



# Effect of Covid-19 Vaccination on Menstrual Pattern Changes: A Systematic Review

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## ABSTRACT

Covid-19 vaccination has proven to be an effective measure to reduce morbidity and mortality. However, some reports have linked Covid-19 vaccination with alterations in menstruation. Considering that menstruation is an important health component for people who menstruate, this information may cause hesitancy to get vaccinated. There are limited systematic reviews regarding the impact of Covid-19 vaccination on changes in menstrual patterns. Therefore, it is necessary to review the available literature on this topic. A systematic review was done in accordance with the PRISMA statement. The literature search was done by hand and on 4 databases: PubMed, EMBASE, ProQuest, and CENTRAL. All found articles were screened based on predetermined criteria. Articles that meet the requirements were critically appraised and analysed. 14 articles consisting of 11 cross-sectional studies and 3 cohorts were found. The outcomes mentioned in the studies include changes in menstrual cycle range, durations, estimated blood quantities, and menstruation symptoms. There are changes in the menstrual pattern after the administration of the Covid-19 vaccination, in the form of irregular menstruation, menorrhagia, worsening of menstruation symptoms, and intermenstrual bleeding. However, these changes only occur temporarily. Therefore, the administration of the Covid-19 vaccination is beneficial for people who menstruate.

**Keywords:** Covid-19 vaccines; Menstruation disturbances; Menstrual irregularities

## ABBREVIATIONS

(PICO) Population Intervention Comparison Outcome; (PRISMA) Preferred Reporting Items for Systematic Reviews and Meta Analyses; (JBI-CAT) Joanna Briggs Institute Critical Appraisal Tool

## INTRODUCTION

The Covid-19 vaccine prevents the spread of the SARS-CoV-2 virus and reduces the risk of morbidity or mortality [1]. As the scope of Covid-19 widens, some post-vaccination side effects

have been reported; one of which is menstrual changes [2]. In the largest surveillance system in the United Kingdom, more than 36,000 menstrual changes post-vaccination have been reported. Meanwhile, around the world, there are various results on menstruation changes post-vaccination [3]. Menstruation is important in women's health, especially during the reproductive period. In this pandemic era, public concern that circumvents this issue is the effect of Covid-19 vaccination on infertility regarding its effects on menstruation. Another concern comes from parents of female adolescents because they think about the child's puberty after the Covid-19 vaccination [3]. A deeper

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understanding of possible menstrual changes post-vaccination is needed for better counselling before the administration of the Covid-19 vaccination. However, no systematic review has discussed the impact of post-covid-19 vaccination on menstruation. Therefore, the presentation of this systematic review aims to determine the impact of the Covid-19 vaccination on menstrual patterns.

## MATERIALS AND METHODS

The clinical question is specified using PICO (Population, Intervention, Comparison, and Outcome) format (Table 1). This clinical question is the basis of our systematic review based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) consensus [4]. We formulated a search strategy using keywords from the clinical question and its synonyms. This search strategy is then finely tuned using the WordFreq and Search Refinery functions from the Systematic Review Accelerator, Bond University, Australia [5]. Details of the search strategy are further explored in the appendices.

**Table 1:** Population intervention comparison and outcome (PICO).

Population	Intervention	Comparison	Outcome
People who menstruate	Covid-19 vaccine	Not vaccinated	Menstrual changes

The literature search was done on the 16<sup>th</sup> and 17<sup>th</sup> of June, 2022 on 4 online databases: PubMed, EMBASE, CENTRAL, and ProQuest. A manual search was also done based on the refer-

ences used in the articles. We independently screened all titles and abstracts found. Studies that are selected by at least 2 researchers are then reviewed entirely by the eligibility criteria (Table 2). All conflicts are resolved by discussion. The search process is reported in a PRISMA flowchart [4].

