A Comparative Study of Serum Lipid Profile and Premenopausal, Perimenopausal and Post-Menopausal Healthy Women: Hospital Based Study in Jharkhand, India

Poonam Kumari[1], Govind Jee Sahay[2], Mehar Bano[3], Richa Niranjan[4]

ABSTRACT

Introduction: The Lipid profile is found to be abnormal in postmenopausal women as compared to their premenopausal counterparts. Study objectives were to know about the relationship of lipid profile and menstrual cycle different phases.

Material and methods: The hospital based cross-sectional study was carried out on total (n=161) healthy women in different phases of menstrual cycle.

Results: The changes in the lipid parameters like total cholesterol, Triglyceride, VLDL, LDL, HDL and AI is found to be highly significant among the various age groups of women.

Conclusion: The lipid profile becomes abnormal as the women approaches perimenopause, postmenopause as compared to their normal menstrual cycle pattern.

Keywords: Serum Lipid Profile, Premenopausal, Perimenopausal, Post-Menopausal Healthy Women

INTRODUCTION

Menopause is a normal life transition in a woman's life when reproductive capacity is lost due to loss of ovarian function resulting in a decrease in circulating oestrogen levels Menopause is an oestrogen deficient state characterised by permanent amenorrhoea lasting for a period of 1 year due to the cessation of ovarian functions.[1] There is considerable variation in the level of estrogen in postmenopausal women occurs during the early postmenopausal years because of continued secretion of estradiol from the ovary and conversion of androstenedione to estrone in fat tissue.[2] In young women, where oestrogen production is high, serum lipids are normal but after menopause, lipid levels are increased resulting in increased incidence of coronary heart diseases. This shows the possible relationship among oestrogen, normal lipid profile and atherosclerosis and the relative immunity to coronary artery diseases (CAD).[3] Natural menopause confers a 3 fold increase in CAD risk and postmenopausal women account for > 30% of the female population at risk for CAD in India.[4,5]

The alterations of serum lipids and lipoproteins in menopause have been shown in previous studies. The hormonal changes associated with menopause e.g. Low plasma levels of oestrogen and marked increase in LH and FSH levels exerts a significant effect on the metabolism of plasma lipids and lipoproteins and the consequent atherosclerosis cardiac related disorders associated with menopause.[1,3] Also, the incidence of CAD has been observed to be increased in postmenopausal women until they become similar to the corresponding rates in men of similar age.[6]

The present study was conducted to assess the relationship of different phases of menstrual cycle and the serum lipid profile in the women of Jharkhand. The estimation of lipo-proteins like HDL and LDL serves as a more reliable tool in predicting the risk of coronary heart disease in perimenopausal and postmenopausal women.

Objective were to assess the changes in serum lipid levels in premenopausal, perimenopausal and postmenopausal women with comparisons being made and to determine the relationship of age and body mass index (BMI) with that of atherogenic index in amongst postmenopausal women.

MATERIAL AND METHODS

Hospital based Cross-sectional study was done for 2 years on healthy female attendants in indoor and outdoor OPD of Medicine and Gynaenaecology Department of Rajendra Institute of Medical Sciences (RIMS), Jharkhand,India. Every Consecutive patient was taken in the study.

Healthy female attendants in different age groups accompanying with the patients attending indoor and outdoor OPD of medicine and gynaecology department of RIMS were included in the study so as to have 4 groups of women like young females with normal menstrual cycle, premenopausal with regular cycle, premenopausal women with irregular cycle and postmenopausal women.

Study subjects: 161 healthy women attending OPD comprises of 4 groups like.

a) 49 young females of age 19-35 years

[1]Assistant Professor, Department of Physiology, GMC Haldwani, Uttarakhand, [2]Professor, Department of Physiology, RIMS Ranchi, Jharkhand, [3]Assistant Professor, Department of Community Medicine, MLB Medical College, Jhansi (UP), [4]Associate Professor, Department of Anatomy, GMC Haldwani, Uttarakhand, India

Corresponding author: Dr Mehar Bano, Assistant Professor, Department of Community Medicine, MLB Medical College, Jhansi (UP)

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b) 49 perimenopausal women of age 40-50 years having regular menstrual cycle
c) 16 perimenopausal women of age 40-50 years having irregular menstrual cycle
d) 47 postmenopausal women of age 40-50 years

Study tools: Lipid profile determination was done using enzymatic methods in the department of Physiology of the same institute.

