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EFFECT OF MENSTRUAL CYCLE LENGTH ON LIPID PROFILE AND INFLAMMATION IN HEALTHY INDIAN WOMEN

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Abstract

Introduction - Several studies show that variations in the length of the menstrual cycle significantly affect lipid and CRP parameters. There is acute paucity of literature comparing lipid profiles and CRP in women with short and prolonged menstrual cycle length in absence of PCOD and other gynecological conditions. The aim of this study was to establish menstrual cycle length as the simplest tool to predict cardiovascular risk. **Objective-** To determine menstrual cycle length and its relationship with lipid profile and CRP. **Method -**The association of lipid and CRP parameters with menstrual cycle length was evaluated in 337 women aged 15-45 years. Based on a questionnaire about menstrual bleeding, participants were divided into three groups: women with short, normal and long menstrual cycles. A menstrual cycle length of 24-38 days was considered normal. Lipid profile and CRP were analyzed during the menstrual cycle in women with short normal and prolonged cycles, and the results were statistically analyzed. **Results** – Mean levels of cholesterol, triglycerides, LDL, VLDL, lipid ratio and CRP were increased in women with short and long menstrual cycles compared to women with normal menstrual cycles, and this increase was significant for TC, TG, VLDL and TC/HDL and TG/HDL ratios, while HDL was significantly lower ($P<0.05$). **Conclusion** - Women with short and long menstrual cycles have a higher risk of developing cardiovascular disease in the coming years compared to women with normal menstrual cycle length.

Keywords: Lipid; Cardiovascular Disease; Predictor; Regularly Menstrual Cycle Length, Short Menstrual Cycle Length, Prolonged Menstrual Cycle Length; C-Reactive Proteins

INTRODUCTION

Menstrual cycle length has been correlated with infertility, ovarian and breast malignancies, type 2 diabetes mellitus, and cardiovascular disease. [1]

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Fluctuations in sex hormone levels are thought to be related to the length of the menstrual cycle because hormones present during the menstrual cycle affect the proliferation and shedding of the endometrium. [2,3,4]

The prevalence of cardiovascular disease (CVD) in women aged 20–39 is half that of men in the same age group [5] The difference in cardiovascular risk between men and pre- and postmenopausal women is due to the cardio protective effect of estrogen role in younger, menstruating women.

However premenopausal and postmenopausal females have notably dissimilar hormonal profiles of which estrogen is the only factor. Various markers of CVD risk determinants including lipid and CRP levels are considered to be related with female ovarian hormones [6]. Overall, short menstrual cycles are associated with reduced per cycle exposure to estradiol whereas long cycle have decreased mean concentrations of progesterone and marginally decreased mean estradiol concentrations as compared with normal-length cycles [4]

Various studies in polycystic ovary syndrome (PCOD) women with irregular menstrual cycles show that lipid and CRP parameters are significantly affected by variations in menstrual cycle length. [7, 8, 9, 10, 11, 12] However, to our knowledge, there is little in the literature regarding the relationship between lipid profiles, CRP and menstrual cycle length in the absence of PCOS and other gynecological diseases. This article aims to provide information to fill this gap and investigate whether menstrual cycle length could be a simpler vital sign, like blood pressure and heart rate, to better predict cardiovascular status in resource-poor locations.

Aims and objectives of the study:

- To define menstrual cycle length
- To find out association between menstrual cycle length, lipid profile and CRP.

SUBJECTS AND METHODS

The study was conducted in the Department of Physiology in close collaboration with the Department of Gynecology and Biochemistry of a leading institute in North India over a period of three years. The research plan was in accordance with the guidelines of the Declaration of Helsinki and was duly approved by the ethical committee of the institute.

Study participants

Participants were selected from among the family members (relatives) accompanying patient attending gynecology OPD of the institute. Out of 710 females of reproductive aged 15-45 years selected for study, only 350 fulfilled the inclusion criteria. 330 females gave consent for the study and 226 completed the study

A simple random sampling technique was used and the sample size was calculated using Cochran's formula. [13] Before starting the study, written consent was obtained from all participants after a detailed explanation of the study in the vernacular language.

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Inclusion Criteria

Females in reproductive age (15-45 years) with no history of PCOD or any other gynacelogical issues were included. The length of the menstrual cycle was considered as the time interval between first days of one bleeding period to first day of next bleeding period. These women were divided in 3 Groups on the basis of average menstrual cycle length from past 6 month [14]:

Group 1 Women with a short length of menstrual cycle of less than 24 days.

Group 2 Women with a normal menstrual cycle length of 24-38 days.

Group 3 Women with prolonged menstrual cycle length of more than 38 days.

