PERIÓDICO TCHÊ QUÍMICA
ARTIGO ORIGINAL

# ALTERAÇÕES NO PERFIL LIPÍDICO DURANTE DIFERENTES FASES DO CICLO MENSTRUAL EM MULHERES JOVENS E EM PRÉ-MENOPAUSA

# LIPID PROFILE CHANGES DURING DIFFERENT PHASES OF MENSTRUATED YOUNG AND PREMENOPAUSAL WOMEN

# تغيرات صورة الدهون في الدم اثناء مراحل مختلفة من اطوار الدورة الشهرية في النساء الشابات والنساء ماقبل سن اليأس

**Noora Kareem Abdul Hasan***
*Department of Biology, College of Science, University of Misan, Maysan, Iraq.*

**Ahmed Aboud Khalifa**
*Department of Biology, College of Science, University of Misan, Maysan, Iraq.*

** Corresponding author*
*E-mail: norakareem655@gmail.com*

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## RESUMO

**Introdução**: As medições do colesterol lipoproteico variam ao longo do ciclo menstrual, correspondendo a concentrações crescentes e decrescentes de gonadotropinas e níveis de hormônios esteroides ovarianos em mulheres jovens, enquanto mulheres em pré-menopausa e aquelas que estão na transição menopáusica são caracterizadas por uma resposta ovariana deficiente à alta secreção de gonadotropina, levando a baixos níveis de esteroides ovarianos. **Objetivos**: Investigar as mudanças no colesterol lipoproteico e suas interações com hormônios esteroides sexuais durante diferentes fases do ciclo menstrual em mulheres jovens menstruadas e mais velhas (pré-menopausa). **Métodos**: A amostra incluiu trinta mulheres saudáveis (com idades entre 20 e 45 anos) divididas em dois grupos (15 mulheres/grupo) de acordo com suas idades (20-25 anos e 40-45 anos). Amostras de sangue foram coletadas no 8º, 16º e 24º dias do ciclo menstrual em ambas as mulheres jovens e mais velhas menstruadas para comparar os parâmetros anteriores entre esses dias para cada grupo e também para comparar esses parâmetros entre dias semelhantes para os dois grupos. As mudanças no perfil lipídico (CT, TG, HDL, LDL e VLDL) foram avaliadas pelos componentes do kit *Bio-Systems*. A análise estatística foi realizada utilizando Análise de Variância de um fator (ANOVA), seguida pelo teste de Duncan, e testes t foram usados para avaliar as diferenças entre os grupos. **Resultados**: CT e TG não aumentaram significativamente no 8º dia do ciclo menstrual, que representa a fase folicular, em comparação com os outros dias (16º e 24º dias). No entanto, LDL aumentou significativamente ($p \leq 0,05$) no 8º dia em comparação com os outros dias. Por outro lado, HDL e VLDL aumentaram no 16º dia do ciclo menstrual, que representa a fase ovulatória.. **Discussão:** CT, TG e LDL aumentaram durante a fase folicular e foram acompanhados por níveis elevados de FSH e estradiol, levando a um perfil lipídico favorável, uma vez que o FSH e o estradiol são considerados reguladores da biossíntese de colesterol e têm uma capacidade de amortecimento. O HDL e o VLDL aumentam (durante os dias de ovulação) para atender aos requisitos da ovulação e garantir uma ovulação bem-sucedida. **Conclusões**: Estudar e avaliar as mudanças no perfil lipídico de acordo com a fase do ciclo menstrual representa uma questão importante para compreender o estado fisiológico e saudável da mulher e prevenir a incidência de doenças cardiovasculares.

**Palavras-chave**: *Colesterol total (CT), Colesterol triglicerídeo (TG), Lipoproteína de alta densidade (HDL), Lipoproteína de baixa densidade (LDL), Lipoproteína de muito baixa densidade (VLDL).*



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## ABSTRACT

**Background**: Lipoprotein cholesterol measurements fluctuated across the menstrual cycle, corresponding to rising and declining concentrations of gonadotropins and ovarian steroid hormones levels in young women, whereas premenopausal women and those who inside the menopausal transition characterized by a poor ovarian response to high secretion of gonadotropin leading to low levels of ovarian steroids. **Aims**: To investigate the lipoprotein cholesterol changes and their interactions with sex steroid hormones during different phases of the menstrual cycle in menstruated young and old (premenopausal) women. **Methods**: The sample included thirty healthy women (aged 20-45 years) divided into two groups with 15 women /group according to their ages (20-25 years) (40-45 years). Blood samples were collected on the 8$^{th}$, 16$^{th}$, and 24$^{th}$ days of the menstrual cycle from both young and old menstruating women to compare the previous parameters between these days for each group and compare these parameters between similar days for the first and second groups. Lipid profile (Total cholesterol (TC), Triglyceride (TG), High density lipoprotein (HDL), Low density lipoprotein (LDL), and Very low density lipoprotein (VLDL) changes be assayed by Bio-Systems Kit components. Statistical analysis was carried out using one-way Analysis of Variance (ANOVA), followed by Duncan's test, and t-tests were used to assess differences between groups. **Results**: TC and TG levels did not significantly increase on the 8th day of the menstrual cycle, which represents the follicular phase, in comparison with the other days (16th and 24th days). However, LDL level increased significantly ($p \leq 0.05$) on the 8th day compared to the other days. On the other hand, HDL and VLDL levels increased on the 16th day of the menstrual cycle, which represents the ovulatory phase. **Discussion**: TC, TG, and LDL levels increased during the follicular phase and were accompanied by high levels of FSH and estradiol, leading to a favorable lipid profile, whereas FSH and estradiol are considered regulators of cholesterol biosynthesis and a buffering capacity. HDL and VLDL levels rise during ovulation to meet the requirements of ovulation and ensure successful ovulation. **Conclusions**: Studying and evaluating changes in the lipid profile according to the menstrual cycle phase of the menstrual cycle represents an important issue in knowing the physiological and healthy woman state and preventing cardiovascular disease incidence.



