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Association Between COVID-19 Vaccines and Menstrual Disorders: A Systematic Review

Laura Esteban-Cledera[1,2], Marcela Villalobos[3], Martín Solorzano[1] and Felipe Villalobos[1]*

[1]*Fundació Institut Universitari per a la recerca a l'Atenció Primària de Salut Jordi Gol i Gurina*

[2]*Departament of Experimental and Health Sciences, Pompeu Fabra University, Barcelona, Spain*

[3]*Faculty of Health Sciences, Open University of Catalonia, Barcelona, Spain*

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***Corresponding author:** Fundació Institut Universitari per a la recerca a l'Atenció Primària de Salut Jordi Gol i Gurina (IDIAPJGol), Barcelona, Spain, Email: fvillalobos@idiapjgol.info

Abstract

Reports on menstrual disorders following COVID-19 vaccination have emerged. This systematic review seeks to address the existing knowledge gap by providing a critical assessment of the existing evidence on the association between COVID-19 vaccines and menstrual disorders. A systematic literature search was conducted across PubMed, Scopus, and Web of Science. Open access, observational cross-sectional, prospective, or retrospective cohort studies, published between January 2021 to December 2023, reporting on association between COVID-19 vaccines and menstrual disorders in women aged 12-55 years old, without pre-existing menstrual disorders, written in English or Spanish, in any setting, were eligible for inclusion. Two independent reviewers screened articles for eligibility, extracted data, and assessed study quality. A total of 31 studies were included in the review. Studies reported menstrual outcomes following vaccination with any dose of the COVID-19 vaccines, Pfizer/BioNTech®, Moderna®, AstraZeneca® and Janssen®. The most common menstrual disorders reported were changes in cycle length, changes in the amount of bleeding, and changes in pain intensity. Most of the studies found an association with the second and third dose, and with Pfizer/BioNTech®, Moderna® and AstraZeneca® vaccines. This systematic review highlights the importance of monitoring and addressing menstrual health concerns in vaccine recipients.

Keywords: COVID-19 vaccine; menstrual disorders; women's health

Introduction

The COVID-19 disease, caused by the SARS-CoV-2 virus, was declared a pandemic by the World Health Organization (WHO) on March 11, 2020. Since then, the rapid development and global deployment of vaccines have played a critical role in the fight against the pandemic, with millions of doses administered since the first vaccines were licensed in December 2020[1]. In response to this health emergency, the European Commission initially approved vaccines developed by Pfizer/BioNTech®, Moderna®, AstraZeneca®, and Janssen®. These vaccines demonstrated efficacy rates in initial clinical trials, providing protection against severe forms of COVID-19 infection and various viral variants. Despite their efficacy, reports of adverse events, including menstrual disorders, have emerged irrespective of the dose and the COVID-19 vaccine type administered [2]. Since June 2022, the European Medicines Agency (EMA) mentioned that 30% of reports on COVID-19 vaccines administrated in women could be related to menstrual disorders [3].

Various systematic reviews have summarized studies evaluating the effect of COVID-19 vaccines on menstrual disorders [4–6]. A review by Al Kadri et al., included 16 cross-sectional studies, and the findings indicated that menorrhagia, oligomenorrhea, and polymenorrhea were the most common menstrual disorders after COVID-19 vaccination. Similar results were found in a review by Nazir M. et al., which included 14 studies, and by Chao M. et al., which included 4 observational studies. However, most of studies included in the reviews were unable to report causal relationship between menstrual disorders and dose or type of COVID-19 vaccines.

The rationale behind conducting this systematic review is to establish a comprehensive understanding of the existing evidence on the association of COVID-19 vaccine on menstrual disorders in women aged between 12 - 55 years old, without pre-existing menstrual disorder.

This approach ensures a well-informed and contextualized foundation for the forthcoming research. Therefore, this study not only contributes to the current literature but also plays a pivotal role in providing essential context and support for the upcoming investigation into this matter within vaccination and women's health. sThe aim of this systematic review is to describe the association between COVID-19 vaccines and menstrual disorders in women aged between 12 - 55 years old, without pre-existing menstrual disorders, with a focus on the evaluation of the association of different COVID-19 vaccine types, and the number of doses administered on menstrual disorders, based on a comprehensive analysis of current evidence.

Materials and Methods

Study design

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [7] and was registered in the International Prospective Register of Systematic Reviews (PROSPERO: ID no. CRD42024505096).

Search strategy and data source

The PECOt (Population, Exposure, Comparator, Outcome, and time) framework was used to structure the search: 1) Population: women aged between 12 - 55 years old, without pre-existing menstrual disorders; 2) Exposure: any dose of the following COVID-19 vaccines: Pfizer/BioNTech®, Moderna®, AstraZeneca® and Janssen®; 3) Comparator: No applicable; 4) Outcome: any menstrual disturbance reported after any dose of COVID-19 vaccines; 5) time: from January 1, 2021 to December 31, 2023. A systematic literature search was conducted across major electronic databases including PubMed, Scopus, and Web of Science, combining keywords, and using the Boolean operators "AND" and "OR". The search strategy was flexible to accommodate studies in Spanish and English language. No filters were applied in the initial search. The identified keywords, including ("COVID-19 vaccine" OR "SARS-CoV-2 vaccine") AND ("menstrual disorders" OR "menstrual disturbances" OR "menstrual irregularities" OR "menstrual cycle" OR "menorrhagia" OR "polymenorrhagia" OR "hypermenorrhoea" OR "oligomenorrhea" OR "abnormal cycle length"), were utilized to search for relevant literature. The search strategy was documented, and results were critically evaluated for relevance and quality. Subsequent iterations and adjustments were made as necessary during the research process (Supplementary Table. 1)

Inclusion and exclusion criteria

The inclusion criteria for this systematic review were: (1) open access, (2) observational cross-sectional, prospective, or retrospective cohort studies, (3) written in English or Spanish, (4) published from January 1, 2021, to December 31, 2023, (5) studies evaluating the association between COVID-19 vaccines and menstrual disorders, (6) in women aged between 12 - 55 years old, without pre-existing menstrual disorders, and (7) vaccinated with any dose of the following COVID-19 vaccines: Pfizer/BioNTech®, Moderna®, AstraZeneca®, Janssen®, (8) in any setting. The exclusion criteria were: (1) reviews, systematic reviews, meta-analysis, clinical trials, case series, or letters to editor, (2) studies which evaluated pregnant women and/or breastfeeding, and (3) studies that were not peer-reviewed.

Study selection and data management

The identified bibliographic citations were transferred to a tool for collecting, examining, and evaluating the titles and abstracts of the citations; this tool was the Rayyan platform (rayyan.qcri.org). Two reviewers independently (L.E.-C. and F.V.) assessed the titles and abstracts of the studies from the search for inclusion. Subsequently, the same reviewers independently reviewed the full text of all potentially eligible articles before making a final decision on eligibility. Any discrepancies were discussed, and a third reviewer acted as a mediator if no consensus was reached (M.V.). In the event of duplicate study populations, the most recent article was considered. Exclusion reasons were recorded, and the inclusion and exclusion process were documented with a flowchart as recommended by the PRISMA guidelines.

Outcomes measures

The main outcome included in this study was the association between any dose of the following COVID-19 vaccines: Pfizer/BioNTech®, Moderna®, AstraZeneca®, Janssen®, and any menstrual disturbance reported in women aged 12-55 years, without pre-existing menstrual disorders.

