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ASSESSMENT OF THE LIPID PROFILE AND ESTROGEN STATUS OF POSTMENOPAUSAL WOMEN CONCERNING THEIR CARDIOVASCULAR HEALTH.

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ABSTRACT

Background: Dyslipidemia is highly prevalent among women. The management of dyslipidemia is a cornerstone in the prevention of both primary and secondary cardiovascular events, such as myocardial infarction, ischemic stroke, and coronary death. All major international guidelines on the treatment of dyslipidemia recommend similar approaches to the management of dyslipidemia in both men and women. Women experience a number of hormonal changes throughout their lifetime, including those changes associated with puberty, menarche, pregnancy, and menopause. Each of these hormonal perturbations can alter serum lipoprotein levels. lipid profile and estrogen status of postmenopausal women concerning their cardiovascular health. **Materials & Methods**: In this hospital based study100 female patients between the age group of 26-70 were included. The lipid profile was assessed using standard methodologies. Statistical analysis were performed using the GraphPad Prism9 stat® Software. Analysis of data was done using one-way ANOVA employing Tukey's test, after analysis. $p<0.05$ was found to be statistically significant. **Results:** In our study population 45% belonged to Grade I obesity, while 19% Grade II obesity and the remaining 36% were found to be non-obese. A statistically significant difference was observed in Triglyceride and HDL cholesterol levels ($p <0.05$). **Conclusion:** Therefore, it can be concluded that menopause leads to changes in lipid profile by causing significant alterations in total and LDL cholesterol and by reducing HDL cholesterol. The elevated LDL and the reduction of cardio protective HDL is an indication that menopause is an independent risk factor for developing cardiovascular disease.

KEYWORDS: Cardiovascular disease. Cholesterol. Postmenopausal women.

INTRODUCTION

The term dyslipidemia is used to denote the presence of any of the following abnormalities, occurring alone or in combination-increased concentration of TC or LDL-C or serum TG or a decreased concentration of HDL-C. Numerous studies conducted in Indians have revealed that various forms of dyslipidemia such as high total and low-density lipoprotein cholesterol (TC and LDL-C), low high-density lipoprotein cholesterol (HDL-C) and high triglycerides (TG) are highly prevalent. At the same time, while extensive guidelines are available for management of dyslipidemia in US and Europe, no specific guidelines exist for lipid management among Indians Several epidemiologic studies have shown that postmenopausal women tend to have significantly different lipid profiles as compared with premenopausal women.[1-2] A number of lipoprotein changes occur that characterize the menopausal transition.[3] Post-menopausal women have increased levels of LDL-C, total cholesterol, and apolipoprotein B as compared with premenopausal women. In the Framingham Study, investigators documented an increase in cholesterol levels that coincided with menopause,suggesting a causal role of menopause in altering lipid levels.[4] In addition to a higher LDL-C, investigators have noted menopause to be associated with a transition in LDL particles to more atherogenic smaller and more dense particles.[5] Total HDLcholesterol and HDL2 also decrease in postmenopausal women.[6] Elevated Lp(a) levels has been associated with an increased CHD risk and has been reported to increase in women following total hysterectomy and oophorectomy.[7]There are many correctable risk factors for ASCVD. Of these, dyslipidemia has the highest population attributable risk for myocardial infarction (MI).[8] Because of its high prevalence and also because of its direct pathogenic association with atherosclerosis. Accordingly, effective management of dyslipidemia remains one of the most important healthcare targets for prevention of ASCVD.

PURPOSE

The purpose of this study is to assess the lipid profile and estrogen status of postmenopausal women concerning their cardiovascular health.

In light of this, the study was taken up with the following objectives:

1. Measurement of weight, height, age and BMI.

2. To determine the serum estrogen level of control, perimenopausal women and postmenopausal women.
3. To determine the serum of HDL, VLDL, LDL, triglycerides and cholesterol levels of control, perimenopausal women and postmenopausal women.
4. To evaluate the relationship between estrogen level with lipid profile in postmenopausal women and to explore the differential effect of estrogen on lipid profile parameters.