**Keywords:** *Total cholesterol (TC), Triglyceride cholesterol (TG), High-density lipoprotein (HDL), Low-density lipoprotein (LDL), Very low-density lipoprotein (VLDL).*



**الملخص**

**الخلفية**: تتباين قياسات كولسترول البروتين الدهني خلال الدورة الشهرية، متناسبة مع ارتفاع وانخفاض تراكيز الهرمونات المغذية للقند والهرمونات الستيرويدية المبيضية في النساء الشابات، في حين تتميز النساء قبل انقطاع الطمث و اللواتي يتواجدن في المرحلة الانتقالية لانقطاع الطمث باستجابة مبيضية ضعيفة تجاه الإفراز العالي للهرمونات المغذية للقند الامر الذي يؤدي إلى انخفاض مستويات الستيرويدات المبيضية. **الأهداف**: دراسة تغيرات كولسترول البروتين الدهني وتداخلاتها مع الهرمونات الستيرويدية الجنسية خلال الاطوارالمختلفة من الدورة الشهرية في كل من النساء الشابات والاكبرعمراً (قبل انقطاع الطمث). **طرائق العمل**: تضمنت عينة الدراسة ثلاثين امرأة سليمة (تتراوح أعمارهن بين 20 الى 45 عامًا) تم تقسيمهن إلى مجموعتين (15 امرأة لكل مجموعة) استنادًا إلى أعمارهن, المجموعة الاولى (20-25 عامًا) والمجموعة الثانية (40-45 عامًا). جمعت عينات الدم في الأيام الثامن, السادس عشروالرابع والعشرون من الدورة الشهرية لكل من مجموعتي النساء الشابات والنساء الاكبرعمراً وذلك لقياس و تقييم مكونات الدهون في الدم (الكولسيرول الكلي, ثلاثي الجلسريد, والبروتين الدهني عالي الكثافة, البروتين الدهني منخفض الكثافة والبروتين الدهني منخفض الكثافة جداً) (بأستخدام مكونات عدة النظام الحيويBio-Systems Kits) لمقارنة المعاييرالدهنية اعلاه بين هذه الأيام لكل مجموعة, ولمقارنة هذه المعاييرايضاً بين الأيام المتماثلة للمجموعتين الأولى والثانية .حيث تم إجراء التحليل الإحصائي بإستخدام تحليل التباين احادي الاتجاه (ANOVA) المتبوع بإختبار دنكن و اختبار**t**. **النتائج**: ارتفعت مستويات الكولسترول الكلي (TC) وثلاثي الجلسريد (TG) وبشكل غير معنوي اما البروتين الدهني منخفض الكثافة (LDL) فقد ارتفعت مستوياته بشكل معنوي ( $p \leq 0.05$) في اليوم الثامن من الدورة الشهرية، والذي يمثل المرحلة الحويصلية، بينما ارتفعت مستويات البروتين الدهني عالي الكثافة (HDL) والبروتين الدهني منخفض الكثافة جداً في اليوم السادس عشر من الدورة الشهرية (والذي يمثل مرحلة التبويض) وبشكل معنوي ($p \leq 0.05$) وغير معنوي على التوالي. **المناقشة**: ان ارتفاع مستويات الكولسترول الكلي (TC) وثلاثي الجلسريد (TG) والبروتين الدهني منخفض الكثافة (LDL) خلال المرحلة الحويصلية وما يصاحب ذلك من ارتفاع في مستويات FSH والاستراديول والذي قد يؤدي إلى تحسين مستويات مكونات الدهون في الدم كونهما يعتبران منظمان للتخليق الحيوي للكوليسترول ولقابليتهما في حفظ توازن الدهون, كما ان الارتفاع في مستويات HDL و VLDL (خلال أيام التبويض) له دور رئيسي في تلبية متطلبات التبويض وضمان نجاح عملية التبويض. **الاستنتاجات**: ان دراسة وتقييم التغيرات الحاصله في صورة الدهون وفقًا لأطور الدورة الشهرية تمثل قضية هامة لفهم الحالة الفسيولوجية والصحية للمرأة والتي قد تمكن من الوقاية من حدوث أمراض القلب والأوعية الدموية.



**الكلمات المفتاحية:** الكوليسترول الكلي (TC) ، ثلاثي الجليسريد (TG) ، البروتين الدهني عالي الكثافة (HDL) ، البروتين الدهني منخفض الكثافة ( *LDL) ، البروتين الدهني منخفض الكثافة جداً (VLDL).*

## 1. INTRODUCTION:

Numerous studies have reported differences in lipoprotein cholesterol levels throughout the menstrual cycle. HDL increased significantly during the follicular phase and a significant decrease in TC and LDL during the luteal phase, whereas estradiol was significantly associated with increased levels of HDL during the follicular phase, and ovarian effects itself (corpus luteum) was associated with significantly reduced levels of TC, HDL, and LDL during the luteal phase. Moreover, the corpus luteum consumes LDL to support steroidogenesis, which depletes circulating LDL during the luteal phase, regardless of the independent action of estradiol and progesterone on the liver (Jensen *et al.*, 2017; Sharma *et al.*, 2022). Furthermore, Fouad Kadhuim 2020 found that the permanence of the estrogen effect is the main cause of ameliorating the lipid profile changes during different phases of the cycle in women aged (25-45 years). In addition, lipoprotein metabolism has been affected by some estrogenic mechanisms such as the increase of VLDL synthesis leading to a subsequent decrease in LDL and increase in HDL, inhibiting hepatic lipase and lipoprotein lipase activity, up-regulating the LDL receptors (Knopp *et al*., 2005), upregulate ATP binding cassette transporter-A1 (ABCA1) that exports HDL generated from excess cellular cholesterol and Apolipoprotein-A1 (APOA1, an essential HDL protein, which enhance HDL production) (Panigrahi and Panda 2018) and suppress hepatic scavenger receptor class B Type 1 (SR-BI) expression leading to decreased hepatic cholesterol uptake from HDL (Ren *et al*.,2018), whereas, LDL and HDL play essential roles in ovarian cholesterol transport, in addition, cholesterol is an important substrate for the synthesis of ovarian sex hormones and follicular development in the follicular phase (Huang *et al*.,2019). In addition, cholesterogenesis regulated by FSH that binds with hepatic FSHRs, activates the Gi2α/β-arrestin-2/Akt pathway and subsequently inhibits the binding of FoxO1 with the SREBP-2 promoter, thus preventing FoxO1 from repressing SREBP-2 gene transcription, this effect, in turn, results in the upregulation of SREBP-2, which drives HMGCR nascent transcription and de novo cholesterol biosynthesis, leading to the increase of cholesterol levels (Guo *et al*.,2019).