Exclusion criteria

We excluded women who had used contraceptives in the past 3 months, were currently using nutritional supplements or prescription medications, pregnant or lactating in the past 6 months, diagnosed with polycystic ovarian disease, recently infected or diagnosed with a chronic disease, with a body mass index of <18 or >35 kg /m2 or autoimmune disease or thyroid disease or coronary artery disease diagnosed by a doctor before the study. Study participants who refused to give consent and decided to withdraw in the interim were also excluded from the study.

Medical examination and Biochemical analysis

Before performing the study, all participants were asked to complete self-administered questionnaires to obtain information about menstrual/medical/family/medical history and lifestyle. Each subject underwent clinical, biochemical, and ultrasound examinations, and trained personnel performed anthropometric measurements on all participants. 5-6 mL of fasting (at least 9-12 h) venous blood samples were collected between 8-10 AM after an overnight fast in a standard vial during the menstrual phase (1-4 days) of the menstrual cycle.

Serum total cholesterol (CHOL) and Troglycerides (TG) concentrations were measured by cholesterol-oxidase-peroxidase (CHOD-POD) method and glycerokinase peroxidase method, respectively. LDL and VLDL were calculated according to the Friedewald formula. Biochemical analysis of lipid profile and CRP was performed using a fully automated Mindray calibrated device. Data related to biochemical parameters and average menstrual cycle length were analyzed using Microsoft Excel data analyzer by one-way ANOVA.

Mean standard deviation was used to describe the main variables. The statistical difference between mean lipids and CRP levels during menstruation among women with normal, short, and long menstrual cycles was evaluated using ANOVA.

RESULTS

Table 1 Compare the demographics and average menstrual length of women with short, normal, and long menstrual cycles. There were no significant differences in age (*P* 0.09), while BMI and waist-to-hip ratio were not significantly higher in women with short or long menstrual cycles (*P* 0.003 and *P* 0.007, respectively) compared to women with normal menstrual cycle

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length. Mean menstrual cycle length was significantly different (*P* 0.00001) between women with short, normal and long menstrual cycle length.

Table 1: Characteristics of study participants

Variable	Females with Short menstrual cycle length (n=38)	Females with normal menstrual cycle length (n=111)	Females with prolonged menstrual cycle length (n=77)	F - value	p-value
Mean Age(years)	27.42±7.35	26.29±7.97	24.63±4.71	2.38	0.09
BMI(kg/m^2)	25.17±3.35	23.07±3.80	24.66± 4.41	5.81	0.003*
Waist/Hip(W/H) ratio	0.89 ± 0.05	0.86 ± 0.06	0.88 ± 0.05	4.99	00.007*
Average length of cycle(in days)	20.89±0.95	29.55±2.7	56.78±17.95	203	0.00001*

Table 2 In women with short, normal, and long menstrual cycle length, the mean lipid profile and CRP levels were compared during the menstrual phase. In comparison to women with normal menstrual cycle length, it was found that women with short and prolonged menstrual cycles had higher mean levels of cholesterol, triglycerides, LDL, VLDL, and CRP. This rise in levels was significant for TC, TG, and VLDL (*P* 0.04, *P* 0.00001, and *P* 0.000001, respectively), while HDL levels were significantly lower (*P* 0.005).

Table 2: Comparison of mean lipid profile and CRP levels during menstrual phase in women with short, normal and prolonged menstrual cycle length

Variable	Females with Short menstrual cycle length (38)	Females with average menstrual cycle length (111)	Females with prolonged menstrual cycle length (77)	F-value	p-value
TOTAL CHOLESTEROL (TC) (mg/dl)	170.94±31.02	164.34 ±29.38	176.14.80±34.94	3.20	0.04*
TRIGLYCERIDES (TG) (mg/dl)	151.81±38.33	89.10 ±14.36	159.11±32.35	197.59	0.00001*
HDL (mg/dl)	46.32±9.45	50.59 ± 10.71	46.16±9.19	5.40	0.005*
LDL (mg/dl)	93.74±34.37	95.91±29.22	98.15 ±36.93	0.24	0.78
VLDL (mg/dl)	30.89± 7.14	17.84±2.87	31.82 ±6.47	197.59	0.000001*
CRP (mg/l)	1.91±0.32	1.71±1.15	1.83±1.35	0.50	0.60

Table 3 Comparison of mean lipid ratios during menstrual phase in women with short, normal and prolonged menstrual cycle length. It was observed that women with short or prolonged menstrual cycle length have significantly raised mean levels of TC/HDL and TG/HDL ratios *(P 0*.0006 & *P0*.000001 respectively) compared to women with normal menstrual cycle length.