MATERIALS AND METHODS

Blood samples were collected from Arora hospital and Bhakna lab diagnostic center and a test was performed in Diagnostic Lab, Amritsar. About 100 samples were taken out of which 13 women served as control who have regular mensuration cycle and belong to age below 45 years, other 75 were postmenopausal women with age group from 40 to 80 years and remaining 12 women served as perimenopausal women having irregular mensuration cycle. Serum estrogen level of all samples were determined by CLIA method using Snibe Magllumi 600 with the help of serum estradiol kit (Figure 1). All lipid profile were determined by semi-biochemistry autoanalyzer with of kit (erba).

Figure 1: Magllumi 600 Snibe.

Blood sample collection

For the collection of sample, a prominent vein was selected and tourniquet was applied and anterior cubital vein area was cleaned with a sterilized cotton swab dipped in spirit. Needles and syringes were properly inspected and then sampling was performed. A cotton swab was held firmly over the vein puncture site as soon as the needle is removed. After removing the needle, the collected blood was dispensed in the tubes. After obtaining the blood, the serum sample was separated for further biochemical analysis. For the preparation of serum, blood was allowed to clot and then centrifuged at 1100 to 2000 rpm for 10 minutes at 4°C. The samples were refrigerated for further use. 5 ml of blood sample was collected from the anterior cubital vein using a sterile disposable syringe and was transferred to a red top tube. Informed consent was taken from subjects. Samples were centrifuged at 1100 to 2000 rpm for 10 minutes to obtain clear serum. Serum sample was obtained from blood for the evaluation of Total Cholesterol (TC), Triglyceride (TG), High-Density Lipoprotein Cholesterol, (HDL-C), Low-Density Lipoprotein Cholesterol (LDL-C) and Very Low-Density Lipoprotein Cholesterol (VLDL-C).

Biochemical investigation

Determination of Cholesterol in serum or plasma by CHOD/PAP method.[9]

The serum cholesterol level was estimated spectrophotometrically at 505 nm by using a commercially available kit (ERBA diagnostics Mannheim GmbH, Mannheim/Germany)

Determination of Triglycerides in serum and plasma by GPO/PAP method.[10]

The serum triglyceride level was estimated spectrophotometrically at 505 nm by using a

commercially available kit (ERBA diagnostics Mannheim GmbH, Mannheim/ Germany)

Determination of HDL Direct

The serum HDL cholesterol level was estimated spectrophotometrically at 505/670 by using a commercially available kit (ERBA diagnostics Mannheim GmbH, Mannheim/Germany)

Determination of LDL Direct

LDL cholesterol was calculated from total cholesterol, triglycerides, and HDL cholesterol level, by using the following formula:

Calculation-

Cholesterol – (VLDL + HDL)

Reference Value: less than 100mg/dl

Determination of VLDL (Very low-density lipoprotein):

VLDL was calculated from TG using the following formula-

Calculation

Conc. of VLDLc (mg/dl) = Triglycerides/5

Reference Value: 2-30 mg/dl

Determination of Total Estrogen by CLIA method (Pagana et al., 2007)

Intended to use: For the direct quantitative determination of Total Estrogens in human serum by an enzyme immunoassay

STATISTICAL ANALYSIS

The data was calculated and analyzed as Mean of observation ± Standard Error. The results so obtained were statistically examined using GraphPad Prism9 stat® Software. Analysis of data was done using one-way ANOVA employing Tukey's test, after analysis. $p<0.05$ was found to be statistically significant. Graph stats Technologies is a global leader of software products for Biostatistics, Molecular Biology, Scientific Graphing & Analysis, Molecular Cloning, and Bioinformatics.

RESULTS

Description of subjects

The information of patients and other parameters were recorded using patient Performa and tabulated (Table 1).

In the present study, patients were divided into three groups. The description of subjects under study is as follows:

Table 1: Data of subjects

Total Population (n=100)		
Controls	**Perimenopausal women**	**Postmenopausal women**
n=13	**n=12**	**n=75**

Comparison between Age, Weight, and BMI of Controls, Perimenopausal and Postmenopausal women (Table 2 and Figure 2).

Table 2: Data of Age, Weight, and BMI of Controls, Perimenopausal and Postmenopausal women.