Because of this controversy, the present study shed some light on the lipid profile changes during different phases of menstruated young and premenopausal women.

## 2. MATERIALS AND METHODS:

### 2.1. Materials

Lipid profile (TC, TG, HDL, LDL, and VLDL) changes be assayed by Bio-Systems Kit components.

### 2.2. Methods

The current study was conducted between 2022 and 2023, following ethical approval from the Training and Human Development Center at the Misan Health Directorate, Ministry of Health (Approval No: 132, Date: 09-03-2023). Thirty healthy women participated in this study, divided into two groups, each comprising 15 women. The first group comprised women aged 20 to 25, while the second group included premenopausal women aged 40 to 45.

Blood samples were collected on the eighth, sixteenth, and twenty-fourth days of the menstrual cycle in both young and premenopausal menstruating women to compare the previous parameters between these days for each group and compare these parameters between similar days for the first and second groups.

Statistical analysis was carried out using one-way Analysis of Variance (ANOVA), followed by Duncan's test, and t-tests were used to assess differences between groups, with a significance level set at $p \leq 0.05$ (Steel *et al*.,1997).

## 3. RESULTS AND DISCUSSION:

### 3.1. Results

#### *3.1.1. Total cholesterol (TC)*

The Total cholesterol (TC) levels increased not statistically on the 8$^{th}$ day in comparison with the 16$^{th}$ and statistically ($p \leq 0.05$) in comparison with the 24$^{th}$ days for the first and second groups ( Figure 1).

In addition, TC increased statistically ($p \leq 0.05$) in

the second group in comparison with the first group for similar days (Figure 2).

#### *3.1.2. Triglyceride cholesterol (TG)*

The Triglyceride cholesterol (TG) levels increased not statistically on the 8th day in comparison with the 16th and statistically ($p \leq 0.05$) in comparison with the 24th days for the first and second groups ( Figure 3).

In addition, TG increased statistically ($p \leq 0.05$) in the second group in comparison with the first group for similar days (Figure 4).

#### *3.1.3. High-density lipoprotein (HDL)*

The first and second groups increased statistically ($p \leq 0.05$) on the 16th day compared with the 8th day and 24th day. (Figure 5).

In addition, HDL decreased statistically ($p \leq 0.05$) (except on the 24th day) at the second group in comparison with the first group for similar days. (Figure 6).

#### *3.1.4. Low-density lipoprotein (LDL)*

LDL increased statistically ($p \leq 0.05$) in the 8th day compared with the 16th day and 24th day for the first and second groups. (Figure 7).

In addition, LDL increased not statistically in the second group compared to the first group for all similar days. (Figure 8).

#### *3.1.5. Very low-density lipoprotein (VLDL)*

VLDL increased not statistically in the 16th day compared with the 8th day and 24th day for the first and second groups. ( Figure 9).

In addition, VLDL increased not statistically in the second group compared to the first group for all similar days. (Figure 10).

### 3.2. Discussion

#### *3.2.1. Total cholesterol (TC)*

This 8th day represents the follicular phase of the cycle that accompanied the high levels of FSH and estradiol, leading to a favorable lipid profile. In contrast, FSH and estradiol are cholesterol biosynthesis regulators and buffering capacities.

During the follicular phase, there was an increase in total cholesterol, corresponding to the rise and peak of estrogen (Panigrahi and Panda, 2018; Sharma *et al*., 2022). Guo and his colleagues 2019 showed that FSH regulated cholesterol biosynthesis via a complex mechanism involving FSH/FSHR binding on the hepatocyte surface followed by different activation steps to approach HMGCR (the rate-limiting enzyme for cholesterol biosynthesis). Furthermore, during the reproductive years, estradiol promotes a favorable lipid profile (Chu *et al.*, 2003).

TC elevation in the second group may be explained by its correlation with the high levels of FSH and the decrease in estradiol levels in the menopausal transition women. In contrast, FSH induced cholesterol biosynthesis via a complex mechanism that ends by de novo cholesterol biosynthesis. In addition, the deficiency in some hormones (including estradiol) led to elevations in serum cholesterol levels. Furthermore, the gradual decrease in the ability to remove cholesterol might also be participating in the age-related disruption of lipid homeostasis, which led to an accumulation of cholesterol and elevated its levels. In premenopausal women, elevated FSH leads to an unfavorable circulating TC disturbance by regulating hepatic cholesterol biosynthesis in the liver. This could be reversed by blocking FSH to reduce serum cholesterol via inhibiting hepatic cholesterol biosynthesis (Guo *et al.*,2019). In addition, Trapani and Pallottini 2010 demonstrate that the causes of age-related disruption of lipid homeostasis include the progressively reduction ability to remove cholesterol through conversion to bile acids and the decreased activity of the bile acid rate-limiting enzyme (cholesterol 7α-hydroxylase C7αOH).

