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

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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 Gynaecology 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

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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.

Serum Precipitating reagent HDL Cholesterol + LDL and VLDL Cholesterol (Supernatant) HDL Cholesterol + LDL and VLDL Cholesterol (Precipitate) Cholesterol ester +H20 Cholesterol esterase Cholesterol + Fatty acids Cholesterol + O2 Cholesterol oxidase Cholesterol + Fatty acids HDL Cholesterol + LDL and VLDL Cholesterol

2H202 + Phenol + 4-aminoantipyrine Peroxidase Red quinine + 4H20

Note: The concentration of cholesterol in the sample is directly proportional to the intensity of the red complex (red quinine) 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°C 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 metaperiodate 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.

$$\text{Triglyceride} + \text{H}_2\text{O}_2 \xrightarrow{\text{lipoprotein lipase}} \text{Glycerol} + \text{Fatty acids}$$

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

$$\text{Glycerol-3-P} \xrightarrow{\text{Glycerol-3-P oxase}} \text{DehydroxyacetoneP} + \text{H}_2\text{O}$$

$$2\text{H}_2\text{O}_2 + 4\text{-aminoantipyrine} + \text{ADPS (N-ethyl-N-Sulfopropyl-n-anisidine)} \xrightarrow{\text{Peroxidase}} \text{Red quinine} + 4\text{H}_2\text{O}$$

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

| 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-2: Comparative study of lipid profile amongst women in 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          | Group 1       | 49           | 140.49±30.50| 23.92     | 0.001   | S            |
|                              | 40-50          | Group 2       | 49           | 144.94±20.87|           |         |              |
|                              | 40-50          | Group 3       | 16           | 135.00±39.85|           |         |              |
|                              | 40-50          | Group 4       | 47           | 198.60±57.06|           |         |              |
| Triglyceride (mg/100ml)      | 19-35          | Group 1       | 49           | 107.84±25.65| 17.804    | 0.001   | S            |
|                              | 40-50          | Group 2       | 49           | 102.14±36.18|           |         |              |
|                              | 40-50          | Group 3       | 16           | 112.69±67.77|           |         |              |
|                              | 40-50          | Group 4       | 47           | 157.55±46.79|           |         |              |
| VLDL Cholesterol (mg/100ml)  | 19-35          | Group 1       | 49           | 21.73±5.36  | 16.93     | 0.001   | S            |
|                              | 40-50          | Group 2       | 49           | 20.62±7.83  |           |         |              |
|                              | 40-50          | Group 3       | 16           | 22.56±13.52 |           |         |              |
|                              | 40-50          | Group 4       | 47           | 31.76±9.59  |           |         |              |
| LDL Cholesterol (mg/100ml)   | 19-35          | Group 1       | 49           | 68.18±25.65 | 23.18     | 0.001   | S            |
|                              | 40-50          | Group 2       | 49           | 74.88±17.93 |           |         |              |
|                              | 40-50          | Group 3       | 16           | 74.25±27.75 |           |         |              |
|                              | 40-50          | Group 4       | 47           | 126.43±60.33|           |         |              |
| HDL Cholesterol (mg/100ml)   | 19-35          | Group 1       | 49           | 50.88±9.23  | 22.27     | 0.001   | S            |
|                              | 40-50          | Group 2       | 49           | 48.55±7.48  |           |         |              |
|                              | 40-50          | Group 3       | 16           | 39.13±9.89  |           |         |              |
|                              | 40-50          | Group 4       | 47           | 39.91±4.89  |           |         |              |
| Atherogenic index (TC/HDL)   | 19-35          | Group 1       | 49           | 2.75±.58    | 53.97     | 0.001   | S            |
|                              | 40-50          | Group 2       | 49           | 3.00±.58    |           |         |              |
|                              | 40-50          | Group 3       | 16           | 3.44±.42    |           |         |              |
|                              | 40-50          | Group 4       | 47           | 4.97±1.49   |           |         |              |

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

| Various groups of women    | Cholesterol (mg/100ml) | Triglyceride (mg/100ml) | VLDL Cholesterol (mg/100ml) | LDL Cholesterol (mg/100ml) | HDL Cholesterol (mg/100ml) | Atherogenic index (TC/HDL) |
|----------------------------|------------------------|-------------------------|----------------------------|----------------------------|----------------------------|--------------------------|
| Group 1 and 2              | P 0.943 Sig NS         | P 0.902 Sig NS          | P 0.915 Sig NS             | P 0.819 Sig NS             | P 0.444 Sig NS             | P 0.523 Sig NS            |
| Group 1 and 3              | P 0.962 Sig NS         | P 0.977 Sig NS          | P 0.987 Sig NS             | P 0.945 Sig NS             | P 0.001 Sig S              | P 0.053 Sig NS             |
| Group 1 and 4              | P 0.001 Sig S          | P 0.001 Sig S           | P 0.001 Sig S              | P 0.001 Sig S              | P 0.001 Sig S              | P 0.001 Sig S              |
| Group 2 and 3              | P 0.813 Sig NS         | P 0.808 Sig NS          | P 0.856 Sig NS             | P 1.000 Sig NS             | P 0.000 Sig S              | P 0.373 Sig NS             |
| Group 2 and 4              | P 0.001 Sig S          | P 0.001 Sig S           | P 0.001 Sig S              | P 0.001 Sig S              | P 0.001 Sig S              | P 0.001 Sig S              |
| Group 3 and 4              | P 0.001 Sig S          | P 0.001 Sig S           | P 0.001 Sig S              | P 0.001 Sig S              | P 0.985 Sig NS             | P 0.001 Sig S              |

