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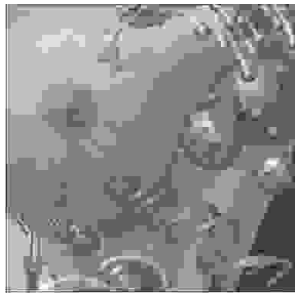

POSTMENOPAUSAL WOMEN;
ATHEROSCLEROTIC RISK FACTORS.

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ABSTRACT... Postmenopausal women are more prone to develop cardiac morbidity due to exhaustive production of estrogens. Postmenopausal women may have 3-4 fold greater risk of atherosclerosis after a natural menopause. **Objectives:** To find correlation between biochemical and physical parameters after the onset of menopause and their effects on disease process in the postmenopausal women. **Design**: Prospective Study. **Setting:** PGMI Lahore. **Period:** From Jan 2000 to Oct 2000. **Material & Methods:** 75 subjects were enrolled in this study and divided into three groups i.e. premenopausal (control), early postmenopausal and late postmenopausal groups. Their physical parameters like weight, waist to hip ratio (WHR) and blood pressure were taken. Biochemical parameters, like cholesterol, triglycerides, high density lipoprotein cholesterol (HDL-C) and low density lipoprotein cholesterol (HDL-C) were estimated by commercial scientific kits. **Results:** Biochemical parameters were mostly non-significant changed ($P > 0.05$) while physical parameters were deviated significantly ($P < 0.001$) when comparisons were made between mean values of various study groups. **Conclusion:** Even at normal values of lipid profile, the postmenopausal women are at risk of developing atherosclerotic lesions because of hypertension, obesity, exhaustive production of estrogen and android type of body fat distribution.

Key words: Post menopause, Hypertension, Waist to hip ratio (WHR), Atherosclerosis.

INTRODUCTION

In western population the rate of heart disease is declining because of health education and magnitude of awareness but it still remains the principal cause of death

in postmenopausal females[1-2]. The women in industrialized countries are the victims of excessive morbidity and mortality due to the atherosclerosis particularly after the onset of menopause[3].

Women develop coronary artery disease (CAD) after the stoppage of menstruation and it is because of exhaustive production of estrogen, an important determinant of cardiovascular disease in women[4].

Epidemiologic data document low rates of coronary heart disease in premenopausal women, a narrowing of the gender gap in CHD mortality after menopause and elevated risk of CHD among young women with bilateral oophorectomy not treated with estrogen. This depicts the significance of estrogen in the well being of women's health care[5].

Estrogen deficiency is a risk factor for osteoporosis and coronary artery disease in postmenopausal women[6].

The few studies have shown that women have much lower rates of CAD then men at the same values for cholesterol, clearly elevated risk for coronary disease in women is evident only at relatively high values of cholesterol (i.e. greater than 260 mg/dl)[7].

In the role of triglycerides have been declared controversial as an independent risk factor in causing CAD[8].

An inverse correlation between high density lipoprotein cholesterol (HDL-C) and triglycerides was reported in England. Since both high concentration of triglyceride rich lipoprotein (VLDL) and low concentration of HDL are well recognized lipid risk factor for arterial disease[9].

Breure[10] in 2001 stated that triglyceride (TG) level is one of several lipid parameters that can help out in the prediction of CAD in postmenopausal women.

Elevated low density lipoprotein cholesterol (LDL-C) and decreased HDL-C concentrations are independent risk factors for coronary heart disease[11].

In large population studies, decreased HDL-C levels are strongly associated with plasma triglyceride concentration, body mass index (BMI), increased alcohol consumption and blood pressure in men. In women, in addition to these parameters, increasing age, menopausal status, plasma glucose and cigarette smoking are also associated with low HDL levels[12].

OBJECTIVES

The major objectives of the study are as follows;

1. To study the effect of estrogen deficiency on various lipid and lipoproteins
2. To elaborate the lipid derangements in postmenopausal women as compared to the premenopausal women
3. To elucidate the prevalence of atherosclerotic changes more after the menopause as a result of changes in the lipid profile in postmenopausal women.

MATERIALS AND METHODS

This study was conducted on seventy five Pakistani females. The subjects were divided into following groups.

1. Premenopausal group (control)

This group consisted of those women who had age range (20-45 years) with regular menstrual cycles. They were not suffering from any metabolic disorders like diabetes and hypertension. Females with H/O hormonal and gynecological diseases were not taken as members of this study group. Alcoholics and smokers females were excluded.

