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Original article

Prediction Of 10 –Year Risk Of Cardiovascular Disease In Post-Menopausal Women In South India.

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ABSTRACT

Background: Menopausal health in our social environment have received minimal awareness among women. Dyslipidaemia, which has been more prevalent among postmenopausal women have made them more susceptible to cardiovascular risks. Objective: To estimate serum lipid profile and atherogenic index of plasma in postmenopausal women compared with premenopausal women. Material and methods: This case control study involved 50 postmenopausal women (cases) aged between 50 -70 years and 50 pre-menopausal women (controls) aged between 30–40 years. Total cholesterol (TC), and their sub fractions: high density lipoprotein cholesterol (HDL-C), very low density lipoprotein cholesterol (VLDL- C), low density lipoprotein cholesterol (LDL-C) and triglycerides (TG) were analysed. Atherogenic index of plasma (AIP); log (TG/HDL –C) was calculated and compared between the cases and control group. These parameters were also compared with 5 yrs post menopausal and 10 yrs postmenopausal women, to assess the cardiovascular risks with increasing years. Results: There was statistically significant increase in TC, TG, LDL-C, VLDL-C and AIP with p value: <0.05 and decrease in HDL-C in postmenopausal women compared with premenopausal women. There was statistically significant derangement of lipid subfractions as the duration of menopause increased. Conclusion: Menopause, undoubtedly alters lipid profile. Atherogenic index of plasma being triglyceride based index definitely can add significant value in assessing atherosclerosis and cardiovascular risks in postmenopausal women.

Introduction

Menopause, is a natural event in the reproductive cycle in all women characterized by cessation of menstrual cycles due to depletion of ovarian follicular reserve. The median age for the final menstrual period is about 51 years, when the oestrogen production is significantly reduced1.Decreased oestrogen during and after menopause have significant impact on physical, psychological and social wellbeing of the woman2.The anti-atherogenic effect of oestrogens and the protection against cardiovascular diseases in women are well established1.There are numerous evidences to indicate that menopause is associated with altered lipid profile such as low high density lipoproteins cholesterol (HDL-C),higher low-density lipoproteins cholesterol (LDL-C) and triglyceride levels(TG)3,central adiposity4, increased diastolic blood pressure5, insulin resistance6 and increased risks of cardiovascular diseases. Many studies have also demonstrated that positive correlation between body mass index and dyslipidaemia as a contributing factor for the development of atherosclerosis and cardiovascular risks6-8. Altered lipid metabolism or dyslipidaemia leads to deposition of fat in the sub endothelium of blood vessels which causes atherosclerosis and coronary artery diseases9. Various studies have been done on the relationship of TG and HDL-C and the ratio of TG to HDL-C have been shown as a strong predictor of myocardial infarction10. Dobisová M suggested Atherogenic Index of plasma, calculated using the formula log (TG/HDL)11 to be better indicator of atherosclerosis. This study aimed to calculate atherogenic index in premenopausal and postmenopausal women from the serum levels of total cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), very low density lipoprotein cholesterol (VLDL-C).

Materials and Methods:

Study design and participants : This case control study involved 50 postmenopausal women (cases) aged between 50 – 70 years and 50 premenopausal women (controls) aged between 30–40 years who came for master health check-up in Trichy Medical College Hospital & Research Centre, Irungalur, Trichy. The study period was for a period of 6 months from May 2017 to Nov 2017. Informed written consent was obtained from the study group. Institutional ethical committee clearance was obtained.

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Exclusion criteria: Those women with history of menstrual disorders were excluded. Other exclusion criteria includes obesity, diabetes mellitus, hypertension, renal diseases, those who had undergone surgical removal of ovaries, hormonal contraception and pregnancy.

Data collection:

A detailed history was elicited for diabetes mellitus, hypertension, renal diseases, menstrual irregularities, surgical removal of ovaries, intake of contraceptive pills and pregnancy. Clinical examination which included weight, height, pulse, systolic and diastolic blood pressure were measured. Systemic examination was done to exclude hepatic and renal pathology.

Sample collection and biochemical measurements

Blood samples were collected after 12-h overnight fasting, and biochemical parameters such as fasting blood glucose (FBG) was estimated by Hexokinase method, and serum levels of urea by Glutamate dehydrogenase method, creatinine by modified Jaffe's method, total cholesterol by cholesterol oxidase –peroxidase method, triglycerides by Glycerol 3-phosphate oxidase method, high-density lipoprotein cholesterol by direct enzymatic method, low density lipoprotein cholesterol by direct enzymatic method, in a fully automatic analyser. Very low- density lipoproteins cholesterol was derived based on the formula: VLDL-C = TG/5.

The atherogenic index of plasma (AIP) was calculated as the logarithmically transformed ratio of concentrations of TG to HDL-C by the formula log (TG/HDL –C)12.

