

# Effects of Menstrual Different Phases on Liver-Kidney Functions in Healthy Women

Shaimaa Mahdi A. Jawad

Kufa University / Faculty of Education for Girls/Iraq  
Corresponding Author: [saymaam.alnaffakh@uokufa.edu.iq](mailto:saymaam.alnaffakh@uokufa.edu.iq)

## ABSTRACT

**Background:** The menstrual cycle is a critical rhythm of life regulated by interactive levels of estradiol, progesterone, luteinizing hormones, and follicular stimulation, during this cycle several metabolic parameters fluctuate in conjunction with sex hormones, therefore, this work was performed to investigate whether the menstrual cycle in healthy women affects the liver and kidney function.

**Materials and Methods:** The study was conducted in the Faculty of Education for girls during the period October 2018–January 2019. It involved the participation of thirty healthy women with age between 18 and 26 years. All participants were non-smokers with no use of contraceptives or hormones. In addition, they confidently mentioned that they had had regular menstrual cycles (between 24 and 32 days).

**Results:** Our findings showed that the liver enzymes (ALT, AST and ALP) levels were higher in the luteal phase than their levels in the follicular phase ( $P \leq 0.05$ ). However, there were no significant differences in the level of blood urea and serum creatinine between the two phases.

**Conclusion:** It can be concluded that the measurement of liver function test can be affected by the phases of menstrual cycle. It is important to take that into consideration when assessing the liver enzymes. It may also be of interest the potential beneficial effect endogenous E2 on liver enzymes.

**Keywords:** Menstrual Cycles in healthy women, liver and kidney function.

## Correspondence:

Shaimaa Mahdi A. Jawad  
Kufa University / Faculty of Education for Girls/Iraq

\*Corresponding author: Shaimaa Mahdi A. Jawad email-address:  
[saymaam.alnaffakh@uokufa.edu.iq](mailto:saymaam.alnaffakh@uokufa.edu.iq)

## INTRODUCTION

The menstrual cycle is associated with significant hormonal changes, primarily due to estrogen and progesterone [1]. The usual length of the menstrual cycle is 21 to 35 days, with an average 26 to 28 days [2]. When there is no fertilization, elevated levels of estrogen and progesterone are produced from the corpus luteum which in turn produce a negative feedback effect on the anterior pituitary. Such effect leads to “shut off” the production of gonadotropins (luteinizing hormone (LH) and follicle-stimulating hormone (FSH). Hence, there will be subsequent decrease in levels of FSH and LH, and estrogen and progesterone from the corpus luteum, respectively [3]. Ultimately, there will be deficient nourishment for the blood vessels of the endometrium resulting in the death of these vessels which will then be sloughed off as menstrual bleeding [4].

Changes in sex hormones during the menstrual cycle is not only accompanied by fluctuation in several metabolic parameters such as serum lipoproteins with altered plasma antioxidant system. It has been mentioned by several studies that plasma lipoproteins and antioxidant status vary from phase to phase during the menstrual cycle. [5-8]

Although it is not well documented, the concentration and/or the activity of serum and liver enzymes potentially fluctuate as well. Such assumption is probably based on changes in hepatic fat content, and that obesity can modulate this fluctuation. [9]

There are several possible pathways to clarify the relationship between liver enzyme levels and sex hormones during the menstruation. One of the organs that are modulated by sex hormones is the liver through estrogen receptors expressed by hepatocytes (ESR1). For example, the metabolic status of liver is mediated by estradiol through estrogen receptors by leading to decreased gluconeogenesis, enhanced lipogenesis and

fatty acid uptake. For this reason, it has been suggested that sex hormones the energy metabolism. [10-13]

Chunwei and colleagues [14] not only found fluctuation in the concentrations of hepatic enzymes during the normal menstrual cycle but also they suppose that such fluctuation is mediated by hormones such as progesterone. In addition, the authors mentioned that the fluctuation in the levels of hepatic enzymes is variable depending on the age and body mass index. Hence, it is important to take into consideration the phase of menstrual cycle when measuring livers function test and/or interpreting findings in menstruating women.

