Original Article

Association of serum lipid profile, body mass index and atherogenic index with cognitive functions in postmenopausal women

R. Kavitha[1], R. Sudha[2], Evangeline Jones[3]

[1]Postgraduate, [2]Assistant professor, [3]Professor and Head of the Department, Department of Biochemistry, Vinayaka Missions Kirupananda Variyar Medical College, Salem, Tamil Nadu, India

ABSTRACT

Background: Cognitive dysfunction has increased in menopausal women, which indicate the initiation of dementia. Body mass index (BMI) have been shown to influence brain development in relationship to early and late measures of cognitive function. A strong interaction between brain areas is involved in cognitive, emotional, and metabolic regulatory functions controlling body weight. **Aim:** To assess serum lipid profile, BMI, atherogenic index of plasma (AIP) and cognitive functions in postmenopausal women and to correlate the serum lipid profile, BMI, AIP with cognitive functions in postmenopausal women. **Methodology:** A cross-sectional study was carried out with 40 premenopausal and 40 postmenopausal at the gynecological outpatient department of Vinayaka Missions Kirupananda Variyar Medical College, Salem. For all the study subjects, the lipid parameters were measured using the standard kits and the cognitive assessment was done by Addenbrooke's cognitive examination (ACE) - ACE-revised (ACE-R). ACE and its revised version (ACE-R) which includes five domains for assessing the mini mental status. **Results:** The BMI, total cholesterol, low-density lipoprotein, triglycerides and AIP were significantly a higher among the post-menopausal women when compared to the premenopausal women ($P < 0.05$). Similarly, the high-density lipoprotein levels were lower in the study group when compared to the control group. All the cognitive parameters including the ACE-R total and the mini mental scale examination score were comparatively higher in the premenopausal women than the post-menopausal and the difference was found to be statistically significant ($P < 0.05$). **Conclusion:** Altered lipid levels have a definite association with decreased cognitive abilities in postmenopausal women. Interventions to lower the lipid levels may be a potential strategy for prevention of cognitive impairment.

Key words: Atherogenic index, Body mass index, Cognitive function, Post-menopausal women

INTRODUCTION

Menopause means permanent cessation of menstruation at the end of reproductive life due to loss of ovarian follicular activity.[1] The effect of the hormonal changes associated with menopause on the serum lipid levels play an important role in most cardiac related disorders associated with menopause.[2] Up to the age of 50 years, the prevalence of coronary artery disease (CAD) among women is lower than among men, but the incidence rises significantly after the menopause. The incidences of coronary heart disease have been observed to be increased in post-menopausal women until they become similar to the corresponding rates in men of similar age.[3] Multiple risk factors have been identified as contributory to the development of CAD. The loss of estrogen often causes marked physiologic changes in the function of the body. Due to the interplay of other hormones and the effect that estrogen has on other important risk factors, post-menopausal women are actually at a higher

Address for Correspondence:
Dr. R.Kavitha, Department of Biochemistry, Vinayaka Missions Kirupananda Variyar Medical College Salem.
E-mail: abikavitha169@gmail.com

risk for developing cardiovascular diseases. A number of changes that occur in the lipid profile after menopause are associated with increased cardiovascular disease risk.[4] There is also derangement of lipoprotein profile independent of age.[5,6] Hypercholesterolemia is a key factor in the pathophysiology of atherosclerosis.[7] After menopause, there is a loss of ovarian function. This results in adverse changes in glucose and insulin metabolism, body fat distribution, coagulation, fibrinolysis, and vascular endothelial dysfunction. At the time of menopause, a woman must readjust her life from one that has been physiologically stimulated by estrogen and progesterone production to one devoid of these hormones.

Cognitive dysfunction has increased in menopausal women which indicate the initiation of dementia. Body mass index (BMI) has been shown to influence brain development in relationship to early and late measures of cognitive function.[8,9] A strong interaction between brain areas is involved in cognitive, emotional, and metabolic regulatory functions controlling body weight.[10] The prevention of cognitive impairment through the identification and management of risk factors is important in woman. As life expectancy increases, women in general experience a longer life after menopause. 60 million women in India are above the age of 55 years. Hence, there is a need to understand the effect of abdominal obesity, serum lipid parameters on cognitive function in postmenopausal women.

Aims and objectives

- To assess serum lipid profile, BMI, atherogenic index of plasma (AIP) and cognitive functions in postmenopausal women
- To correlate the serum lipid profile, BMI, AIP with cognitive functions in postmenopausal women with premenopausal women.

