Assessment of the Cardiovascular Profile in Pre- and Post-Menopausal Women: An Observational Study

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Abstract

Aim: The aim of the present study was to assess the abnormalities in the cardiovascular profile in postmenopausal women.

Material & Methods: A cross-sectional comparative study on 100 women who were either postmenopausal or premenopausal and were between the age group of 40 to 55 years was carried out over a period of ten months in the Department of Obstetrics and Gynaecology.

Results: Out of 100 women, 40 belonged to <45 years, 50 belonged to 45-52 years and 10 women belonged to >52 years. There were 15% CHD cases and 3% stroke cases based on self-reporting. Women with early menopause (<45 years) tend to have lower educational level (P for trend <0.001), and higher parity (P for trend <0.05). 16 patients had diabetes who belonged to <45 years. There was a decreased trend toward CHD presence with increasing age at natural menopause (P for trend <0.05). Each one year delay of age at menopause was associated with 3% reduction in CHD presence compared with women with menopause at ages 45−52 years. Our findings also showed a linear relationship between menopausal age and the presence of stroke (P for trend <0.001). Each one year delay in age at menopause was associated with 5% reduction in stroke presence. Women with early age at menopause (<45 years) had higher prevalence of stroke than those with menopause at ages 45−52 years after adjustment for potential risk factors. In the age adjusted model, women with later age at menopause (> 52 years) was inversely associated with presence of stroke compared with those with menopause at ages 45−52 years. However, the association was no significant when we further adjusted other confounding factors.

Conclusion: Our study demonstrated that early age at natural menopause is associated with the presence of CHD and stroke among women. The effect of menopausal age on cardiovascular disease can be taken into consideration for the prevention.

Keywords: Cardiovascular Disease; Coronary Heart Disease; Diagnostic Medicine; Medical Risk Factors; Menopause; Women's Health

Introduction

Cardiovascular disease is the leading cause of death for women. [1], accounting for 50% of cases, of which 20% are attributable to ischemic heart disease (IHD) and 13% to stroke. [2] Menopause is an important event in women's lives, possibly contributing to the development of CVD, which is associated with changes in the cardiovascular risk profile, markers of metabolic health, and subclinical atherosclerosis [3] The risk of CVD increases with the onset of menopause, and this is mainly seen among women with early menopause (EM) (i.e., when the age at menopause is <45 years) or premature ovarian insufficiency (POI), which is diagnosed if the age at menopause is <40 years). [4]

Menopausal status is associated with an increased risk for cardiovascular diseases mainly due to changes in body fat distribution, glucose metabolism, and serum lipids. [5] Traditionally, menopause is defined as the absence of menstruation with no other cause for 12 consecutive months. [6] The menopausal transition is characterized by ovarian hormone changes, menstrual cycle irregularities, and an increased risk for cardiovascular diseases. [7] Hormonal factors like the cardio protective role of estrogen are thought to be responsible. [8,9,10] Hypertension and central obesity too play a contributory role. [11,12,13] Cardiovascular risk has been shown to manifest at a lower level of adiposity and abdominal obesity in Asian Indians as compared to their Western counterparts. [14,15] Menopause is associated with a significant increase of blood pressure, body mass index (BMI), obesity, and body fat distribution. [16]

Menopause involves atherogenic changes in the lipid profile. Postmenopausal women have higher levels of total cholesterol, triglycerides, and low-density lipoprotein (LDLC), as well as reduced levels of high-density lipoprotein (HDL-C). [17] In addition, after menopause, the risk of developing metabolic syndrome (MetS) increases because of impaired glucose metabolism, weight gain, and central abdominal obesity. [17,18]

Other important factors increasing the risk of CVD in women are type 2 diabetes, hypertension, and obesity. Women with diabetes have a 1.81-fold higher risk of death from ischemic heart disease and a five-fold higher risk of heart failure than their nondiabetic counterparts. [19] Postmenopausal women are especially prone to CVD—as estrogen levels decline, so does their protective vasodilating effect and the resulting blood pressure benefits. [20] CVD is a serious problem among women entering menopause. The changing hormonal environment predisposes them to an increased risk of CVD due to the accumulation of risk factors such as visceral obesity, dyslipidemia, impaired glucose homeostasis, hypertension, and non-alcoholic fatty liver disease. Therefore, the aim of our study was to analyze the association of menopause with CVD risk factors and subclinical markers of cardiometabolic disease.

Material & Methods

A cross-sectional comparative study on 100 women who were either postmenopausal or premenopausal and were between the age group of 40 to 55 years was carried out over a period of ten months in the Department of Obstetrics and Gynaecology, NMCH, Sasaram, Bihar, India.