S. No.	Subjects	Weight (kgs)	Height (inches)	BMI (kg/m^2)
1	Controls	67.5±4.0	62.6±0.8	26.8±1.6
2	Perimenopausal women	64.8±3.2	61±0.8	26.8±1.1
3	Postmenopausal women	69.2±1.2	62.2±0.3	29.5±0.7

(Data represented as Mean ± SE)

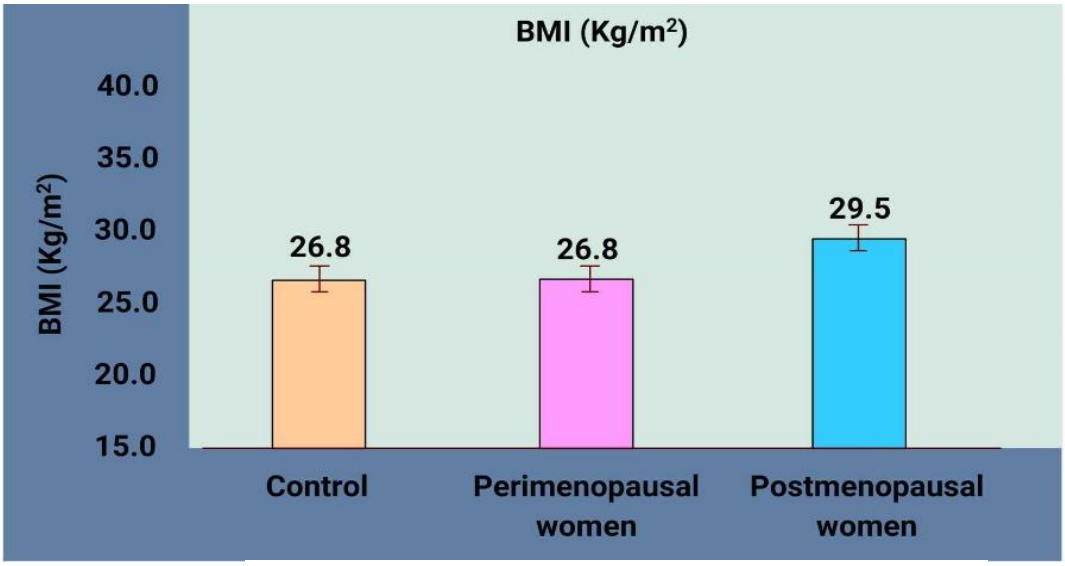

Figure 2: BMI in postmenopausal women, perimenopausal women, and control.

The average value of BMI in postmenopausal women was (29.5±0.7) mg/dl, in perimenopausal women (26.8±1.1) mg/dl and the control (27.5±1.6) mg/dl. The mean value of BMI of postmenopausal women was higher as compared to perimenopausal women and control.

Comparison of Serum Total Cholesterol, Triglyceride, HDL-Cholesterol, LDL-Cholesterol, VLDL Cholesterol, and Serum Estrogen levels of Controls, Perimenopausal and Postmenopausal women (Table 3 and Figure 3)

Table 3: Data of biochemical parameters Total Cholesterol, Triglyceride, HDL-Cholesterol, LDL-Cholesterol, VLDL-Cholesterol and Serum Estrogen levels of Controls, Perimenopausal and Postmenopausal women.

S.no	Subject	Cholesterol (mg/dl)	Triglyceride (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)	Serum Estrogen (pg/ml)
1	Control group	168.3±5.4	108.2±7.5	42.1±1.4	104.6±3.6	21.6±1.5	65.9±10.9
2	Perimenopausal women	190.9±8.1	156.7±7.4	47.4±2.0	111.9±5.7	31.3±1.5	95.0±19.0
3	Postmenopausal women	207.8±6.2	230.3±13.6	24.1±1.8	140.2±7.0	46.1±2.7	22.8±1.0