METHODOLOGY

The postmenopausal state in the present study was defined as age above 45 years and the absence of a menstrual cycle for the last 12 months. The experiment protocol was approved by Ethics Committee of the college. A cross-sectional study was carried out with 40 pre-menopausal and 40 postmenopausal women at the gynecological outpatient department of Vinayaka Missions Kirupananda Variyar Medical College, Salem. The study was conducted for a period of 6 months from May 2014 to November 2014. Each subject was briefly explained the purpose, procedure and confidentiality prior to their written informed consent. Participants were categorized into a study group (postmenopausal women) and control group (pre-menopausal women). After detailed enquiry of the medical history of the subjects, women on the oral contraceptive pill, hormonal replacement therapy, drugs that alter the cardiovascular functions were excluded from the study. Fasting venous samples (5 ml) were collected, and samples were centrifuged. Serum was separated and was analyzed colorimetrically. Total cholesterol (TC) was estimated by CHOD-PAP method.[11] Triglyceride (TG) was estimated by glucose oxidase-peroxidase method. High-density lipoproteins (HDL) were analyzed by kits (supplied by Roche Diagnostic Gmbh D-68298 Mannheim).[12] The concentration of very low-density lipoprotein cholesterol (VLDL-C) and LDL-C was estimated according to the Friedewald's equation.[13] According to Friedewald, LDL-C can be calculated as follows: LDL = TC – HDL – TG/5 (mg/dl). Cognitive function was evaluated by Addenbrooke's cognitive examination (ACE) - ACE-revised (ACE-R). ACE[14] and its revised version (ACE-R)[15] were developed as a brief test of cognitive functions. This includes the mini mental scale examination (MMSE), consists of five domains, each representing a specific cognitive function: (1) Attention and orientation (18 points), (2) memory (26 points), (3) fluency (14 points), (4) language (26 points), and (5) visuospatial ability (16 points). The total score of ACE-R is 100 points, which includes the MMSE score (30 points). Higher scores indicate better cognitive functioning.

Statistical analysis

Statistical analysis was done using SPSS version 16.0. Results were presented as a mean and Standard deviation. Test for significance was calculated using student *t*-test, and correlation analysis among variables was done using the Pearson's correlation test. The *P* value of < 0.05 was considered as statistically significant.

RESULTS

Table 1 shows the various physical and biochemical parameters measured among the study population. It is inferred from Table 1 that BMI, TC, LDL, triglycerides, and AIP were significantly higher among the postmenopausal women when compared to the premenopausal women ($P < 0.05$). Similarly, the HDL

levels were lower in the study group when compared to the control group, and the difference was found to be statistically significant ($P < 0.05$).

Table 2 shows the cognitive function assessed among the pre and postmenopausal women. It is seen from Table 2 that all the cognitive parameters except the language, the scores including the ACE-R total and the MMSE were comparatively higher in the premenopausal women than the post-menopausal and the difference was found to be statistically significant ($P < 0.05$).

Table 1: Anthropometric and laboratory data of study subjects

Variable	Mean±SD		*P* value
	Premenopausal women	Postmenopausal women	
Number	40	40	
BMI	24.5±3.33	29.9±2.42	0.032*
WHR	0.78±0.04	0.84±0.03	6.24
TC (mg/dl)	160.05±38.82	216.35±49.05	0.002*
TG (mg/dl)	175.89±55.12	161.75±52.82	0.050*
HDL (mg/dl)	47.63±4.58	46.41±5.95	0.023*
LDL (mg/dl)	74.52±36.60	87.76±30.45	0.666
AIP	0.19±0.15	0.16±0.19	0.024*

AIP: Atherogenic index of plasma, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, TG: Triglycerides, TC: Total cholesterol, WHR: Waist-hip ratio, BMI: Body mass index, SD: Standard deviation, **P* value statistically significant

Table 2: Cognitive function among the study subjects

Variables	Mean±SD		*P* value
	Premenopausal women	Postmenopausal women	
Attention	16.15±1.46	13.76±2.07	0.0004*
Memory	23.47±1.42	22.05±2.30	0.0381*
Fluency	13.47±0.77	12.11±1.61	0.0045*
Language	23.15±1.86	22.70±2.64	0.5618
Visuospatial	14.15±1.38	12.41±1.12	0.0001*
ACE-R total	83.10±5.63	71.05±11.54	0.0007*
MMSE	25.78±1.81	23.94±3.36	0.0458*

MMSE: Mini-mental scale examination, **P* value statistically significant, SD: Standard deviation, ACE-R: Addenbrooke's cognitive examination revised

