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COVID-19 VACCINES AND ALTERATIONS IN MENSTRUAL CYCLE-A MATTER OF CONCERN?

Arshiya Mubeen Batool[1]*, Neha Fatima[2], Farzana Shereen[3], Tanuja Paipuru[4] and C. Uma Sree Devi[5]

[1,2,3]PharmD (PB) Post Graduate, Department of Pharmacy Practice, Aster Prime Hospital Ameerpet, Sultan ul Uloom College of Pharmacy, JNTUH, Telangana, India.
[4]0MBBS, MS-Obstetrics & Gynaecology, Consultant OB/GYN at Aster Prime Hospital, Ameerpet, Hyderabad, India.
[5]MBBS, MD-Anaesthesiology, at Aster Prime Hospital, Ameerpet, Hyderabad, India.

***Corresponding Author: Dr. Arshiya Mubeen Batool**
PharmD (PB) Post Graduate, Department of Pharmacy Practice, Aster Prime Hospital Ameerpet, Sultan ul Uloom College of Pharmacy, JNTUH, Telangana, India.

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ABSTRACT
A prospective observational study was conducted among the South Indian female population in the gynecology department of the tertiary care hospital in Hyderabad, Telangana. for a period of 13 months in 352 patients from September 2021 to October 2022. Our study aimed to analyze the menstrual changes experienced by these women after the administration of the first and second doses of the COVID-19 vaccines available in the Indian market, namely, Covishield, Covaxin, and Sputnik V. The patient's responses before and after vaccination were recorded. A follow-up was conducted after their first and second doses of vaccination, respectively, and baseline characteristics were observed, recorded, and evaluated to determine the effects of these vaccinations on the menstrual cycle. In the study conducted, 165 females, were in the age group of 15–24 years. 140 females, were 25–34 years old. 35 females,were 35–44 years old. 12 females, were in the age group of 45–54 years. In the given study population, comorbid disease conditions were observed in 11 females with asthma, 12 females with diabetes mellitus, 4 females with hypertension, and 30 females with thyroid disease. 34 females had PCOD, and 5 females had other underlying comorbidities. Among 352 females, 71 (20.2%) of them were vaccinated by Covaxin, 261 (74.1%) were vaccinated by Covishield, and 20 (5.7%) were vaccinated by Sputnik V. Changes in menstrual cycle such as duration,flow, changes in abdominal pain or cramps, changes in vaginal discharge episodes, and body pain or leg pain after the first and second doses of vaccination was recorded. The changes were found to be reversible and not a matter of concern for the majority of the study population, which is 79.8%.e also included in the study.

KEYWORDS: Side effects of COVID-19 vaccines, menastrual cycle abnormalities, SARS-COV2, NSAIDS, female, Menstruation, gynecology.

INTRODUCTION
Menstruation affects more than half of the world's population, and menstrual disorders are extremely common and detrimental. [1] Improper menstruation can lead to anemia [2], which harms the quality of life and is a significant socio-economic challenge for women, their family members, health care providers, and society.[3–7]

The International Federation of Gynecology and Obstetrics (FIGO) has defined standard parameters for typical menstruation, such as menstrual frequency, duration, regularity, and volume, and deviation from these may indicate abnormal uterine bleeding.[8] Menstrual cycle features are increasingly being identified as "vital signs," acting as both indicators and potential determinants of physical health and well-being.[9] Menstrual cyclicity is an obvious indicator of good health and fertility.

Menstrual characteristics do not remain constant from month to month throughout an individual's life.[10-12]

Concerns about a potential connection between coronavirus disease 2019 (COVID-19) vaccination and menstrual irregularities may end up causing vaccine hesitancy. Unfortunately, menstrual cycle outcomes were not collected in the clinical trials of the current COVID-19 vaccines.[13-16] VAERS (Vaccine Adverse Event Reporting System) somehow doesn't effectively gather details concerning menstrual cycles, and by May 2021, just a small number of women (fewer than 200) had self-reported menstrual-related problems to VAERS.[17]

The recent incident of the severe acute respiratory syndrome coronavirus 2 (SARSCoV2) outbreak, formerly known by the interim name 2019 novel coronavirus (2019nCoV), in the city of Wuhan in China's Hubei province in 2019–2020, has now been causing massive numbers of mortality and morbidity in humans with coronavirus infection diseases (COVID19) with fever, severe respiratory illness, and pneumonia. [18,19,20]

To determine whether there is a link between COVID-19 vaccination and menstrual cycle changes. We enrolled 352 vaccinated females aged 18 to 50, and we tracked their menstrual cycles before and after vaccination. We present an analysis of a prospective observational study here.

Compared to men, women seem to report side effects more frequently. According to a study by the CDC, 78.7% of the adverse event reports filed within the first month of immunization in the United States involved women. 15 out of the 16 people who experienced anaphylaxis after receiving a vaccine were girls, according to another study. These results are consistent with a 2013 study on the H1N1 vaccine administered during the 2009 flu pandemic, which discovered a higher incidence of hypersensitivity reactions among females of reproductive age than in other study population subgroups. This gender disparity may be influenced by pregnancy hormones such as estrogen and testosterone. According to a mouse study, estrogen stimulates the body to produce more antibodies, which boosts the immune system's reaction. [21-26]

Below, we have mentioned the vaccines, their types, and their side effects that have been included in our study.

Table 1: Types of Vaccines and Their side effects.

