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Original research article

Correlation of homocysteine with lipid profile in pre & post-menopausal women

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Abstract

In Premenopausal women the levels of reproductive hormones are variable and the effects of hormonal withdrawal are present and they may have menstrual cycles which may be regular or irregular. Perimenopause or menstrual transition is the period preceding the menopause characterized by irregular menses and missed cycles which is associated with increase in follicle stimulating hormone levels (> 20 IU/mL). The clinical data pertaining to all patients were recorded as per proforma. A detailed history was taken pertaining to last menstrual period, year of menopause, history of diabetes mellitus, hypertension, cardiac events, and drug intake. The study showed the positive correlation of plasma homocysteine with TC, LDL, VLDL, TG in postmenopausal and premenopausal women and negative correlation of plasma homocysteine with HDL.

Keywords: Homocysteine, lipid profile, pre & post-menopausal women

Introduction

The global burden of cardiovascular disease is increasing rapidly and it is the leading cause of death in women around the world. Cardiovascular disease develops 7 to 10 years later in women than in men. The life expectancy is longer in women when compared to men. The larger proportion of the elderly population is constituted by women and they are more prevalent for CVD [1].

In Premenopausal women the levels of reproductive hormones are variable and the effects of hormonal withdrawal are present and they may have menstrual cycles which may be regular or irregular [2].

Perimenopause or menstrual transition is the period preceding the menopause characterized by irregular menses and missed cycles which is associated with increase in follicle

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stimulating hormone levels (> 20 IU/mL) [3].
Menopause is a normal physiological process that marks the end of a women's reproductive life. Complete absence of menstrual cycle over a period of one year defines that a woman has attained menopause. The median age at menopause is around 50 in Western industrialized societies. In United States it is around 49.8, in Britain it is 50.8 and in South Africa 48.7. Black women in South Africa and United States attain an earlier menopause than white women. The median age in subcontinent is around 44 years. Many factors determine the age at menopause, nutrition, however is important. The reason for Indian women attaining early menopause could be due to insufficient nutrition [4].
Parity, nutrition, race and smoking are some of the factors that influence the age at menopause by at most three years either side of normal median age. Almost all the women, who attain menopause, experience the erratic changes that occur in body as the female reproductive hormone declines and characterized by "hot flush", mood change, elevation in the blood pressure and subsequently signs and symptoms of cardiovascular disease [5, 6].

Methodology

Inclusion criteria

Confirmed post-menopausal women who are attending the Gynecology outpatient department were included in the study as cases.
Regular menstruating pre-menopausal women were included in the study as controls.

Exclusion criteria

- Known case of hypertension.
- Obesity.
- Known case of diabetes mellitus.
- Known case of cardiovascular disease.
- Known case of hepatic, metabolic and renal disease
- Any neoplasia.
- Arthritis or any other inflammatory disease.
- And those who are on hormone replacement therapy or lipid lowering drugs.
- Subjects with history of surgical menopause.

Sample size

Total 96 samples has been derived by calculating alpha and beta errors using the formula
$N= (z\alpha+ z\beta)^2 \times S^2 \times 2 \div d^2$

Where
S = standard deviation.
d = difference.

- 48 pre-menopausal women as controls.
- 48 post-menopausal women as cases.

The clinical data pertaining to all patients were recorded as per proforma. A detailed history was taken pertaining to last menstrual period, year of menopause, history of diabetes mellitus, hypertension, cardiac events, and drug intake.

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Collection of blood samples

After getting the informed consents from the subjects, 2.5ml of fasting blood samples were collected for lipid profile in a plain vacutainer tube and 2.5 ml of blood sample were collected in EDTA tubes for homocysteine estimation. This however, was done after the 7th day of the last menstrual period for premenopausal group.
Samples were centrifuged at 3000 rpm to separate serum and plasma for the analysis of lipid profile and homocysteine estimation.
The following methods were used for the analysis of lipid profile parameters and homocysteine estimation.

1. Total cholesterol by enzymatic CHOD-PAP method.
2. Triglycerides by enzymatic GPO-PAP method.
3. HDL cholesterol by direct method.
4. LDL cholesterol by Friedwald's formula.
5. VLDL cholesterol by using formula = Triglycerides/5.
6. Total plasma homocysteine levels by enzymatic method.

Data collected was entered in MS Excel 2010 and analyzed using SPSS version 18. Descriptive statistics like percentage, mean and standard deviation are applied for the analysis. Inferential statistical tests like student t test were applied to compare the means between two groups.