Inclusion Criteria

Women aged 40-55 years

Women with natural menopause

Willing to participate

Exclusion Criteria

Women with premature/surgical menopause, renal disease, liver disease, endocrine disorders including diabetes mellitus, alcohol consumption, smokers and those with collagen vascular disease as well as women taking any form of hormone replacement therapy were excluded.

Methodology

Thus, 100 patients satisfying the inclusion criteria were subjected to a detailed questionnaire (with special focus on cardiovascular risk factors and health) which included past history with reference to the duration, investigation and treatment of cardiac disease or hypertension, a history of major diseases like diabetes mellitus, tuberculosis, renal, liver diseases and other endocrine diseases. Family history of diabetes mellitus, hypertension, tuberculosis, and ischemic heart disease including angina, MI and sudden cardiac death was enquired into. A detailed menstrual history (to help rule out any premature or surgical menopause) and an obstetric history was noted; especially for any form of contraception used including oral contraceptive pills and their compositions. A thorough general examination was performed and anthropometric measurements of BMI, WHR, vitals and presence of signs of CCF and atherosclerosis were taken note of. A detailed system wise clinical examination with special attention to the cardiovascular system was done. The subjects underwent routine investigations like complete blood count, urinalysis and biochemical investigations like fasting and 2 hours post-glucose, blood glucose levels, blood urea, serum creatinine, lipid profile (total cholesterol, LDL-C, HDL-C, VLDL-C and triglyceride). Chest X-ray, electrocardiography and echocardiography were done in each of the subjects.

Results

Table 1: Characteristics of participants according to age at natural menopause

	Age at menopause			P- Value
	45 (n=40)	45−52 (n=50)	>52 (n=10)	
Age	63.63±8.08	63.51±8.52	63.66±7.38	0.921
Married (%)	36	42	8	0.936
CHD	8	6	1	0,885
Stroke	1	1	1	0.790
Primary or below (%)	10	12	2	0.000
Current smokers (%)	3	2	1	0.912
Current drinkers (%)	4	3	1	0.512
Physical activity (yes, %)	32	40	8	0.713
Parity	2.07±1.12	2.01±1.16	1.95±1.05	0.001
Miscarriage (yes, %)	28	32	7	0.723
Ever contraceptive use (yes, %)	8	7	2	0.589
Ever HRT use (yes, %)	3	2	1	0.763
Family history of CHD (yes, %)	4	6	1	0.000

Family history of stroke (yes, %)	7	4	1	0.123
BMI (kg/m^2)	24.26±3.43	24.19±3.51	24.53±3.45	0.014
WHR	0.87±0.06	0.86±0.10	0.86±0.06	0.385
SBP (mmHg)	138.28±23.22	138.40±23.32	138.49±22.81	0.782
DBP (mmHg)	77.72±12.28	78.08±12.18	78.48±12.16	0.047
Triglycerides (mmol/L)	1.56±1.19	1.57±1.09	1.59±1.10	0.285
LDL−C (mmol/L)	2.79±0.89	2.82±0.90	2.82±0.90	0.368
HDL−C (mmol/L)	1.56±0.46	1.56±0.44	1.56±0.44	0.899
Total cholesterol (mmol/L)	4.93±1.14	4.98±1.12	5.00±1.15	0.031
Fasting glucose (mmol/L)	5.96±1.68	5.97±1.64	5.98±1.61	0.707
Diabetes (%)	16	10	2	0.702
Hypertension (%)	24	15	6	0.202

Out of 100 women, 40 belonged to <45 years, 50 belonged to 45-52 years and 10 women belonged to >52 years. There were 15% CHD cases and 3% stroke cases based on self-reporting. Women with early menopause (<45 years) tend to have lower educational level (P for trend <0.001), and higher parity (P for trend <0.05). 16 patients had diabetes who belonged to <45 years.