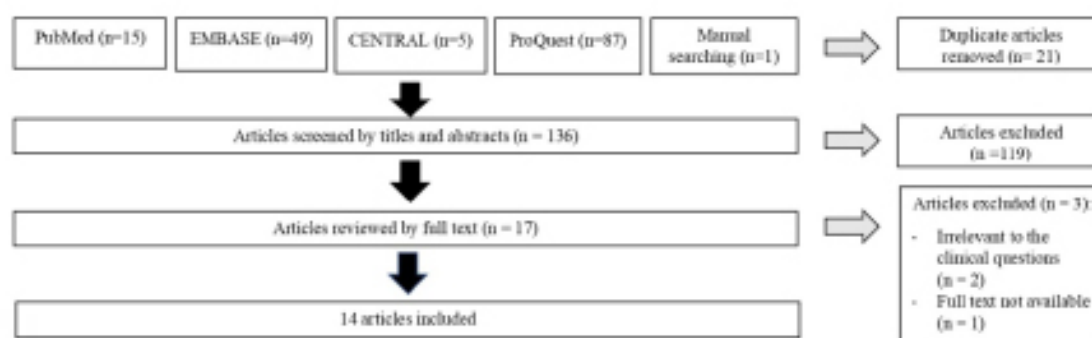
**Table 2:** Eligibility criteria.

Inclusion Criteria	Exclusion Criteria
Hard data (experimental or observational studies)	Soft data (editorials, news articles)
In English or Bahasa	Full text not available (including conference abstracts)
Subjects are otherwise healthy	

Two researchers independently appraised each identified article using the Joanna Briggs Institute Critical Appraisal Tool (JBI CAT) [6]. Data extraction was also done by 2 independent researchers using an online questionnaire that include the study methods (year, location, and design), subjects (population size and eligibility criteria), intervention (vaccination status and type of vaccine), results, and other notable findings. Differing opinions are resolved by discussion. The conclusion is then graded according to the GRADE consensus [7].

## RESULTS

14 studies fulfill the eligibility criteria (Figure 1). All studies found are observational studies from the last 2 years (2021-2022). 11 of those studies use a cross-sectional study design [8-18]. The other 3 studies are cohort studies [19-21].



**Figure 1:** The PRISMA flowchart.

The characteristics of the studies found can be explored in Table 3.

**Table 3:** Characteristics of included studies.

Article ID (year)	Population (N)	Intervention	Results
Alghamdi, et al. (2021)* [8]	Vaccinated adults, Saudi Arabia. (2,874)	Pfizer (1,846) vs AstraZeneca (1,028)	Abnormal menstrual cycle: Pfizer vaccine: 18 (0.69%) subjects (1 <sup>st</sup> dose); 1 (0.22%) subject (2 <sup>nd</sup> dose) vs AstraZeneca vaccine: 7 (0.45%) subjects (1 <sup>st</sup> dose)
Almohaya, et al. (2021)* [9]	Vaccinated adults, Saudi Arabia. (2,302)	Pfizer vaccine (single arm)	Lengthening of the menstrual cycle: 8 subjects
Anjorin, et al. (2022)* [10]	Vaccinated adults, Afrika. (455)	Covid-19 vaccine (single arm)	Menstrual changes: 5 subjects (0.5%)
Araminda, et al. (2022)* [11]	Vaccinated general population, Indonesia. (298)	Moderna (138) vs AstraZeneca (160)	Abnormal menstrual cycle post-vaccination: Moderna 46 subjects (15.4%) vs Astra Zeneca 24 subjects (8%)
Dar-Odeh, et al. (2022)* [12]	Vaccinated doctors and dentists aged 22-71 years old, Saudi Arabia and Jordan. (384)	Covid-19 vaccine (single arm)	Menstrual changes: 15 (4.8%) of 314 reproductive-age female subjects.
Goldlin, et al. (2021)* [13]	Vaccinated adults in a teaching hospital. (209)	Covishield vaccine (single arm)	Menstrual changes: 1 subject (0.16%)