Statistical analysis:

Analysis was done using SPSS VERION 23. (IBM SPSS Inc.,Chicago,Illinois,USA) Results were presented as mean ± SD. The Student t test was used for comparison of quantitative variables. Analysis of variance (ANOVA) was done for multiple comparisons among variables. P values less than or equal to 0.05 were considered as significant.

Results:

The mean, standard deviation of clinical and biochemical parameters were depicted in Table 1 .The mean age, BP, fasting blood glucose, urea, creatinine was estimated to fulfil the exclusion criteria in the study population.

There were statistically significant increase ($P<0.05$) in TC, TG, LDL-C and VLDL-C in the postmenopausal women compared to premenopausal women. There was decrease in HDL-C in the postmenopausal women when compared to the premenopausal women with p value being insignificant. This difference in lipid profile and AIP was more significant with 5 yrs post menopausal and 10 yrs postmenopausal women with more risks with increasing years.

The AIP (log TG/HDL-C) was 0.67± 0.24 in post-menopausal women which significantly higher than 0.47±0.25 in premenopausalwomen.($p<0.05$).

(5.04%). In the present survey 120 (86.33%) participants were residing in their own houses while 19 (13.67%) were residing in rented houses. Regarding employment status of the women, 66 (47.48%) were in some or other employment and remaining 73 (52.52%) were home makers. According to modified Kuppuswamy classification for socioeconomic status (SES), 27 (19.42%) belonged to class I, 70(50.36%) were from class II, 25(17.99%) were from class III, 16(11.51%) belonged to SES class IV,and 1(0.72%) participant was from SES class V.The respondents were asked to mention few reasons which lead to non-utilization of public health care facilities. The common reasons that were given by the study participants are shown in table 1.

The study questionnaire also included statements related to problems faced at the public health care facilities acting as barriers for their utilization. These barriers were grouped as those related to health care delivery, general care delivery, and medical care delivery. The response of the study participants about problems related to health care delivery are represented in figure 2.

Lack of personal attention in public health facilities as opted by 69.78% study participants was noted to be the prime problem faced while accessing health care delivery. The next problem related to health care at public health facilities was lack of co-operation by the hospital staff as perceived by 35.25% respondents. These were followed by poor quality of treatment and inhospitable attitude of the hospital staff as considered by 28.78% respondents for each. Apart from all these, corrupt practices followed by some paramedical staff at public health care facilities was also a problem according to 20.86 % study participants. The next group of problems faced was categorized related to general care delivery which is presented graphically in figure 3.

As obvious from figure 3, poor sanitation at public health facilities emerged as an important factor as perceived by 64.03 % of the females in the study. Poor surroundings and ineffective hospital administration were the other problems related to general care delivery at the public health care facilities in view of 51.08 % and 42.45% respondents respectively. The multiple response type question also had statements regarding no respect to the patients and uncommitted paramedical and labour staff which were chosen as a problem perceived by 34.53 % and 25.18 % study participants respectively.

Under the heading of medical care delivery related problems that can be possibly faced at public health facilities, a total of five statements were placed. Lack of modern technology was perceived as a problem by 81(58.27 %) study participants. Similarly, lack of well-furnished and equipped rooms was perceived as problem according to 81(58.27%). Other medical care related problems viz. lack of medical facilities, less building capacity, and location at inconvenient places were perceived by49 (35.25%), 46 (33.09%), and 22 (15.83%) women respectively (see figure 4).

Table 1 Distribution of clinical and biochemical parameters

Variables	Premenopausal (n=50)	Postmenopausal (n=50)	P value
Age	31±5	57±3	0.00*
BMI	23.2±2.1	22.4±2.4	0.17
Systolic BP(mmHg)	121±3	123±6	0.107
Diastolic BP(mmHg)	70±8	80±5	0.06
FBG(mg/dl)	79±9	88±7	0.89
Urea (mg/dl)	27±5	26±6	0.25
Creatinine (mg/dl)	0.6±0.3	0.7±0.3	0.814
TC(mg/dl)	146.81±24.58	202.70±20.08	0.000*
LDL-C(mg/dl)	88.08±19.59	126.75±25.92	0.001*
HDL-C(mg/dl)	41.52±10.52	35.85±10.14	0.061
TG(mg/dl)	125.00 ±50.35	188.50 ±87.63	0.008*
VLDL-C(mg/dl)	21.46±7.31	38.75±13.81	0.001*
AIP	0.47±0.25	0.67± 0.24	0.0091*

* p < 0.05 statistically significant

Fig 1 Bar chart showing distribution of lipid profile and AIP among the study group