Vaccines	Types	Side effects
Covishield	Recombinant, replication-deficient chimp adenovirus vector encoding the sars-cov-2 spike (s) glycoprotein.	Pain at the injection site, nausea, dizziness, fatigue, a mild fever, headache, muscle pain, and chills. **Menstrual abnormalities (based on reported cases) such as cramps, and increased or decreased flow. Rare cases: increased vaginal discharge. A very rare case of menstrual blood clots.**
Covaxin	Whole-virion inactivated vero cell-derived vaccine	Injection site pain, rashes, headache, fatigue, fever, abdominal pain, and vomiting. Rare cases: swelling of the throat and face. **Menstrual changes: a delay in periods or early periods, sometimes bleeding.**
Sputnik v	Human adenoviral vector-based vaccine	Sore arm, tiredness, low fever. Extremely rare cases: breathing difficulties, convulsions, muscle weakness, hypertension, in addition to headache. **Menstrual changes: increased abdominal cramps; a 30-day menstrual cycle increased to 45 days; increased vaginal discharge.** [27-28]

Search strategy

The literature search for this article was carried out using the keywords "side effects of COVID-19 vaccines" on ncbi.nlm.nih.gov, "menstrual cycle disturbances after COVID-19 vaccination" on Sage journals, and "Covid-19 vaccines and the menstrual cycle" on NIH. All the various aspects, such as retrospective, prospective, and observational studies, from both review and research articles, have been taken into consideration for the literature work.

METHODOLOGY

Our study is a prospective observational study of the South Indian female population, including patients referred to the Department of Gynaecology at Aster Prime Hospital, Hyderabad, for treatment of PCOS or PCOD and menstrual abnormalities from September

2021 to October 2022. The total sample collected to determine menstrual abnormalities was 352. The subjects selected were the outpatients on examination and based on the data provided by the patients. We collected the remaining data from the non-patient female South Indian population through a Google Forms survey. This study has been approved by the Institutional Review Board of Aster Prime Hospital, Ameerpet. Data from each individual is collected with their consent and convenience.

A carefully curated and designed data form was used to collect data and to conduct a survey which includes details like age, weight, height, occupation, marital status, comorbidities, treatments or therapies if any disease is present, the number of pregnancies, type of vaccine, previous menstrual cycle date, changes after the first dose and second dose i.e.,(duration, flow, clots, abdominal pain, episodes of vaginal discharge, body pains/ leg pain, about lifestyles i.e., (smoking, alcohol consumption, etc.), history of any surgery/surgeries in past 6 months, history of heavy menstrual bleeding, how long the menstrual changes last (were they temporary or permanent), how much in months did it take to go back to normal, did they seek any medical help, and did they opt for any medical treatment for the menstrual change (if yes, what are the medications being prescribed ?)

RESULTS AND DISCUSSION

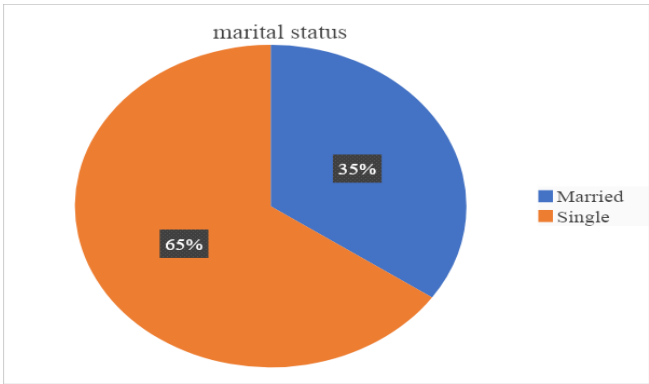

Figure 1: Marital status.

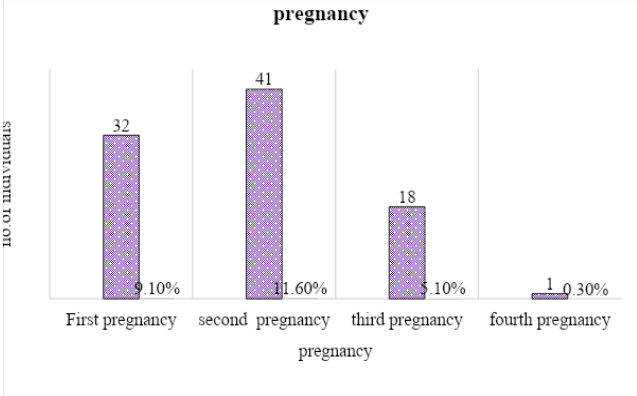

Figure 2: Number of pregnancies.

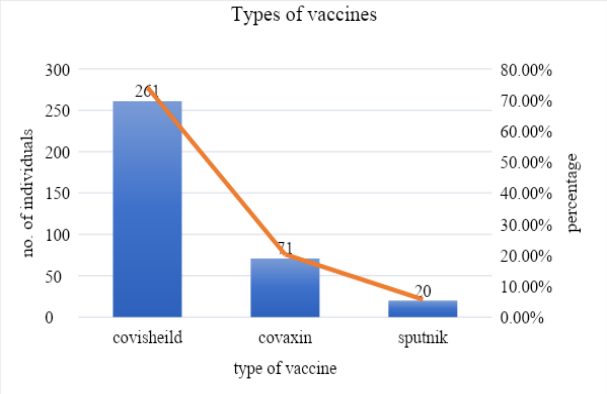

Figure 3: Types of vaccines.