Iguacel, et al. (2021)* [14]	Vaccinated adults, Spain. (1,446)	Covid-19 vaccine (single arm)	Abnormal menstrual cycle: 1.1% subjects (1 <sup>st</sup> dose); 0.5% subjects (2 <sup>nd</sup> dose) Normal menstrual cycle after 1-3 months follow-up post-vaccination: 273 subjects (79.8%); and 4-6 months follow-up post-vaccination: 294 subjects (85.9%)
Kezia, et al. (2022)* [15]	Vaccinated adults, Indonesia. (342)	Sinovac-CoronaVac vaccine (single arm)	Irregular menstrual cycle post-vaccination: 50%-60% (1 <sup>st</sup> dose); 60-70% (2 <sup>nd</sup> dose)
Lagana, et al. (2022)* [16]	Vaccinated female adults with a normal menstrual cycle before vaccination, Italy (164)	1 <sup>st</sup> (9) and 2 <sup>nd</sup> (8) doses of AstraZeneca vs Pfizer (133; 133) vs Moderna (19; 14) vs JnJ (3; 0)	Abnormal menstrual cycle post-vaccination: 66.3%
Muhaidat, et al. (2022)* [17]	Vaccinated people who menstruate, the Middle East and North Africa Regions. (2,269)	Covid-19 vaccine (single arm)	Dysmenorrhea or abnormal menstrual cycle: Moderna vs Pfizer OR=0.593 (CI=0.561-0.628); Johnson and Johnson vs Pfizer OR=0.992 (CI=0.909-1.083) Lengthening of menstrual cycle post-vaccination in comparison to pre-vaccination: 1 <sup>st</sup> dose 0.71 days (CI=0.47-0.94), 2 <sup>nd</sup> dose 0.91 days (CI=0.63-1.19).
Sa, et al. (2022)* [18]	Vaccinated general population, U.S.A(6,183)	mRNA vaccines (Moderna, Pfizer) vs JnJ vaccine	Lengthening of menstrual cycle in vaccinated in comparison to unvaccinated population: 1 <sup>st</sup> dose 0.64 days (CI=0.27-1.01), 2 <sup>nd</sup> dose 0.79 days (CI=0.40-1.18).
Edelman, et al. (2022)** [19]	Vaccinated females aged 18-45 years old with a normal menstrual cycle prior to vaccination, U.S.A. (3,959)	Covid-19 vaccine (2,403) vs unvaccinated (1,556)	Menstruation disorder consisted of the abnormal menstrual cycle, increased bleeding, and dysmenorrhea: Pfizer 1 <sup>st</sup> dose 0.6% and 2 <sup>nd</sup> dose 0.4%; AstraZeneca 1 <sup>st</sup> dose 0.2% dan 2 <sup>nd</sup> dose 0.2%.
Rogers, et al. (2022)** [20]	Vaccinated general population aged 18-65 years old, UK (6,855)	1 <sup>st</sup> (196) and 2 <sup>nd</sup> (3,141) dose of Pfizer vaccine vs 1 <sup>st</sup> (176) and 2 <sup>nd</sup> (2,661) dose of AstraZeneca vs other vaccines (681)	Increased bleeding after 1 <sup>st</sup> dose RR=1.90 (CI=1.69-2.13), 2 <sup>nd</sup> dose RR=1.84 (CI=1.66-2.03)
Trogstad, et al. (2021)** [21]	Female with the normal menstrual cycle and aged 18-30 years old, Norway (8,576)	1 <sup>st</sup> dose of Covid-19 vaccine (388) vs 2 <sup>nd</sup> dose (5,212) vs unvaccinated (88)	

\*Cross-sectional study design; \*\*Cohort study design

Results of the critical appraisal using JBI CAT are reported in **Table 4** with 3 answer options (Yes (+), Uncertain (?), and No (-)) [6]. 6 studies use online-based self-reported questionnaires; thus we deemed the measurement tools to not be valid (Q3,

Q7) [8,9,12-16]. 8 studies ignore possible menstruation-specific confounders due to being a general report of all post-vaccination side effects [8-16]. All 3 cohort studies lacked proper and adequate follow-up periods (Q9, Q10) [19-21].

**Table 4:** Critical appraisal of included articles using JBI CAT.

Appraisal Tool	Article ID	Criteria	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11
JBI CAT for cross-sectional studies	Alghamdi, et al. [8]		+	+	?	+	+	-	-	+			
	Almohaya, et al. [9]		+	+	?	+	+	-	-	+			
	Anjorin, et al. [10]		+	+	+	+	+	-	-	+			
	Araminda, et al. [11]		+	+	+	+	+	?	?	+			
	Dar-Odeh, et al. [12]		+	+	?	+	+	-	-	+			
	Goldlin, et al. [13]		+	+	?	+	+	-	-	+			
	Iguacel, et al. [14]		+	+	?	+	+	-	-	+			
	Kezia, et al. [15]		+	+	?	+	+	-	-	+			
	Lagana, et al. [16]		+	+	+	+	+	+	+	+			
	Muhaidat, et al. [17]		+	+	+	+	+	-	+	+			
JBI CAT for cohort studies	Sa, et al. [18]		+	+	+	+	+	+	+	+	Q9	Q10	Q11
	Edelman, et al. [19]		-	+	+	+	+	+	+	+	?	?	+
	Rogers, et al. [20]		+	+	+	+	+	+	+	+	-	?	+
	Trogstad, et al. [21]		?	+	+	-	-	?	+	+	?	?	-