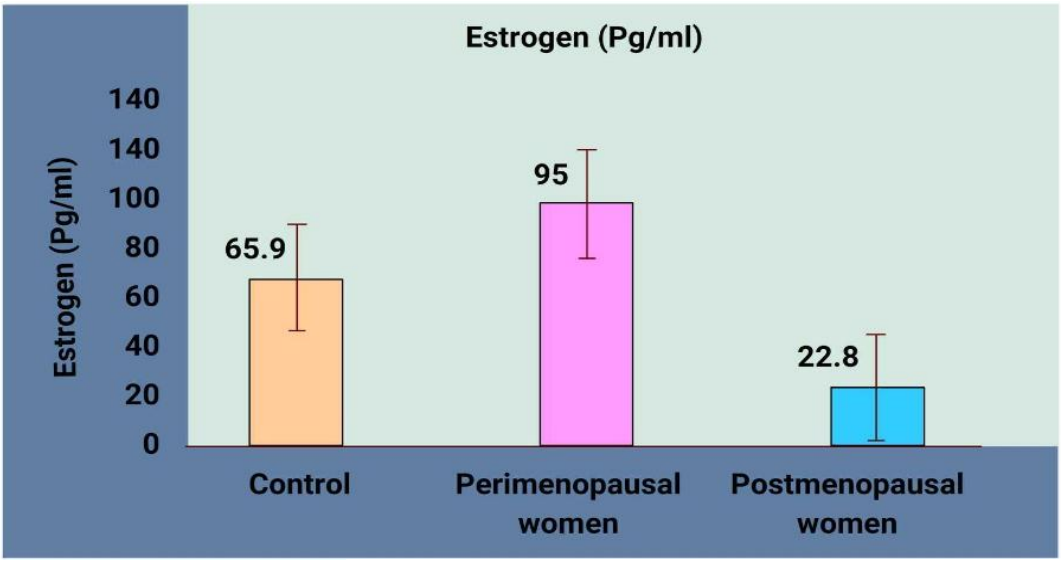

Figure 3: Serum Estrogen levels in postmenopausal women, perimenopausal women, and control.

The mean value of serum estrogen in postmenopausal women was (22.8±1.0) mg/dl, in perimenopausal women was (95.0±19.0) mg/dl and in controls was (65.9±10.9) mg/dl.

Comparison of Total HDL Cholesterol in postmenopausal women, perimenopausal women, and control (Figure 4).

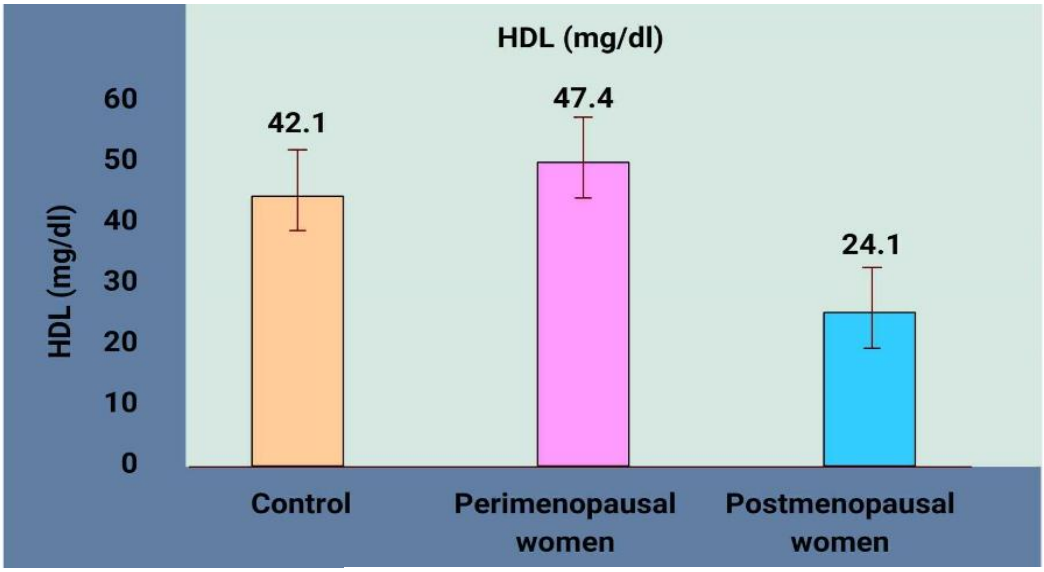

Figure 4: Total HDL Cholesterol in postmenopausal women, perimenopausal women, and control.

