

# Menstrual Cycle Abnormalities During Aura Of Covid - 19

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## Abstract

Menstruation is a physiological phenomenon for any female starts at the age of 11-15 years (menarche) and for most of the women end (menopause) by 45-50 years. The normal menstrual cycle relies on the action and interaction of hormones released from hypothalamic-pituitary-ovarian axes. With beginning of COVID-19 a lot of discussions on impact of this pandemic on women's menstruation indicated that women may experience menstrual changes. Unfortunately it is currently unclear how many women have experienced menstrual cycle changes and is it exactly caused by this exposure? Still unknown. This study was done to confirm or exclude this observation. A prospective cross-sectional study was conducted in Basrah \ Iraq from November 2020 to November 2021. 150 Women who previously had normal cycle, experienced menstrual irregularity six months after infected with COVID 19 pandemic was encouraged to voluntarily participate by direct questionnaires and filled the predesigned questionnaire paper. The questionnaire consist of four domain : The first domain : consist of socio –demographic with mean age  $30.8\pm 9.1$ .

The second domain : include the type of menstrual cycle patterns : risk of amenorrhea in this study is only 37.3% , menorrhagia is high 46% , dysmenorrhea 45.3% and 40.7% cycle length more than 35 days The third domain : estimated relation of state of vaccination with menstrual irregularity which reveal significant association between vaccination and dysmenorrhea with P-value 0.049 , the fourth domain: estimated relationship between ( menorrhagia and dysmenorrhea ) and patient's health ,physical, psychological and social activities which showed menorrhagia(heavy cycle) and dysmenorrhea has a negative impact on women's physical and psychological aspect with P-value 0.023 , 0.001 respectively. This study showed some sort of menstrual irregularity like increasing rate of dysmenorrhea ,heavy cycle and significant association of vaccination with dysmenorrhea but still not conclusive due to smaller sample size. So larger sample size more cohort studies is needed to confirm this association

## Introduction

Menstruation is a physiological condition that affects all females. For the majority of women, it begins (menarche) at around age 11 to 15 and ends (menopause) around age 45 to 50. The action and interaction of hormones secreted by the hypothalamic-pituitary-ovarian axes is essential for a healthy menstrual cycle (1).

Normal variation exist within women over life span and between women in relation to characteristics such as BMI ,parity and exercise , also menstrual cycle features such as volume , pain , PMS symptoms are subjective and data are self-reported( 2)

FIGO (international federation of gynecology and obstetrics) give the typical standardized definition of menstruation regarding menstrual frequency (<24-38days), duration(up to 8 days), regularity( shortest to longest≤9 days) and volume, any deviation for this regarded abnormal (3).

With beginning of COVID-19 a lot of discussions on impact of this pandemic on women's menstruation indicated that women may experience menstrual changes, unfortunately it is currently unclear how many women have experienced menstrual cycle changes and is it exactly caused by this exposure? Still unknown

COVID 19 pandemic declared in March 2020 by WHO (4). An infectious disease caused by acute respiratory syndrome coronavirus 2 (SARS-coV-2) transmitted from infected person via small liquid particles respiratory droplets, this infection can be asymptomatic or may range from mild to severe symptoms leading to death it has caused nearly five million deaths and over 287 million confirmed positive cases (5), first discovered in Wuhan, China in late December 2019. Therefore infected person need to be isolated from others, the impact of this isolation may cause depression and stress, feeling of loneliness, fear of death, loss of social contact and financial loss. This stress has severe psychological impact on women (6). A study showed that severe stress and anxiety caused by COVID 19 pandemic was found to be high enough to effect the menstrual cycle in women (7), Other US study in April 2020 found higher rates of psychological distress among adult, compared with 2018 (8)

The COVID-19 sickness may have an impact on the hypothalamic-pituitary-ovarian-endometrial axis, altering the menstrual cycle. It also induces temporary amenorrhea as a protective mechanism, allowing energy resources to be diverted from reproduction to the immunological response. Progesterone is primarily anti-inflammatory, and its sharp decline before menstruation causes an influx of inflammatory cells to the local endometrium, which causes darkening and menstruation. Menstrual blood loss is reduced by vasoconstriction of spiral arteries and activation of the local coagulation system (10)

It is proposed that ACE2(angiotensin converting enzyme 2) receptors are present on ovarian and endometrial tissue and hence COVID infection may hypothetically affect ovarian\ endometrial response to menses by alteration of endometrial leukocyte number\ phenotype So COVID -19 associated with endometrial cell dysfunction and alteration of coagulation system both components of endometrial function at menstruation (11,12).