In terms of renal function test during the menstrual period, data available are still limited. However, previous studies performed on mice and rats have reported that females were less vulnerable to kidney damage or kidney diseases when compared to males. Interestingly, the ovaries of females were removed, these females became as vulnerable as males to the same degree of kidney injury. The secret seems to be estrogen, while in men; it is not as noticeable as it is in women. [15] As such literature reviews debate of the role of female hormones in kidney disease; we considered that the effect of hormones on normal renal tissue may have protective effects, rendering the kidneys less vulnerable to injury. [16]

Another study indicated that there is no correlation between the increase in the luteal phase and creatinine clearance at the clinical level during the normal menstrual cycle in spite of the statistically significant increase in the luteal phase. Importantly, at the time of ovulation, there is no significant reduction in creatinine clearance. [17] Nevertheless, the interaction among endogenous sex hormone and uric acid rates in pre-menopausal women has not been explained, while its variability over the menstrual cycle in pre-menopausal women have not been identified. [18]

**Aims**

Clinical laboratory diagnosis is a fundamental necessity to provide adequate treatment in most diseases. Therefore, it is necessary to exclude any interference from other conditions that may give a false positive or negative results which lead to resulting an inappropriate diagnosis and/or treatment. Therefore, this study was conducted to determine the effect of the menstrual cycle in healthy women on liver and kidney function.

**Materials and Methods**

**Place and Time of Study**

This study was carried out at the Faculty of Education for women (October 2018–January 2019).

**Participants and their criteria**

Thirty women were enrolled in this work. They were healthy women with age between 18 and 26 years. They were non-smokers, not using any contraceptive or hormonal preparation, and well oriented with full knowledge about their regular menstrual cycles (between 24 and 32 days) [19].

**Preparation of blood samples**

Five milliliters of venous blood were obtained by antecubital venipuncture using G 23 needles from healthy women in two periods. The first collection was performed when the participants reached the follicular phase which is corresponding to the day 1–3 of the cycle while the second collection was performed when the participants reached the luteal phase which is corresponding to day

14–16 of the cycle. Blood samples were placed in plain test tubes and allowed to clot at room temperature. Tubes were centrifuged (3000 rpm for 10 minutes), serum was collected and transferred into plastic tubes as aliquots and stored at -20° until be used for measurement of the concentration levels of liver enzymes, “including alanine aminotransferase (ALT), aspartate aminotransferase, alkaline phosphatase (ALP)” and each of urea and creatinine levels, were measured via colorimetric method on a chemistry analyzer (Beckman coulter AU480, Germany).

**Statistical Analysis**

SPSS 19.0 program was used to perform statistical analysis and generate figures. The data are expressed as a mean ± standard error of mean (SEM). A paired student's T-test was used to compare between different parameters in two periods and  $P < 0.05$  was considered statistically significant.

**RESULTS**

Mean levels of ALT, AST and ALP varied significantly according to phases of the menstrual cycle in healthy women. Lower mean levels of liver enzymes observed in the luteal phase of menstrual period. (Table 1, Fig. 1)

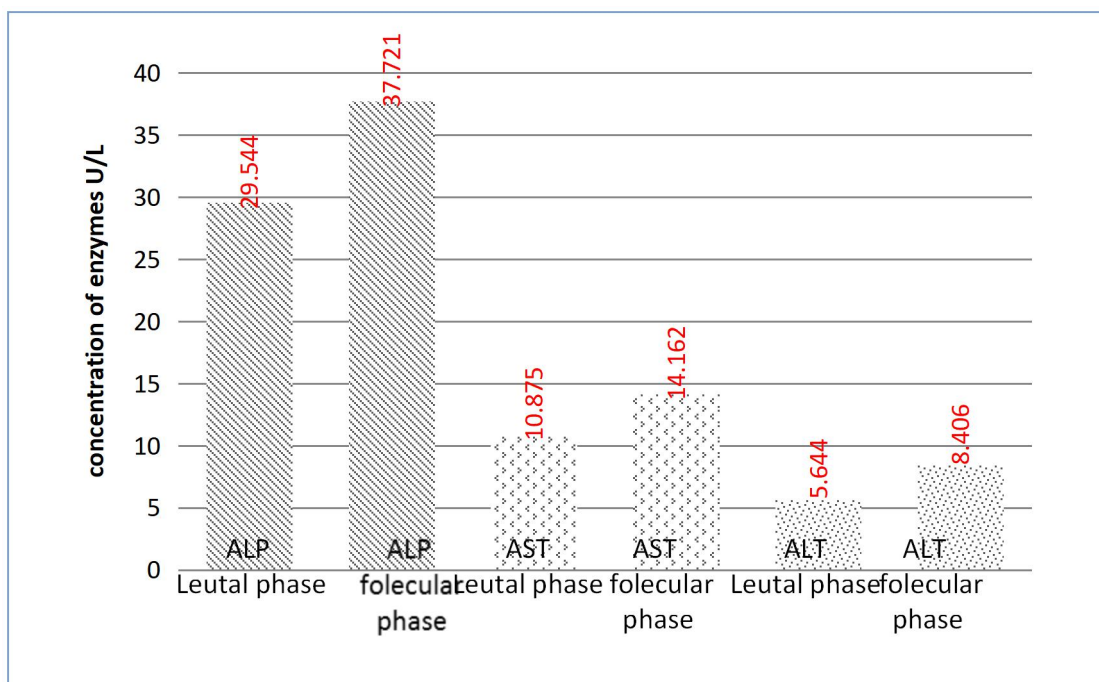
**Table 1:** This table shows the serum concentrations of liver enzymes (IU/L) in women when reached the follicular phase and those in women who reached the luteal phase of menstrual cycle.