Data extraction and data synthesis

Two independent reviewers extracted all relevant information from the included studies into a standardized Excel template and compared it to ensure accuracy. The data of interest were title, author, publication year, study design, sample size, age, inclusion criteria, study duration, vaccination status, menstrual disorders reported, association between exposure and outcome, and conclusion.

Analysis of study quality

To assess the quality of studies included in this systematic review, The Joanna Briggs Institute Critical Appraisal Tools (JBI) checklist was applied [8]. This checklist, developed by the Faculty of Health Sciences at the University of Adelaide, is structured

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independently based on the specific study design to be assessed

Results

Study selection

The primary search elicited 300 articles. After the removal of duplicates (100), 200 articles were screened for review of the full text. Of these, 169 studies were excluded based on different reasons. A total of 31 observational studies (12 cohort and 19 cross-sectional) were included for the analysis (Figure 1). Most of the studies (n = 24) were outside of Europe (EE.UU., Israel, Lebanon, Japan, Saudi Arabia, Jordan, Palestine, Syria, Egypt, Sudan, Libya, India, Latin America and Trinidad and Tobago)[9–32], while only 7 studies were conducted in Europe (UK, Netherlands, Germany, Denmark, Sweden, Spain and Hungary)[33–39]. (Supplementary Table. 2).

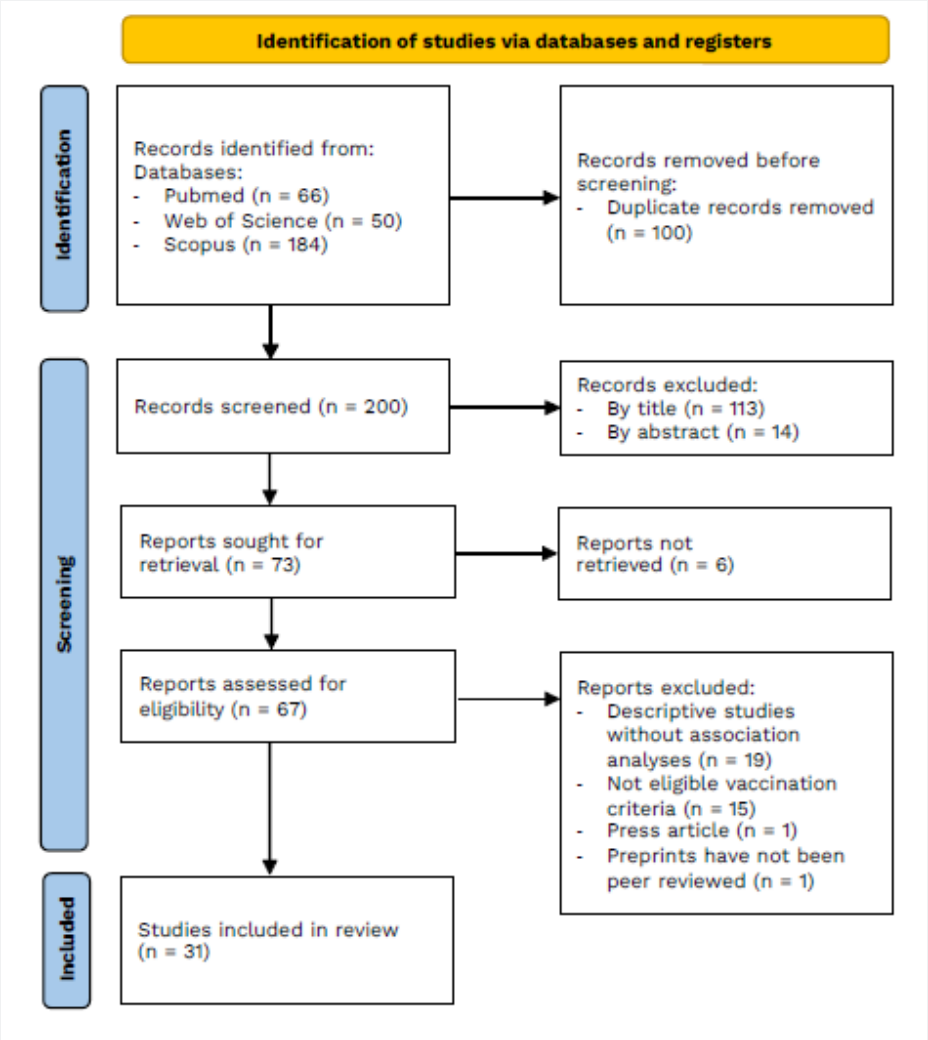

Figure 1: PRISMA Flow Chart

Quality appraisal

The quality of 31 studies was objectively assessed using a validated tool. Taken together, the studies provide useful evidence on the association between COVID-19 vaccination and menstrual disorders. However, during the assessment, it was found that some studies have methodological deficiencies, particularly in the identification and management of confounding factors, so it is suggested that the findings should be interpreted carefully. (Supplementary Table. 3)

Inclusion Criteria and Population Characteristics: Of the 31 studies included in this review, 28 clearly described the inclusion criteria for participants and the context in which they were conducted, allowing for a better assessment of the applicability of the results. Only 3 studies lack a detailed description of the setting and characteristics of the included female population.

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Exposure and Outcome Measurement: In nearly all studies (n=30), exposure measurement was conducted in a valid and reliable manner, as was the validity and reliability of outcome measurements. However, in one of the included studies, standardized criteria or validated methods were not used to measure outcomes.

Identification and Management of Confounding Factors: In 21 of the included studies, potential confounding factors that could influence the association between COVID-19 vaccination and menstrual disorders in the studied population were identified. This means that a third of the studies did not consider these variables, potentially compromising the internal validity of their findings. Although a considerable number of studies identified confounding variables, only 13 implemented clear strategies to manage them (such as statistical adjustments or the use of multivariate regressions).

Study characteristics

A total of 3,060,573 women were the study population included in this review from 31 studies. Of these, 2,946,448 (96.27%) women were from one retrospective cohort study conducted in Sweden. For most of the studies, the female population was represented by women over the age of 18 years old in general. Seven studies included female adolescents aged between 12–17 years old. The various types of vaccines administered to the women include Pfizer/BioNTech®, Moderna®, AstraZeneca® and Janssen®. In most studies, the Pfizer/BioNTech® vaccine was the most administered vaccine. The majority of the studies (n = 21) used self-reported (online) questionnaires to assess the presence of menstrual disorders, often spread through social media, whereas some used retrospective data (n=10).

COVID-19 vaccines and menstrual disorders

A wide variety of menstrual disorders were reported in the studies. The most common disorders included changes in cycle length (n = 19), changes in the amount of bleeding (n = 13), and changes in pain intensity (n =11), and other menstruated changes, menstrual disturbances, menstrual symptoms or irregular menstruation (n=6). Various studies reported more than one menstrual disorder.

Seventeen studies found an association between COVID-19 vaccines and menstrual disorders and one study found a weak and inconsistent association. Of these, 7 studies reported an association by dose of COVID-19 vaccine, 5 studies by type of COVID-19 vaccine, 2 studies by both conditions, and 4 did not stratify by dose or by type of COVID-19 vaccine. The results are heterogeneous, most of the studies found an association after the second and third dose, and Pfizer/BioNTech®, Moderna® and AstraZeneca® were associated with menstrual disorders.