After receiving the COVID 19 vaccination, a variety of menstrual cycle modifications, including short cycles, long cycles, heavier or lighter menstrual flows, have been recorded. However, the mechanism by which COVID vaccines affect menstrual cycles is yet unknown. Changes in menstrual cycle characteristics were observed after receiving the flu and HPV vaccines (13), while the precise mechanism by which immunization affects menstruation is still unknown (expected to be transient). In a study conducted at Oregon Health and Science University in Portland, USA, Alison and Edelman et al. found that the COVID19 immunization was related with just a minor increase in cycle duration (longer time between bleeding) compared to uninfected individuals. (14)

Treatment of COVID may also play role in changes in menstrual cycle, antipyretic and analgesia used during COVID-19 may affect endometrial prostaglandin synthesis which in turn affect menstrual cycle (15)

Also dexamethasone may affect menstrual cycle through cortisol action (16)

IN this survey we try to find or exclude any menstrual cycle abnormality during the aura of COVID 19

## Material and methodology

A prospective cross-sectional study was conducted in Basrah \ Iraq from November 2020 to November 2021.

. After taking their consent, participants were reviewed using a predesigned questionnaire which includes information regarding the demographic features and about their menstrual history including changes following COVID pandemic and whether these changes affect their life. 150 Women who previously had

normal cycle, experienced menstrual irregularity six months after infection with COVID 19 were participated.

The inclusion criteria: women in the reproductive age, all of them had infected with COVID19 six months before, of different social classes who had regular cycle before the pandemic

exclusion criteria: women with age less than 11 and more than 45 year ( as they may be affected by hormonal changes), pregnant , lactating, history of ovarian problems , hypothalamic menopause ,drugs uses like combine oral contraceptive pills ,heavy exercise and smoker .

The questionnaire consist of Data about:

The first domain: consist of socio -demographic (age 12-45) years, level of education, social class, marital status, had vaccine (regardless the type) and medical history which may affect menstruation).

Social states depend on patient monthly income (salary) 500 \$(less than 500 \$ is low social class, more than 750\$ relatively higher class) place of residency and family members

The second domain: include the type of menstrual cycle patterns : menstrual cycle patterns: assessed by frequency, duration, regularity and volume

Frequency defined: as interval between menstrual cycle, duration: interval from beginning to the end of menstrual bleeding, regularity: as variation of menstrual cycle length

The volume was assessed subjectively depending on numbers of pads used before, presence of clots before and after the pandemic

Dysmenorrhea: as pain during first few hours before menstruation, amenorrhea: as absence of menstruation

Regular menstruation determined by definition of FIGO so in this study frequency was between 22-35, duration of bleeding 3-7 , amount depend on personal perception

The third domain: the estimated relationship between monthly irregularity and vaccination status (independent of type) (absent, present). (Amenorrhea, dysmenorrhea, and heavy cycles).

The fourth domain: estimated relationship between (menorrhagia and dysmenorrhea) and patient's health (physical, psychological and social activities).

Whether these symptoms affect their daily routine activity, need to use medication, absence from work or class, mood swing, depression, Personal relationship, sexual activity , Financial: from Costs of the pads

## Ethical considerations

This study was conducted after obtaining the approval of Basrah University, College of Medicine Review Board (BMCRB No. )

## Statistical analysis

Using SPSS version 26 software, the data were examined. Frequencies and percentages were employed to portray qualitative data, whereas the mean, standard deviation, and median (minimum-maximum) were used to provide quantitative data. Shapiro Wilk and Kolmogorove Smirnov were used to test quantitative variables. Chi-Square was used to analyze the relationship. A probability value of 0.05 or less was deemed significant.