Table 2: ORs (95%CI) for CHD and stroke according to age at natural menopause

	Age at menopause			Per 1-y increase in	*P* for
	≤45	45−52	>52	age at menopause	trend
CHD					
Model1	1.34(1.18−1.51)	1.00	1.07(0.94−1.21)	0.97(0.96−0.98)	0.004
Model2	1.33(1.15−1.53)	1.00	1.03(0.90−1.19)	0.97(0.96~0.99)	0.006
Model3	1.33(1.13−1.57)	1.00	1.05(0.90−1.23)	0.97(0.95−0.98)	0.017
stroke					
Model1	1.55(1.23−1.97)	1.00	0.71(0.53−0.96)	0.95(0.93−0.98)	0.000
Model2	1.53(1.16−2.02)	1.00	0.70(0.50−1.01)	0.96(0.93−0.99)	0.000
Model3	1.69(1.25−2.30)	1.00	0.73(0.49−1.07)	0.95(0.92−0.98)	0.000

There was a decreased trend toward CHD presence with increasing age at natural menopause (P for trend <0.05). Each one year delay of age at menopause was associated with 3% reduction in CHD presence compared with women with menopause at ages 45−52 years. Our findings also showed a linear relationship between menopausal age and the presence of stroke (P for trend <0.001). Each one year delay in age at menopause was associated with 5% reduction in stroke presence. Women with early age at menopause (<45 years) had higher prevalence of stroke than those with menopause at ages 45−52 years after adjustment for potential risk factors. In the age adjusted model, women with later age at menopause (> 52 years) was inversely associated with presence of stroke compared with those with menopause at ages 45−52 years. However, the association was no significant when we further adjusted other confounding factors.

Discussion

CVDs include disorders like coronary heart disease, cerebrovascular disease, rheumatic heart disease, arterial disease, peripheral arterial disease, congenital heart disease, deep vein thrombosis and pulmonary embolism. CVD is the main cause of morbidity and mortality in both men and women in developed countries. Studies have shown that low estrogen levels correlate with coronary artery disease in men. [21] CVD occurs more frequently in men than in women before menopause. [22] Although IHD in females occurs 7–10 years later compared with males, mostly due to the protective effect of estrogens on the atherosclerotic process, there is a steady increase in this risk after the transition to menopause. [23] This is mostly evident in women with early menopause (EM; defined as age at menopause <45 years) or premature ovarian insufficiency (POI; defined as age at menopause <40 years). [24]

Out of 100 women, 40 belonged to <45 years, 50 belonged to 45-52 years and 10 women belonged to >52 years. There were 15% CHD cases and 3% stroke cases based on self-reporting. Women with early menopause (<45 years) tend to have lower educational level (P for trend <0.001), and higher parity (P for trend <0.05). 16 patients had diabetes who belonged to <45 years. There was a decreased trend toward CHD presence with increasing age at natural menopause (P for trend <0.05). Each one year delay of age at menopause was associated with 3% reduction in CHD presence compared with women with menopause at ages 45−52 years. Menopause affects many metabolic biomarkers more than the process of aging. [25] Postmenopausal women experience changes in the metabolism of

lipoproteins, fatty acids, and amino acids. These changes are independent of age, and potentially underlie the link between menopause and cardiometabolic diseases. As stated by Gurka et al [26], the severity of MetS and five risk factors for heart disease may increase before menopause faster than after menopause. Women may exhibit vasomotor or other menopausal symptoms before menstruation ceases. [27] For many years, researchers have been trying to understand the impact of selected determinants of increased CVD risk in postmenopausal women. [28] It has been observed that in addition to the accumulation of CVD risk factors during menopause (e.g., increased fasting blood glucose, higher blood pressure, and increased blood lipid levels), the incidence of type 2 diabetes, which is a major CVD risk factor, also increases. [29] In addition, menopausal symptoms, such as hot flashes, night sweats, sleep disturbances, depression, and anxiety are associated with an unfavorable cardio metabolic profile, and thus with an increased risk of CVD. [30]

Our findings also showed a linear relationship between menopausal age and the presence of stroke (P for trend <0.001). Each one year delay in age at menopause was associated with 5% reduction in stroke presence. Women with early age at menopause (<45 years) had higher prevalence of stroke than those with menopause at ages 45−52 years after adjustment for potential risk factors. In the age adjusted model, women with later age at menopause (> 52 years) was inversely associated with presence of stroke compared with those with menopause at ages 45−52 years. However, the association was no significant when we further adjusted other confounding factors. The risk of CVD increases with the passage of time since menopause. [31] There is probably a link between the time since menopause and some traditional CVD risk factors, such as MetS and obesity. [32] Cho et al [33], on the other hand, noted that women who were 10–14 years after menopause were more likely to have higher TG levels.

Some researchers speculate that the age of menopause contributes to CVD risk, and this relationship is bidirectional. The Framingham Heart Study revealed that higher total cholesterol, SBP, and DBP, as well as other CVD risk factors are associated with earlier menopause, irrespective of smoking. [34] Moreover, it was observed that the first CVD event before the age of 35 was associated with a doubling of the risk of early menopause, while the occurrence of a CVD event after the age of 35 was associated with menopause at the age of 51. [35] It is therefore likely that poorer cardiovascular health before menopause may influence the onset of natural menopause. The age at which women reach natural menopause is considered a predictor of reproductive, somatic, and cardiometabolic aging, as well as women's overall health.