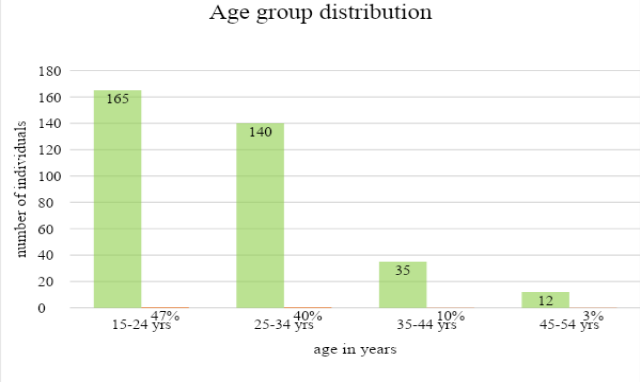

Figure 4: Age group distribution.

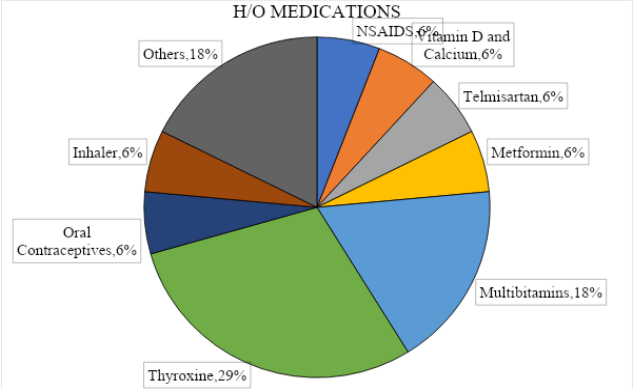

Figure 5: History of medications.

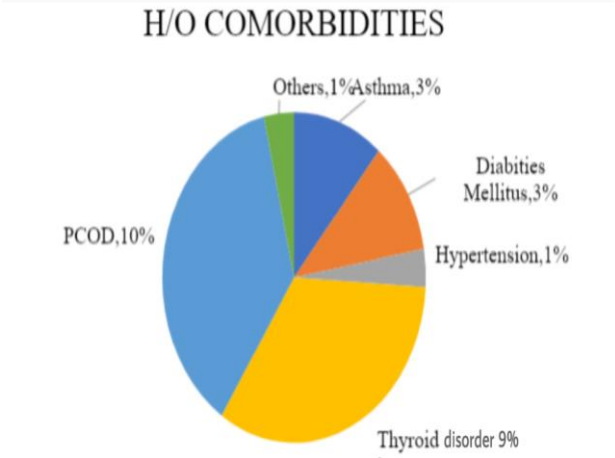

Figure 6: History of comorbidities.

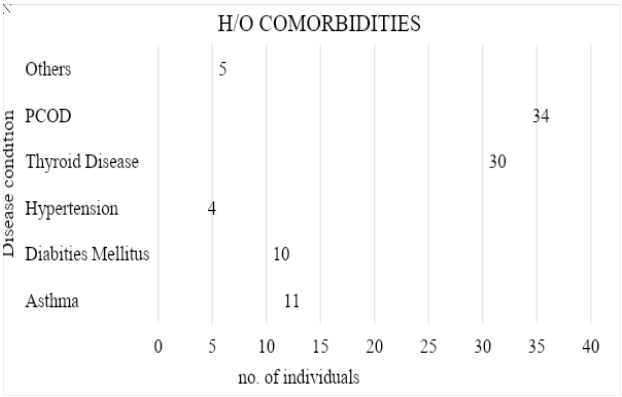

Figure 6: History of comorbidities.

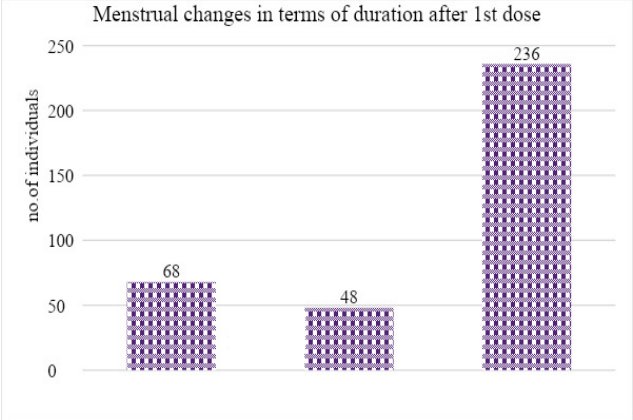

Figure 7: Menstrual changes-duration after the first dose.

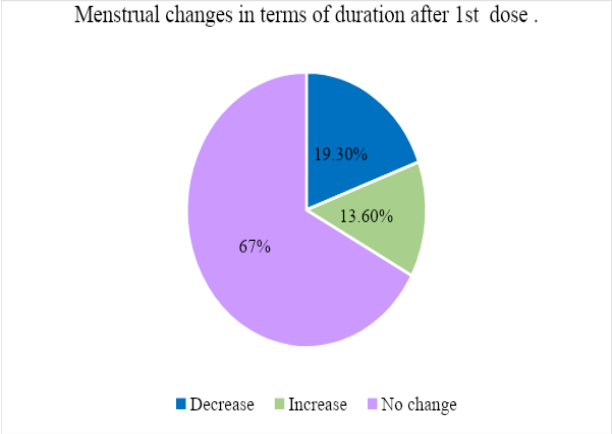

Figure 7: Menstrual changes-duration after the first dose.