Methodology: After taking informed consent from the healthy women, blood samples were collected after an overnight fast of 10-12 hours. About 5 ml of blood was withdrawn in a dry autoclaved syringe or disposable syringe and poured after removing the needle in plain sterilised vial. After an hour or so when the serum had separated it was drained, centrifuged and stored at 2-6 degree centigrade for a period of 2-3 days in refrigerator until they were analysed. Analysis was done for total cholesterol, triglyceride and HDL cholesterol. VLDL cholesterol and LDL cholesterol were estimated using Friedewald's equation.

Estimation of HDL Cholesterol and Total cholesterol by Precipitation and enzymatic methods (Allain et al):

Total Cholesterol

Principle: Serum low density and very low density lipoproteins are selectively precipitated by Mg++ phosphotungustate and removed by centrifugation, cholesterol associated with soluble HDL fraction is measured using enzymatic procedure.

$$\text{Serum} \xrightarrow{\text{Precipitating reagent}} \underset{\text{(Supernatant)}}{\text{HDL Cholesterol}} + \underset{\text{(Precipitate)}}{\text{LDL and VLDL Cholesterol}}$$

$$\text{Cholesterol ester} + H20 \xrightarrow{\text{Cholesterol esterase}} \text{Cholesterol} + \text{Fatty acids}$$

$$\text{Cholesterol} + 02 \xrightarrow{\text{Cholesterol oxidase}} \text{Cholestenone} + H202$$

$$2H202 + \text{Phenol} + \text{4-aminoantipyrine} \xrightarrow{\text{Peroxidase}} \text{Red quinine} + 4H20$$

Note: The concentration of cholesterol in the sample is directly proportional to the intensity of the red complex (red quinone) which is measured at 500nm.

HDL Cholesterol: The samples, precipitating reagents and the reconstituted reagents which were used for the estimation of total cholesterol were brought to room temp. Prior to use and were mixed well and centrifuged at 3500-4000 rpm for 10min. Then separated the clear supernatant immediately and determine the HDL cholesterol content. Then incubated for 5 min at 37^0C and mixed well and finally read in the photoelectric colorimeter.

Estimation of Triglyceride: Serum triglyceride was estimated by enzymatic method.

Principle: Triglyceride is measured by determining the amount of glycerol liberated after hydrolysis of triglycerides by saponification with alcoholic potassium hydroxide. The liberated glycerol is oxidised by potassium metaperoxidate to formaldehyde and the excess oxidant is destroyed by reduction with sodium arsenite. The formaldehyde thus produced is determined photometrically by the chromotropic acid colour reaction. The lipid extract of serum must therefore be freed from other sources of glycerol, in particular phospholipids and from glucose which on oxidation can also yield formaldehyde. Silicic acid is used to absorb these interfering substances from the isopropyl ether solution.

$$\text{Triglyceride} + H_20 \xrightarrow{\text{lipoprotein lipase}} \text{Glycerol} + \text{Fatty acids}$$

$$\text{Glycerol} + \text{ATP} \xrightarrow{\text{Glycerol kinase}} \text{Glycerol-3-phosphate} + \text{ADP}$$

$$\text{Glycerol-3-P04} \xrightarrow{\text{Glycerol-3-P04 oxidase}} \text{DehydroxyacetoneP04} + H_20$$

$$2H_20_2 + \text{4-aminoantipyrine} + \text{ADPS (N-ethyl-N-Sulfopropyl-n-anisidine)} \xrightarrow{\text{Peroxidase}}$$

Red quinone+H20

The intensity of the purple coloured complex formed during the reaction is directly proportional to the triglycerides concentration in the sample and is measured at 546nm.

Estimation of VLDL Cholesterol and LDL Cholesterol: Formulae have been described for the determination of serum VLDL Cholesterol and serum LDL Cholesterol concentration from serum total cholesterol, HDL Cholesterol and serum triglycerides values. According to the Friedewald's equation:
1. LDL CHOL (mg/dl) = Total CHOL- Triglycerides/5 – HDL CHOL
2. VLDL CHOL (mg/dl) = Triglycerides/5

STATISTICAL ANALYSIS

The data was collected, tabulated and analysed using percentages, one way anova and Post Hoc test for pair wise comparison among the 4 groups of women. The analysis was done using SPSS-18. Pearson correlation was used for the relationship of age and body mass index (BMI) with that of atherogenic index in postmenopausal women in the study.