2. Early postmenopausal group

Twenty five women with age range 46-60 years were included in this group, who had developed natural menopause. Those who had undergone oophorectomy (surgical menopause) were not selected as the subjects for this study. Subjects with H/O gynecological and hormonal disorders were excluded, along with alcoholics and smoker females.

3. Late postmenopausal group

This group included those 25 women who were living with menopause since long. They had age range of 61-80 years. Females with surgical menopause were excluded alongwith other exclusion criteria.

Subjects were selected from the outpatient departments of services and Jinnah Hospitals Lahore. They were recruited in the research process after having their due consent on printed proforma. They were told that 10cc blood will be taken and physical examination will be performed.

On the day of enrolment, the subjects were narrated fully about the protocol of the study. They were advised to continue their normal daily diet and working routine. They were also informed about the date and time on which the fasting blood samples would be collected[13].

After taking prior consent of the patient, 10ml blood was taken after the 30 minutes rest from the median cubital vein with the help of a sterile disposable syringe in the morning at 8-9 AM on the day of sampling after an overnight fasting of about 12-14 hours. All the samples were centrifuged at a speed of 4000 rpm for 15 minutes. The plasma and serum were separated from the above samples, then they were placed in capped sample storage cubes and placed in refrigerator. All the samples collected on different days depending upon the availability of subjects were analyzed simultaneously on fixed dates. Blood pressure was measured by mercury sphygmomanometer[14]. The waist to hip ratio (WHR) was taken by measuring the circumference of waist and hip in centimeters. The weight of the subjects was measured by clinical weighing machine. The biochemical tests were performed by the commercially available scientific kits for lipid profile.

RESULTS

The distribution of the subjects is depicted in Table-I.

Table-I. Distribution of Subjects

Group	No. of Subjects	Age Range	Description
G-I	25	20-45 Years	Premeopausal group (control)
G-II	25	46-60 years	Early postmenopausal group (Experimental I)
G-III	25	61-80 years	Late postmenopausal group (Experimental II)

The above mentioned groups were further elaborated to explain the mean age, mean values of serum cholesterol, triglycerides HDL-cholesterol and LDL-cholesterol and to exhibit any type of correlation between the mean values of biochemical parameters among each other in experimental and control groups. The variation in systolic and diastolic blood pressures are shown in figures 1 and 2 because blood pressure is a necessary sequale of atherosclerotic changes going on in the vasculature of postmenopausal subjects. The variations in mean values of weight, systolic blood pressure, diastolic blood pressure and waist to hip ratio are shown in tables V-VII.

The biochemical markers are tabulated in the form of their mean values with standard deviations in table II, III and IV. The table II exhibit the comparison of biochemical markers with the significance and non-significance as below. It was noted that only triglycerides were significantly changed in late postmenopausal women in comparison with control group while other parameters like cholesterol, LDL-C and HDL-C remained non-significant in the comparison as shown in Table III. This fact was also noted that in the process of comparison between early postmenopausal and late postmenopausal groups, there was no significant change was found as depicted in table IV.

Table-II. Comparison of biochemical parameters between premenopausal and early postmenopausal groups				
Biochemical parameters	**Premenopausal group (control)n=25**	**Early postmenopausal group (ex n= 25)**	**P. Value**	**Significance**
Cholesterol mg/dL	181.8 ± 66.2	185.3 ± 46.4	>0.05	N.S
Triglycerides mg/dL	148.8 ± 23.5	153.5 ± 20.4	>0.05	N.S
HDL- cholesterol mg/dL	52.6 ± 17.1	48.4 ± 8.0	>0.05	N.S
LDL cholesterol mg/dL	112.7 ± 61.4	120.7 ± 39.2	>0.05	N.S
N.S = Non-significant *H.S = Highly significant*				

Table-III. Mean values of comparison of cholesterol, triglycerides, HDL-C and LDL-C between premenopausal and late postmenopausal groups				
Biochemical parameters	**Premenopausal group (control)n=25**	**Late postmenopausal group (ex n= 25)**	**P. Value**	**Significance**
Cholesterol mg/dL	181.8 ± 66.2	218.3 ± 53.2	>0.05	N.S
Triglycerides mg/dL	148.8 ± 23.5	186.4 ± 38.6	>0.001	H.S
HDL- cholesterol mg/dL	52.6 ± 17.1	45.8 ± 11.4	>0.05	N.S
LDL cholesterol mg/dL	112.7 ± 61.4	138.6 ± 56.0	>0.05	N.S