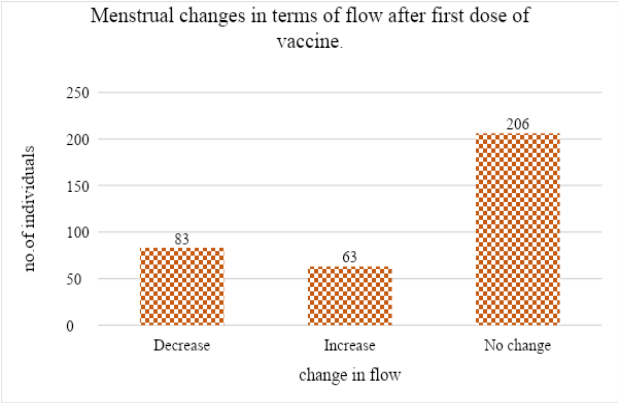

Figure 9: Menstrual changes-flow after the first dose.

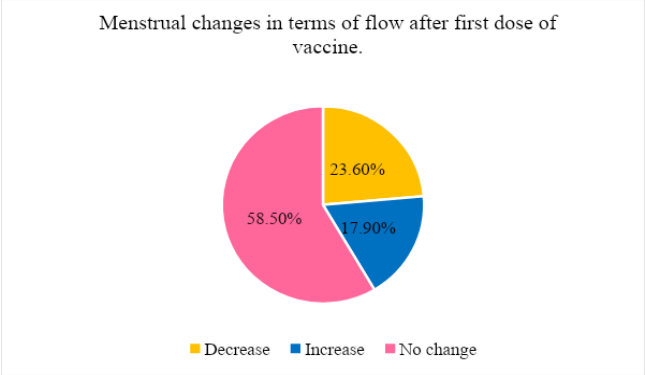

Figure 9: Menstrual changes-flow after the first dose.

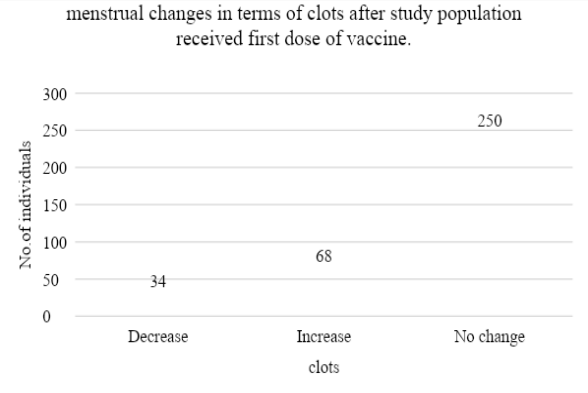

Figure 10: Menstrual changes: clots after the first dose.

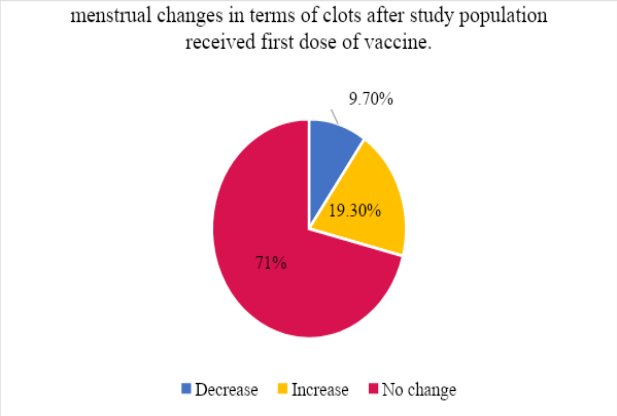

Figure 10: Menstrual changes: clots after the first dose.

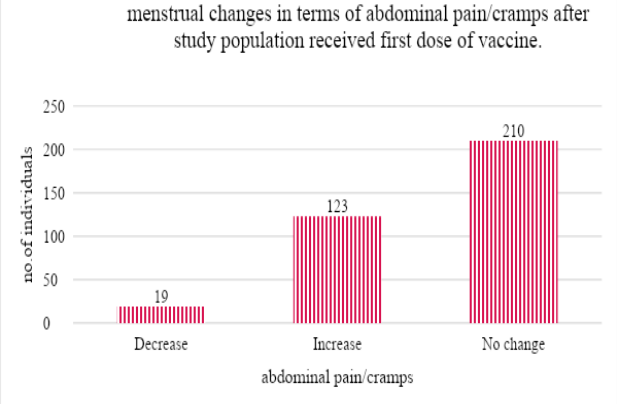

Figure 11: Menstrual changes: abdominal pain/cramps after the first dose.

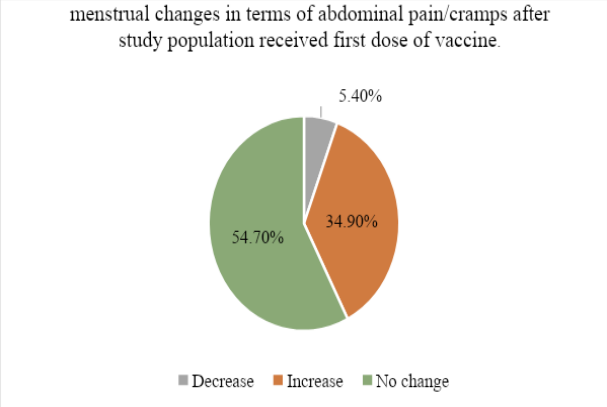

Figure 11: Menstrual changes: abdominal pain/cramps after the first dose.

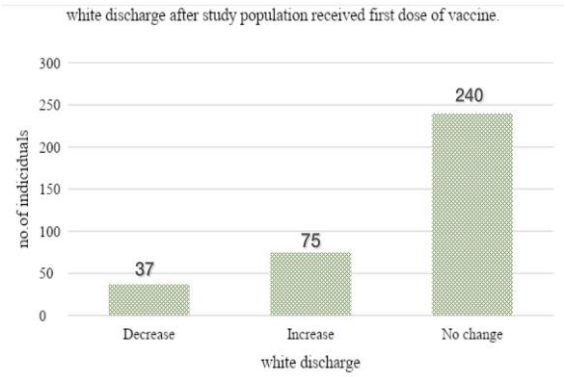

Figure 12: Menstrual changes: white discharge after the first dose.