The average value of serum HDL level in post-menopausal (24.1±1.8) mg/dl, in perimenopausal women (47.4±2.0) mg/dl and control (42.1±1.4) mg/dl (Table 3). The level of serum HDL was significantly lower(p=0.0001) p<0.005 in postmenopausal than in the perimenopausal and control (Figure 4).

Comparison of VLDL-Cholesterol in postmenopausal women, perimenopausal women, and control.(Figure 5).

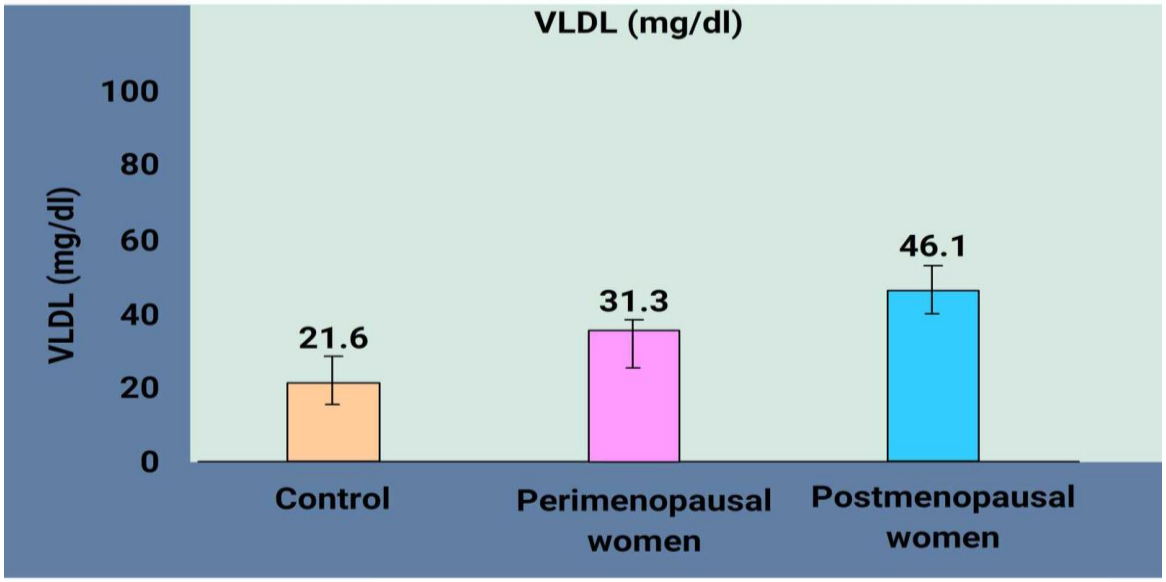

Figure. 5: LDL-Cholesterol in postmenopausal women, perimenopausal women, and control.

The average value of serum LDL levels in postmenopausal women (140.2±7.0) mg/dl in perimenopausal women was (111.9±5.7) mg/dl and control women was (104.6±3.6) mg/dl (Table 3). The mean value of LDL in postmenopausal women was higher (p=0.0360) p<0.005than perimenopausal women and control (Figure:5).

Comparison of VLDL-Cholesterol in postmenopausal women, perimenopausal women, and control