## Results

**Table (1): Demographic characteristics and medical history**

Variable	Mean±S.D	Median (Min.-Max.)
Age	30.83±9.100	32 (12-45)
	<b>Frequency</b>	<b>Percent</b>
<b>Education:</b>		
No formal	9	6.0
Primary school	32	21.3
Secondary school	55	36.7
College (undergraduate)	5	3.3
Graduate	49	32.7
<b>Marital status:</b>		
Yes	97	64.7
No	53	35.3
<b>Occupation:</b>		
Homemaker	69	46.0
Working	60	40.0
Student	21	14.0
<b>Social class*:</b>		
Upper	2	1.4
Middle	80	55.9
Lower	61	42.7
<b>Had a vaccine:</b>		
Yes	75	50.0
No	75	50.0
<b>Chronic disease:</b>		
Yes	4	2.7
No	146	97.3

<b>Total</b>	<b>150</b>	<b>100.0</b>
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\* Seven missed cases, data expressed in numbers, (%) and mean

**Table (1)** shows that the study sample mean age was 30.83 years and the minimum and maximum ages were 12 and 45 years respectively. Most of the women were secondary school certificate holders, about two-thirds of them were married, 46% of them were housewives, and more than half of them came from the middle level social class. Regarding their medical history only 2.7% of the study women had a chronic disease

**Table (2) incidence of menstrual changes.**

<b>Variable</b>	<b>Frequency</b>	<b>Percent</b>
<b>Dysmenorrhea (spasmodic) after COVID-19:</b>		
Yes	68	45.3
No	82	54.7
<b>Heavy after COVID-19:</b>		
Yes	69	46.0
No	81	54.0
<b>Irregular cycle after COVID-19:</b>		
Yes	86	57.3
No	64	42.7
<b>Length of cycle after COVID-19:</b>		
Less than 21	31	20.7
21-35	58	38.7
More than 35	61	40.7
<b>Duration of cycle after COVID-19:</b>		
Less than 3	13	8.7
3-7	102	68.0
More than 7	35	23.3
<b>No. of pads\ day after COVID-19:</b>		
1-2	29	19.3
3-5	87	58.0
More than 5	34	22.7

<b>Amenorrhea (absent menses more than a month) developed after COVID-19:</b>		
Yes		
No	56	37.3
	94	62.7
<b>Total</b>	<b>150</b>	<b>100.0</b>

**Table 2** presents data regarding the menstrual changes occurred six months after COVID-19 infection, values expressed in numbers and percentage (%). Almost half of participant had irregular, heavy, dysmenorrhea and length of cycle more than 35days, while only 37.3% had amenorrhea

**Table (3): Effect of vaccine on patient's menstrual cycle (dysmenorrhea, heavy cycle and amenorrhea)**

	<b>Heavy cycle No. (%)</b>	<b>Dysmenorrhea No. (%)</b>	<b>Amenorrhea No. (%)</b>
Vaccinated	35 (50.7)	40 (58.8)	29 (51.8)
Unvaccinated	34 (49.3)	28 (41.2)	27 (48.2)
P-Value	0.870	0.049	0.736

When menstrual abnormalities were investigated among those whom were vaccinated and non-vaccinated, it was found that dysmenorrhea was the only abnormality significantly statistically associated with COVID - 19 vaccination.

**Table (4): Effect of menstrual irregularity (dysmenorrhea, heavy cycle) during COVID on women's health**

<b>Health</b>	<b>Dysmenorrhea</b>			<b>Menorrhagia(heavy cycle)</b>		
	<b>Absent</b>	<b>Present</b>	<b>p-value</b>	<b>Absent</b>	<b>Present</b>	<b>p-value</b>
Physical	49	59	0.0001	43	65	0.0001
Psychological	55	42	0.498	59	38	0.023
Social	29	31	0.203	31	29	0.640

It is clear in that dysmenorrhea was found to have negative effect on physical aspect of women's health and it's statistically significant, while menorrhagia had a negative effect on both physical and psychological aspect of women's health

## Discussion

Menstruation is one of major concern in reproductive women's health affects large number of women throughout their reproductive life from adolescence till menopause

During aura of COVID 19 a lot of studies documented that there is significant increase in the numbers of women experience menstrual irregularity.