Discussion

This systematic review summarized evidence on the association between COVID-19 vaccination and menstrual disorders. Our findings are consistent with recent systematic reviews that reported that menstrual disorders such changes in cycle length, changes in the amount of bleeding, and changes in pain intensity are common after COVID-19 vaccination in women aged 12-55 years, without pre-existing menstrual disorders. In addition, in most studies, the Pfizer/BioNTech® vaccine was the most administered vaccine. Heterogeneous results were found regarding menstrual disorders after specific COVID-19 vaccine brands. Some studies did not find differences between the vaccine brands whereas others found that Pfizer/BioNTech®, Moderna® and Astra Zeneca resulted in a higher rate of menstrual disorders, especially after second and third doses.

Research gaps

The systematic review reveals some research gaps in the current literature exploring the association between COVID-19 vaccination and menstrual disorders. Firstly, most studies employ observational designs, which limits the ability to draw definitive conclusions about causality between vaccination and menstrual disorders [40,41]. Without experimental or longitudinal research, it remains challenging to establish a clear association. Additionally, there is a notable lack of investigation into the biological mechanisms that might explain potential links between vaccines and menstrual disorders; exploring these mechanisms is crucial to understanding underlying causes and requires further study. Another gap lies in the scarcity of research addressing the long-term impact of vaccination-related menstrual disorders, with few studies examining the persistence or consequences of these changes over time [42]. Furthermore, many studies did not stratify findings by important factors, such as age, pre-existing clinical conditions, or other relevant variables, which could influence susceptibility or response to vaccination. Addressing these gaps is essential to produce more comprehensive, generalizable findings and to enhance our understanding of this possible side effect of COVID-19 vaccination.

Implications for further research

In further research on menstrual disorders related to vaccination, several areas require deeper exploration. More longitudinal studies are needed to follow women before and after vaccination to determine the timing and type of menstrual changes. Additionally, research should focus on the impact of different vaccine doses and types, as disorders appear more common after the second or third doses. Lastly, specific age groups, particularly adolescents near menarche and perimenopausal women, need targeted studies to assess any age-related differences in the occurrence of these disorders following vaccination [43].

Limitations

This systematic review on the association between COVID-19 vaccines and menstrual disorders faces some limitations that impact the strength and generalizability of its conclusions. A significant limitation is the heterogeneity among the included studies, as variability in study designs, methods of assessing

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menstrual disorders, and populations studied creates challenges in directly comparing results. This diversity restricts the ability to draw overarching conclusions and reduces the generalizability of findings to broader populations. Additionally, the quality of studies varies, with some relying heavily on self-reported data, which may introduce potential biases related to recall accuracy and subjective interpretation of symptoms. Another limitation is the frequent lack of control for confounding factors, which may influence menstrual outcomes and complicate the ability to isolate the effect of COVID-19 vaccination. Addressing these limitations in future research is essential to strengthen the evidence and provide clearer insights into this association.

Conclusions

In conclusion, this systematic review provides evidence suggesting an association between COVID-19 vaccination and various menstrual disorders, particularly following the second and third vaccine doses, with Pfizer/BioNTech®, Moderna®, and AstraZeneca® vaccines most frequently implicated. Common menstrual disorders reported included alterations in cycle length, bleeding amount, and pain intensity. However, the observational nature of most studies, reliance on self-reported data, and variability in study designs and populations limit the strength of causal inferences and generalizability of the findings. Future research with more robust methodologies, including controlled, longitudinal studies, is needed to better understand these associations, explore underlying biological mechanisms, and evaluate the potential long-term impact of COVID-19 vaccination on menstrual health.

Author Contributions

Conceptualization, L.E.-C., M.V., and F.V.; methodology, M.V. and F.V.; formal analysis, L.E.-C., M.V. and F.V.; investigation, L.E.-C., M.V. and F.V.; data curation, L.E.-C., M.V. and F.V.; writing-original draft preparation, L.E.-C., M.V., M.S., and F.V.; writing-review and editing, L.E.-C., M.V., M.S., and F.V.; supervision, M.V. and F.V. All authors have read and agreed to the published version of the manuscript.

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Supplementary Table 1: Full Search Strategy.

Database	Key words
Pubmed/MEDLINE	("COVID-19 vaccine" OR "SARS-CoV-2 vaccine") AND ("menstrual disorders" OR "menstrual disturbances" OR "menstrual irregularities" OR "menstrual cycle" OR "menorrhagia" OR "polymenorrhagia" OR "hypermenorrhoea" OR "oligomenorrhea" OR "abnormal cycle length")
Web of Science	(TS= ("COVID-19 vaccine" OR "SARS-CoV-2 vaccine")) AND (TS= ("menstrual disorders" OR "menstrual disturbances" OR "menstrual irregularities" OR "menstrual cycle" OR "menorrhagia" OR "polymenorrhagia" OR "hypermenorrhea" OR "oligomenorrhea" OR "abnormal cycle length"))
SCOPUS	TITLE-ABS-KEY ("COVID-19 vaccine" OR "SARS-CoV-2 vaccine") AND TITLE-ABS-KEY ("menstrual disorders" OR "menstrual disturbances" OR "menstrual irregularities" OR "menstrual cycle" OR "menorrhagia" OR "polymenorrhagia" OR "hypermenorrhea" OR "oligomenorrhea" OR "abnormal cycle length")

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Supplementary Table 2: Characteristics of included studies.

Author	Year	Country	Study design	Population	Vaccine(s) administered (types and doses)	Mentsrual disorders	Association	Conclusion
Al-Mehaisen L.M.M., et al.	2022	Jordan	Cross-sectional study, web-based survey	n= 1,506 vaccinated women. Age 18 - 55 years old.	Vaccine status. Pfizer/BioNTech (n=691 (45.9%), Astra Zeneca (n=224, 14.9%, and others (Sinopharm n= 591 (39.2%). n=526 (34.9%) 1 dose; 980 (65.1%) 2 doses.	43.5% had only one period after receiving the vaccine, and 24.4% reported that the first period was early. 76% reported no changes regarding the duration of menstrual cycle and 60% reported no changes in the menstrual flow. No new episodes of dysmenorrhea were found.	The association between the date of the last dose of vaccine with period timings, period duration, period volume, and dysmenorrhea after vaccine and period timings and period volume was found to be significant. Astra-Zeneca was significantly associated with new episodes or increased dysmenorrhea	There was a change in the menstruation timings and flow after vaccination.
Alahmadi A.M., et al.	2022	Saudi Arabia	Retrospective cohort study	n= 673 reproductive-aged women with a normal menstrual cycle. Age 18-45 years old.	Vaccine status: 76.5% have received three vaccine doses against COVID-19. Pfizer/BioNTech: 75,8%, 1 dose or 74.3% 2 doses. Astra Zeneca: 23% and 21.8% for the first and second dose, respectively.	Menstrual changes were observed among 45.9% after the first dose: increased menstrual pain (22.9%) and increased menstrual bleeding (14.3%), whereas menstrual changes were observed among 42.8% after the second dose: increased menstrual pain (21.4%) and intermenstrual bleeding (12.5%).	Bivariate analysis showed that women who have had two doses of the vaccine were significant more likely to report menstrual changes than those who have had three doses (61.4% vs. 50.9%). Regarding second type of vaccine, Moderna vaccine was significant associated with the highest rate of menstrual changes (65.4%), whereas Astra Zeneca was significant associated with the lowest rate (44.9%).	The COVID-19 vaccination is associated with a minor and transient change in the menstrual cycle, resulting mainly more menstrual pain and increased bleeding
Almomani E.Y., et al.	2023	Jordan	Cross-sectional study, survey	n=564 vaccinated women. Age >16 years old.	Vaccination status: Pfizer/BioNTech (n=312, 55%); Oxford–AstraZeneca (n=68, 12.0%); Sinopharm (n=179; 32.0%) not included Moderna vaccine (n=3, 1.0%). Dose information: 90,6% had two doses of the same vaccine type; all third vaccine doses were Pfizer/BioNTech vaccine.	Before vaccination, 18% of participants had menstrual irregularities; post vaccination 52% experienced menstrual irregularities.; (after first dose (n=102, 35.2%); second dose (n=187, 64.5%); third shot (n=1, 0.3%)	Bivariate analysis showed that menstrual irregularities were significantly higher post-vaccination compared to pre-vaccination in women. Vaccine type analysis revealed no analysis was made by vaccine dose.	This study provides evidence that post-COVID-19-vaccine physiological adverse effects during the menstrual cycle were frequently observed in vaccinated women. Fortunately, all studied post-vaccine adverse events concerning menstrual cycle irregularities during menstruations were short-terms and subsided within 3 months on average.

