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Research Paper

Study of Cardiovascular Risk Factors Amongst Peri And Post Menopausal Women And Their Correlation With Serum Estradiol Levels

Medical Science

KEYWORDS : cardiovascular risk, serum estradiol, serum HDL, serum LDL, post-menopausal

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ABSTRACT

Menopause is permanent cessation of menstruation beginning 12 months after final menses. Cardiovascular risk is increased in postmenopausal women attributable to decreased serum estradiol levels. This study was conducted to study cardiovascular risk factors amongst peri and post menopausal women correlating it with serum estradiol levels. 100 women included in study were divided as group I comprising of 50 perimenopausal and group II comprising of 50 postmenopausal women. Routine investigations including serum lipid profile and serum estradiol measurements were done. Prevalence of cardiovascular risk factors was higher while serum estradiol was lower in postmenopausal group .Increased serum estradiol was associated with higher serum HDL and lower serum LDL and VLDL thus reducing the risk of cardiac diseases. Thus based on these observations, it may be said that menopausal transition represents a time of substantial adverse changes in cardiovascular risk factors for women and estradiol appears to play a cardioprotective role.

Menopause is permanent cessation of menstruation following loss of ovarian activity which, by definition begins 12 months after last menses. Changes from normal ovulatory cycle to cessation of menses known as perimenopausal phase starts 5- 10 years prior to menopause, marked by irregularity of menstrual cycles.

There has been an increase in life expectancy of Indian women , and more women are living beyond 65 years of age, thus, experiencing the consequences of gonadal hormone loss for >20 years of life, increased morbidities and compromised quality of life after menopause.

Coronary Heart Disease is the leading cause of morbidity and mortality in men and postmenopausal women. Menopause increases the risk of coronary heart disease for women still further. Risk of cardiovascular diseases in women lag behind approximately by 10 years compared to men. However, there is a marked increase in incidence of cardiovascular diseases among postmenopausal women.[1] The risk of cardiovascular disease is increased by two fold among women who undergo bilateral oophorectomy compared with premenopausal women [2]. Therefore it has long been postulated that estrogen is cardioprotective, and that the changes in level of estrogen in postmenopausal period contributes to increased risk of cardiovascular diseases.

During reproductive years, women are protected from coronary heart disease due to increased level of HDL which is a consequence of effect of estrogen and lower level of testosterone. Total and LDL cholesterol are lower in premenopausal women than in men, although the levels gradually increase with ageing and after menopause they rise rapidly [3].

The present study was conducted to study the prevalence of risk factors for cardiac diseases in premenopausal and post menopausal women and their correlation with serum estradiol levels thus, trying to bring forth the protective role of estrogen in cardiac diseases.

MATERIALS AND METHODS

The study was a cross sectional study conducted in department of Obstetrics and Gynaecology of King George's Medical University, Lucknow .

Total of 100 cases were included in the study and divided into two groups after taking informed consent from them. Group I included 50 perimenopausal women while Group II included 50 postmenopausal women.

Subjects not giving consent , those on hormone replacement therapy , having acute illness, with known, suspected or past history of breast or endometrial cancer , with undiagnosed abnormal genital bleeding, active deep venous thrombosis or thromboembolic disorders or a history of these conditions, with active arterial thrombosis or documented history of these conditions were excluded from the study.

Detailed history and examination including height, weight, systolic and diastolic blood pressure, waist and hip measurement was done for all the patients. All routine investigations including serum lipid profile (serum cholesterol , serum LDL, serum VLDL, serum HDL, serum triglyceride) and serum estradiol measurement was done.

The obtained data was analyzed using the SPSS software.

RESULTS

The mean age of perimenopausal group was 44.74±5.42 years while that of postmenopausal group was 55.24±6.15 years. The difference between the two groups was statistically significant for age. Both the groups were comparable for area of residence (rural/urban), socioeconomic status, and religion.

Distribution of cardiovascular risk parameters was studied in both the groups. Systolic and diastolic blood pressure, serum VLDL, serum triglyceride, serum cholesterol /HDL, serum LDL/ HDL was significantly more in group II as compared to group I. Serum estradiol and serum HDL was significantly more in group I as compared to group II. (Table 1)

Higher prevalence of cardiovascular risk factors was seen in group II as compared to group I. Women with serum estradiol levels <40 pg/ml were significantly higher in group II as compared to group I.(Table 2)

For both the groups, association was studied between cardiovascular risk factors and serum estradiol levels. Higher levels of serum cholesterol, serum LDL, serum triglycerides and low levels of serum HDL showed significant association with lower serum estradiol levels. In group II higher waist hip ratio, serum cholesterol, serum triglyceride and low serum HDL were significantly associated with lower serum estradiol levels. (Table 3)