Although SARS-COV2 virus can infect human race irrespective of age ,a study was done in India by Savitesh and Poonam in 2021 ; suggested higher chance of infection among female with lower age group

age of 18-35 which is the commonest age group for female infected with COVID 19 virus ( 17), ,The mean age in present study is ( 30.8 ±9.1) and this is in agreement with Savitesh and poonam et al study

Depending on patient monthly salary , number of family members and place of residency , In the current study most of our participant of are of middle and low social classes (55.9 % ,42.7% ) respectively , this study is in consistent with a lot of studies which showed association of social class with degree and severity of COVID19 (18,19) . The first observational studies reported that severity of COVID -19 depend not only on physical conditions such as Age, cardiovascular, obesity but also on socioeconomic status (SES) indicator such as lower educational level among various population (20) . In European populations those who had NO qualification ( lower educational level) had higher risk of sever COVID-19 (21) ,Other study in USA also showed that lower level of education is risk factor for sever infection (22) .

Excessive stress during aura of COVID19 is one of the most common concern among women in reproductive age group around the world. it can lead to immunological , physiological ,psychological and behavioral changes which can lead to menstrual irregularity , stress has inhibitory effect on hypothalamic pituitary gonadal axis (HPG) so it suppress GnRH release and glucocorticoid inhibit luteinizing hormone LH release and estrogen and progesterone production by ovary which presumably result in amenorrhea(6, 23,24 ) . In contrast to these studies Risk of amenorrhea in the present study is low, only (37.3 %) had amenorrhea this may be related to either smaller sample size which result in higher bias or depend on the severity of COVID19.

57.3% of the patients complaining of some sort of menstrual irregularity which is consistence with a lot of studies (7, 9)

Menorrhagia is considered to be one of the most significant cause of ill health in women. One in 20 women aged 30-49 years consults her general practitioner each year with heavy menstrual loss (25)

Almost half of women in Phelan's et al study reported menorrhagia and dysmenorrhea are the main perceptype type of menstrual irregularity compared to before the pandemic. In line with this study nearly half of patients reported menorrhagia and dysmenorrhea (46%, 45.3%) and this in consistence with study done by Phalen et al. (6)

A study published in journal of obstetrics and gynecology 2019 found that there is small association between cycle length and coronavirus disease 2019 and vaccination (14) their periods themselves ,which came almost a day later on average and the effect is transient . (40.7%) of patients reported increase menstrual length (more than 35 days) in this study

Although the public were hesitant to get the vaccine , Shortly after giving coronavirus vaccines women started reporting menstrual changes , some said their period were late others reported heavier bleeding than usual or painful bleeding (dysmenorrhea) and the effect is transient . Several studies showed link between COVID -19 vaccine and menstrual irregularities (26) this study showed significant association between COVID-19 vaccination and dysmenorrhea with (p-value of 0.049)

In 2022 a study was done by Nadia Muhaidat et al. investigated the prevalence and impact of menstrual abnormalities after COVID 19 vaccine and showed a possible link between COVID19 vaccine and menstrual irregularity (27) and this in disagreement with this study which showed no statistical significance between menstrual abnormality ( menorrhagia and amenorrhea ) with P-value ( 0.870 , 0.736 respectively ) and vaccination .

Studies showed that although menorrhagia rarely threatens life , it has negative effect on women's personal, family , social and work life and it decreases quality of life .Shankar et al in 2008 conducted review of studies evaluating quality of life in women's suffering from menorrhagia and revealed that their life were

adversely affected by menorrhagia (28,29 ). Other study documented that irregular menstrual cycle negatively impact the quality of life of women of reproductive age. COVID 19 infection, lockdown policies may exacerbated physical, social and psychological states for Women how showed significant increase in suffering from physical, mental health symptoms (30, 31). In this study both dysmenorrhea and menorrhagia had significant impact on our patient's physical and psychological in a negative way (p-value 0.001, 0.023) respectively and this in agreement with Shankar et al and previous studies also

## Conclusion

COVID-19 still a new topic, little is known about its morbidity and studies still under researches. Pattern of infection differ from country to country in term of severity, vaccination, lock down and stress which could probably affect menstruation. This study showed some sort of menstrual irregularity like increasing rate of dysmenorrhea ,heavy cycle and significant association of vaccination with dysmenorrhea but still not conclusive due to smaller sample size.

So study with larger sample size and more cohort studies is needed to confirm this association.

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