Table-IV. Comparison of mean values of cholesterol, triglycerides, HDL-C and LDL-C between early postmenpausal and late postmenopausal groups (values are given in Mean ± S.D)				
Biochemical parameters	**Early Postmenopausal group n=25**	**Late postmenopausal group (n= 25)**	**P. Value**	**Significance**
Cholesterol mg/dL	185.3 ± 48.4	218.3 ± 53.2	>0.05	N.S
Triglycerides mg/dL	153.5 ± 20.4	186.4 ± 38.6	>0.05	H.S
HDL- cholesterol mg/dL	48.4 ± 8.0	45.8 ± 11.4	>0.05	N.S
LDL cholesterol mg/dL	12.07 ± 39.2	138.6 ± 56.0	>0.05	N.S

Table-V. Comparison of mean values of weight, waist to hip ratio (WHR), and blood pressure (systolic and Diastolic) between premenopausal and early postmenopausal groups (values are given in Mean ± S.D)				
Biochemical parameters	**Premenopausal group n=25**	**Early postmenopausal group (n= 25)**	**P. Value**	**Significance**
Weight (Kg)	59.4 ± 9.2	60.9 ± 11.1	>0.05	N.S
WHR	0.9108 ± 0.0421	1.077 ± 0.0329	<0.001	H.S
Systolic blood pressure (SBP) mm Hg	113.6 ± 9.0	131.0 ± 13.3	<0.001	H.S
Diastolic blood pressure (DBP) mm Hg	78.9 ± 7.0	91.6 ± 8.3	<0.001	H.S

Table-VI. Comparison of mean values of weight, waist to hip ratio (WHR), and blood pressure (systolic and diastolic)between premenopausal and late postmenopausal groups (values are given in Mean ± SD)

Biochemical parameters	Premenopausal group (n=25)	Early postmenopausal group (n= 25)	P. Value	Significance
Weight (Kg)	59.4 ± 9.2	81.0 ± 9.6	<0.001	H.S
WHR	0.9108± 0.0421	1.263 ± 0.1320	<0.001	H.S
Systolic blood pressure (SBP) mm Hg	113.6 ± 9.0	140.5 ± 18.5	<0.001	H.S
Diastolic blood pressure (DBP) mm Hg	78.9 ± 7.0	91.6 ± 8.3	<0.001	H.S

Table-VII. Comparison of mean values of weight, waist to hip ratio (WHR), and blood pressure (systolic and diastolic) between early postmenopausal and postmenopausal groups (values are given in Mean ± SD)

Biochemical parameters	Premenopausal group (n=25)	Late postmenopausal group (n= 25)	P. Value	Significance
Weight (Kg)	60.9 ± 11.1	81.0 ± 9.6	<0.001	H.S
WHR	1.0776 ± 0.0329	1.263 ± 1320	<0.001	H.S
Systolic blood pressure (SBP) mm Hg	131.0 ± 13.3	140.5 ± 18.5	<0.001	H.S
Diastolic blood pressure (DBP) mm Hg	91.6 ± 8.3	96.2 ± 8.9	<0.001	H.S

Fig-1. Variations in systolic B.P in premenopausal, early postmenopausal and late postmenopausal

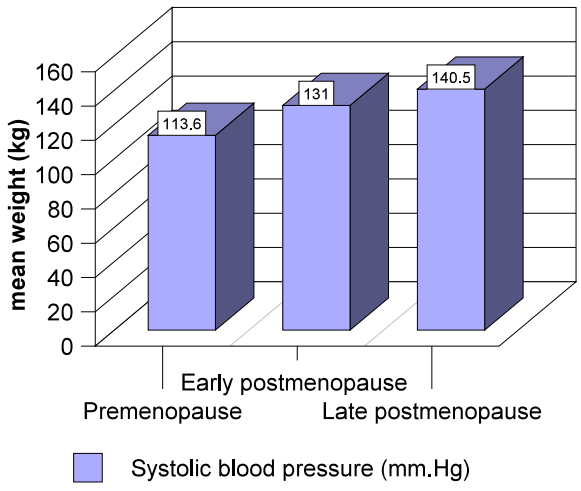
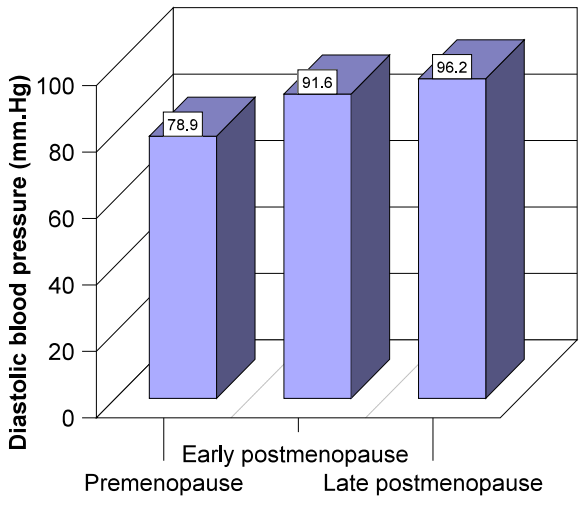