Phases	Follicular phase Mean ± S.E	luteal phase Mean ± S.E
Parameters		
ALT (U\L)	8.407 ±0.387*	5.645 ±0.648
AST(U\L)	14.163 ±1.193*	10.875 ± 0.806
ALP(U\L)	37.721 ± 2.216*	29.544 ±1.599

\*Significant at level ( $P \leq 0.05$ ). S.E: Stander Error

ALT: Alanine aminotransferase

AST: aspartate aminotransferase ALP: Alkaline phosphatase



**Fig. 1:** Concentration of Alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase in

serum of healthy women within two phases of menstrual cycle.

No significant differences ( $P > 0.05$ ) were noticed in both phase of cycle in healthy women in terms of urea and creatinine levels (Table 2).

**Table 2:** This table shows the serum concentrations of serum urea and creatinine (mg\dl) in women when reached the follicular phase and those in women who reached the luteal phase of menstrual cycle.

Phases	Follicular phase Mean $\pm$ S.E	luteal phase Mean $\pm$ S.E	p. Value
Parameters			
Urea (mg\dl)	21.829 $\pm$ 1.116	21.819 $\pm$ 1.304	N.S
Creatinine(mg\dl)	0.497 $\pm$ 0.015	0.536 $\pm$ 0.012	N.S

S.E: Stander Error N.S: Non- significant

## DISCUSSION

In this study, it was demonstrated that there is a correlation between the menstrual cycle and metabolic processes in healthy women. The findings of this study showed an increase in the level of liver enzymes in the first phase of the menstrual cycle, and the reason for this increase may be due to stress associated with or prior to the menstrual cycle, and stress in turn affects the structure and permeability of the cell membranes [20]. This leads to the release of liver enzymes and increases their concentration in the blood.

In addition, the absence of estrogen hormone during the first phase of the menstrual cycle, which is known to be a scavenger of free radicals induced by stress and a barrier to the stress mechanism itself, which contributes to a rise in oxidative stress and the incidence of oxidative stress due to free radicals or the so-called Reactive Oxygen Species. [21]

And that the presence of these unstable molecules can cause damage to the cells of the body due to a defect in the cell membranes. These molecules can attack the hepatic cell membrane by breaking the acyl chain of phospholipids in the cell membrane, leading to dynamic changes such as fluidity and permeability, which increase the penetration of hepatic enzymes into the blood. [22] However, this decline in the amount of estrogen is increasing comparatively and steadily, as well as less stress on the woman's body during this time. Therefore, we find that the rise is proportional to the level of liver enzymes and it returns to normal after the elimination of the stimuli. [23]

Konstandi et al [24] reported cyclic changes in hepatic expression of genes in the animal model during the estrous cycle. Various transcription factors, including Srebp-1c, the main regulator of hepatic lipogenesis, have been observed. In addition, gene expression changes in response to variations in sex hormones tend to be partly motivated by regulation of hepatic insulin signaling. It is therefore possible that the variations in ALT indicate the inherent effect of sex hormones on the liver, most likely through subtle changes in the fat content of the liver.

The results of the current study showed that there was no significant difference in the concentration of urea in the serum of women between the two periods of the menstrual cycle. This finding is consistent with other studies that have shown no significant difference in urea concentrations at various stages of the menstrual cycle. [25-26] although some other studies have shown that women experience a higher incidence of high urea levels in the blood after menopause, to which scientists attribute the explanation of the role of protective sex hormone in menopause. [27]

It was also noticed that there was no significant difference in the concentration of creatinine despite the presence of an increase in the level of creatinine in the second period, but it was not statistically significant, as this result was in agreement with other studies [17, 25] as it confirmed that there was no change in creatinine clearance at the clinical level during a normal menstrual cycle, of particular around the time of ovulation. However, according to Gault and Chafe, there was high and low decrease in creatinine the renal function test in the follicular phase and near ovulation, respectively. [26]

## CONCLUSION

These results show the significance of taking into account the menstrual cycle stage in the measurement of liver enzymes in pre - menopausal women and confirm the suspected beneficial effects of endogenous E2 on liver enzyme levels and the changes in urea and creatinine levels between this group of healthy women was modest

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