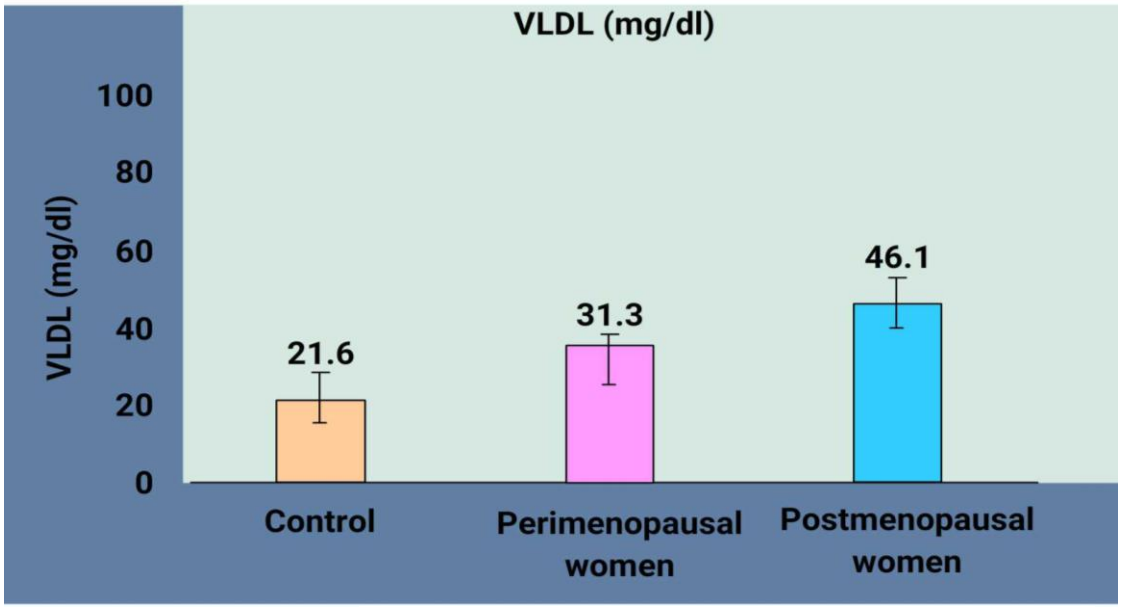

Figure 6: VLDL-Cholesterol in postmenopausal women, perimenopausal women, and control.

The average value of serum VLDL level in post-menopausal women (46.1±2.7) mg/dl, in perimenopausal women was (31.3±1.5) mg/dl and in control was (21.6±1.5) mg/dl (Table 3). These were calculated by the friedwald equation. The mean value of VLDL in postmenopausal women was significantly higher (p=0.0002) p<0.005 in postmenopausal women than the perimenopausal women and control (Figure 6).

Differential evaluation of Levels of Total Cholesterol, Triglyceride, HDL-Cholesterol, LDL-Cholesterol, VLDL in postmenopausal women in different Estrogen ranges (Table 4 and Figure 4). Evaluation of Percentage data of no. of postmenopausal women in different Estrogen ranges.

Table 4: - Data of postmenopausal women in different Estrogen ranges.

S.no.	Estrogen levels (pg/ml)	No. of postmenopausal women (75)	Percentage of postmenopausal women
Range I	4 – 18 pg/ml (13.6)	25	34%
Range II	18.1- 32.2 pg/ml (24.7)	40	53%
Range III	>32.2 pg/ml (37.9)	10	13%