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.
Indeed, there is a decrease in TC, and increase in 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. The antiatherogenic effect of estrogens and the protection of females against CVD, especially coronary heart disease are well described during the premenopausal period. Indeed, there is convincing evidence that menopause is associated with a pro-atherogenic lipid profile characterised by low HDL, higher LDL and TGs levels.

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. 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. 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-significantly correlated with BMI. This finding is in contrast to the study done in outside india in another developing country in Cameroon, 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.

REFERENCES

1. Sacks FM, Murray AM et al. Hormone Therapy to Prevent Disease and Prolong Life in Postmenopausal Women. Ann Int Med 1992;117:202-352.
2. Matthews KA, Cauley J. Menopause and mid-life changes. In: Hazzard WR, Blass JP, Ettinger WH Jr, Halter JB, Ouslander JG, eds. Principles of Geriatric Medicine and Gerontology. 4th ed. New York, NY:McGraw-Hill; 1999;179 –190.
3. Do KA, Green A et al. Longitudinal Study of Risk Factors for Coronary Heart Disease Across the Menopausal Transition. Am J epidemiology 2000;151:584-593.
4. Bang HO, Dyerberg J et al: Acta Med Scand 1972; 192:85.
5. Barbara B, Sherwin, Morrie M, Gelfand et al. Postmenopausal Oestrogen and Androgen Replacement and Lipoprotein Lipid Concentration. Am J Obstet Gynecol 1987; 156:414-419.
6. Berg G, Mesch V et al. Lipid and Lipoprotein Profile in Menopausal Transition. Effects of Hormones, age and Fat Distribution. Hormone and Metabolic Research 2004; 36: 215-220.
7. Dosi R, Bhatt N, Shah P, Patell R. Cardiovascular Disease and Menopause. J Clin Diag Res, 2014; 8: 62-4.
8. Pahwa MB, Seth S, Seth RK. Lipid Profile in Various Phases of Menstrual Cycle and its Relationship with Percentage Plasma Volume Changes. Clin Chim Acta, 1998; 273: 201-7.
9. Waren MP, Halpert S. Hormone Replacement Therapy: Controversies, Pros and Cons. Best Pract Res Clin Endocrino Metab 2004; 18: 317-32.
10. Jensen J, Nilas L et al. Influence of Menopause on Serum Lipid and Lipoprotein. Maturita 1990; 154: 2349-2355.
11. Edr HA, Gidiz LL. The Clinical Significance of the Plasma High Density Lipoprotein. Med Clin North Am 1982; 66: 431-434.
12. Igweh JC, Aaloamaka CP. Cholesterol Profile of Adult Residents in Eastern Nigeria. O J Med 2003; 15: 46-50.
13. Oknofua EE, Lawal A et al. Features of Menopause and Menopausal Age in Nigerian Women. Int J Gynaecol Bstemet 1990; 31 341-5
14. Sarrel PM. Ovarian Hormone and the Menopause. JAMA, 287:387-498;1990.
15. Usoro CAO, Adikwuru CC et al. Lipid Profile of Postmenopausal Women in Calabar, Nigeria. Pak J of Nutrition 2006; 5: 79-82.
16. Mathews KA, Wing RR et al. Influence of the Perimenopause on Cardiovascular Risk Factors and Symptoms of Middle Aged Healthy Women. Arch Int Med 1994; 154: 2349-2355.
17. Purnajita Sen, Sandeep Das, Dipayan Choudhuri. Correlates of Cardiometabolic Risk Factors Among Women of Tribal Community of Tripura. Indian Journal of Public Health 2017; 61(3).
18. Jobert Richie N Nansseu, Vicky Jocelyne Ana Moor, Murielle Elsa D Nouaga, Bertrand Zing- Awona, Gladys Tchanana and Arthur Ketcha. Atherogenic Index of Plasma and Risk of Cardiovascular Disease Among Cameroon Postmenopausal Women. Lipid in Health and Disease 2016; 15:49.

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