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Table 3: Comparison of mean lipid ratio during menstrual phase in women with short, normal and prolonged menstrual cycle length

Variable	Females with Short menstrual cycle length (38)	Females with average menstrual cycle length (111)	Females with prolonged menstrual cycle length (77)	F-value	p-value
TC/HDL	3.86±1.18	3.39±0.91	3.97 ± 1.19	7.58	0.0006*
TG/HDL	3.47 ±1.04	1.86±0.57	3.59±1.07	110.17	0.000001*
LDL/HDL	2.16 ±1.09	2.02±0.83	2.25 ±1.11	1.35	0.25

DISCUSSION

In the current study the lipid profile and CRP values are compared in females with short, normal, and prolonged menstrual cycle lengths.

The fact that the study was conducted on females with irregular menstrual cycle duration for the previous six months, without PCOS or other gynecological problems, gives the study's findings clinical value.

The study's key results were that women with irregular menstrual cycle duration had higher levels of biochemical variables including lipid profile and CRP that are known to contribute to CVD. Lipid profile and CRP are recognized as biochemical indicators of potential CVD in the future.

The majority of earlier research discovered that lipid levels were greater in women with irregular menstrual cycle duration compared to controls. The study also showed that women with short or prolonged menstrual cycle length had greater levels of lipids than did women with normal menstrual cycle length, albeit some lipid indicators did not show a statistically significant difference between the groups. Similar to this, while the difference did not achieve statistical significance, CRP levels were greater in women with short and long menstrual cycles compared to those with normal cycle length.

It is possible that lipid parameters may be elevated much earlier, even before inflammation begins, in women with irregular menstrual cycle length compared to women with normal length of menstrual cycle, as indicated by the significant increase in lipid parameters and the insignificant difference in CRP in these subjects when compared to normal subjects.

The results of our investigation are entirely consistent with a few globally conducted studies of a comparable nature. [8,9,10,12, 15, 16,17] In these earlier research, women whose cycles lengthen during their lifetimes had the highest TG readings. The lowest TG concentrations are found in women whose cycle patterns have moved toward shorter cycles. Even while greater total and LDL cholesterol levels and lower HDL cholesterol levels have been detected in women with extended cycle length, the other blood lipids HDL, LDL, and TC did not demonstrate a meaningful relationship. [15] Another research, however, discovered that despite a slight correlation with TG concentration, indicators of cardiovascular risk, including HDL and TG, did not substantially correlate with the menstrual cycle pattern. [16]

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According to our findings, women with short or lengthy menstrual cycles may have elevated lipid and CRP levels as a result of reduced estradiol levels. Estrogen has a positive impact on lipoprotein metabolism by upregulating the LDL receptors, upregulating ATP-binding cassette transporter-A1 (ABCA1) and apolipoprotein-A1 (APOA1), a key HDL protein, which increase HDL production, and suppressing the activity of the hepatic scavenger receptor class B type 1 (SR-BI), which results in less hepatic cholesterol uptake from HDL. [19]

Progesterone, on the other hand, is hypothesized to counteract the stimulatory effects of estrogen or have no effect on lipoprotein metabolism. [20]

Estrogen appears to largely enhance the light subtype of VLDL, which is weak in atherogenicity, resulting in overall positive benefits [21] and protecting against atherosclerosis, even though these alterations would also tend to raise TG levels. In addition to down-regulating adhesion molecules such intracellular adhesion molecule 1 and E-selectin, estrogen lowers levels of tumor necrosis factor-alpha [22], interleukin-8, and platelet activating factor. This results in a reduction in the recruitment of leukocytes [23]. By preventing the release of cytochrome c from the mitochondria, estrogen can block the apoptotic process in endothelial cells, reducing the subsequent vascular inflammation [24]. By reducing the activity of natural killer cells, macrophage TNF, and inhibiting T-cell growth and activity, progesterone has anti-inflammatory effects[25].

Therefore, estrogen is often responsible for the antiatherogenic action of reproductive hormones on lipid and CRP levels.

Therefore, we may infer that elevated blood lipid levels found in women with short and long menstrual cycles may be caused by an estrogen-related decline in lipoprotein lipase (LPL) function. Lower HDL levels in women with irregular menstrual cycle length are likely caused by a decrease in estrogen output.

It's interesting to see that higher BMI was linked to longer menstrual periods. According to the findings of our study, obesity may cause prolonged cycles and a suppression of reproductive hormones.

Limitations of study:

This study was subjected to bias since it was based on a questionnaire on menstrual bleeding patterns. Another drawback is that we have connected questionnaire data with biochemical data without obtaining estimations of oestrogen and progesterone hormone levels due to funding limitations.

CONCLUSION

Finally, we may draw the conclusion that abnormalities in length of menstrual cycle may show to be the straightforward critical indication for forecasting women's risk of CVD. This is especially useful in our resource-poor countries, where women's health is often put on the back burner.

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These results highlight the potential negative health effects of menstrual cycle length disorder in women and emphasize the significance of monitoring menstrual cycle features throughout a woman's reproductive life in order to avoid CVD and atrial fibrillation in females.

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Nil.

Conflicts of interest

No conflicts of interest.

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