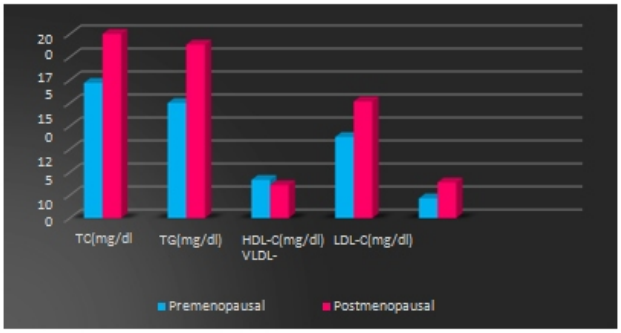
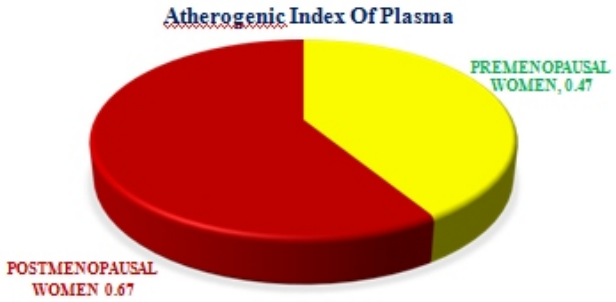


Fig 2 Pie Chart showing distribution of AIP among the study group



The mean, standard deviation of TC, and its sub-fractions in premenopausal, 5 years postmenopausal and 10 years postmenopausal women are presented in table 2.

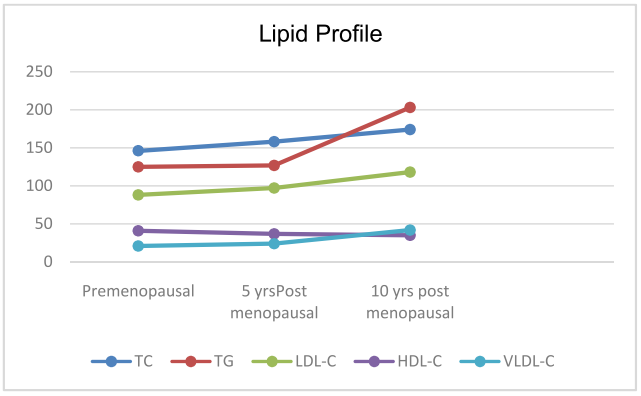
Table 2 Showing lipid profile and duration of menopause

Parameters	Premenopausal(n=50)	5 years Postmenopausal(n=26)	10 years Postmenopausal(n=24)	P value
TC(mg/dl)	146.81±24.58	158.82±24.31	174.89±18.02	0.117
LDL-C(mg/dl)	88.08±19.59	97.18±17.86	118.0±27.69	0.04*
HDL-C(mg/dl)	41.52±10.52	37.17±7.78	35.33±10.31	0.646
TG(mg/dl)	125.00 ±50.35	127.33±36.95	203.20±56.14	0.001*
VLDL-C (mg/dl)	21.46±7.31	24.27±5.66	42.0±9.02	0.000*
AIP	0.47±0.25	0.49±0.16	0.74±0.24	0.01*

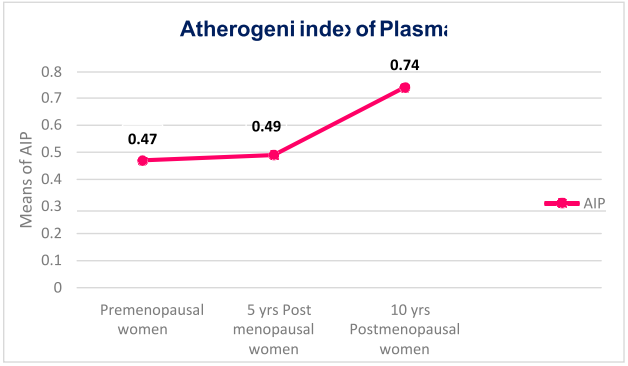
* p < 0.05 statistically significant

Apart from a decrease in HDL-C that was insignificant (p:0.64), there were statistically significant increase in other lipid sub fractions and AIP with the duration of menopause (p<0.05)

Fig 3 Lipid profile in 5 yrs and 10 yrs postmenopausal women



Means of AIPFig 4 ANOVA Means Test



Discussion:

The peril of non-communicable diseases have encroached both developed and developing countries and cardiovascular diseases, one of the significant non-communicable disease, have solely attributed for 30% of deaths worldwide in 2005 only13.Coronary Artery Disease (CAD) is more prevalent among men than women upto the age of 50 years but after 50 years this incidence is overturned causing increased prevalence

of CAD in women14. Most probable reason behind this could be the loss of cardio protective effect of oestrogen which is slowly downturned in women after menopause. Therefore, it necessitates screening of every women undergoing menopause for early diagnosis and prevention of CVD.