#### *3.2.2. TG*

The elevation in TG may be correlated with the high levels of both FSH and estradiol on this 8th day due to their roles in promoting lipid biosynthesis ending with TG increase. The follicular phase is characterized by an increase in both the follicle-stimulating hormone (FSH) and estradiol (Uenoyama *et al*., 2021). Simeon and his colleagues 2022 found that TG has higher values at the follicular phase due to the production of high estrogen levels from developing follicles. In addition, Zhu and his colleagues 2018 showed that FSH treatment increased lipid biosynthesis and lipid droplet formation through the Gai/ $Ca^{2+}$/cAMP regulatory element-binding protein (CREB) pathway. Furthermore, Luo and his colleagues 2017 showed that estrogen is an important factor in

maintaining TG homeostasis and up-regulates serum concentrations of Apolipoprotein A5 (APOA5), which possesses a strong ability to decrease serum TG levels.

However, premenopausal women (second group) are accompanied by an imbalance of lipid profiles caused by a deficiency of estradiol that plays a prominent role in lipid homeostasis, besides the continual impacts of FSH secretion on the TG increase. The present findings and thoughts are in consent with many studies. Kawamura and his colleagues 2020 showed that women aged 30 - 45 years have increased and decreased FSH and estradiol levels, respectively. Warjukar and his colleagues 2020 found that premenopausal healthy women (with regular menstrual cycles) have significant lipid parameter (TG increase) differences due to estradiol decrease. Moreover, triglyceride negatively correlates with estrogen in premenopausal women (Swarnalatha and Ebrahim, 2012).

#### *3.2.3. High-density lipoprotein (HDL)*

The rise in HDL (during the ovulatory days and beyond) is crucial for successful ovulation. HDL is necessary to both approach lipids homeostasis and correct ovulation without any defects during these days. The present findings and thoughts are in line with many studies. HDL levels increased in ovulatory days during the menstrual cycle (Mumford *et al*.,2011; Panigrahi and Panda,2018; Sharma *et al*.,2022). HDL is generated from excess cellular cholesterol exported by ATP-binding cassette A1 (ABCA1A) expressed in theca cells. Its deficiency inhibits successful ovulation through cholesterol accumulation in the ovarian follicle (Futamata *et al*.,2023). Moreover, Quiroz and his colleagues 2020 found that HDL and oocyte ABCA1 transporters regulate mouse oocyte cholesterol homeostasis and contribute to female fertility. Furthermore, Hamdi and his colleagues 2010 mentioned that HDL is the primary lipoprotein in human follicular fluid and is important in ovulation and fertilization. Moreover, Panigrahi and Panda 2018 mentioned that estradiol upregulates ABCA1 and APOA1, the essential HDL proteins that enhance HDL production. In addition, estradiol also increases VLDL synthesis, leading to a subsequent decrease in LDL and an increase in HDL.

The deficiency in HDL in the second group may be attributed to the bad behavior of lipoproteins caused by the low present levels of estradiol (which plays a prominent role in lipids homeostasis) during transitional and progressive age. Lipid pattern changed (HDL decrease) with loss of estradiol effect during the menopausal transition (Swarnalatha and Ebrahim, 2012; Inaraja *et al*., 2020).

Moreover, HDL levels decreased in aging women due to their low level of estradiol and the highest activity of hepatic lipase, which enhances the uptake and catabolism of HDL (Fatima and Sreekantha, 2017). However, HDL is not always good cholesterol, and large HDL particles were found to become dysfunctional during the menopause transition. In contrast, its ability to promote cholesterol efflux capacity (CEC) from macrophages becomes weaker (El Khoudary *et al*., 2021).

#### *3.2.4. Low-density lipoprotein (LDL)*

The behavior of lipoproteins and their relationship with the sex hormones is still unclear. Nevertheless, estradiol (perhaps FSH) plays a role in lipid metabolism physiologically due to its benefit impacts, especially during the growth and repair period (follicular phase), through its ability in lipid homeostasis and maintenance via several routes, such as a modulator of the hepatic LDL receptors (LDLR),up–regulated the LDL uptake and its ability to prevent PCSK9 mediated LDLR degradation in liver cells. Many studies mentioned that estradiol has physiologically beneficial effects on lipid metabolism during the follicular phase ( Mumford *et al*.,2010; Faulds *et al*.,2012; Ko *et al*.,2020). Also, several studies indicated that the peak levels of LDL observed during the follicular phase occurred simultaneously with increased levels of estrogen, which is associated with an improved lipid profile (Mumford *et al*.,2011; VaShiShta *et al*.,2017; Panigrahi and Panda, 2018; Sharma *et al*.,2022). Huang and his colleagues 2019 found that LDL and HDL play essential roles in ovarian cholesterol transport. In contrast, cholesterol is an important substrate for synthesizing ovarian sex hormones and follicular development in the follicular phase.

It seemed that the chronological age besides the estradiol deficiency is beyond these lipid (LDL) alterations in these premenopausal women, in addition to the continuing effects of FSH secretion on the LDL increase. Several researchers indicated that menopausal transition women have a deficiency of estradiol and increased activity of plasma LPL that causes elevation of LDL along with downregulation of LDLR (Mallick *et al*.,2015; Fatima and Sreekantha,2017; Warjukar *et al*.,2020). Moreover, Song and his colleagues 2016

mentioned that higher FSH is related to higher levels of LDL. In contrast, FSH participated in hepatic LDL metabolism via attenuated degradation of LDL and inhibited LDLR expression in liver tissue. However, Lee and his colleagues 2022 showed no correlation between FSH and lipid profile.