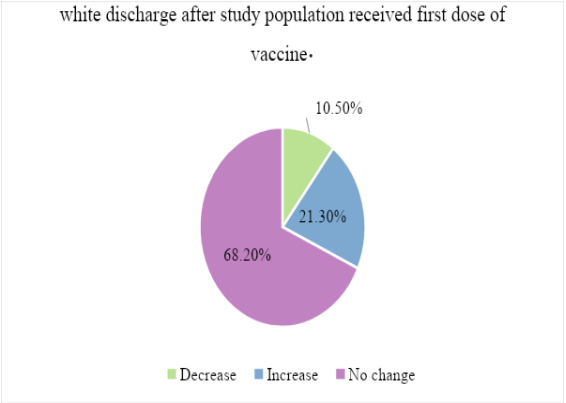

Figure 12: Menstrual changes: white discharge after the first dose.

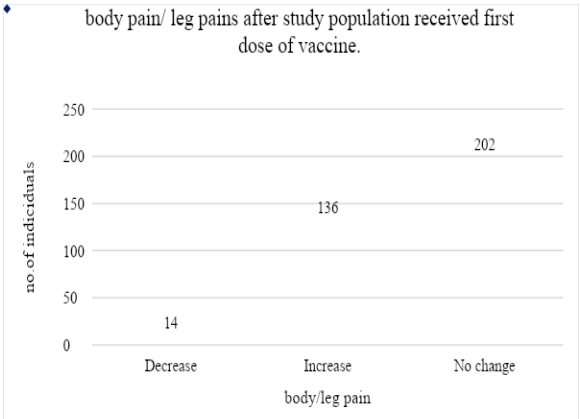

Figure 13: Menstrual changes: body pain/ leg pains after the first dose.

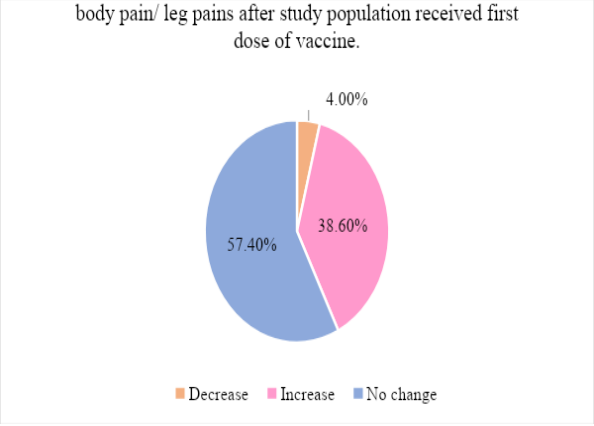

Figure 13: Menstrual changes: body pain/ leg pains after the first dose.

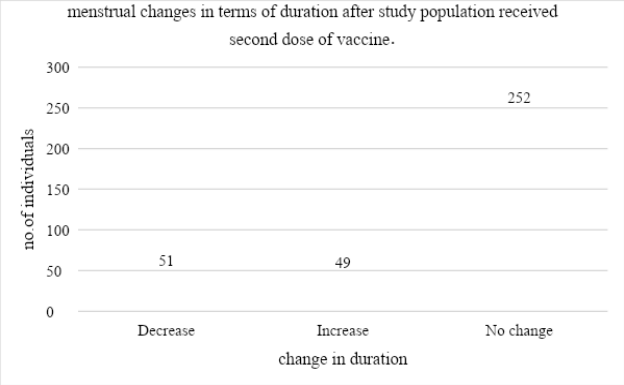

Figure 14: Menstrual changes: duration after the second dose.

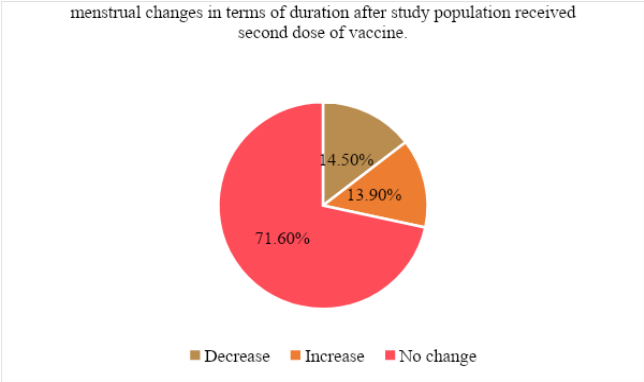

Figure 14: Menstrual changes: duration after the second dose.

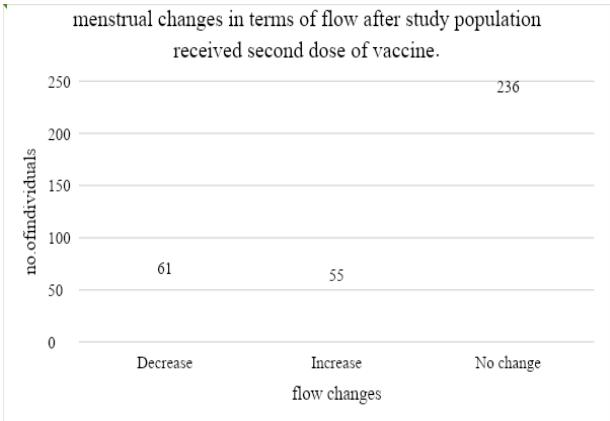

Figure 15: Menstrual changes: flow after the second dose.

