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Research Article

Influence of menstrual cycle phases on serum levels of lipids and lipoprotein ratios in eumenorrheic women

Kirti Gupta[1]*, Keerti Mathur[2], Manisha Sankhla[3]
[1]Ph.D. scholar, [2]Senior Professor, [3]Senior Demonstrator, Department of Physiology, S.M.S. Medical College, Jaipur (Raj.) – 302004, India

***Corresponding author**
Mrs. Kirti Gupta,
Email: kirtigupta_in@yahoo.com

Abstract: It is believed that the cyclic variations in sex hormones across the menstrual cycle may have effects on the lipid profile and hence on cardiovascular health. Thus, the purpose of study was to find out the serum levels of lipids and lipoprotein ratios in different phases of menstrual cycle in eumenorrheic women. One hundred and twenty young healthy female subjects of reproductive age group (17-27 years), having regular menstrual cycle, were examined to find out the serum levels of total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), very low-density lipoprotein cholesterol (VLDL-C), TC/HDL-C ratio, LDL-C/HDL-C ratio and TG/HDL-C ratio in follicular phase (on 7th day) and in luteal phase (on 21st day). Significant higher ($p>0.0001$) levels of HDL-C and significant lower ($p>0.0001$) levels of TC, TG, LDL-C, VLDL-C, ratios of TC/HDL-C, LDL-C/HDL-C and TG/HDL-C were observed in luteal phase as compared to follicular phase. These changes may be associated with high levels of sex hormones in the luteal phase. So, these cyclic variations in lipid levels may need to be considered in the design and interpretation of studies in reproductive age women and in the clinical management of their cholesterol.
Keywords: Follicular phase, lipoprotein ratios, luteal phase, menstrual cycle, serum lipids, sex hormones

INTRODUCTION

The relationship between the menstrual cycle and blood lipid status is of considerable interest since due to the cyclic nature of circulating levels of sex hormones in menstruating women and their possible impact on the levels of lipids and lipoproteins, and hence coronary heart disease (CHD) risk, it is important to determine how these levels vary between the follicular and luteal phases of the menstrual cycle.

Measurement of Low-density lipoprotein cholesterol (LDL-C) concentration has been the prime index of cardiovascular disease. However, several lipoprotein ratios or "atherogenic indices" such as TC/HDL-C and LDL-C/HDL-C ratios are considered risk indicators with greater predictive value than isolated parameters used independently, particularly LDL-C [1]. TG/HDL-C ratio also has been reported as a significant predictor of extensive coronary heart disease [2]. The levels of above ratios may also vary across the normal menstrual cycle.

Menstrual cycle is the result of complex interacting processes involving interaction of the hypothalamus, pituitary, ovaries, uterus, prostaglandins and neuroendocrine factors [3].

The normal menstrual cycle is a twenty eight days period characterised by three phase's namely follicular, ovulatory and luteal phases. The follicular phase is characterised by a low level of estrogen, while during the ovulatory phase, there is rise in estradiol, lutenizing hormone (LH) and follicle stimulating hormone (FSH). The luteal phase is characterised by increased levels of progesterone and estrogen [4].

Female sex hormones not only play an important role in the reproduction but also influence other systems in the body. Estrogen is the primary sex hormone amongst the female species and is cardinal towards the normal functioning of the female reproductive system. Apart from being cardinal to the reproductive system, estrogen is also believed to aid in enhancing the levels of HDL-C (good cholesterol) and reducing the levels of LDL-C (bad cholesterol), thereby maintaining the healthy functioning of the heart [5]. It also has been shown that the cessation of estrogen production after menopause can increase a woman's risk for heart disease [6].

On the other hand, variations in the serum lipid levels (cholesterol) in relation to changes in the sex

hormones also have been reported throughout the normal menstrual cycle in the women of reproductive age group [7].

Although changes in levels of TC/HDL-C and LDL-C/HDL-C ratios have been evaluated throughout the normal menstrual cycle but studies regarding TG/HDL-C ratio have not been reported in relation to normal menstrual cycle, to the best of our knowledge.

Thus, the present study was aimed to find out the serum levels of lipids and lipoprotein ratios in different phases of normal menstrual cycle in the eumenorrheic women.

MATERIAL AND METHODS

The present study was carried out on 120 normal healthy and regularly menstruating female subjects (age 17-27 years) selected from the S.M.S. Medical College & attached Hospitals, Jaipur. Study was carried out in the Upgraded Department of Physiology, S.M.S. Medical College, Jaipur. Permission from the institutional ethical committee and an informed written consent from all the subjects were obtained. After recording the detailed menstrual history (i.e. age at menarche, date of last menstruation, cycle length and days of bleeding), the subjects were then subjected to sample collection.

Five ml of fasting blood samples were drawn from antecubital vein from each subject during the follicular phase (on 7^{th} day of the cycle) and luteal phase (on 21^{st} day of the cycle) after taking full antiseptic precautions.

Serum levels of Total Cholesterol (TC), Triglyceride (TG) and High Density Lipoprotein Cholesterol (HDL-C) were measured spectrophotometrically by CHOD-PAP method [8], GPO method [9] and Precipitation method [10], respectively using enzymatic kits. While, serum levels of Low Density Lipoprotein Cholesterol (LDL-C) and Very Low Density Lipoprotein Cholesterol (VLDL-C) were measured by Friedewald's Formula [11]. Serum levels of TC/HDL-C, LDL-C/HDL-C and TG/HDL-C ratios were also calculated.