#### *3.2.5. Very low-density lipoprotein (VLDL)*

The increased tendency in VLDL, accompanied by the current high levels of HDL (Figure 5 ) to provide the ovulation requirements, may be attributed to the estradiol role in lipid metabolism (VLDL) directly and or indirectly, as well as the actions of other hormones (such as kisspeptin, LH and prolactin that secreted during the ovulatory days) that facilitated ovulation process and may be contributed in lipid metabolism. VLDL levels increase during the follicular to ovulatory phase, the menstrual cycle (Gupta *et al*., 2015; VaShiShta *et al*., 2017; Panigrahi and Panda, 2018). The oocyte (as a rapidly growing cell) has a considerable demand for energy and cholesterol. Therefore, it appears that ApoB-containing lipoproteins (VLDL) might have a nourishing function that the TG-poor HDL lipoproteins are not able to fulfill properly (Stouffer *et al*., 2007; Gautier *et al.*, 2010). Moreover, estradiol exerts a regulatory control for every step of the lipid metabolism chain.

In contrast, estradiol mediates the packaging of circulating fatty acid into TG-rich VLDL particles by the liver. In addition, some of estradiol's protective effects in the liver are likely indirectly due to estrogen signaling adipose tissue to limit the release of serum fatty acid made into TG, which is matched with increased VLDL-TG secretion. Moreover, estradiol also increased VLDL levels by regulated LPL, which is responsible for hydrolyzing TG to chylomicrons and VLDL (Saxena *et al*., 2012; Palmisano *et al.*, 2017; Berad, 2019).

Furthermore, kisspeptin, LH, and prolactin have many roles in lipid metabolism (VLDL). In contrast, exogenous KP 10 was associated with a significant elevation in hepatic lipids synthesis and transport in quails. In contrast, LH receptors (LHR) expression is intimately associated with cholesterol transport, synthesis, and steroidogenesis in the ovary, whereas increased prolactin receptor signaling is associated with an increase in VLDL cholesterol levels (Wang and Menon, 2005; Wu *et al*., 2013; van der Sluis *et al.*, 2014).

Despite this slight elevation in VLDL in the second group, the disruption of lipid homeostasis related to progressive age may be caused by the deficiency of estradiol ( during this transition period ), which plays an essential role in lipid homeostasis via different mechanisms. Estradiol deficiency in menopausal transition women causes a relative accumulation of small VLDL particles due to increased VLDL catabolism, resulting in more VLDL residual particles. Additionally, the converse implication of estrogen-mediated reductions in fatty acid delivery to the liver and estrogen-mediated increases in VLDL-TG export leads to fat accumulation (Liu *et al*., 2015; Fatima and Sreekantha, 2017; Palmisano *et al*., 2017; Berad, 2019; Warjukar *et al.*, 2020).

## 4. CONCLUSIONS:

Studying and evaluating the lipid profile changes according to the menstrual cycle phase represents an important issue in knowing the physiological and healthy woman state and preventing cardiovascular disease incidence. This may help manage and control cardiovascular disorders and other pathological conditions associated with alterations in lipid profile, especially in premenopausal women.

## 5. DECLARATIONS

### 5.1. Study Limitations

No limitations were known at the time of the study.


### 5.2. Acknowledgements

The authors thank Prof. Dr. Asad Yahea for his invaluable assistance in analyzing our data.

### 5.3. Funding source

The authors funded this research.


### 5.4. Competing Interests

There are no conflicts of interest.

## 6. HUMAN AND ANIMAL-RELATED STUDIES

### 6.1. Ethical Approval

Misan Health Directorate /Training and Human Development Center/Knowledge Management Division.

Number 123/Date 2023

### 6.2. Informed Consent

The consent of the participants was obtained to publish this study.

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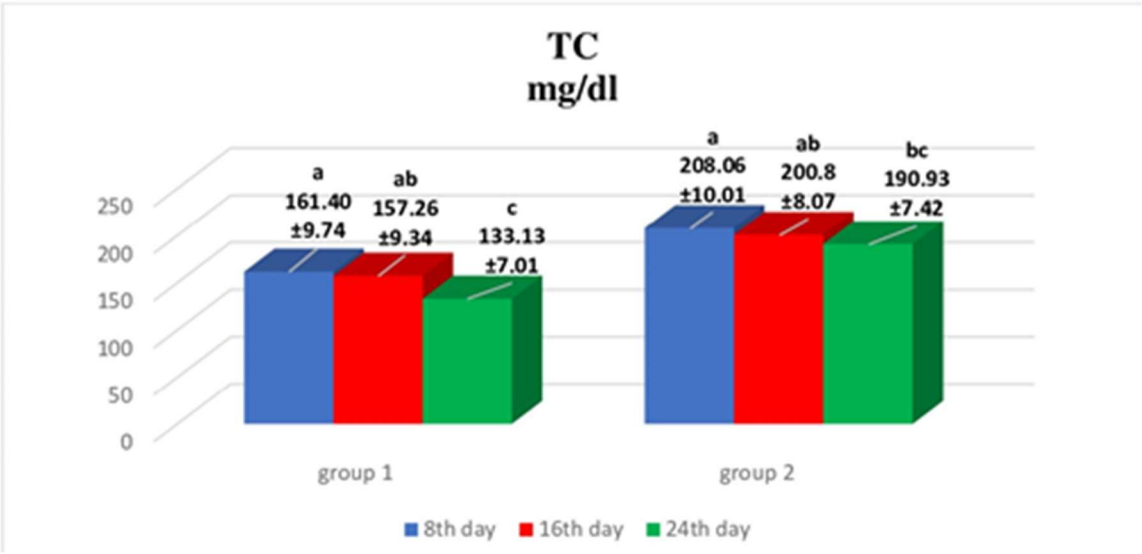