RESULTS

There were similar proportions of 30.43% of normal young healthy females aged 19-35 years and normal healthy females aged 40-50 years with regular menstrual cycle. The postmenopausal females were only 29.2% (table-1).
Group 1: Premenopausal
Group 2: Perimenopausal (regular menstrual cycle)
Group 3: Perimenopausal(irregular menstrual cycle)
Group 4: Postmenopausal
The changes in the lipid parameters like total cholesterol, Triglyceride, VLDL, LDL, HDL and AI is found to be highly significant among the various age groups of women i.e young healthy women in age group 19-35 years (Group 1), women with regular menstrual cycle in age group 40-50 years (Group 2), women with irregular menstrual cycle in the age group 40-50 years (Group 3) and postmenopausal women in the age group 40-50 years (Group 4). The test of significance used is one way anova ($p < 0.05$) (table-2).
With the increase in age, among the 2 groups of women i.e in women 19-35 years of age and other group of women 40-50 years with regular menstrual cycle, there is increase in

Groups	Type of group	Number	%
Healthy young females of age 19-35 years with regular menstrual cycle	Group 1 (Premenopausal)	49	30.43%
Healthy females of age 40-50 years with regular menstrual cycle	Group 2 (Perimenopausal with regular menstrual cycle)	49	30.43%
Healthy females of age 40-50 years with irregular menstrual cycle	Group 3 (Perimenopausal irregular menstrual cycle)	16	9.94%
Postmenopausal women of age 40-50 years	Group 4 (Postmenopausal)	47	29.2%
Total		161	100.00%

Table-1: Distribution of studied women according to different stages of menstrual cycle

Serum Lipid	Age (in years)	Type of group	No. of cases	Mean±SD	'F' value	P value	Significance
Cholesterol (mg/100ml)	19-35	Group1	49	140.49±30.50	23.92	0.001	S
	40-50	Group2	49	144.94±20.87			
	40-50	Group3	16	135.00±39.85			
	40-50	Group4	47	198.60±57.06			
Triglyceride (mg/100ml)	19-35	Group1	49	107.84±25.65	17.804	0.001	S
	40-50	Group2	49	102.14±36.18			
	40-50	Group3	16	112.69±67.77			
	40-50	Group4	47	157.55±46.79			
VLDL Cholesterol (mg/100ml)	19-35	Group1	49	21.73±5.36	16.93	0.001	S
	40-50	Group2	49	20.62±7.83			
	40-50	Group3	16	22.56±13.52			
	40-50	Group4	47	31.76±9.59			
LDL Cholesterol (mg/100ml)	19-35	Group1	49	68.18±25.65	23.18	0.001	S
	40-50	Group2		74.88±17.93			
	40-50	Group3		74.25±27.75			
	40-50	Group4		126.43±60.33			
HDL Cholesterol (mg/100ml)	19-35	Group1		50.88±9.23	22.27	0.001	S
	40-50	Group2		48.55±7.48			
	40-50	Group3		39.13±9.89			
	40-50	Group4		39.91±4.89			
Atherogenic index (TC/HDL)	19-35	Group1		2.75±.58	53.97	0.001	S
	40-50	Group2		3.00±.58			
	40-50	Group3		3.44±.42			
	40-50	Group4		4.97±1.49			

Table-2: Comparative study of lipid profile amongst women in different stages of menstrual cycle

Various groups of women	Cholesterol		Triglyceride		VLDL Cholesterol		LDL Cholesterol		HDL Cholesterol		Atherogenic index	
	P	Sig	P	Sig	P	Sig	P	Sig	P	Sig	P	Sig
Group 1 and 2	.943	NS	0.902	NS	0.915	NS	0.819	NS	0.444	NS	0.523	NS
Group1 and 3	.962	NS	0.977	NS	0.987	NS	0.945	NS	0.001	S	0.053	NS
Group 1 and 4	0.001	S	0.001	S	0.001	S	0.001	S	0.001	S	0.001	S
Group 2 and 3	0.813	NS	0.808	NS	0.856	NS	1.000	NS	0.000	S	0.373	NS
Group 2 and 4	0.001	S	0.001	S	0.001	S	0.001	S	0.001	S	0.001	S
Group 3 and 4	0.001	S	0.001	S	0.001	S	0.001	S	0.985	NS	0.001	S

Table-3: Pair wise comparision among the various women in different stages of menstrual cycle using Post Hoc Multiple Comparision Tests

serum cholesterol, LDL and AI while decrease in HDL, TG, VLDL. But all these changes are not found to be significant (figure-1) (table-3).