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Alsalman M., et al.	2022	Saudi Arabia	Cross-sectional study	n= 399 women. Mean age 25.54 years old.	Number of dosis: 1 dose 5 (1.3%); 2 doses 76 (19%); 3 doses 317 (79.4%); 4 doses 1 (0.3%).	53.9% of the participants reported post-vaccination menstrual bleeding abnormality in terms of a heavy or irregular cycle.	There were no significant associations between menstrual bleeding changes after receiving the vaccine and the type of booster shot, previous history of COVID-19 infection, and age group. However, women who received three doses were at a significant greater risk of post-vaccination menstrual bleeding abnormality.	Despite vaccination being the most effective way to prevent COVID-19, it does have an impact on menstrual bleeding in terms of menorrhagia and metrorrhagia.
Alvergne A., et al.	2022	United Kingdom	Prospective/restrospective study	Prospective cohort (n=79): women >18 years old who had a gynaecological problem and were planning to receive the first or second dose of the vaccine. Retrospective cohort (n=1273): women >18 years old, who have received at least one dose of the COVID-19 vaccine, have periods or withdrawal bleeds and who have a record of the dates of these, and the date or dates they received the vaccine.	1 dose, n = 1,012; 2 dose, n= 635. Prospective cohort: 82.3% Pfizer/BioNTech, 14% Moderna, 3.8% AstraZeneca. Retrospective cohort: 61% Pfizer/BioNTech, 10.7% Moderna, 27.1% AstraZeneca, 0.6% Janssen and 0.4% Not specified.	Late period: Compared to the day on which the participant had expected their period, pre-vaccine periods occurred on average 0.17 days early, whereas the period following dose one occurred mean of 2.3 days late (significantly different from pre-vaccination cycles) and the period following dose two occurred a mean of 1.3 days. The differences between pre-vaccination cycle timing and post-dose 1 and -dose 2 timing remained significant.	This study found no significant change to self-reported menstrual flow in the period or withdrawal bleed following vaccination, either in spontaneously cycling participants, or in those using hormonal contraception.	These findings suggested that COVID-19 vaccination can lengthen the menstrual cycle and that this effect may be mediated by ovarian hormones. Importantly, this study found that the menstrual cycle returns to its pre-vaccination length in unvaccinated cycles.

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Barabás K., et al.	2022	Hungary	Restrospective cohort	n= 1563 individuals. Aged: 15-49 years old.	62.2 % of the vaccine recipients received mRNA-based vaccine (56.3 % Pfizer/BioNTech, 5.9 % Moderna), 23.8 % received adenovirus vaccine (10.2 % Astra Zeneca, 12.4 % Sputnik, 1.2 % Janssen) and 8.5 % received the traditional, inactivated virus vaccine (Sinopharm), while 5.3 % received more than one type of vaccines	Menstrual cycle length shortening (29.9%) and prolongation (more than 7 days; 22.2%) was reported. In addition, 13.9 % of female individuals had a missed period post-vaccination, while 7.8% suffered from prolonged bleeding lasting for more than 2 weeks. The rest of the individuals (26.2%) had other menstrual problems. The most frequently reported problems included the followings: irregular bleeding (12.2%), heavier bleeding (4.3%), strong menstrual cramps (2.8%) and period reappearance (2%).	There was no association found between the vaccination and the menstrual cycle changes.	This study provided evidence on the reproductive health safety of COVID-19 vaccines and indicates that the effect of COVID-19 vaccines and SARS-CoV-2 infection on the menstrual cycle may be negligible compared to the effect of depression.
Bissgaard Jensen C., et al.	2023	Denmark	A population-based cohort study	n=13,648 menstruating women. Age 16-65 years old.	Vaccination status: Pfizer/BioNTech n= 10,684 (78%), Moderna n= 2,664 (20%), others n= 69 (<1%). n= 1274 (9%) 1 dose; n= 12,343 (90%) 2 doses; 32 (<1%) 3 doses.	30% of menstruating women reported menstrual changes following COVID-19 vaccination. Common reported changes were longer, shorter, and more irregular menstrual cycles, as well as heavier bleeding.	Pre-vaccination menstrual regularity and vaccine type were not associated with reporting any menstrual change. No analysis were made by number of doses.	We found that 30% of menstruating women reported menstrual changes following COVID-19 vaccination and several potential risk factors including stress, vaccine concerns, severe COVID-19 infection, and immediate vaccine symptoms were associated with these reports.
Dabbousi A.A., et al.	2023	Lebanon	Cross-sectional study	n= 505 premenopausal vaccinated women. Aged 18 - 55 years old.	AstraZeneca (60) 11.9%; Pfizer/BioNTech (410) 81.2%; Sputnik (20) 4%; Sinopharm (10) 2%; Moderna (1) 0.2%. Do not know (4) 0.8%. 2 doses: (426) 84.4%.	Heavy menstrual bleeding was decreased after vaccination, where the number of women having heavy bleeding decreased by 6% after vaccine. Light menstrual bleeding was increased by 7% after vaccination. In addition, regularity was affected by vaccination, where the number of women having regular cycles decreased after taking the vaccine by 8%. Concerning the duration, it shifted to less than 5 days or more than 7 days after vaccination.	None of the vaccines was significantly associated with menstrual irregularities.	Our findings support the fact that the COVID vaccine has effects on the menstrual cycle, explaining the findings reported by many women post-vaccination. Moreover, it shows that some diseases are associated with the alteration of the menstrual cycle.