This study also analyzed correlation of serum estradiol levels

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and different cardiovascular risk factors. In group I, a significant and mild inverse correlation of serum estradiol was observed with serum cholesterol, inverse moderate correlation of serum estradiol was observed with serum LDL, serum VLDL, and serum triglyceride, a strong positive correlation of serum estradiol was observed with serum HDL whereas a strong inverse correlation of serum estradiol was observed with serum cholesterol/HDL and serum LDL/HDL. All other correlations were weak and not significant statistically. In group II all correlations of serum estradiol except with serum VLDL and serum triglyceride were significant statistically. Weight, serum cholesterol/HDL and serum LDL/HDL had a mild inverse correlation with serum estradiol. BMI, diastolic blood pressure, waist hip ratio had a moderate inverse correlation with serum estradiol while systolic blood pressure, serum cholesterol and serum LDL had a strong inverse correlation with serum estradiol. Serum HDL had a perfect correlation with serum estradiol. (Table 4)

Table 1
Distribution of parameters for cardiovascular risk factors in both the groups

Parametres	Group I (premenopausal)	Group II (postmenopausal)	P value
Mean BMI (kg/m^2)	24.01±3.635	24.42±2.195	0.496
Mean WHR(waist hip ratio)	0.83±0.051	0.81±0.064	0.105
Systolic BP (in mm Hg)	122.16±10.47	131.28±7.67	<0.001
Diastolic BP (in mm Hg)	79.56±5.23	84.32±4.97	<0.001
Serum Cholesterol (mg/dl)	187.49±21.85	190.88±37.93	0.585
Serum LDL (mg/dl)	103.71±24.89	109.05±33.10	0.365
Serum VLDL (mg/dl)	19.18±8.21	31.98±13.57	<0.001
Serum HDL(mg/dl)	64.60±14.71	51.37±11.69	<0.001
Serum Triglyceride (mg/dl)	144.20±14.37	163.07±52.46	0.016
Serum Cholesterol/HDL	3.12±1.13	3.81±1.05	0.002
Serum LDL/HDL	1.78±0.93	2.26±1.21	0.026
Serum Estradiol (pg/ml)	69.77±22.61	42.82±17.78	<0.001

Table 2
Comparison of different cardiovascular risk factors in both the groups

S no	Parametres	Group I (n=50)		Group II(n=50)		P value
		No.	%	No.	%	
1.	BMI > 25 kg/m^2	10	20	21	42	0.017
2.	Waist Hip Ratio >0.81	22	44	29	58	0.161
3.	Hypertension (>=140/90 mm Hg)	2	4	11	22	0.007
4.	Serum Cholesterol >200mg/dl	13	26	18	36	0.280
5.	Serum LDL >100 mg/dl	15	30	27	54	0.015
6.	Serum HDL <50 mg/dl	8	16	26	52	<0.001
7.	Serum Triglycerides>150mg/dl	12	24	24	48	0.012
8.	Presence of any one of the above	21	42	39	78	<0.001
9.	Presence of two or more of the above	18	36	31	62	0.02
10.	Serum estradiol (<40 pg /ml)	4	8	27	54	<0.001

Table 3 - Association between cardiovascular risk factors and mean serum estradiol levels in both the groups

	Cardiovascular risk factor	Group I			Group II		
		No. of subjects	Mean estradiol levels	P value	No. of subjects	Mean estradiol levels	P value
1.	BMI (kg/m^2)						
	18.0-25.0	40	71.84±22.53	P=0.197	29	51.86±22.54	P=0.626
	>25.0	10	61.46±22.08		21	25.9±22.08	
2.	WHR						
	<=0.81	22	66.19±17.82	P=0.327	29	49.26±18.11	P=0.002
	>0.81	28	72.58±25.74		21	33.92±13.12	
3.	Hypertension						
	no	48	69.83±22.71	P=0.414	39	40.4±17.04	P=0.878
	yes	2	68.30±28.43		11	39.51±16.65	
4.	Serum cholesterol						
	<200 mg/dl	37	77.82±19.76	P<0.001	32	47.44±17.54	P=0.013
	>= 200 mg/dl	13	46.86±12.21		18	34.60±15.43	
5.	Serum LDL						
	<=100 mg/dl	35	78.81±19.86	P<0.001	23	53.5±16.88	P=0.607
	>100 mg/dl	15	48.67±12.29		27	33.72±12.95	
6.	Serum-HDL						
	>=50 mg/dl	42	75.26±20.08	P<0.001	24	48.14±20.61	P=0.041
	<50 mg/dl	8	40.95±9.42		26	37.91±13.28	
7.	Serum Triglyceride						

	<= 150 mg/dl	38	77.36±19.64	P<0.001	26	52.91±18.30	P<0.001
	>150 mg/dl	12	45.72±12.23		24	32.68±10.14	

Table 4

Bivariate correlation of serum estradiol levels and different cardiovascular risk parameters in group I and group II