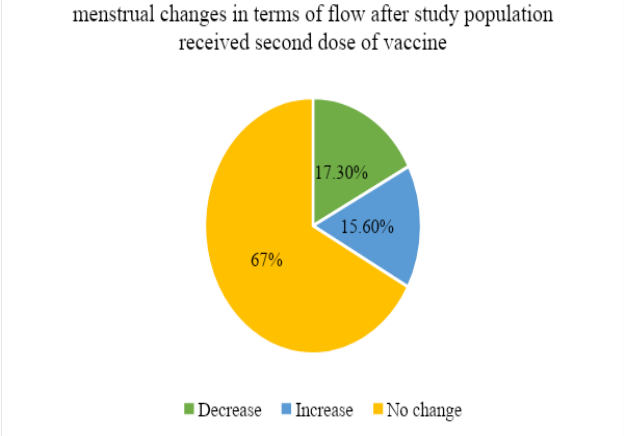

Figure 15: Menstrual changes: flow after the second dose.

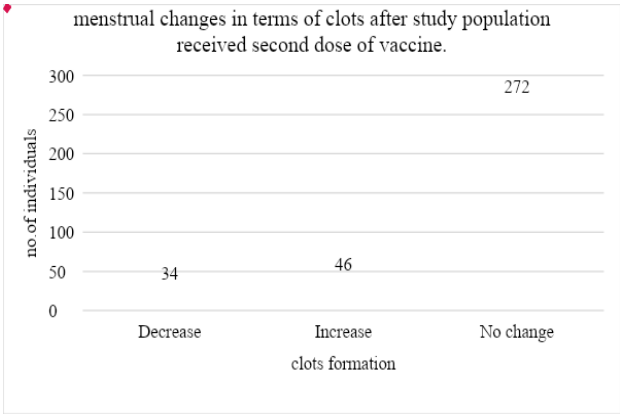

Figure 16: Menstrual changes: clots after the second dose.

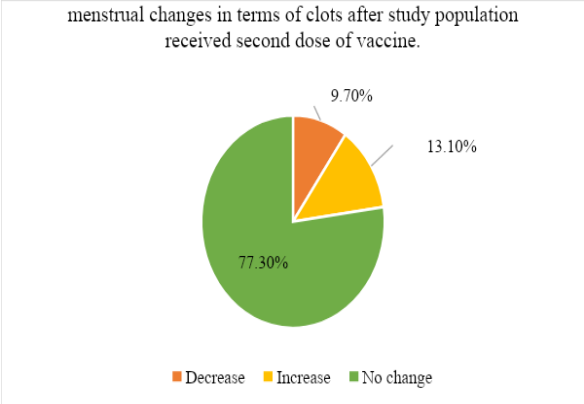

Figure 16: Menstrual changes: clots after the second dose.

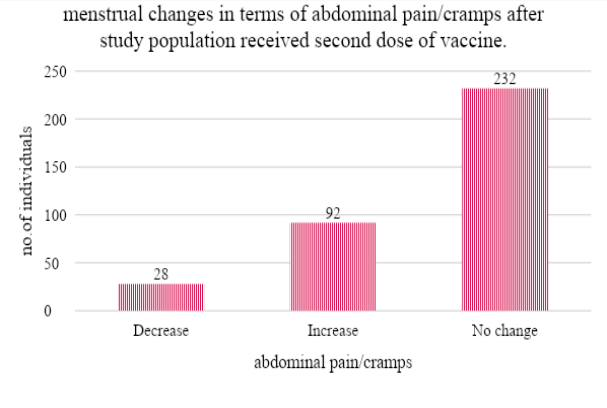

Figure 17: Menstrual changes: abdominal pain/cramps after the second dose.

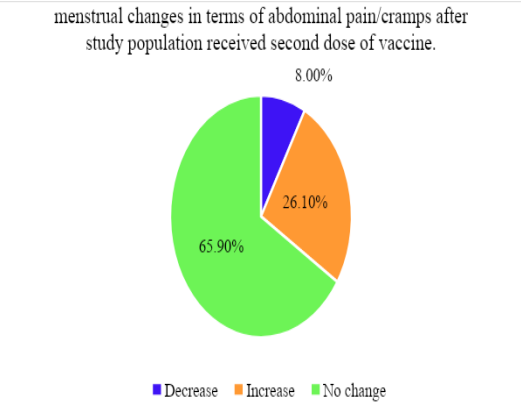

Figure 17: Menstrual changes: abdominal pain/cramps after the second dose.

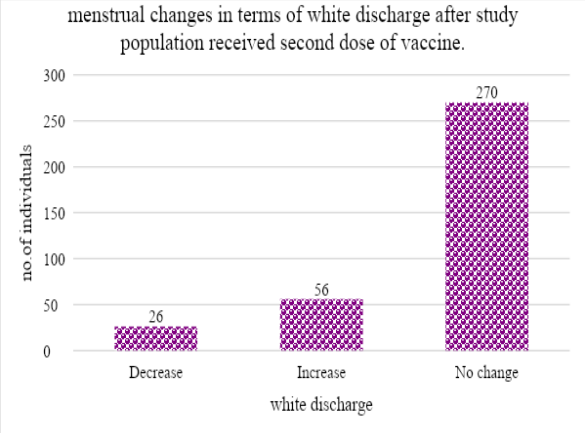

Figure 18: Menstrual changes: white discharge after the second dose.