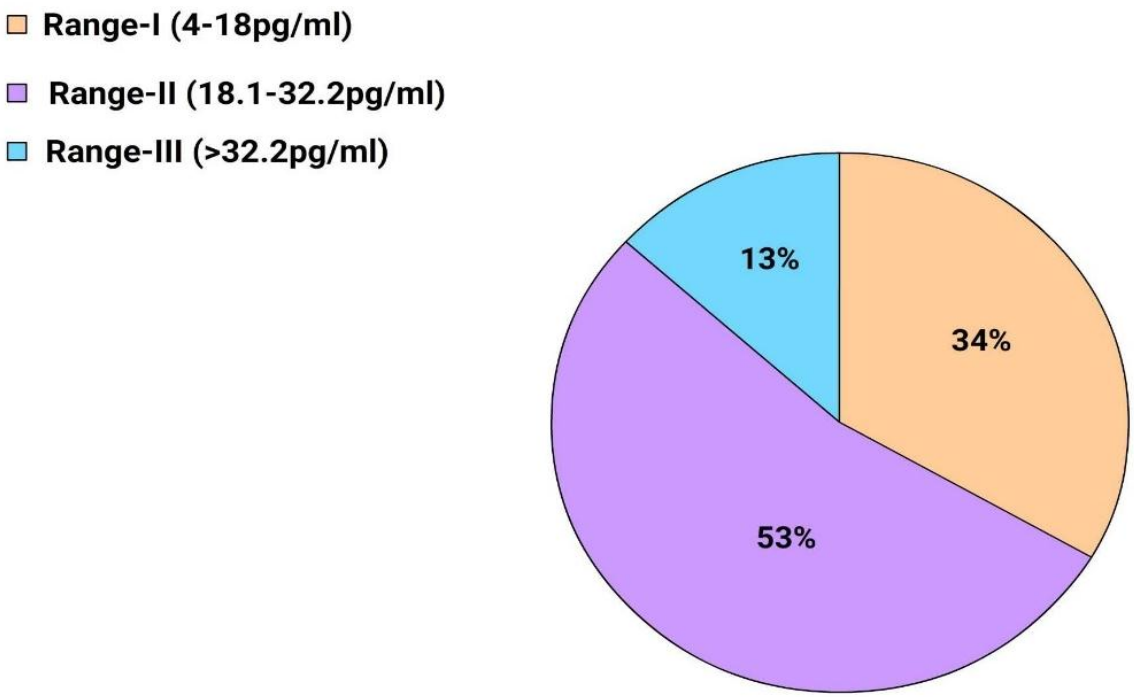

Figure 4: Population %age of postmenopausal women with different Estrogen ranges.

The serum estrogen levels of all the 75 postmenopausal were determined. The result presented in (Table 4) indicates that out of a total of 75 postmenopausal women, 34% postmenopausal women (25) have estrogen levels in range-I, 53% postmenopausal women (40) have estrogen levels in range-II, 13% postmenopausal women (10) have estrogen level in range-III. The present study shows that maximum postmenopausal women have estrogen level in range of 18.1-32.2 mg/dl (Figure 4).

Different estrogen ranges and their association with lipid profile at the high-risk level (Table 5 and Figure 5).

Table 5: Percentage data of cholesterol, TG, HDL, LDL, VLDL of postmenopausal women having Estrogen ranges.

Percentage (%) of no. of subjects															
Subject	Cholesterol			Triglyceride			HDL			LDL			VLDL		
	Normal	Borderline	High risk	Normal	Borderline	High risk	Normal	Borderline	High risk	Normal	Borderline	High risk	Normal	Borderline	High risk
Estrogen range-I (4-18pg/ml)	52	24	24	8	36	56	28	60	12	48	36	16	8	32	60
Estrogen range-I (18.1-32.2 pg/ml)	50	30	20	15	42	43	35	60	5	47	28	25	15	35	50
Estrogen range-I (>32.2 pg/ml)	10	70	20	40	40	20	0	100	0	10	90	0	40	30	30