***Figure 1.*** The levels of TC changes during different phases of the menstrual cycle in both groups.

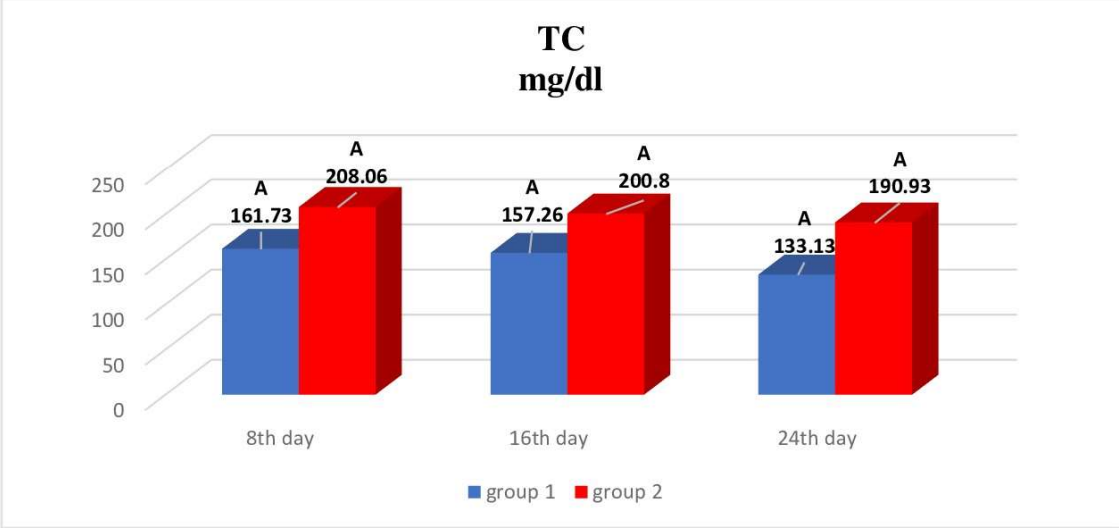


***Figure 2.*** The levels of TC for similar days in different phases between both groups.

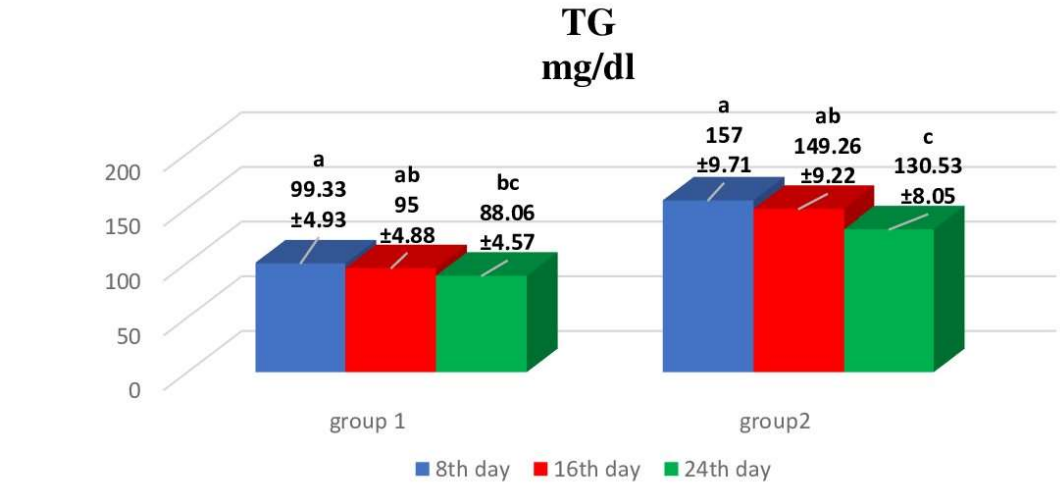


***Figure 3.*** The levels of TG during different phases of the menstrual cycle in both groups.

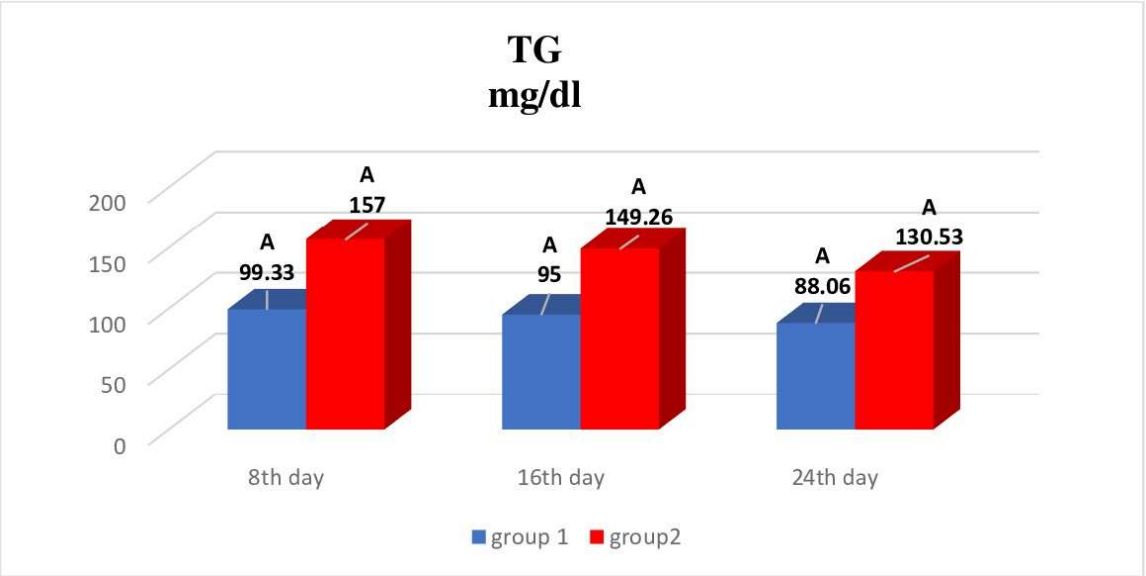