Results

Table 1: Correlation of Homocysteine with lipid profile in post-menopausal women

	Post-menopausal women Correlation coefficient(r)	**P-value**
Total Cholesterol	0.027	0.8
HDL	-0.085	0.9
LDL	0.032	0.93
VLDL	0.017	0.99
TG	0.018	0.99

Table 2: Correlation of Homocysteine with lipid profile in pre-menopausal women

	Pre-menopausal women Correlation coefficient(r)	**p-value**
Total Cholesterol	0.048	0.7
HDL	-0.15	0.28
LDL	0.053	0.71
VLDL	0.044	0.76
TG	0.049	0.73

Table 1 and table 2 showed the positive correlation of plasma homocysteine with TC, LDL, VLDL and TG in postmenopausal and premenopausal women and negative correlation of plasma homocysteine with HDL.

Discussion

Lipid profile has been extensively used around the globe as a conventional marker of cardiovascular disease by various studies. These markers display cellular lipid interaction and the physiological functions of serum lipid bearing proteins and aids in clinical decision making and the risk types. Along with this conventional marker, a newer marker helps in early prediction of risks, its types and status of morbidity. There is a need for a newer

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biomarker which can facilitate more authentic and fast diagnosis of CVD. Novel cardiovascular risk factors may play a decisive role in the early diagnosis of ischemic heart disease, especially in women with suspected myocardial ischemia, but without electrocardiographic, echocardiographic or angiographic findings. Hcy is one such marker of CVD. Not many studies have been carried out in India on homocysteine and lipid profile to assess risk factor of CVD in postmenopausal women. Hence the present study has included Homocysteine as a newer marker along with lipid profile to assess the cardiovascular risk [7].

After menopause the incidence of cardiovascular disease may be partly caused by changes in plasma lipid levels that occur following menopausal transition. The increased risk of cardiovascular disease following menopause is mainly attributed to endocrine influences on lipid profile, especially when the other risk factors such as diabetes, hypertension and obesity are ruled out or maintained under normal condition.

The global burden of cardiovascular disease is rapidly increasing and it is one of the leading causes of death in women around the world. Estrogen deficiency has been linked to the rapid increase in CVD in women who have undergone the natural or surgical menopause. Menopause is a risk factor for CVD because estrogen withdrawal has a detrimental effect on cardiovascular function and metabolism. The menopause compounds many traditional cardiovascular disease risk factors (CVRFs), including changes in body fat distribution from a gynoid to an android pattern, reduced glucose tolerance, hyperhomocysteinemia, abnormal plasma lipids, increased blood pressure, increased sympathetic tone, endothelial dysfunction, and vascular inflammation [8].

Increase in plasma homocysteine level is one of the risk factor for cardiovascular disease and many studies have strongest epidemiological evidence for a clear association between Hyperhomocysteinemia and vascular risk.

Reduction in the estrogen production level in the ovaries after menopause results in derangement in the lipid profile and Hyperhomocysteinemia resulting in increased risk of cardiovascular diseases.

A study by Giardina EG showed that more than 450,000 women succumb to heart disease annually and 250,000 die of coronary heart disease [9].

Trudy L Bush in his epidemiological study on “Cardiovascular disease in postmenopausal women” showed that older women die of CVD than men do, although at every age, women have lower rates of CVD than men. In 1986 in the United States, 337,024 women compared to 333,348 men died from ischemic heart disease or cerebrovascular disease [10].

A study conducted by Fernandez Miranda *et al*. showed that in post-menopausal women increased homocysteine concentration together with hypercholesterolemia will contribute to the raise of their cardiovascular risk [11].

Another study by Ozkan Y *et al*. [12] showed that post-menopausal women had higher total homocysteine and total cysteine levels than premenopausal women among the controls

A study carried out by Masse P G *et al*. [13] stated that mean fasting plasma total homocysteine concentration of post-menopausal group was 2 fold higher than the value found for control group, thus post-menopausal women are exposed to higher plasma homocysteine concentration and deleterious cardiovascular effects.

Two meta-analyses of observational data demonstrated that by lowering the plasma homocysteine levels cardiovascular disease risks also reduced. Wald *et al*. evaluated 20 prospective studies and concluded that lowering homocysteine concentration by 3µmol/l decreased the risk of ischemic heart disease by 16% and stroke by 24% [14].

A second meta-analysis of 18 retrospective and 12 prospective studies determined that a 25% reduction in homocysteine levels was associated with an 11% lower ischemic heart disease risk and a 19% lower stroke risk.

A comparative study by Dr Maulik S. Varu *et al*. [15] showed that mean level of serum total cholesterol and serum LDL were significantly higher in post-menopausal women and levels

significantly increase with increase in the duration of menopause, while the serum level HDL were significantly lower in post-menopausal women and level significantly decreased with increase in duration of menopause.

Conclusion

The study shows the positive correlation between homocysteine and altered lipid profile in pre and postmenopausal women. All these alteration may be because of decrease in estrogen level in postmenopausal women.

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