In groups 1 and 3 i.e. 19-35 years and 40-50 years with irregular menstrual cycle, there is increase in TG, VLDL, LDL and AI and decrease in HDL and TC but the change is found to be significant in case of HDL level.

In groups 1 and 4 i.e. 19-35 years and 40-50 years (Postmenopausal), there is increase in serum TC, TG, VLDL, LDL and AI and decrease in HDL. The increase in all the parameters of lipid profile is more as the women arrives in the menopause stage. Also, the changes in lipid profile in postmenopausal women are found to be significant as menopause alters the lipid profile.

Variables	Perimenopausal women n=65	Post menopausal women n=47
Hypertriglyceridemia (≥150mg/dl)	5 (7.7%)	24 (51.1%)
Reduced HDL-C (<50mg/dl)	45 (69.2%)	46 (97.9%)

Table-4: Comparision of Triglyceridemia and Reduced HDL-C in perimenopausal and postmenopausal women

Variables	Number	Correlation coefficient (r)	P value
Age and AI	47	0.431	0.002
Mean age of postmenopausal women is 48 ± 1.77			
BMI and AI	47	0.073	0.626
Mean BMI of postmenopausal women is 25 ± 1.06			

Table-5: Correlation of age, BMI with Atherogenic Index (AI) amongst postmenopausal women

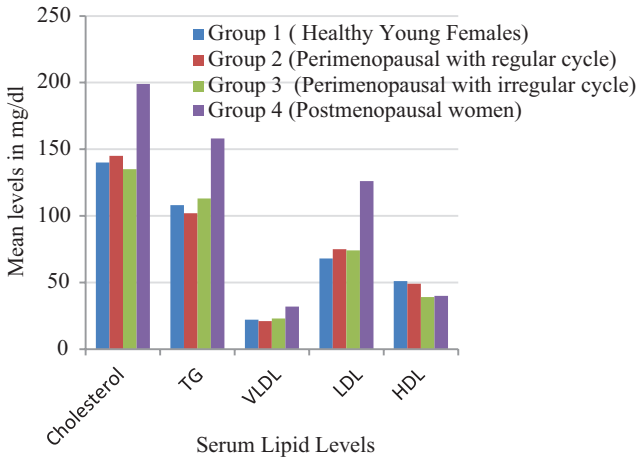

Figure-1: Bar Diagram Showing Changes in Lipid Levels in Different Groups of Women

In groups 2 and 3 i.e. women of same age group but one with regular menstrual cycle and the other with irregular menstrual cycle, there is decrease in TC, and increase in TG, VLDL, LDL and also slightly increase in AI and increase in HDL but the change is found significant in case of HDL.

In groups 2 and 4 and groups 3 and 4 i.e when women with regular and irregular menstrual cycle are compared with postmenopausal women, then the changes are found to be significant in all the parameters of lipid profile except in HDL which is not found to be significant in women with irregular menstrual cycle.

Hence, from the changes in lipid profile in normal young healthy females, 40-50 years age group of women with regular menstrual cycle and irregular menstrual cycle respectively, the increase or decrease in the lipid parameters are not found significant with increase in age among women and till there is no disturbance in the menstrual cycle of a women. Also, with increase in age and with irregularity in the menstrual cycle, the decrease in HDL is found to be significant only. Similar change is observed in the lipid parameters when women with regular menstrual cycle are compared with irregular menstrual cycle. (decrease in HDL is significant)

With increase in age and the women enters the menopause transition, the increase in the lipid parameters like TC, TG, VLDL, LDL and AI and decrease in HDL are found to be highly significant. Similar change is observed in the lipid profile when women with regular and irregular menstrual cycle are compared with postmenopausal women as observed in the comparison made in normal healthy women and postmenopausal women. Only change is that the decrease in HDL is not found to be significant when women with irregular menstrual cycle are compared with postmenopausal women. It could be explained that as perimenopause is a slow process and the change gradually spreads over the next 4-5 years.

There was a comparatively higher percentage of hypertriglyceridemia and reduced HDL-C in postmenopausal women in the current study (table-4).

In our study, the AI is positively and significantly correlated with age and non-significantly correlated with BMI (table-5).