Conclusion

Our study demonstrated that early age at natural menopause is associated with the presence of CHD and stroke among women. The effect of menopausal age on cardiovascular disease can be taken into consideration for the prevention.

References

1. Roth GA, Johnson C, Abajobir A, Abd-Allah F, Abera SF, Abyu G, et al. Global, regional, and national burden of cardiovascular diseases for 10 causes, 1990 to 2015. J Am Coll Cardiol .2017; 70(1):1–25.
2. Wilkins E, Wilson L, Wickramasinghe K, Bhatnagar P. European Heart Network. European Cardiovascular Disease Statistics 20 17.
3. Wellons, M.; Ouyang, P.; Schreiner, P.J.; Herrington, D.M.; Vaidya, D. Early menopause predicts future coronary heart disease and stroke: The Multi-Ethnic Study of Atherosclerosis (MESA). Menopause 2012, 19 ,1081–1087.
4. Stevenson, J.C.; Collins, P.; Hamoda, H.; Lambrinoudaki, I.; Maas, A.H.E.M.; Maclaran, K.; Panay, N. Cardiometabolic health in premature ovarian insufficiency. Climacteric 2021, 24, 474–480.
5. Carr MC. The emergence of the metabolic syndrome with menopause. J Clin Endocrinol Metab. 2003; 88(6):2404–11.
6. Organization WH. Research on the menopause in the 1990s: report of a WHO scientific group. 1996; 866:1–107.
7. El Khoudary SR, Greendale G, Crawford SL, Avis NE, Brooks MM, Thurston RC, et al. The menopause transition and women's health at midlife: a progress report from the Study of Women's Health Across the Nation (SWAN). Menopause. 2019; 26(10):1213–27.
8. Debra F. Skafar, RuiXu, Juan Morales, Jeffrey Ram and James R Sowers. Female sex hormones and cardiovascular disease in women. Journal of Clin Endocr Metabol. 1997; 82(12); 3913-18.
9. Campos H, Walsh BW, Judge H, Sacks FM. Effect of estrogen on very low density lipoprotein and low density lipoprotein subclass metabolism in postmenopausal women. Journal of Clin Endocr. Metabolism. 1997; 82: 3955-63.
10. Mendelsohn ME, Karas RH. The protective effects of estrogen on cardiovascular system. New England Journal of Medicine. 1999;(340): 1801-11.
11. Trémollières FA, Pouilles JM, Cauneille C, Ribot C. Coronary heart disease risk factors and

menopause: a study in 1684 French women. Atherosclerosis. 1999; 142(2): 415-23.

12. Jouyandeh Z, Nayebzadeh F, Qorbani M, Asadi M.Metabolic syndrome and menopause. J Diabetes Metab Disord. 2013; 12(1).

13. Marjani A, Moghasemi S. The Metabolic Syndrome among PostmenopausalWomen in Gorgan. Int J Endocrinol. 2012; 953627.

14. Mohan V, Rao GHR. Type 2 Diabetes in South Asains. 1 sted. New Delhi: South Asian Society on Atherosclerosis and Thrombosis; 2007.

15. Misra A, Khurana L. The metabolic syndrome in South Asians: Epidemiology, clinical correlates and possible solutions. International Diabetes Monitor. 2009; 21: 92-101.

16. Paduszyńska A, Banach M, Maciejewski M, Dąbrowa M, Bielecka-Dąbrowa A. The outcomes of hypertension treatment depending on gender in patients over 40 years of age. Prz Menopauz 2021; 19: 174-8.

17. Crandall, C.J.; Barrett-Connor, E. Endogenous sex steroid levels and cardiovascular disease in relation to the menopause: A systematic review. Endocrinol. Metab. Clin. N. Am. 2013, 42,227–253.

18. El Khoudary, S.R.; Thurston, R.C. Cardiovascular implications of the menopause transition: Endogenous sex hormones and vasomotor symptoms. Obstet. Gynecol. Clin. N. Am. 2018, 45, 641–661.

19. Dal Canto, E.; Ceriello, A.; Rydén, L.; Ferrini, M.; Hansen, T.B.; Schnell, O.; Standl, E.; Beulens, J.W. Diabetes as a cardiovascular risk factor: An overview of global trends of macro and micro vascular complications. Eur. J. Prev. Cardiol. 2019, 26, 25–32.