## DISCUSSION

Studies found in our search had inconsistent definitions of menstrual changes. Studies by Muhaidat et al., Lagana et al., and Rogers et al., use a set of conditions which is considered abnormal [16,17,20]. Lagana et al., defined abnormal menstruation as a menstrual cycle of <25 days or >36 days, menstruation duration of <3 days or >7 days, and an abnormal estimated blood loss in comparison to previous menstruations [16]. In comparison, Muhaidat et al., reported menstrual cramps, menstrual cessation, worsening of premenstrual symptoms and intermenstrual bleeding as its conditions [17]. Other studies either did not prespecify what counts as menstrual changes, or only choose a single condition [9,16,18,21]. These menstrual changes appear variably in different populations. 3 studies mentioned that menstrual disorders are one

of the rarer post-vaccination side effects in Africa (0.5%), India (0.16%) and Spain (1<sup>st</sup> dose: 0.7%, 2<sup>nd</sup> dose: 0.25%) [10,13,14]. In contrast, menstrual disorders are the second most common side effect (4%, 8%) in female doctors and dentists in Jordan and Saudi Arabia [12]. But, it is consistent that the majority of menstrual changes happen mostly after the first dose (46.7%) in comparison to the second dose (32.4%) or after both doses (20.9%) [17]. One possible cause of the differences between populations is the preferred vaccine used in said population. Post-vaccination menstrual changes were more common after Pfizer-BioNTech than AstraZeneca [8,20]. However, there was no statistically significant difference found [20]. Another study by Sa et al., also found that Pfizer-BioNTech had unfavorable odds ratio for menstrual changes in comparison to Moderna (0.593%, 95% CI=0.561-0.628) and Johnson & Johnson (0.992, CI 0.909-1.083) [18] (Tables 5-8).

**Table 5:** PubMed Search Strategy (June 16 2022, 09:54:21 PubMed Time).

No.	Query	Results (n)
1	(Covid[Title/Abstract])OR(Covid-19[Title/Abstract])OR(SARSCoV-2[Title/Abstract])OR(BNT162[Title/Abstract])OR(mRNA-1273[Title/Abstract])OR(COVID-19 aAPC[Title/Abstract])OR(INO-4800[Title/Abstract])OR(LV-SMENP-DC COVID-19 [Title/Abstract])OR(Ad5-nCoV[Title/Abstract])OR(ChAdOx1 COVID-19[Title/Abstract])OR(MNA SARS-CoV-2 S1 Subunit[Title/Abstract])	251.328
2	(Vaccin*[Title/Abstract])OR(Postvaccin*)OR(Booster Shot[Title/Abstract])	379.218
3	1 AND 2	33.051
4	(Covid-19 Vaccines[MeSH Terms])	12.996
5	3 OR 4	34.492
6	(Menstruation Disturbances[MESH Terms])OR(Menstrual Cycle[MESH Terms])OR(Oligomenorrhea[MESH Terms])OR(Amenorrhea[MESH Terms])	59.401
7	(Menstrua*[Title/Abstract])OR(Intermenstrua*[Title/Abstract])OR(Premenstrua*[Title/Abstract])OR(Menses[Title/Abstract])OR(Oligomenorrhea[Title/Abstract])OR(Polymenorrhea[Title/Abstract])OR(Amenorrhea[Title/Abstract])OR(Hypomenorrhea[Title/Abstract])OR(Dysmenorrhea[Title/Abstract])	73.191
8	6 OR 7	96.124
9	5 AND 8	15

**Table 6:** CENTRAL Search Strategy (June 17 2022, 05:41:33 PubMed Time).

No.	Query	Results (n)
1	("COVID"):ti,ab,kw OR ("COVID-19"):ti,ab,kw OR ("SARS Co-V"):ti,ab,kw OR ("BNT162"):ti,ab,kw OR ("mRNA-1273"):ti,ab,kw (Word variations have been searched)	10.387
2	("COVID-19 aAPC"):ti,ab,kw OR ("INO-4800"):ti,ab,kw OR ("LV-SMENP-DC COVID-19"):ti,ab,kw OR ("Ad5-nCoV"):ti,ab,kw OR ("ChAdOx1 COVID-19"):ti,ab,kw (Word variations have been searched)	24
3	("MRNA SARS-CoV-2 S1 Subunit"):ti,ab,kw (Word variations have been searched)	0
4	1 OR 2 OR 3	10.839
5	("Vaccin*"):ti,ab,kw OR ("Postvaccin*"):ti,ab,kw OR ("Booster Shot"):ti,ab,kw (Word variations have been searched)	28.097
6	4 AND 5	1.412
7	MeSH descriptor: [COVID-19 Vaccines] explode all trees	147
8	6 OR 7	1.412
9	MeSH descriptor: [Menstruation Disturbances] explode all trees	2.141