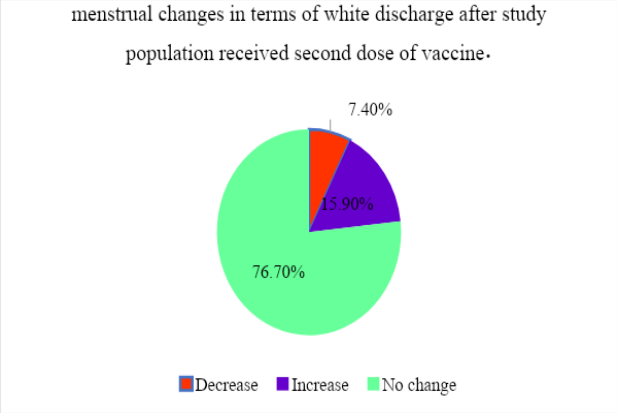

Figure 18: Menstrual changes: white discharge after the second dose.

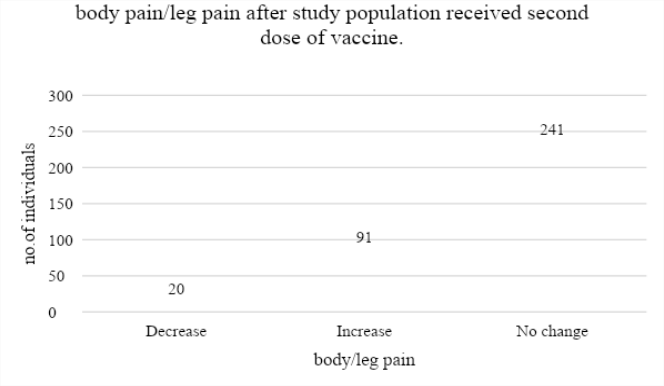

Figure 19: Menstrual changes: body pain/leg pains after the second dose.

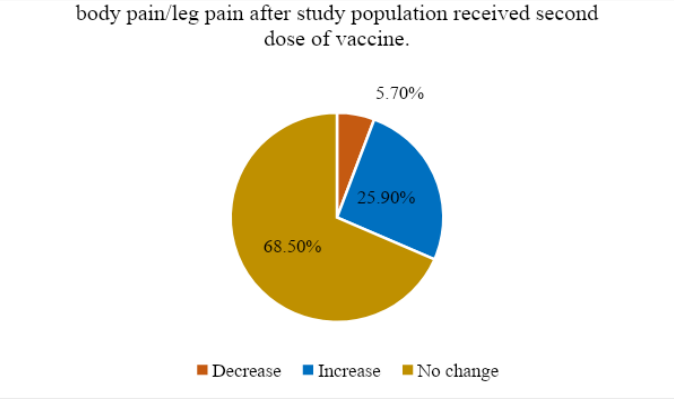

Figure 19: Menstrual changes: body pain/leg pains after the second dose.

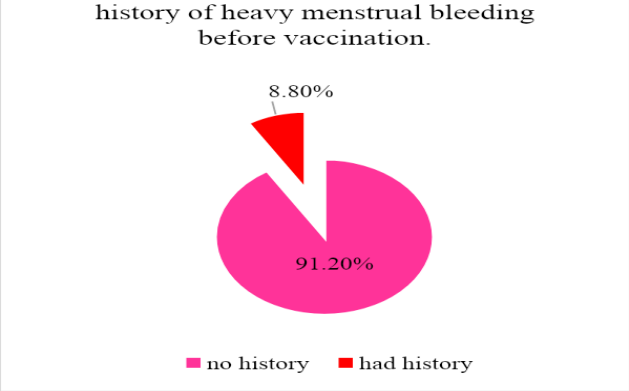

Figure 20: History of heavy menstrual bleeding before vaccination.

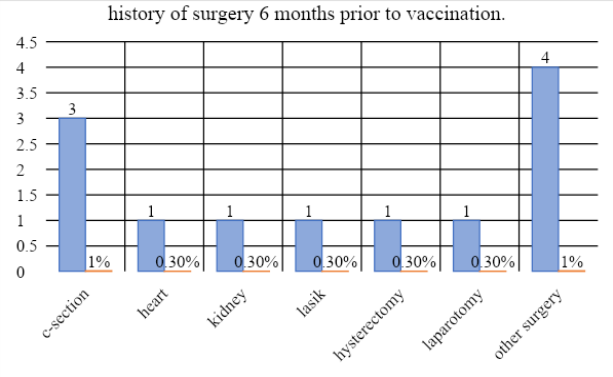

Figure 21: History of surgery 6 months prior to vaccination.

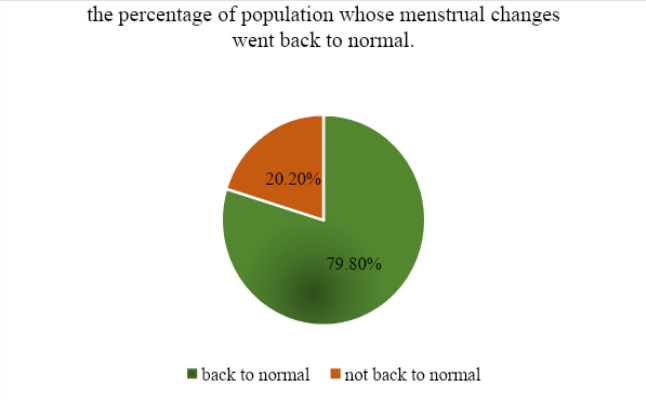

Figure 22: The percentage of population whose menstrual changes went back to normal.