The data thus obtained was subjected to statistical analysis using the Student paired 't' test. The significance level was considered at $p<0.05$.

RESULTS

The mean serum levels of TC, TG, HDL-C, LDL-C, VLDL-C, and ratios of TC/HDL-C, LDL-C/HDL-C and TG/HDL-C during the follicular and luteal phases of menstrual cycle are presented in Table 1. In the present study, the mean serum levels of all the lipids except HDL-C were found to be decreased significantly ($p<0.0001$), whereas HDL-C levels were found to be significantly increased ($p<0.0001$) in the luteal phase as compared to the follicular phase.

Mean serum values of TC/HDL-C, LDL-C/HDL-C and TG/HDL-C ratios were 3.161 ± 0.4703, 1.92 ± 0.4395 and 1.20 ± 0.2961 in the follicular phase and these were significantly ($p<0.0001$) lower in the luteal phase i.e. 2.888 ± 0.4539, 1.676 ± 0.4305 and 1.05 ± 0.2638, respectively.

Table-1: Mean±SD levels of serum lipids and lipoprotein ratios during follicular and luteal phases of menstrual cycle.

Parameters	Follicular phase (Mean ± SD)	Luteal phase (Mean ± SD)	p value
Total Cholesterol (mg / dl)	161.9 ± 9.789	155.9 ± 11.73	<0.0001*
Triglycerides (mg / dl)	61.53 ± 11.87	56.52 ± 11.76	<0.0001*
HDL-Cholesterol (mg / dl)	52.2 ± 7.42	55.07 ± 7.717	<0.0001*
LDL-Cholesterol (mg / dl)	97.43 ± 11.5	89.56 ± 13.88	<0.0001*
VLDL-Cholesterol (mg / dl)	12.31 ± 2.375	11.31 ± 2.352	<0.0001*
TC / HDL-C Ratio	3.161 ± 0.4703	2.888 ± 0.4539	<0.0001*
LDL-C / HDL-C Ratio	1.92 ± 0.4395	1.676 ± 0.4305	<0.0001*
TG / HDL-C Ratio	1.20 ± 0.2961	1.05 ± 0.2638	<0.0001*

Data expressed as mean ± SD, * Highly significant.

DISCUSSION

Present study has revealed the relationship between the different phases of menstrual cycle and blood lipids status in the eumenorrheic women. A significant ($p< 0.0001$) higher levels of HDL-C have been observed in the luteal phase as compared to the follicular phase of the menstrual cycle. Nduka EU *et al.* [12] also reported the significant increase in the levels of HDL-C during the luteal phase as compared to the follicular phase which supports our study results.

The levels of TC, TG, LDL-C and VLDL-C were found to be significantly lower ($p< 0.0001$) during the luteal phase as compared to follicular phase in the present study. Consistent with present study, Mumford SL *et al.* [13] and Barnett JB *et al.* [7] also observed a significant decrease in the serum levels of TC, TG and LDL-C during the luteal phase compared with the follicular phase of normal menstrual cycle.

The significant ($p< 0.0001$) lower ratios of TC/HDL-C, LDL-C/HDL-C and TG/HDL-C in the luteal phase compared with the follicular phase were observed in present study tend to indicate the sum of the effects of increased HDL-C as well as decreased levels of TC, LDL-C and TG in these two menstrual cycle phases. These findings were supported by Devi K *et al.* [14].

Above results may coincide with the increased level of estrogen and progesterone, which is characteristic of luteal phase [15]. Mumford SL *et al.* [13] also reported that the lower levels of TC and LDL-C were associated with increased levels of estrogen in the luteal phase.

Estrogen exerts a favorable effect on lipoprotein metabolism by increasing VLDL-C synthesis leading to subsequent decrease in LDL-C and increase in HDL-C [16]. Estrogens appear to (i) upregulate the LDL receptors [17]; (ii) upregulate ATP-binding cassette transporter-A1 (ABCA1) and apolipoprotein-A1 (APOA1, a major HDL protein, which increases HDL synthesis) [18]; and (iii) suppress hepatic scavenger receptor class B type 1 (SR-BI) expression leading to decreased hepatic cholesterol uptake from HDL-C [19]. Although these changes would also tend to increase triglyceride levels, estrogen appears to primarily increase the light subtype of VLDL-C that lacks atherogenicity, thus leading to overall beneficial effects [20].

Thus, the cyclic fluctuations in the serum lipid levels during different phases of normal menstrual cycle need to be considered in the screening and medical monitoring of reproductive aged women.

Therefore, based on present findings, different phases of the normal menstrual cycle should be taken into account when evaluating lipoprotein cholesterol levels among reproductive-aged women.

CONCLUSION

In conclusion, present results suggest that understanding variations in lipoprotein cholesterol levels throughout the menstrual cycle is very important because these may be useful in clinical implications regarding the appropriate timing of measurement and implications on the design and interpretation of studies in women of reproductive age. Such fluctuations may prove to be clinically significant in the long run.

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