10	MeSH descriptor: [Oligomenorrhea] explode all trees	47
11	MeSH descriptor: [Amenorrhea] explode all trees	342
12	9 OR 10 OR 11	2.141
13	("Menstrua*"):ti,ab,kw OR ("Intermenstrua*"):ti,ab,kw OR ("Premenstrua*"):ti,ab,kw OR ("Menses"):ti,ab,kw OR ("Oligomenorrhea"):ti,ab,kw (Word variations have been searched)	1.727
14	("Polymenorrhea"):ti,ab,kw OR ("Amenorrhea"):ti,ab,kw OR ("Hypomenorrhea"):ti,ab,kw OR ("Dysmenorrhea"):ti,ab,kw (Word variations have been searched)	4.864
15	12 OR 13 OR 14	7.045
16	8 AND 15	5

**Table 7:** ProQuest Strategy (June 17 2022, 09:14:02 PubMed Time).

No.	Query	Results (n)
1	((AB, TI("COVID" OR "COVID-19" OR "SARS COV-2" OR "bnt162" OR "mrna-1273" OR "covid-19 aapc" OR "ino-4800" OR "lv-smenp-dc COVID-19" OR "ad5-ncov" OR "chadox1 COVID-19" OR "MRNA SARS-CoV-2 S1 Subunit") AND AB, TI("Vaccin*" OR "Postvaccin*" OR "Booster Shot")) OR MESH("COVID-19 Vaccines")) AND (MESH("Menstruation Disturbances" OR "Menstrual Cycle" OR "Oligomenorrhea" OR "Amenorrhea") OR AB, TI("Menstrua*" OR "Intermenstrua*" OR "Premenstrua*" OR "Menses" OR "Oligomenorrhea" OR "Polymenorrhea" OR "Amenorrhea" OR "Hypomenorrhea" OR "Dysmenorrhea"))	87

**Table 8:** EMBASE Strategy (June 17 2022, 23:30:01 PubMed Time).

No.	Query	Results (n)
1	'covid':ab,ti OR 'covid-19':ab,ti OR 'sars cov-2':ab,ti OR 'bnt162':ab,ti OR 'mrna-1273':ab,ti OR 'covid-19 aapc':ab,ti OR 'ino-4800':ab,ti OR 'lv-smenp-dc covid-19':ab,ti OR 'ad5-ncov':ab,ti OR 'chadox1 covid-19':ab,ti OR 'mna sars-cov-2 s1 subunit':ab,ti	265.834
2	'vaccin*':ab,ti OR 'postvaccin*':ab,ti OR 'booster shot':ab,ti	444.94
3	1 AND 2	34.167
4	'sars-cov-2 vaccine'/exp	19.651
5	3 OR 4	37.9
6	'menstrua*':ab,ti OR 'intermenstrua*':ab,ti OR 'premenstrua*':ab,ti OR 'menses':ab,ti OR 'oligomenorrhea':ab,ti OR 'polymenorrhea':ab,ti OR 'amenorrhea':ab,ti OR 'hypomenorrhea':ab,ti OR 'dysmenorrhea':ab,ti	95.121
7	'menstruation disorder'/exp OR 'menstrual cycle'/exp	193.483
8	6 OR 7	217.721
9	5 AND 8	60
10	9 AND [embase]/lim	49