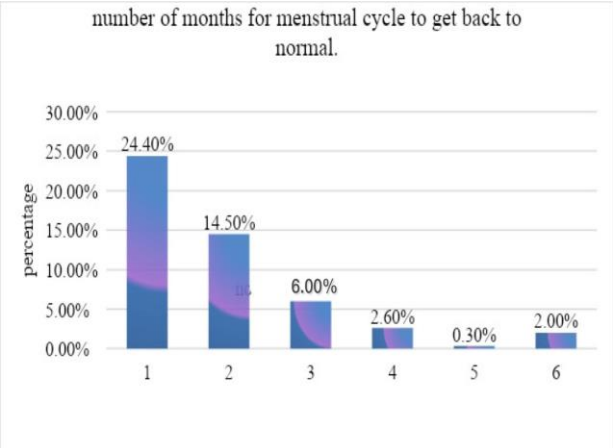

Figure 23: Number of months for menstrual changes to get back to normal.

CONCLUSION

COVID-19 was a massive outbreak that affected billions of people around the globe. This pandemic left the entire world in utter chaos. Even scientists and medical team experts were helpless as this deadly virus took the lives of billions of people, and they couldn't save their lives. It was discovered that the virus harmed people's immunity, so we needed to boost and spark ours. Different vaccines were formulated that helped build an immune response against COVID-19. All medications and vaccines have side effects, whether minor or severe. Females observed changes in their menstrual cycle after vaccination. Changes in the menstrual cycle are a matter of concern, and hence there was a need to record what changes were observed in the menstrual cycle after vaccination.

In our study, we recorded the changes in terms of menstrual flow, clot formation, abdominal cramps, white discharge, and body and leg pain after the first and second doses of COVID vaccination. Major factors, i.e., the medication history of the patient and comorbid disease conditions, were also taken into consideration. Medication history included NSAIDS, vitamin D, calcium supplementation, telmisartan, metformin, multivitamins, thyroxine, oral contraceptives, inhalers, and a few other medications. Also included were comorbid conditions like asthma, diabetes mellitus, hypertension, thyroid disorders, and PCOD and PCOS. Other factors, like heavy menstrual bleeding and surgery, were also taken into consideration.

All the baseline characters were recorded. Our study population consisted of females aged 15 to 54. Among the 352 study participants, 121 were married and 229 were unmarried. A major factor, the number of pregnancies, was also taken into consideration. 32 females were primigravida, 41 females were gravida 2, 18 females were gravida 3, and one of them was gravida 4. The majority of the 352 were vaccinated with Covishield, with 261 receiving it, followed by Covaxin (71), and Sputnik (20 receiving it). A small number of females had changes in their menstrual cycle. The changes were found to be reversible and not a matter of concern for the majority of the study population, which is 79.8%.

Changes observed in the study population

1. **Menstrual changes in terms of duration**

- After the "first" dose of the vaccine: A decrease in the duration of menstruation was seen in 68 females (19.3%).
- An increase in the duration of menstruation was seen in 48 females (13.6%).
- No changes were seen in 236 females (67%).
- After the "second" dose of the vaccine: A decrease in the duration of menstruation was seen in 51 females (14.5%).
- An increase in the duration of menstruation was seen in 49 females (13.9%).
- No changes were seen in 252 females (71.6%).

2. **Menstrual changes in terms of flow**

- After the "first" dose of the vaccine: A decrease in the flow of menstruation was seen in 83 females (23.6%).
- An increase in the flow of menstruation was seen in 63 females (17.9%).
- No changes were seen in the 206 females (58.5%).
- After the "second" dose of the vaccine: A decrease in flow was seen in 61 females (17.3%).
- An increase in flow was seen in 55 females (15.6%).
- No changes were seen in 236 females (67%).

3. **Menstrual changes in terms of clots**

- After the "first" dose of the vaccine: A decrease in clots were seen in 34 females (9.7%).
- An increase in clots was seen in 68 females (19.3%).
- No changes were seen in the 250 females (71%).
- After the "second" dose of the vaccine: A decrease in clots was seen in 34 females (9.7%).
- An increase in clots was seen in 46 females (13.1%).
- No changes were seen in 272 females (77.3%).

4. **Menstrual changes in terms of abdominal pain/cramps**

- After the "first" dose of the vaccine: A reduction in abdominal cramps was seen in 19 females (5.4%).
- An increase in cramps was seen in 123 females (34.9%).
- No changes were seen in the 210 females (59.7%).
- After the "second" dose of the vaccine: A decrease in cramps was seen in 28 females (8.0%).
- An increase in cramps was seen in 92 females (26.1%).
- No changes were seen in the 232 females (65.9%).

5. **White discharge**

- After the "first" dose of the vaccine: A decrease in white discharge was seen in 37 females (10.5%).
- An increase in white discharge was seen in 75 females (21.3%).
- No changes were seen in the 240 females (68.2%).
- After the "second" dose of the vaccine: A decrease in white discharge was seen in 26 females (7.4%).
- An increase in white discharge was seen in 56 females (15.9%).
- No changes were seen in 270 females (76.7%).

6. **Body pain/ leg pains**

- After the "first" dose of the vaccine: A decrease in leg pain was seen in 14 females (4.0%).
- An increase in leg pain was seen in 136 females (38.6%).
- No changes were seen in the 202 females (57.4%).
- After the "second" dose of the vaccine: A decrease in leg pain was seen in 20 females (5.7%).
- An increase in leg pain was seen in 91 females (25.9%).
- No changes were seen in 241 females (68.5%).

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Ethical
Approved.

Conflict of interest
The author declares no conflicts of interest.

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