20. Garcia, M.; Mulvagh, S.L.; Merz, C.N.; Buring, J.E.; Manson, J.E. Cardiovascular disease in women: Clinical perspectives. Circ. Res. 2016, 118, 1273–1293.

21. Bajelan M, Roodi NE, Daloee MH, Farhangnia M, Kuchaksaraei AS. The effect of low testosterone and estrogen levels on progressive coronary artery disease in men. Reports of Biochemistry & Molecular Biology. 2019 Jul; 8(2):168.

22. Stanhewicz AE, Wenner MM, Stachenfeld NS. Sex differences in endothelial function important to vascular health and overall cardiovascular disease risk across the lifespan. American Journal of Physiology-Heart and Circulatory Physiology. 2018 Dec 1;315(6):H1569-88.

23. Maas AH, Rosano G, Cifkova R, Chieffo A, van Dijken D, Hamoda H, Kunadian V, Laan E, Lambrinoudaki I, Maclaran K, Panay N. Cardiovascular health after menopause transition, pregnancy disorders, and other gynaecologic conditions: a consensus document from European cardiologists, gynaecologists,

and endocrinologists. European Heart Journal. 2021 Mar 7;42(10): 967-84.

24. Stevenson JC, Collins P, Hamoda H, Lambrinoudaki I, Maas AH, Maclaran K, Panay N. Cardiometabolic health in premature ovarian insufficiency. Climacteric. 2021 Sep 3; 24(5):474-80.

25. Wang Q, Ferreira DL, Nelson SM, Sattar N, Ala-Korpela M, Lawlor DA. Metabolic characterization of menopause: cross-sectional and longitudinal evidence. BMC medicine. 2018 Dec;16(1):1-2.

26. Gurka MJ, Vishnu A, Santen RJ, DeBoer MD. Progression of metabolic syndrome severity during the menopausal transition. Journal of the American Heart Association. 2016 Aug 3;5(8):e003609.

27. Reed SD, Lampe JW, Qu C, Copeland WK, Gundersen G, Fuller S, Newton KM. Premenopausal vasomotor symptoms in an ethnically diverse population. Menopause. 2014 Feb 1;21(2):153-8.

28. Juppi HK, Sipilä S, Cronin NJ, Karvinen S, Karppinen JE, Tammelin TH, Aukee P, Kovanen V, Kujala UM, Laakkonen EK. Role of menopausal transition and physical activity in loss of lean and muscle mass: a follow-up study in middle-aged Finnish women. Journal of clinical medicine. 2020 May 23;9(5):1588.

29. Muka T, Oliver-Williams C, Kunutsor S, Laven JS, Fauser BC, Chowdhury R, Kavousi M, Franco OH. Association of age at onset of menopause and time since onset of menopause with cardiovascular outcomes, intermediate vascular traits, and all-cause mortality: a systematic review and meta-analysis. JAMA cardiology. 2016 Oct 1;1(7):767-76.

30. Janssen I, Powell LH, Matthews KA, Jasielec MS, Hollenberg SM, Bromberger JT, Sutton-Tyrrell K, Everson-Rose SA. Relation of persistent depressive symptoms to coronary artery calcification in women aged 46 to 59 years. The American journal of cardiology. 2016 Jun 15;117(12):1884-9.

31. Zhou H, Zhang C, Ni J, Han X. Prevalence of cardiovascular risk factors in non-menopausal and postmenopausal inpatients with type 2 diabetes mellitus in China. BMC endocrine disorders. 2019 Dec;19(1):1-9.

32. Akinkuolie AO, Buring JE, Ridker PM, Mora S. A novel protein glycan biomarker and future cardiovascular disease events. Journal of the American Heart Association. 2014 Sep 23; 3(5):e001221.

33. Cho GJ, Lee JH, Park HT, Shin JH, Hong SC, Kim T, Hur JY, Lee KW, Park YK, Kim SH. Postmenopausal status according to years since menopause as an independent risk factor for the metabolic syndrome. Menopause. 2008 May 1;15(3):524-9.

34. Kok HS, van Asselt KM, van der Schouw YT, van der Tweel I, Peeters PH, Wilson PW, Pearson PL, Grobbee DE. Heart disease risk determines menopausal age rather than the reverse. Journal of the American College of Cardiology. 2006 May 16;47(10):1976-83.

35. Zhu D, Chung HF, Pandeya N, Dobson AJ, Hardy R, Kuh D, Brunner EJ, Bruinsma F, Giles GG, Demakakos P, Lee JS. Premenopausal cardiovascular disease and age at natural menopause: a pooled analysis of over 170,000 women. European journal of epidemiology. 2019 Mar 15;34:235-46.