This cross-sectional study had emphasized comparison of the lipid profile pattern between pre and postmenopausal women. The study also highlights the atherogenic indices between two groups. The study was carried out in 100 apparently healthy women; among them 50 were premenopausal and 50 were postmenopausal. The average age of premenopausal group was and 31±5 that of postmenopausal group was 57±3.

In this present investigation, t here were statistically significant increases in TC, TG, LDL, VLDL and AIP (p :<0.05)when post-menopausal women were compared to their premenopausal counterparts. There was also a decrease in the HDL of postmenopausal women (p: 0.064) when compared to the premenopausal counterparts. These results were consistent with the study conducted by Ifueko in 2013, in which TC, TAG, and LDL-C were increased significantly with " value < 0.001 in postmenopausal women than in premenopausal women15.

Derby et al. (2009), in his study showed a result of significant increase in TC and LDL-C while TAG was increased non significantly and there was no changes in HDL-C in postmenopausal women when compared to premenopausal women16. A study done by Peters et al. in 1999 found significantly increased TC and LDL-C but the increase in TAG and HDL-C was nonsignificant in postmenopausal women than in premenopausal women17. This controversy in the level of HDL-C in postmenopausal women is attributed by the authors to variation in study population, life style interventions, and duration of menopause. Most studies showed significant increase in LDL cholesterol levels. This absolute increase in LDL-C may be due to the decrease in oestrogen that stimulates the synthesis of LDL receptor which directly causes reduction of LDL receptor after menopause.

The atherogenic indices obtained in the present study showed TC/HDL with average of 0.47 in premenopause and 0.67 in postmenopausal women. The elevated TC, LDL-C and atherogenic index in postmenopausal women in this study has been attributed to hormonal changes associated with menopause i.e. low plasma levels of oestrogen and marked increase in luteinizing and follicle stimulating hormone levels which exerts a significant effect on the metabolism of plasma lipids and lipoproteins18 . The increase in cardiovascular risks may be associated with alterations in the lipid profile characterized by increased triglycerides and low HDL-C levels. The atherogenic link between high triglycerides and HDL-C is due to the higher plasma concentration of triglyceride rich, very low-density lipoprotein that generates small, dense LDL-C during lipid exchange and lipolysis. These LDL-C particles accumulate in the circulation and form small, dense HDL-c particles, which undergo accelerated catabolism, thus closing the atherogenic circle19. Protasio et al., explained that ratio of triglycerides to HDL-C was found to be a powerful independent indicator of extensive coronary disease20.

The lower TC, LDL-C and atherogenic index levels of the premenopausal women in this study could be explained by the anti-atherosclerotic action of oestrogen which maintains high level of HDL-C and low level of LDL-C and TAG. There is mass clearance of LDL-C from the plasma results probably from accelerated conversion of hepatic cholesterol to bile acids and increased expression of LDL receptors on cell surfaces. Increase in production of apolipoprotein A-I and decrease in hepatic lipase activity facilitate increase of HDL-C. Oestrogen hormone regulates mRNA production for specific proteins of lipid metabolism such as lipoprotein lipase (LPL) and hormone sensitive lipase (HSL) and reduces the synthesis of apoB-100, specific for LDL-C in adipose tissue21.Thus pre-menopausal women have lower cardiovascular risks than post-menopausal women.

The duration of menopause, in this study, also had impact on the lipid profile with statistically significant increase in the TG, LDL-C and atherogenic index ($p<0.05$) and decrease in HDL-C. ($p<0.05$). These results were consistant with the results of the study by Nwagha et al. in 2010 about lipid profile and atherogenic index in postmenopausal women22. Derby et al and Pansini F et al in their study showed increase in HDL-C with the duration of menopause suggesting HDL-C is not only dependent on menopausal status but also on other factors like weight gain and other associated metabolic disorders16, 23 .

The results of this present study showed higher levels of lipid profile and atherogenic index in postmenopausal women compared with pre-menopausal women. Still, further longitudinal studies with large sample size are needed to corroborate and confirm these results.

Conclusion:

This present study revealed altered lipid profile and higher atherogenic index in postmenopausal women compared to pre-menopausal women. The Atherogenic Index of Plasma, which can be easily calculated from the standard lipid profile values, act as an adjunct that significantly adds predictive value for the development of cardiovascular diseases than the individual lipid profile values and other ratios like TC/HDL-C, LDL/HDL-C. AIP can be used for routine screening for CVD in women undergoing menopause along with dietary interventions and increased physical activity.

Limitations:

The limitation of the study is small-sample size and single-centered study. Due to logistic and socioeconomic difficulties, follow up of the subjects with dyslipaedimia was not done to ascertain the percentage who developed athersclerosis. Larger, community-based prospective multi-centric studies, with follow up of the study group are needed to further assess whether AIP could be used as a valuable tool to predict the risk of CVD.

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