***Figure 4.*** The levels of TG for similar days in different phases between both groups.

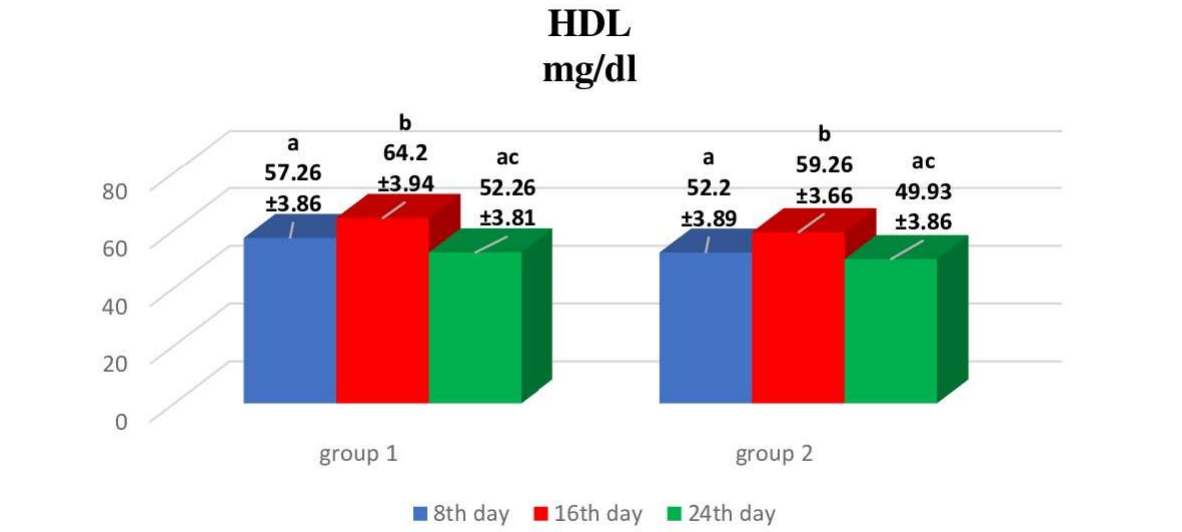


***Figure 5.*** The levels of HDL changes during different phases of menstrual cycle in both groups.

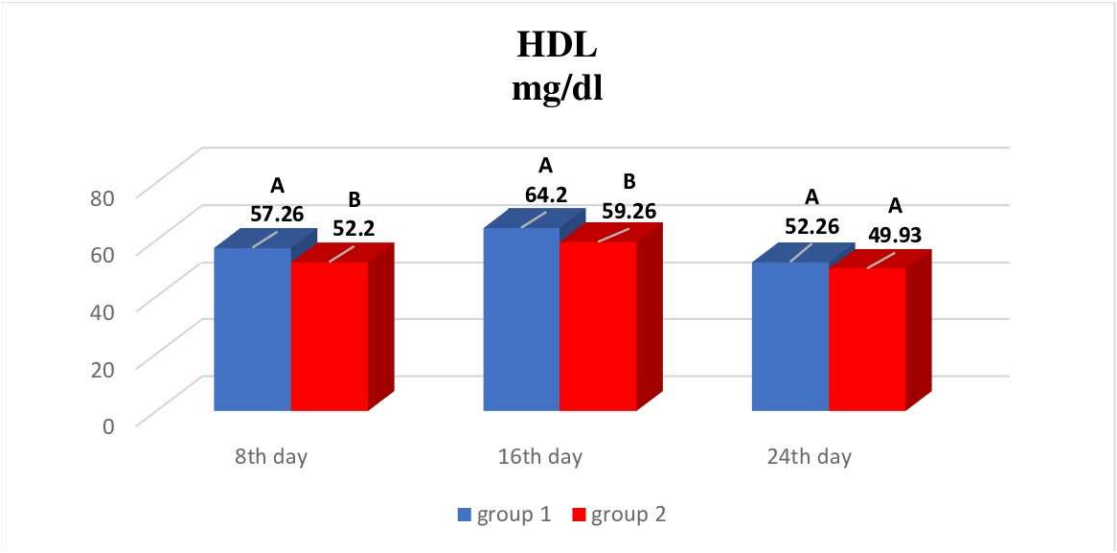


***Figure 6.*** The levels of HDL for similar days in different phases between both groups.

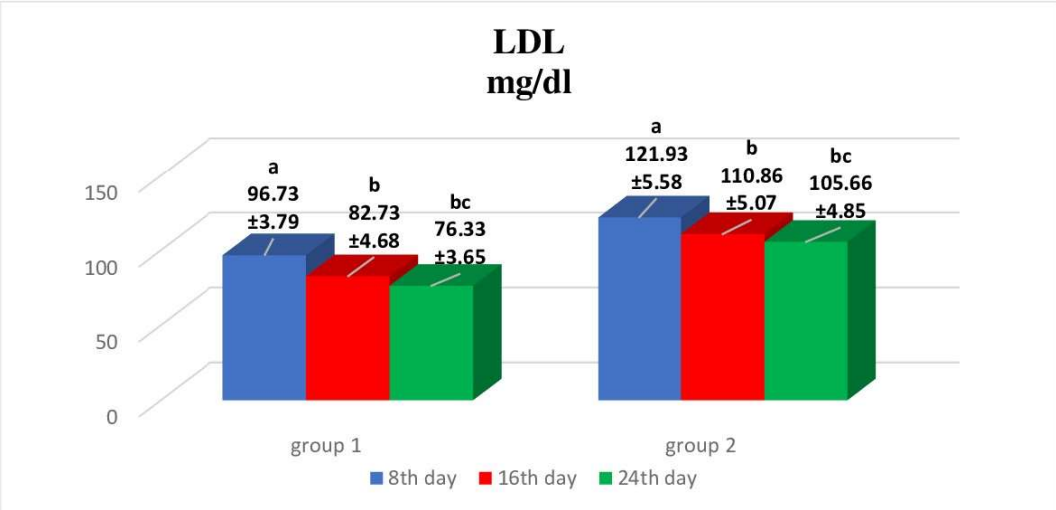


***Figure 7.*** The levels of LDL change during different phases of the menstrual cycle in both groups.