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Duijster J.W., et al.	2023	The Netherlands	Case reports cohort study	Over 24 000 spontaneous reports of menstrual abnormalities and over 500 episodes (n= 16,929 women) of menstrual abnormalities.	Most women who reported a menstrual abnormality, received the Pfizer/BioNTech vaccine (79.0%, n= 19,076), followed by Moderna (11.3%, n= 2,727), Janssen (6.8%, n= 1,647) and AstraZeneca (2.6%, n= 614).	Amenorrhoea/oligomenorrhoea was the most reported menstrual abnormality (33.3%), followed by heavy menstrual bleeding (29.4%) and irregular blood loss (22.7%) with no substantial differences between vaccines. In total, 38 case reports of menstrual abnormalities were considered serious by the reporter according to the CIOMS criteria. which the majority received the Pfizer vaccine (80.5%). A total of 7068 women sent in a case report of heavy menstrual bleeding, of which the majority followed Pfizer vaccination (78.0%).	Significant associations were observed for the age group 25–34 years (OR 2.18; 95% CI 1.45–3.41) and the Pfizer/BioNTech vaccine (OR 3.04; 95% CI 2.36–3.93).	This study found an incidence of menstrual disorders of 41.4 per 1000 female participants aged ≤54 years. This was complemented with the analysis of >24 000 case reports received through the spontaneous reporting system in the Netherlands.
Edelman A., et al.	2022	U.S.A.	Cohort; Retrospective study	n=3,959 participants. Age 18-45 years old.	Vaccination status (n=2,403): Pfizer/BioNTech (55%), Moderna (35%), Janssen (7%); Unspecified (3%). Number of doses: at least 1 dose n=2,403 (100%); 2 doses n=1,919 (79.85%)	NA	The vaccinated cohort experienced a less than 1-day unadjusted increase in the length of their menstrual cycle during the first vaccine cycle compared with their three pre-vaccination cycles (0.71-day increase, 98.75% CI 0.47–0.94); After adjusting for confounders, the difference in the change in cycle length by vaccination status was 0.64 days (98.75% CI 0.27–1.01). During the second vaccine cycle, a slightly higher proportion of participants had a change in cycle length of 8 days or more (6.5% vaccinated, p=0.017). After adjusting for confounders, the difference in the change in cycle length for the second vaccine cycle by vaccination status was 0.79 days (98.75% CI 0.40–1.18). We found no changes in unadjusted menses length for either the first or second vaccination cycle. There were no differences in adjusted menses length changes by vaccination status for either vaccine cycle.	This study did no find population-level clinically meaningful change in menstrual cycle length associated with COVID-19 vaccination. These findings support and help explain the self-report of changes in cycle length. Individuals receiving two COVID-19 vaccine doses in a single cycle do appear to experience a longer but temporary cycle length change. COVID-19 vaccination is not associated with changes in menses length. .

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Farah S., et al.	2023	Lebanon	Retrospective cross-sectional study	n= 304 COVID-19 vaccinated participants. Aged 18 - 65 years old.	All participants were fully vaccinated and Pfizer/BioNTech was the prevalent type of vaccination, except for only one woman who received AstraZeneca and two others who did not recall the type of vaccination received.	A total of 21 (6.9%) women had a change in cycle length, by a mean of 12.88 ± 16.21 days after the first dose, of whom seven (2.3%), 13 (4.3%), and one (0.3%) reported a decrease, increase, or complete absence of menses, respectively. A higher number of women (28 [9.2%]) reported changes after the second dose, by a mean of 14.31 ± 16.74 days, of whom seven (2.3%), 18 (5.9%), and two (0.7%) had a decrease in length, increase, or complete absence of menses, respectively. On the other hand, 21 (6.9%) women experienced changes after the third dose, with a mean of 14.54 ± 14.85 days, of whom four (1.3%), 15 (4.9%), and two (0.7%) had a decrease in length, increase, or complete absence of menses, respectively. As for menstrual flow, 17 (5.6%) participants reported a change after the first dose, with most (10 [3.3%]) complaining of a lighter flow compared with seven (2.3%) who had heavy menses. A higher number (22 [7.2%]) had flow changes after the second dose, with 13 (4.3%) and nine (3.0%) reporting lighter and heavier flow, respectively. Almost similar results were seen after the third dose, while 21 (6.9%) reported flow changes, of whom 13 (4.3%) and eight (2.6%) complained of lighter and heavier flow, respectively.	As for the change in symptoms after vaccination, women with polycystic ovary syndrome significant were seven times more prone to have changes in their symptoms after the first dose of vaccination (OR, 7.52 [95% CI, 1.02–55.60]), and those who were taking chronic medications significant reported nine and four times more changes after the first and second dose, respectively (OR, 9.55 [95% CI, 0.97–93.64]; and OR, 4.24 [95% CI, 0.92–9.54] P = 0.045). Surprisingly, women with fibroids were less likely to report significant changes in symptoms after the second and third doses (OR, 0.86 [95% CI, 0.63–1.16]; and OR, 0.857 [95% CI, 0.63–1.16]).	COVID-19 vaccine influences the cycle length, flow, duration of menstruation, symptoms, and breakthrough bleeding without an effect on postmenopausal vaginal bleeding. Age, level of education, BMI, underlying comorbidities, and use of chronic medications are significantly associated with changes in menstrual length, flow, and symptoms.

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Gopaul, C.D., et al.	2023	Trinidad and Tobago	Cross-sectional study	n= 657 pre-and post-menopausal women, with the majority drawn from the reproductive age group (25-44 years).	1st. dose: Janssen (n=10) 3.2%, Oxford AstraZeneca(n=157)49.5%, Pfizer/BioNTech (n=46) 14.5%, Sinopharm (n=104) 32.8%. 2nd. dose: Oxford-AstraZeneca (n=153) 48.3%, Pfizer/BioNTech (n=42) 13.2%, Sinopharm (n=97) 30.6 %.	There was a significant association in menstrual symptoms between the pre- and post-vaccination period. The frequency of menstrual cycle regularity had changed significantly post-vaccination compared to the cycle regularity before COVID-19 vaccination. The frequency of the period length and period flow had significantly decreased after the first and second cycle dose vaccination compared to the menstrual period length and period flow before the COVID-19 vaccination. For instance, moderate period flow decreased after the first dose vaccination (65.5%) and the second dose vaccination (61.4%) compared to 72.6% who had reported moderate period flow prior to the COVID-19 vaccination.	Expose to COVID-19 vaccination resulted in a significant change in the women's menstrual period flow, but did not have a significant effect on the women's menstrual cycle length. The participants' menstrual period length was not significantly longer after the first dose compared to the second dose vaccination.	The study concludes that although COVID-19 vaccines tend to negatively affect women's menstrual cycles, these changes are short-lived.
Harinton E., et al.	2023	U.S.A.	Cross-sectional, nationwide study	n= 5,314 reproductive-age women. Age 18–55 years old.	Vaccine status: Pfizer/BioNTech n= 2,150 (59,8%); Moderna n= 1,245 (34,21%), Jansen n=244 (6,71%).	There were no differences in average cycle length in the 6 months preceding or 6 months after vaccination or infection	No significant association in cycle length after vaccination.	In this cohort of reproductive-age women tracking their menstrual cycles, neither receipt of the COVID-19 vaccine nor recent SARS-CoV-2 infection led to meaningful aberrations in menstrual cyclicity.
Hosoya S., et al.	2024	Japan	Prospectively or retrospectively recorded data	n= 22,509 menstruating women. Age 18 - 57 years old.	Vaccination status: 9,048 first dose; 8,545 primary series (first and second doses), and 4,768 boosters. 68.0% and 67.4% of the women received the Pfizer/BioNTech vaccine for the first and second doses, and 53% Moderna vaccine as the booster.	NA	Significant greater degree of menstrual cycle prolongation after the booster dose than after the first and second doses when administered in different cycles and slight prolongation persisting in consecutive cycles after the booster dose.	Booster dose against COVID-19 may have a greater and longer-lasting effect on menstrual cycle than the primary-series doses.