Table 3: Correlation analysis of ACE-R score with the lipid profile in postmenopausal women

Parameters	r value	*P* value
TC	–0.693	0.002*
TG	–0.482	0.050*
HDL	0.549	0.023*
LDL	0.113	0.666
AIP	–0.544	0.024*

AIP: Atherogenic index of plasma, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, TG: Triglycerides, TC: Total cholesterol, ACE-R: Addenbrooke's cognitive examination revised, **P* value statistically significant

Table 3 shows the Pearson's correlation analysis for ACE-R score with the lipid profile parameters among the postmenopausal women. It is inferred from Table 3 that there was strong negative correlation for TC, TG, and AIP, that is as their level increases the ACE-R score decreases and similarly a positive correlation was observed for HDL, as its level decreases the ACE-R score decreases and both these differences were found to be statistically significant.

DISCUSSION

Menopause is a normal condition that all women experience as they age. At the physiological level, menopause happens because of a decrease in the ovaries' production of the hormones estrogen and progesterone. Estrogens have several cardioprotective mechanisms that change the vascular tone by increasing nitrous oxide production. Oestrogens stabilize the endothelial cells, they enhance antioxidant effects and alter fibrinolytic protein. All these are cardioprotective mechanisms which get lost with the onset of menopause.[7] Many estrogen actions are potentially relevant to cognitive changes occurring after menopause, but for most the clinical implications are yet unclear. Estrogen enhances synaptic plasticity, neurite growth, hippocampal neurogenesis, and long-term potentiation. The latter is a physiologic process involved in the formation of episodic memories. Estrogen protects against apoptosis and against neural injury in a variety of experimental settings, including toxicity induced by excitatory neurotransmitters, β-amyloid, oxidative stress, and ischemia.[16]

As compared to premenopausal women, mean level of total serum cholesterol and serum LDL were significantly higher in postmenopausal women whereas the serum HDL levels was significantly lower in postmenopausal women since factors affecting serum lipid profile were excluded, these changes may be related to deficiency of estrogen occurring after menopause The present study correlates well with results of Usoro *et al*.,[17] who found statistically significant increase in serum TC and serum LDL and statistically significant decrease in serum HDL after menopause. The present study also correlates with results of Igweh *et al*.,[7] who found statistically significant increase in serum LDL and statistically significant decrease in serum HDL after menopause. Lipid profile is affected by metabolic conditions and alterations in lipid metabolism that have been

implicated in atherosclerosis and coronary heart disease.[6,18] Results from this study on lipid profile in postmenopausal women indicate that menopause alters the lipid profile in women. Estrogen, one of the important female sex hormone has a role in lipid metabolism, which affects the serum cholesterol and lipoprotein levels thereby indirectly having a role in coronary heart disease. The increase in the LDL cholesterol level after menopause might be caused by decreased LDL receptor activity.[19]

The post-menopausal decrease of estrogen concentration explains the cognitive and psychic impairments observed in that period. Both clinical studies and preclinical research provide data indicating the protective role of estrogens for the cognitive functioning and the protective function of estrogens in the examined neurotoxicity models, including the neurotoxicity related to amyloid beta, as well.[20,21] Poor performance on memory tasks is common among obese individuals across the adult lifespan. Our study suggests that obesity is associated with decreased cognitive function in postmenopausal women, and the finding is in par with the study done by Nayanathara *et al*.[22] in Karnataka. The present findings are also consistent with studies demonstrating the decrements in cognitive functions in adults with increased body weight. Larger body mass requires more blood flow for optimal functioning; the brain is deprived of blood flow that it normally receives under circumstances when the body is not as large.[23,24] In turn, this lack of essential blood flow could be a contributing factor to poor cognitive performance in individuals with a larger BMI.

CONCLUSION

Altered lipid levels have a definite association with decreased cognitive abilities in postmenopausal women. Interventions to lower the lipid levels may be a potential strategy for prevention of cognitive impairment. Early detection of dementia will improve the quality of life in post-menopausal women by proper medication and lifestyle modification.