DISCUSSION

Menopause is a natural event in the ageing process of a woman and signifies the end of reproductive years with cessation of cyclic ovarian functions as manifested by cyclic menstruation. While premenopausal women have a lower incidence of cardiovascular diseases (CVD) compared with men of the same age, the incidence of the disease in women increases dreadfully after the age of 50 years.[7] The anti-atherogenic effect of estrogens and the protection of females against CVD, especially coronary heart disease are well described during the premenopausal period.[8] Indeed, there is convincing evidence that menopause is associated with a pro-atherogenic lipid profile characterised by low HDL, higher LDL and TGs levels.[9]

In the present study, group 1 and 2, group 1 and 3, group 2 and 3 belonged to premenopausal/ perimenopausal group. In these groups, it was found that there was no significant difference in the total cholesterol level. In pre/perimenopausal women, there was significant reduction in the cardioprotective HDL-C and significant increase in the atherosclerotic index (TC/HDL). It indicates that as age increases, atherogenic index increases and women become sensitive for CAD. The lower LDL-C levels of the premenopausal/ perimenopausal women could be explained by the increased HDL-C which scavenges cholesterol esters, reducing its availability for LDL-C formation.

These findings are also consistent with the findings of other studies.[10,11,12] It has also been estimated that for any 1mg/dl increase in HDL-C, there is a 30% decrease in the risk of coronary artery diseases and 4.7% decrease in risk of mortality from cardiovascular diseases.[13]

Also, in the present study, group 1 and 4, group 2 and 4 and group 3 and 4 belonged to premenopausal/ perimenopausal/ postmenopausal groups. It shows that there is significant increase in serum level of cholesterol, LDL-C cholesterol, atherogenic index and decrease in HDL-C in postmenopausal women when compared with younger women of age 19-35

years (Premenopausal) i.e group1, perimenopausal with regular menstrual cycle i.e group 2 while in perimenopausal with irregular menstrual cycle i.e group 3, decrease in HDL-C level was not found significant. The elevated total cholesterol, LDL-C and atherogenic index in postmenopausal women and women older than 40 years has been attributed to hormonal changes and failure of ovarian follicular development, where the plasma oestradiol levels that reduces the risk of coronary heart diseases falls below the levels seen in premenopausal women.[14]

The total cholesterol, LDL-C and TC/HDL-C (atherogenic index) were significantly higher and HDL-C lower in postmenopausal women and women older than 40 years when compared to perimenopausal and women between the age-ranges of 19-35 years. This agrees with the findings of Usoro et al, 2006 who also demonstrated higher TC, LDL-C and TGs in menopausal transition and postmenopausal women in comparison with premenopausal women.[15] A similar observation was also made by Mathew et al, 1994 in postmenopausal Caucasians women.[16]

Results from the present study reveals that in postmenopausal women, lipid profile in postmenopausal women indicate that menopause alters the lipid profile in women. Alterations in lipid profile have been associated with age. The TC, LDL-C and AI were significantly higher and HDL-C lower in women above 40 years when compared to those of women of aged between 19-35 years.

In a study done on tribal women in tripura, the author has found comparatively lesser percentage of hypertriglyceridemia i.e 34.33% in postmenopausal women unlike 51.1% in our study. Similar picture is also seen in context to reduced HDL-C level which is also much higher (97.9%) amongst postmenopausal women in the present study unlike 33.73% in a study in Tripura.[17] This difference may be due as our study has been conducted few years back and as awareness regarding risk factors for non communicable diseases is being spread through government initiatives.

Regarding the relationship of AI with age and BMI amongst postmenopausal women in the current study, it was revealed that the AI is positively and significantly correlated with age and non-significanly correlated with BMI. This finding is in contrast to the study done in outside india in another developing country in Camerron, Africa where authors have found that AI was positively and significantly correlated with BMI but not with age.[18] It may be due to as our study has recruited healthy postmenopausal women. Our study has also revealed comparatively higher mean value of AI in postmenopausal women (4.96 ± 1.48) unlike in a study in Cameroon where it is 0.21 ± 0.27.[18]

CONCLUSION

Hence, as the changes in lipid profile correlates directly with the change of oestrogen level. It accounts for increased CAD risk in perimenopausal women compared to premenopausal women. The risk maximises in menopause in the women. The estimation of lipo-proteins like HDL and LDL serves as a more reliable tool in predicting the risk of coronary heart disease in perimenopausal and postmenopausal women.

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