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Khan G. A., et al.	2023	Saudi Arabia	Retrospective observational cross-sectional study	n= 383 COVID-19 vaccinated participants. Age 18 - 55 years, all of whom were experiencing menstruation.	1 dose (1.57 %); 2 doses (17.49%); 3 doses (79.63%) 4 doses (1.31%). 64.23% participants had received the Pfizer/BioNTech vaccine or a combination of the Pfizer/BioNTech vaccine and AstraZeneca or Moderna vaccines. Few participants had received only the AstraZeneca (7.05%) or only the Moderna (0.26%) vaccines.	All participants before and after at least one dose of a COVID-19 vaccine, as regularity, flow volume, dysmenorrhea, and intermenstrual bleeding.	The association between COVID-19 vaccine administration and menstrual changes to identify the likely associated factors. No statistically significant change in duration of cycle was found. Women without PCOS experienced significant less change in dysmenorrhea than those with PCOS (23.88% vs 37.78%).	Data suggest significant associations between COVID-19 scepticism, the use of hormonal contraceptives, and the reported post-vaccine menstrual disturbances.
Lessans N., et al.	2022	Israel	Cross-sectional study, questionnaire based	n= 219 vaccinated women with Pfizer/BioNTech COVID-19 vaccine. Age 18–50 years old.	Vaccine status: Pfizer/BioNTech (100%).	23.3% (n= 51) experienced irregular bleeding and 37% (n= 83) reported any menstrual change (including irregular bleeding, mood changes or dysmenorrhea) following vaccination.	Bivariate analyses were made comparing two populations those who experienced irregular bleeding and menstrual change and those who do not experience. No analysis was made by dose.	High rates of irregular bleeding and menstrual changes after receiving the Pfizer/BioNTech vaccine
Ljung R., et al.	2023	Sweden	Cohort; Retrospective study	n=2,946,448. Age 12-74 years old.	Vaccination status (all unvaccinated at baseline): Pfizer/BioNTech; Moderna; AstraZeneca. Number of doses: 1 dose (n=64,139); 2 doses (n=863,396); 3 doses: (n=1,645,367)	More than 99% of menstrual disturbance (19 329/19 443 cases in the National Patient Register) or bleeding disorder diagnoses (9370/9407 cases) in the overall study population were from specialist outpatient care. In the subpopulation where primary care data were available (n=1 156 260, approximately 40% of the Swedish female population), about 11% (666/6207 cases) of the diagnoses reflecting premenopausal and postmenopausal bleeding, and 19% (2119/11 344 cases) of diagnoses of menstrual disturbance were recorded in primary healthcare.	The adjusted hazard ratio for menstrual disturbance after vaccination with any dose compared with unvaccinated periods was 1.13 (95% CI 1.04 to 1.23) in the one to seven days risk window and 1.06 (1.01 to 1.11) in the 8-90 days risk window. Adjustment for covariates strongly attenuated or almost completely removed the weak associations noted in the dose specific crude analyses. The strongest adjusted association observed was a 26% increased risk of menstrual disturbance among women aged 12-49 years in the one to seven days risk window (1.26 (1.11 to 1.42)) after the first dose. The adjusted hazard ratio for premenopausal bleeding after vaccination with any dose compared with unvaccinated periods was not statistically significative.	This study observed weak and inconsistent associations between COVID-19 vaccination and healthcare contacts for postmenopausal bleeding, and even less consistent for menstrual disturbance, and premenstrual bleeding. Extensive adjustment for confounding attenuated most risk estimates. The patterns of association are not consistent with a causal effect. These findings do not provide any substantial support for a causal association between COVID-19 vaccination and healthcare contacts related to menstrual or bleeding disorders.

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Lukac S., et al.	2023	Germany	Cross-sectional study	n= 1,726 participants. Aged >18 years old.	Vaccination status (n=1,699; 98,4%) 1st. dose: Pfizer/BioNTech (n=1070; 65.1%; Janssen (n=35, 2.1%); Moderna (n=145; 8.8%); AstraZeneca (n=391; 23,8%); Others (n=3; 0,2%) 2nd. dose: Pfizer/BioNTech (n=1403; 85.7%; Janssen (n=1, 0.1%); Moderna (n=188; 11.5%); AstraZeneca (n=44; 2,7%); Others (n=2; 0,1%). 3rd. dose: Pfizer/BioNTech (n=1392; 93.8%; Janssen (n=2; 0.1%); Moderna (n=84; 5.7%); AstraZeneca (n=5; 0,3%); Others (n=1; 0,1%).	Three menstrual cycle parameters—CL, MD, and BV. n=483; 28% of participants answered their cycle had change after infection/vaccination. In vaccinated women (first vaccination: 13,4% change after first dose; 16,1% change after second dose; 11,9% change after third dose)	There was a significant change about CL from before to after immunization/infection, with 21.1% of participants reporting changes in the CL categories. Likewise, there was a significant change in BV, with 17.5% and 4.4% of participants reporting an increase or a decrease, respectively. Overall, 13.6% of participants reported changes in the MD categories (7.4% increase, 6.2% decrease); however, the change from before to after immunization/infection regarding MD categories was not significant.	Data showed that more than one-quarter of women who were vaccinated or infected experienced changes in the menstrual cycle, which were temporary but could last for up to more than 6 months and occurred especially after the second vaccination. The most affected parameter was CL followed by BV. Changes in MD were not statistically significant.
Matar, S G., et al.	2023	6 Arab countries (Jordan, Palestine, Syria, Egypt, Sudan and Libya)	Cross-sectional study	4,942 (all vaccine 2919). Menstruating female participants over 18 years of age were included, and women who were pregnant, breastfeeding, taking oral contraceptives or any other hormonal therapy, using intrauterine devices, or those who had endometriosis or polycystic ovary syndrome were excluded. means 24 years	1 dose (33.9 %); 2 doses (59.8%); 3 doses (1.2%) and 1 dose de Janssen 5.5%. AstraZeneca 24.3%; Janssen 4,6%; Moderna 1.7%; Pfizer/BioNTech 27.2%; Sinopharm or Sinovac 24,7%; Sputnik 17,4%.	Participants who received one or more dose of COVID-19 vaccine had a significantly higher frequency of pelvic pain (84.5%) than the unvaccinated participants (81.6%). Similar outcomes were reported for back pain experienced by vaccinated participants (82.9%) versus non-vaccinated participants (77.9%), thigh pain (63.9% vs. 61%), nausea (43% vs. 40%), tiredness (89.7% vs. 87.1%,), pelvic pain (85.6% vs. 81.9%), and taking painkillers for the pain without prescription (62.7% vs. 57.2%). All significant.	In all the three regression models applied on the data, receiving the vaccine was a significant predictor for higher frequency of all pelvic pain, back pain, nausea, general weakness, menstrual pain, unprescribed analgesics use, more frequent bowel movement, and more loose stool status, after adjustment for demographics.	This study indicated that COVID-19 vaccine may have an effect on menstruation in terms of menstrual pain and bleeding heaviness.