Fig-2. Mean values of diastolic blood pressure (DBP) in premenopausal, early postmenopausal and late postmenopausal groups



The comparisons pertaining to waist to hip ratio showed significant change ($P < 0.001$) depicting that atherosclerotic risk is present in experimental subjects (Table V-VII).

Systolic and diastolic blood pressure also exhibited significant changes ($P < 0.001$) as shown in (Table V-VII). The body weight is also significantly altered in two comparisons ($P < 0.001$) while it is non-significantly changed in one comparison (Table V).

DISCUSSION

Menopause is associated with a gain in fat mass and loss of lean body mass but these changes in body composition are not prevented by hormone replacement (HRT) therapy[15].

Lipid profile was noted in this study in previous decades the evaluation of the serum cholesterol was used as the sole informative marker of coronary artery disease in subjects of both gender. Now a days high plasma LDL/HDL ratio is more informative[16]. In present study, there was no significant change noted ($P > 0.05$) in the mean concentration of cholesterol among premenopausal, early postmenopausal and late postmenopausal groups (Table II, III, IV). Our results of study are consistent with the results of a Chinese research accomplished by Lien et al. (1996)[17] in which it was assessed that with low level of serum cholesterol still there is high risk of coronary artery disease in postmenopausal women.

The biologically important lipids are fatty acids and their derivatives, the neutral fats (triglycerides) the phospholipids and related compounds. The triglycerides are made up of three fatty acids bound to glycerol[18]. In this study there was found highly significant change ($P < 0.001$) between mean concentrations of triglycerides of late postmenopausal group (Table IV). In other two comparisons there was non-significant ($P > 0.05$) change in mean concentration of triglycerides (Table II, III).

Our study correlates with the results of Breuer (2001)[10] who stated that triglyceride (TG), level is one of several lipid parameters that can help in prediction of heart disease risk in postmenopausal women.

In this study, HDL has been reported as a good marker of atherosclerosis in postmenopausal women because its mean concentration was significantly lower ($P < 0.001$) in late postmenopausal women as compared to premenopausal and early postmenopausal women (Table II, III, IV).

In 1992, Demirovic et al.[19] reported that there was no significant association between high-density lipoprotein (HDL) and menopausal status in either black or white US women.

Our study is partially consistent with the above mentioned research. The predictivity of HDL for atherosclerosis in postmenopausal women is appreciated with certain exceptions. In this study no significant change was found ($P > 0.05$) among premenopasual, early postmenopausal and late postmenopausal groups regarding the mean concentration of serum low-density lipoprotein (Tables II, III, IV).

This finding is very much close to the report of Bhatnagar and Durrington[20] who stated that with normal level of LDL there is risk of coronary artery disease in postmenopausal women.

The weight gain in women after the onset of menopause doubtlessly ameliorates the gender difference in the development of atherosclerosis and later on coronary artery disease[21]. In this study weight is known to be partially significant in the development of CAD. In present study, the waist to hip ratio was calculated of all the participants of the study. There was highly significant changes ($P < 0.001$) in all the comparisons possibly made (Table V-VII). This study is in consistent with the results of Tuck[22] that high waist to hip ratio have a high risk for the development of CAD in postmenopausal women.

CONCLUSIONS

Postmenopausal women are at higher risk of development of coronary artery disease even with no deviation of lipid profile from the normal physiological values, because obesity, increased waist to hip ratio (WHR) and hypertension are the potent factors even with normal lipid profile for the development of atherosclerosis in postmenopausal women.

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