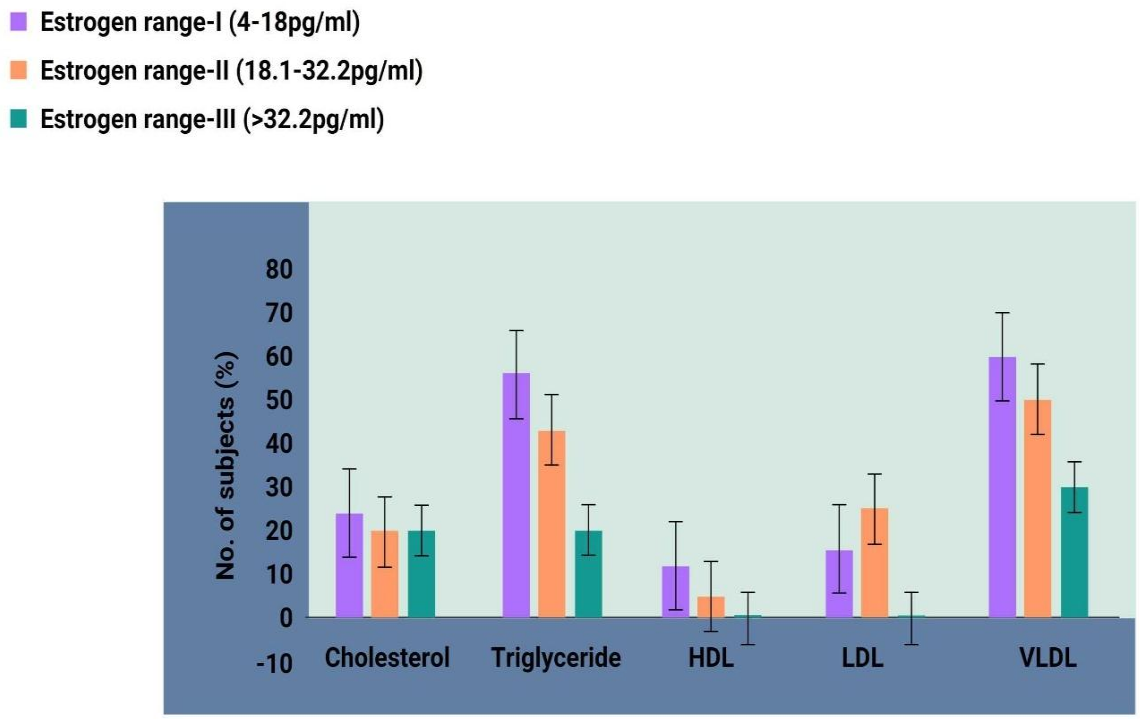

Figure 5: Percentage of different lipid parameters associated with the estrogen range-I illustrate that 24% of women have cholesterol, 56% women have TG, 12% women have HDL, 16% women have LDL, and 60% women have VLDL at high-risk levels. The percentage of different lipid parameters showed in the figure associated with estrogen range-II illustrate that 20% of women have cholesterol, 43% women have TG, 5% women have HDL, 25% women have LDL, and 50% women have VLDL at high-risk levels. The percentage of different lipid parameters showed in the figure associated with estrogen range-III illustrate that 20% of women have cholesterol, 20% women have TG, 0% women have HDL, %0 women have LDL, and 30% women have VLDL at high-risk levels (Table.5).

DISCUSSION

The present study was undertaken to evaluate the levels of serum lipid profile in pre- and postmenopausal women. The incidence of CHD in women is significantly lower before menopause, a protection that has been attributed to the effects of estrogen. Natural menopause confers a 3-fold increase in CHD risk.[11] In the Nurses' Health Study cohort, women undergoing bilateral oophorectomy had up to an 8-fold increase in risk of CHD.[12]After age 50 years, cholesterol levels plateau in men; however, levels of low-density lipoprotein (LDL) cholesterol increase an average of 0.05 mmol/L (2 mg/dL) per year between ages 40 and 60 years in women.[13] At least part of this increase results from declining levels of estrogen, which result in down-regulation of the LDL receptor on the liver.[14] A high LDL cholesterol level is a strong predictor of CHD risk in women younger than 65 years and a somewhat weaker predictor in women aged 65 years and older. Increases in levels of total cholesterol, very-low-density lipoprotein (VLDL) cholesterol, and triglycerides have also been observed after menopause.[15] Menopause is the permanent amenorrhea, which lasts at least for a period of 1-year due to the cessation of ovarian function.[16] (Padubidri VG, 2004) This results in changes in metabolism ofglucose and insulin, body fat distribution, coagulation, fibrinolysis, and vascular endothelial dysfunction.[17]

CONCLUSION

From this study, we concluded that

- Postmenopausal women have significantly lower ($p<0.05$) serum estrogen as compared to control and perimenopausal women.
- Women in menopause have lower concentration of HDL ($p<0,05$) and high concentration of Cholesterol ($p<0.05$), TG ($p<0.05$), LDL ($p<0.05$) and VLDL($p<0.05$) in relation to women with regular menstruation. The concentration of estrogen shows a negative correlation with VLDL and triglycerides concentration in women in menopause, while the correlation with HDL concentration is positive.
- Maximum postmenopausal women (53%) have estrogen level in range 18.1-32.2pg/ml whereas 34% postmenopausal women have estrogen level in range 4-18pg/ml and only 13% postmenopausal women have estrogen level in range >32.2pg/ml.
- With the increase in levels of serum estrogen, the no. of women having high risk levels of serum HDL, LDL, Cholesterol, TG and VLDL decreased.
- The decline of estrogen levels in postmenopausal women raised all lipid profiles (except HDL), but a prominent effect was seen in VLDL and TG levels.
- Adverse changes in lipid profile in postmenopausal women under study have an increased risk of having complications of cardiovascular disease in near future. Early and timely detection and primary

prevention can avoid morbidity and mortality in this high-risk population.

- Estrogens therapy in these postmenopausal women may result in the improvement of lipid metabolism.

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