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Mínguez-Esteban I., et al.	2022	Spain	Cross sectional; Survey	n=746 participants. Age 18-45 years old	Vaccination status: (all had at least two doses) First dose: 70% received Pfizer/BioNTech; 30% received Moderna. Second dose: 69% received Pfizer/BioNTech; 31% received Moderna. Third dose: 22% Pfizer/BioNTech; 21% Moderna; 57% had not received the first dose.	65% of the women perceived significant changes in their menstrual cycle after being administered the vaccines, irrespective of the type of vaccine or number of doses. (n=484). - Most of them (n=316) reported more than one alteration on their menstrual cycle. Categories: duration of menstrual cycle, bleeding amount, pain, absence of menstrual cycle.	The results support the presence of one or more MC alterations even 5 months after vaccination, irrespective of the type of vaccine or combination between them, number of doses or time since last dose.	The results of this study support the existence of a correlation between mRNA vaccine administration and pain, duration of the menstrual cycle and bleeding amount disregarding type of vaccine, number of doses or time since last dose. Finally, a correlation between pain, duration and bleeding was found both before and after COVID-19 vaccination.
Mahfouz M.S., et al.	2023	Saudi Arabia	Analytical cross-sectional study, online web-based survey	n= 729 COVID-19 vaccinated women. Age 18-45 years old	Vaccination status: n= 275 (37.7%) 2 doses; n= 447 (61.3%) 3 doses. Vaccine type in the first dose: Pfizer/BioNTech (n= 563, 77.2%), Astra Zeneca (n= 157, 21.5%) and Moderna (n=9, 1.3%)	Prevalence of menstrual change was between 60.9% - 66.3%, in the age group of 25-34 and 35-45 years were more affected. Abnormalities were related to delayed menstruation and changes in pain intensity.	No significant association between dose of COVID-19 vaccine received and menstruation change. No analysis was made by vaccine type.	There is a considerable increase in menstrual disorders following vaccination. Because there is no apparent cause for these post-vaccine disturbances, and their effects are difficult to anticipate, it is preferable to warn those concerned and encourage them to learn more about the biological changes causing these problems.
Muhaidat N., et al.	2022	Jordan	Cross-sectional study, online self-administered survey	n=2,269 women. Age 14 - 54 years old	Vaccination status: Vaccine type: Pfizer/BioNTech (48.4%), Astra Zeneca (13.4%) and other (Sinopharm (35.3%). 85.4% received two doses.	66.3% of participants reported menstrual symptoms post-vaccination, of which 46.7% experienced them after their first dose, 32.4% after second dose and 20.9% after both doses.	Vaccine type did not significantly influence the incidence of abnormalities. No analysis were made by number of doses.	The study showed a possible link between the COVID-19 vaccine and menstrual abnormalities that have impacted their quality of life
Namiki T., et al.	2022	Japan	Cross-sectional study, web-based survey	n= 309 vaccinated women with Pfizer/BioNTech COVID-19 vaccine. Mean age 31.9 years old.	Vaccine status: Pfizer/BioNTech (n=308, 100%). n= 308 (100%) 1 dose; n=308 (100%) 2 doses, and n= 305 (99.02%) 3 doses.	Abnormal bleeding was 0.6%, 1.0%, and 3.0% for the first, the second, and third doses, respectively. Irregular menstrual cycles were more common than abnormal bleeding: 2.0%, 4.9%, and 6.6% for the first, second, and third doses, respectively	Abnormal bleeding occurred more commonly after the third dose than after the first dose. An irregular menstrual cycle was significantly more common after the second and third doses than after the first dose.	The present study showed that the effects of COVID-19 vaccination on menstruation seem limited.

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Qashqari F.S.S., et al.	2022	Saudi Arabia	Restrospective study	n= 673 reproductive women aged 18-45 years old with a normal menstrual cycle (cycle length between 21 and 35 days and duration of menstruation less than 8 days) and those who received two doses of COVID-19 vaccines regardless of the type of vaccine.	76.5% of participants received 3 doses. The Pfizer/BioNTech vaccine was the most reported either for the 1st. dose (75.8%) or 2nd. dose (74.3%), followed by Astra Zeneca (23% and 21.8% for the 1st. dose and 2nd. dose, respectively).	Menstrual changes were observed among 45.9% of participants after the first dose, primarily increased menstrual pain (22.9%) and increased menstrual bleeding (14.3%), whereas menstrual changes were observed among 42.8% of patients after the second dose; in general, increased menstrual pain (21.4%) and intermenstrual bleeding (12.5%).	The Moderna vaccine was significant associated with the highest rate of menstrual changes (65.4%), whereas Astra Zeneca was associated with the lowest rate (44.9%).	COVID-19 vaccination is associated with minor and transient changes in the menstrual cycle. Women who received at least two doses of the vaccine primarily reported more menstrual pain and increased bleeding, but these changes resolved within a short period amongst most participants.
Qazi, T.B., Bashir, et al.	2023	India	Cross-sectional study	n= 300 reproductive women. Aged 15–49 years old.	n= 211 (70%) received the Covishield vaccine (Astra Zeneca) and the remaining 89 (30%) received Covaxin vaccine (Bharat Biotech).	n= 202 (67.3%) reported no changes in the regularity of menstrual cycles following COVID-19 vaccination. Only 30 (10%) reported a change in the regularity of menstruation and 68 (22.7%) reported a change in the regularity of their cycles. Among these, 6 (20%) reported having a prolonged cycle, 9 (30%) reported having a missed cycle, and 15 (50%) reported having a delayed cycle. 33 (11%) reported a change in cycle duration after vaccination. Among these 33 who reported a change in cycle duration, 18 (54.5%) reported decreased duration of the menstrual cycle after COVID-19 vaccination and 9 (27.4%) reported increased duration. 6 (33.3%) reported the occurrence of cramps along with pain after vaccination. The duration of pain was increased in 18 (6%) after menstruation. Among the total participants, 74 (24.7%) reported a change in menstrual flow after vaccination: increased menstrual flow was reported by 12 (16.2%), decreased menstrual flow was reported by 44 (59.5%), and decreased flow along with blood clots was reported by 18 (24.3%).	A significant association was found between the type of vaccination received and regularity of cycles, a change in the duration of the cycle, a change in intensity of pain after vaccination, and a change in menstrual flow after vaccination. There was no significant association between the type of COVID-19 vaccination and the change in the duration of the pain after vaccination.	There was a significant association between the type of vaccine used and the changes in the menstrual cycle after vaccination.

