North Africa also showed similar results¹⁰.

In the present study, people who had a diagnosis of medical disorder (Tuberculosis, thyroid disorder, PCOS, or chronic skin condition) did not differ in experiencing menstrual abnormalities from those who were medically healthy. Our findings are consistent with a recent study done in the MENA region where thyroid disorders, PCOS, and symptoms of menstrual abnormalities were not associated¹⁰. Though, it is difficult to propose this considering the small number of participants who had been diagnosed with medical disorders. The mechanism behind these post-vaccination menstrual changes is still unknown. However, it has been proposed that endocrine abnormalities and immune-mediated mechanisms are responsible for this^{4,17}. Participants who had previously contracted SARS-CoV-2 infection were excluded from our study, therefore the results that are reported cannot possibly be the consequence of an immune response to the disease, as was the case in a study where odds of reporting any changes in the menstrual cycle were increased due to prior COVID-19 infection⁶.

The strength of this study is that it is a pioneer study, done in India, assessing menstrual pattern post-COVID-19 vaccination. An online questionnaire was used instead of face-to-face interview, in light of the ongoing pandemic situation, to limit transmission of the virus. The limitations are that it is retrospective in nature, with recall and selection bias, and small sample size. A control group could have been taken to compare the findings that were observed. Assessment of menstrual pattern was only done for one-month post-vaccination although further follow-up is desirable. Prospective studies recruiting a large sample and longer follow-up are needed.

Conclusion

In our study, heavy bleeding and menstrual irregularity were commonly present following COVID-19 vaccination. It opens a new domain of counselling women prior to vaccination about menstrual disturbances so that they can be more receptive and prepared for the same. The

mechanism underlying the potential effects of the COVID-19 vaccine on menstruation needs to be studied. Larger prospective studies with extended follow-up are required to fully understand the problem.

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