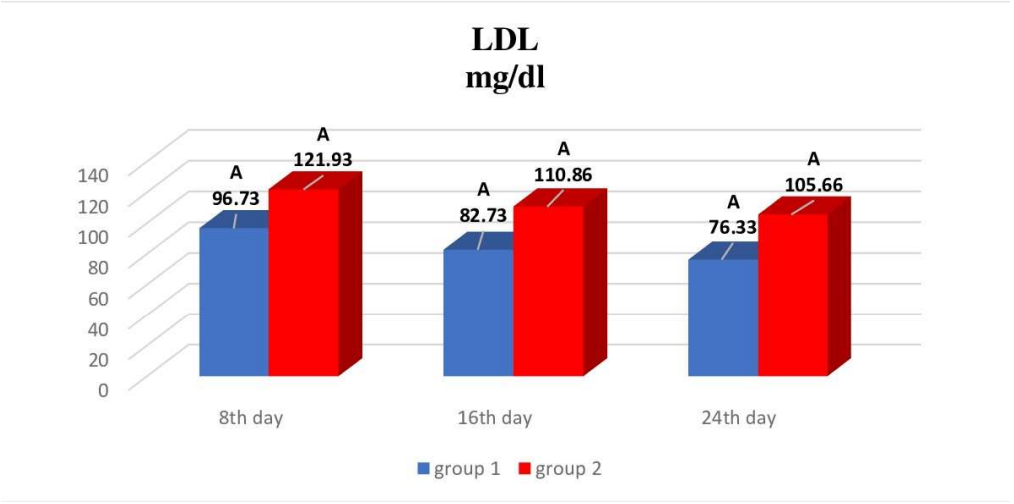


***Figure 8.*** The levels of LDL for similar days in different phases between both groups.

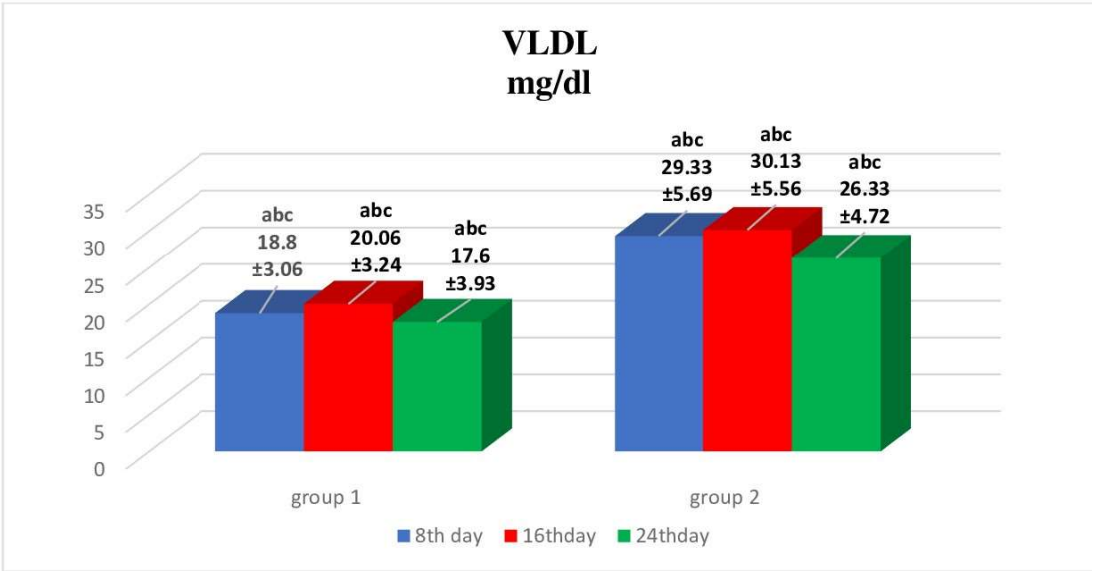


**Figure 9.** The levels of VLDL change during different phases of the menstrual cycle in both groups.

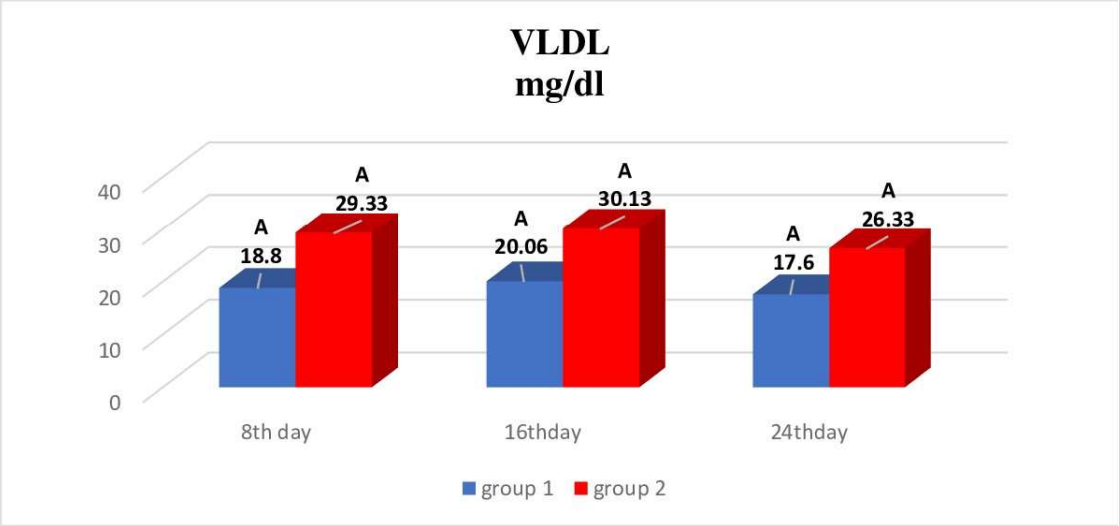


***Figure 10.*** The levels of VLDL for similar days in different phases between both groups.