Changes in menstrual cycle duration were found after the 1<sup>st</sup> dose of AstraZeneca (55.6%), Pfizer-BioNTech (41.4%), Moderna (52.6%), and Johnson & Johnson (66.7%) vaccines [16]. The average menstrual cycle duration significantly increased from 27+6 days (pre-vaccination) to 28.1+10 days (post-vaccination) [17]. This finding is supported by Edelman et al., who also reported significant menstrual cycle duration change in the vaccinated population in comparison to the unvaccinated cohort [19]. Increased menstrual cycle duration can be due to increased menstruation duration (6+0.03 days to 6+0.05 days) or delayed menstruation (0.4%) [9,17]. Menorrhagia is also reported in 78 cases (3.4%) [17]. Relative risk of increased menstrual bleeding was 1.90 (95% CI: 1.69-2.13) and 1.84 (95% CI=1.66-2.03) respectively after the 1<sup>st</sup> and 2<sup>nd</sup> dose of vaccination [21]. The risk of increased menstrual bleeding can be due to changes in estimated menstrual bleeding, menstruation frequency, or the aforementioned menstruation duration. Changes in the estimated amount of menstrual blood, which is the most common cause, were found after the first dose of As-

traZeneca (66.7%), Pfizer-BioNTech (47.4%), Moderna (52.6%), and Johnson & Johnson (66.7%) [16]. Changes in menstruation frequency are also reported after the first dose of AstraZeneca (66.7%), Pfizer-BioNTech (57.1%), Moderna (47.4%), and Johnson & Johnson (33.3%) vaccines [16]. In Indonesia, Sinovac-CoronaVac vaccine is more extensively used during the earlier vaccination effort. Menstrual changes post-Sinovac-CoronaVac administration happens in 20.2% of patients during the first 3 months [15]. During the next 3 months, the percentage decreases to 14.1% [15]. Results of other vaccines in Indonesia show that irregular menstruation is more likely found patients given Moderna (15.4%) than AstraZeneca (8%) vaccines (p=<0,000) [11].

The mechanism of Covid-19 vaccination altered menstruation is still unknown. However, a hypothesis links this phenomenon to vaccine-induced thrombocytopenia and the immune system that also occurs in various other types of vaccines, such as Measles Mumps Rubella (MMR), hepatitis A, hepatitis B, and oth-



ers [17]. Thrombocytopenia could explain frequent menstrual bleeding [18]. In addition, the increased menstrual disturbance after the Covid-19 vaccination was also associated with anxiety or stress because the Covid-19 vaccine was still newly discovered [13]. Another hypothesis is the ability of mRNA-based vaccines that were assessed to induce novel immune responses that could affect the hypothalamic-pituitary-ovarian axis [19].

Menstrual changes that occurred post-Covid-19 vaccination have negatively affected the quality of life of more than 50% of women [17]. A slight change in menstruation could be a problem, especially for someone who planning or avoiding pregnancy [19]. However, menstrual changes that occur are generally moderate (54%) and did not require hospitalization [20]. Data showed that 92.3% of women who experience menstrual disorders after the 1<sup>st</sup> dose of vaccination still continue to get the 2<sup>nd</sup> dose of vaccination [21]. It is because menstrual disorders that occur are generally temporary and do not affect fertility [12]. Therefore, giving Covid-19 vaccination is still considered to have greater benefits than not clinically significant menstrual changes [19,21]. This study describes various changes in menstruation after Covid-19 vaccination with various types of vaccines, either mRNA or vector-based. This broad discussion topic is supported by an article search strategy designed to be as sensitive as possible. The limitation of this study lies in the lack of articles specifically written to discuss the PICO carried. In addition, the majority of studies found are based on online self-reporting, so there is a risk of memory and representational bias. Based on these considerations, the researchers assess that the synthesis of evidence in this article meets the very low-GRADE criteria [7]. This shows that quality research is still very much needed in this area of science.

## CONCLUSION

Based on the studies that have been described, there are variations in menstrual changes after the Covid-19 vaccination seen from the cycle, duration, frequency, quantity of bleeding, and other complaints related to menstruation. The mechanism behind this is still unclear, but it is associated with thrombocytopenia, stress, and effects on the hypothalamic-pituitary-ovarian axis. Menstrual changes after the Covid-19 vaccination can affect women's quality of life, but only temporarily. Therefore, giving the Covid-19 vaccination is still beneficial for reproductive women.

## DECLARATION

### Ethics approval and consent to participate

Not applicable

### Consent for publication

Not applicable

### Availability of data and materials

All data generated or analysed during this study are included in this published article [and its supplementary information files].

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## AUTHORS CONTRIBUTION

**Conceptualization:** N.I.M., N.K.P.S and A.R

**Methodology:** N.K.P.S

**Investigation:** N.I.M., N.K.P.S and A.R

**Data curation:** N.I.M. and N.K.P.S

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**Writing-review and editing:** A.R

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Not applicable.

## CONFLICT OF INTEREST

The authors declare that they have no conflict of interests.

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