Independent variable	Serum Estradiol			
	Group I		Group II	
	"r"	"p"	"r"	"p"
Body weight	-0.091	0.530	-0.30	0.037
BMI	-0.066	0.649	-0.596	<0.001
Systolic BP	-0.273	0.055	0.911	<0.001
Diastolic BP	-0.013	0.928	-0.611	<0.001
WHR	0.068	0.638	-0.533	<0.001
Serum Cholesterol	-0.30	0.037	-0.743	<0.001
Serum LDL	-0.596	<0.001	-0.730	<0.001
Serum HDL	0.911	<0.001	1.000	<0.001
Serum VLDL	-0.611	<0.001	-0.165	0.252
Serum Triglyceride	-0.533	<0.001	-0.130	0.368
Serum CHO/HDL	-0.743	<0.001	-0.459	0.001
Serum LDL/HDL	-0.730	<0.001	-0.414	0.003

DISCUSSION

Estradiol, secreted by ovary is one of the important female sex hormones which has a role not only in ovulation and reproduction but also has an important role to play in other body functions and lipid metabolism, which affects the serum cholesterol and lipoprotein levels thereby indirectly having a role in cardiovascular health.

The difference was statistically significant for two groups with regard to systolic and diastolic BP as also seen in study by Shefali pandey et al [4]and Ramin Heidari et al[5]. Studies have provided a conflicting set of evidences between menopausal status and blood pressure probably because blood pressure is an interplay of not only serum estradiol but also other multiple mechanisms both genetic and non genetic [6]including hormonal influences on vascular tone and remodelling , the renin angiotensin system, and oxidative stress[7]. Women in their premenopausal period have lower blood pressure than men of same age; however blood pressure begins to increase in post menopausal phase. Early onset of menopause and longer duration of post menopausal period are associated with higher blood pressures [8], also hypertension is seen more frequently in women with hypoestrogenic states [9, 10]. SWAN study [11], Chin Shan community cardiovascular cohort study [12] failed to find any relationship between hormonal changes during menopausal transition and blood pressure. However, Healthy Women study[13] observed that increases in blood pressure were greater during postmenopause than in perimenopausal period, which is similar to our study.

Perhaps the strongest evidence linking menopause with adverse changes in cardiovascular risk is that suggesting proatherogenic changes in lipid profile. In present study, all lipid profile markers were found to be raised significantly in group II as compared to group I except Serum HDL which was found to be lower. Also serum estradiol was significantly more in perimenopausal group compared to postmenopausal group. Similar findings were found in study by Bhagya et al[14]. The decrease in HDL after menopause can be attributed to hormonal changes. Serum HDL decreases and LDL cholesterol increases after menopause, HDL/LDL and HDL/Cholesterol decreases with age attributable to decrease in estradiol. The best indicator of developing atherosclerotic heart disease is ratio of plasma LDL to HDL, lower the ratio lowers the risk. A high level of LDL (bad cholesterol) in plasma is associated with increased deposition of cholesterol in arterial wall and higher incidence of heart attacks while reverse effects are seen with HDL (good cholesterol). J.C. Igweh et al [15] reported significant reduction in HDL, VLDL and significant increase in LDL in postmenopausal women. Okonofua et al [16]reported that for any 1 mg/dl increase in HDL-C, there is a 3% decrease in risk of coronary artery disease and 4.7% decrease in risk of mortality from cardiovascular disease. In Chin Shan community cardiovascular cohort study [12] total cholesterol was the only lipid which changed significantly from premenopausal to postmenopausal group. SWAN study[11] showed that changes in lipids during early stage of menopause transition were minimal, with total cholesterol, LDL cholesterol, and triglycerides peaking during late perimenopause and early postmenopause. HDL levels also peaked during late perimenopause and early postmenopause but leveled off thereafter. Thus, based on present study and other available studies it can be suggested that adverse changes in lipid profile occur from perimenopause to postmenopausal phase, consequently, increasing the cardiovascular risk.

In present study on an average group I women had significantly less risk factors for CHD as compared to group II as also seen in study by F.A. Tremollieres et al [17].

In the present study on bivariate analysis we found significant and mild inverse correlation between serum estradiol and diastolic blood pressure, serum cholesterol, serum LDL and serum triglyceride. Further there was significant and moderate inverse correlation between serum estradiol and systolic blood pressure, serum VLDL, serum Cholesterol/HDL and serum LDL/HDL. Strong positive correlation was observed between serum estradiol and serum HDL. These findings are also supported by study by AAS Majumdar et al [18] who showed serum estradiol as a strong predictor of coronary artery disease. Irene Lambrinoudaki et al [19] observed that high endogenous estradiol was related to pro atherogenic lipid profile in post menopausal women. However in present study lower serum estradiol levels were associated with cardiovascular risk factors like increased CHO/HDL, waist hip ratio and increased LDL/HDL ratio suggesting usefulness of serum estradiol as a predictor for cardiovascular outcome.

CONCLUSIONS

On basis of present study and previous studies, menopausal transition represents a time of substantial adverse changes in cardiovascular risk factors for women. Women and their clinicians should be aware of these risk factors and steps to control them at an earlier stage may decrease the future risk of cardiac disease. Our study had its limitations because of small sample size. Larger studies are needed to evaluate the cardioprotective effect of estradiol on cardiovascular status and also to evaluate the role of hormone therapy in decreasing cardiovascular risk.

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