REFERENCES

1. Dutta DC. Textbook of Gynaecology.6th ed. Missouri: Elsevier; 2013. p. 55-61.
2. Do KA, Green A, Guthrie JR, Dudley EC, Burger HG, Dennerstein L. Longitudinal study of risk factors for coronary heart disease across the menopausal transition. Am J Epidemiol 2000;151:584-93.
3. Berg G, Mesch V, Boero L, Sayegh F, Prada M, Royer M, *et al.* Lipid and lipoprotein profile in menopausal transition. Effects of hormones, age and fat distribution. Horm Metab Res 2004;36:215-20.
4. Stampfer MJ, Willett WC, Colditz GA, Rosner B, Speizer FE, Hennekens CH. A prospective study of postmenopausal estrogen therapy and coronary heart disease. N Engl J Med 1985;313:1044-9.
5. Spencer CP, Godsland IF, Stevenson JC. Is there a menopausal metabolic syndrome? Gynecol Endocrinol 1997;11:341-55.
6. Bales AC. In search of lipid balance in older women. New studies raise questions about what works best. Postgrad Med 2000;108:57-60, 66, 69-72.
7. Igweh JC, Nwagha IU, Okaro JM. The effects of menopause on the serum lipid profile of normal females of South East Nigeria. Niger J Physiol Sci 2005;20:48-53.
8. Mathuranath PS, Nestor PJ, Berrios GE, Rakowicz W, Hodges JR. A brief cognitive test battery to differentiate Alzheimer's disease and frontotemporal dementia. Neurology 2000;55:1613-20.
9. Gunstad J, Lhotsky A, Wendell CR, Ferrucci L, Zonderman AB. Longitudinal examination of obesity and cognitive function: Results from the Baltimore longitudinal study of aging. Neuroepidemiology 2010;34:222-9.
10. Whitmer RA, Gunderson EP, Barrett-Connor E, Quesenberry CP Jr, Yaffe K. Obesity in middle age and future risk of dementia: A 27 year longitudinal population based study. BMJ 2005;330:1360.
11. Kaplan A, Lavernel LS. Disorder of carbohydrate. In: Clinical Chemistry: Interpretation and Techniques. 2nd ed. Philadelphia: Lea and Febiger; 1983.
12. Herbert K. Lipids. In: Kaplan LA, Pesce AJ, editors. Clinical Chemistry: Theory, Analysis and Correlation. St. Louis: C.V. Mosby; 1984. p. 1182-230.
13. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972;18:499-502.
14. Mathuranath PS, Nestor PJ, Berrios GE, Rakowicz W, Hodges JR. A brief cognitive test battery to differentiate Alzheimer's disease and fronto temporal dementia. Neurology 2000;55:1613-20.
15. Mioshi E, Dawson K, Mitchell J, Arnold R, Hodges JR. The addenbrooke's cognitive examination revised (ACE-R): A brief cognitive test battery for dementia screening. Int J Geriatr Psychiatry 2006;21:1078-85.
16. Henderson VW. Cognitive changes after menopause: Influence of estrogen. Clin Obstet Gynecol 2008;51:618-26.
17. Usoro CA, Adikwuru CC, Usoro IN, Nsonwu AC. Lipid profile of postmenopausal women in calabar, Nigeria. Pak J Nutr 2006;5:79-82.
18. Taddei S, Virdis A, Ghiadoni L, Mattei P, Sudano I, Bernini G, *et al.* Menopause is associated with endothelial dysfunction in women. Hypertension 1996;28:576-82.
19. Bonithon-Kopp C, Scarabin PY, Darne B, Malmejac A, Guize L. Menopause-related changes in lipoproteins and some other cardiovascular risk factors. Int J Epidemiol 1990;19:42-8.
20. Manly JJ, Merchant CA, Jacobs DM, Small SA, Bell K, Ferin M, *et al.* Endogenous estrogen levels and Alzheimer's disease among postmenopausal women. Neurology 2000;54:833-7.
21. Petanceska SS, Nagy V, Frail D, Gandy S. Ovariectomy and

17beta-estradiol modulate the levels of Alzheimer's amyloid beta peptides in brain. Neurology 2000;54:2212-7.
22. Nayanatara AK, Pai SR, Shetty SB, Bhagyalakshmi K, Anupama N, Kin RD, *et al*. Effect of abdominal obesity and serum lipid markers on cognitive functions in postmenopausal Indian women. World J Pharm Pharm Sci 2014;3:2106-13.
23. Manson JE, Willett WC, Stampfer MJ, Colditz GA, Hunter DJ, Hankinson SE, *et al.* Body weight and mortality among women. N Engl J Med 1995;333:677-85.
24. Ylikoski R, Ylikoski A, Raininko R, Keskivaara P, Sulkava R, Tilvis R, *et al.* Cardiovascular diseases, health status, brain imaging findings and neuropsychological functioning in neurologically healthy elderly individuals. Arch Gerontol Geriatr 2000;30:115-30.

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