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Ríos Calderón K., et al.	2023	Latino-america	Cross-Sectional; Survey	n= 4,087. Age 18-50 years old.	Vaccination status: mRNA: Pfizer/BioNTech and Moderna (n=1,931); Inactivated virus: Sinovac; Sinopharm (n=720); Chimpanzee viral vector: AstraZeneca (n=631); Human viral vector (n=431); Combined (n=374). Number of doses: 1 dose (n=341); 2 doses (n=2,998); 3 or more doses (n=748)	86.5% (3535/4087) of the participants reported menstrual changes following one or more doses of COVID-19 vaccine. A greater relationship was observed with the appearance of menstrual changes and: 1) being aged 18-34 years, 2) a single type of commercial vaccine, 3) a single dose and 4) residing outside Latin America; but without statistical significance.	In the analysis of menstrual changes by age group according to mechanism of action, it was observed that women between 18-34 years of age vaccinated with mRNA and inactivated virus showed significant more menstrual changes compared to the 35-50 years age group.	The results showed that at least 8 to 9 out of 10 patients presented menstrual changes associated or not with dysmenorrhea, after the application of the COVID-19 vaccine, regardless of the mechanism of action. It was also possible to detect with statistical significance that some mechanisms of action, such as the inactivated virus, were associated with a greater or lesser frequency of these symptoms when compared specifically with other mechanisms of action.
Saleh Alzahrani H., et al.	2023	Saudi Arabia	Observational cross-sectional study	n= 1,066 women. Age 18-50 years old.	Vaccine status: n= 422 (39.6%) 2 doses, n= 644 (60.4%) 3 doses. First doses: Pfizer/BioNTech n=842, (79.9%), AstraZeneca n= 202 (18.9%), Moderna n= 9 (0.8%).	Menstrual irregularity after receiving the COVID-19 vaccine was prevalent among 281 participants, (26.4%). Common abnormalities included irregular menstruation (12.0%) and increased time between one cycle and the next cycle (7.5%)	No significant association by vaccine type and number of doses.	Our study findings show that the number and types of COVID-19 vaccines were not associated with menstrual abnormality.
Wali R., et al.	2023	Saudi Arabia	Cross-sectional study	n= 297 women. Age 15 - 50 years old.	Vaccine status: 74% Pfizer/BioNTech, 25% Astra Zeneca, and 1% Moderna. n= 295 (99%) 2 doses, n= 187 (63%) 3 doses.	22 (9.69%) first-dose recipients and 33 (14.6%) second-dose recipients expressed heavy menses, and 20 (16.39%) after the third dose. 35 (21%) stated they had "painful periods" after the first dose, 47 (28%) after the second dose, and 28 (17%) after the third dose.	No significant association between vaccine type and the number of doses on monthly cycle, heavy menses and premenstrual symptoms.	COVID-19 vaccination remains necessary to prevent severe infection and is safe for females of reproductive age, whether trying to get pregnant or lactating, and has no significant effect on the menstrual cycle.
Wang S., et al.	2022	U.S.A. / Canada	Cohort; Prospective study	n= 3,858 participants. Age >18 years old.	Vaccination status (n=3527) Pfizer/BioNTech (n=2145, 60.8%); Moderna (n=1282, 36.4%); Janssen (n=84, 2.4%); Astra Zeneca (n=9; 0.3%); Unknown (n=7, 0,2%). No information on the number of doses.	17.6% of women reported cycles >32 days, and 22.75 reported irregular cycles.	COVID-19 vaccination was associated with a 48% higher risk of change to longer cycles. (multivariable-adjusted model OR: 1.48 [1.00-2.19]). Vaccine type: The association of vaccination status with change in cycle length was significative in Pfizer/BioNTech (OR: 1.53 [1.03-2.29]) and Moderna (OR: 1.53 [1.01-2.31]. No analysis was made by vaccine dose.	This study found that COVID-19 vaccination may be associated with a short-term change toward longer menstrual cycles. These changes were not explained by differences in health-related behavioral factors or pandemic-related stress. In addition, these menstrual disturbances did not seem to be related to vaccine type.

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Wesselink A.K., et al.	2023	U.S.A. / Canada	Cohort; Prospective study	n=1,137. Age between 21-45 years old	Vaccination status (n=437): 32.3 % Moderna-Spikevax; 60.9 % Pfizer/BioNTech; 6.6 % Janssen and 0.2 % Astra Zeneca. (they only analyze Pfizer/BioNTech and Moderna). Number of doses: At least 1 dose.	On the first and second follow-up questionnaires following the first dose, the prevalence of irregular cycles was 22.7% and 20.4% respectively. After the second dose was 24.8% and 17.7%. The prevalence of bleed lengths 7 days and menses that required 20 tampons/pads was similar by vaccination status. The prevalence of menstrual pain requiring medication was 29.8 % (95 % CI: 24.1%, 35.5%) on unvaccinated follow-up questionnaires and 34.8 % (95% CI: 27.4%, 42.2%) and 31.9% (95% CI: 25.9%, 37.9%) on the first and second follow-up questionnaires after the first dose, respectively.	No significant association found	In this prospective cohort study, this study found a one-day average delay in menses and a higher prevalence of long menstrual cycles following COVID-19 vaccination, which resolved by the next menstrual cycle. Other menstrual cycle characteristics, including cycle regularity, bleed length, heaviness of bleed, and menstrual pain, were not strongly associated with COVID-19 vaccination
Zhang B., et al.	2022	U.S.A.	Cohort; Retrospective study	n=14,431 reports related to menstrual disorders in female. Mean age 35 years old.	Vaccine status: Pfizer/BioNTech (n=9,613; 73.28%); Moderna (n=2,748; 20.95%); Janssen (n=742; 5.66%); Unknown (n=15) Dose: 1 dose: Pfizer/BioNTech (n=4,966; 51.66%); Moderna (n=1,388; 50,51%); Janssen (n=465; 62,67%); Unknown (n=9; 60%) 2 doses: Pfizer/BioNTech (n=3,563; 37,06%); Moderna (n=923; 33,59%); Janssen (n=1; 0.13%); Unknown (n=2; 13.33%) 3 doses: Pfizer/BioNTech (n=65; 0.68%); Moderna (n=17; 0.62%); Janssen (n=0; 0%); Unknown (n=0; 0%).	The COVID-19 vaccine group reported 2,698 cases (20.57%) of menstruation delayed, 2,088 cases (15.92%) of Intermenstrual bleeding, and menorrhagia was reported only 28 cases (0.21%). The non-COVID-19 vaccine group reported 251 cases of metrorrhagia (19.12%), 301 cases of amenorrhea (22.90%) and only 6 cases of Intermenstrual bleeding (0.46%).	This study found a potential association signal between COVID-19 vaccine and menstrual disorders occurrences with ROR = 7.83 and fulfilled the lower criterion of ROR 95% CI >1 and number of cases >3.	From the signal detection results, there was a statistically significant correlation between the COVID-19 vaccine and reports of adverse reactions to menstrual disorders, and COVID-19 may contribute to menstrual disorders in young adult female (30–49 years).

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Supplementary Table 3: Quality Appraisals.

Author (year)	Were the criteria for inclusion in the sample clearly defined?	Were the study subjects and the setting described in detail?	Was the exposure measured in a valid and reliable way?	Were objective, standard criteria used for measurement of the condition?	Were confounding factors identified?	Were strategies to deal with confounding factors stated?	Were the outcomes measured in a valid and reliable way?	Was appropriate statistical analysis used?
Al-Mehaisen L.M.M., et al. (2022)	No	No	Yes	Yes	No	No	Yes	Yes
Alahmadi A.M., et al. (2022)	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Almomani E.Y., et al. (2023)	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Alsalman M., et al. (2022)	Yes	Yes	No	Yes	Yes	No	Yes	Yes
Alvergne A., et al. (2022)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Barabás K., et al. (2022)	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Bissgaard Jensen C., et al. (2023)	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Dabbousi A.A., et al. (2023)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
Duijster J.W., et al. (2023)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Edelman A., et al. (2022)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Farah S., et al. (2023)	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Gopaul, C.D., et al. (2023)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Harinton E., et al. (2023)	No	No	Yes	Yes	No	No	Yes	Yes
Hosoya S., et al. (2024)	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Khan G. A., et al. (2023)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Lessans N., et al. (2022)	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Ljung R., et al. (2023)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Lukac S., et al. (2023)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Matar, S G., et al. (2023)	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Mínguez-Esteban I., et al. (2022)	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Mahfouz M.S., et al. (2022)	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Muhaidat N., et al. (2022)	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Namiki T., et al. (2022)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Qashqari F.S.S., et al. (2022)	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Qazi, T.B., Bashir, et al. (2023)	Yes	Yes	Yes	No	No	No	Yes	Yes
Ríos Calderón K., et al. (2023)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
Saleh Alzahrani H., et al. (2023)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Wali R., et al. (2023)	No	No	Yes	Yes	No	No	Yes	Yes
Wang S., et al. (2022)	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Wesselink A.K., et al. (2023)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Zhang B., et al. (2022)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
YES (n, (%))	28 (90.32)	28 (90.32)	30 (96.77)	30 (96.77)	21 (67.74)	13 (41.9)	30 (96.77)	30 (96.77)
NO (n, (%))	3 (9.67)	3 (9.67)	1(3.22)	1(3.22)	10 (32.25)	18 (58.06)	1(3.22)	1(3.22)

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