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Original article

Age at menopause and its association with comorbidities in older women

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Abstract: *Background* — Menopause age is a potential mediator of subsequent mortality, morbidity, and quality of life after menopause.
Objective — Since limited studies have reported an association between age at menopause and chronic diseases in the elderly population, this study aimed to investigate this association.
Methods — This retrospective cohort study was conducted among elderly women aged ≥60 years living in the northern part of Iran. Demographic characteristics, history of harmful habits (smoking), and self-reported age at menopause were collected through direct interviews. Participants were divided into three groups based on the age at menopause (normal menopause age: 45–54 years; early menopause: <45 years; and late menopause: ≥55 years). The situation with chronic diseases including diabetes, hypertension, cognitive impairment and depression was compared between the three groups.
Results — A total of 811 eligible elderly women (mean age 68.93±6.72 years) were included in the study. The mean age at menopause was 47.12±5.82 years. Among them, 537 women (66.2%) had normal menopause age, 83 (10.2%) experienced late menopause, and 191 (23.6%) reported early menopause. An inverse correlation was detected between menopause age and geriatric depression score (r=-0.093; P=0.008); however, the three menopause age groups had no significant association with diabetes (P=0.579), hypertension (P=0.532), or cognitive impairment (P=0.077).
Conclusion — Although we did not find a statistically significant association between menopause age and diabetes mellitus, hypertension and cognitive impairment, chronic diseases (especially, depressive disorders) should be given more attention in elderly women.

Keywords: menopause, aging, comorbidity.

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Introduction

Women's health, especially the prevention of communicable and noncommunicable diseases, is among the most important issues in health care and health policy development [1]. Hence, in recent years, there has been increasing attention to issues related to menopause and hypoestrogenism. It is worth noting that proper management of menopause can affect the quality of life and life expectancy of women [2].

The World Health Organization reported that in 2019, the global life expectancy was 73.4 years and the healthy life expectancy (HALE) was 63.7 years [3]. Given the increasing life expectancy of women, they are expected to spend about a third of their lives in menopause. Therefore, implementing appropriate strategies to promote healthy longevity and active ageing in postmenopausal women is a necessity for all countries [4-6].

Differences between men and women have been recognized in various health outcomes such as cardiovascular, psychiatric and inflammatory disorders; however, numerous physiological, socioeconomic, epidemiological, and behavioral determinants have been proposed to explain this difference. Menopause has been identified as an important physiological factor influencing various health outcomes in women [7, 8]. The association between various comorbidities with decreased follicular activity and the hormonal transition associated with menopause has not been clearly investigated. Some evidence has revealed an association of reduced estrogen concentration with cardiometabolic and cognitive disorders [2, 9]. However, other studies have reported the influence of covariates other than menopausal status [10, 11].

Every year, 47 million women worldwide experience menopause. The World Health Organization estimates that by 2030, there will be more than 1.2 billion postmenopausal women globally [12]. While most women experience menopause between the ages of 45 and 55 years, approximately 5-10% may experience menopause earlier, between the ages of 40 and 45 years. Menopause occurs before age of 40 years in 1-3% of the female population [13].

Age at menopause may be influenced by a wide range of familial, environmental, behavioral, and lifestylefactors [14] and may be a potential mediator of subsequent mortality, morbidity, and quality of life after menopause [13, 14]. Since just a few studies have reported an association between age at menopause and chronic disorders in the elderly population [2, 9], our study aimed to investigate this issue.

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Material and Methods

Study design

This retrospective cohort study was conducted within the framework of a cohort project (Amirkola Health and Aging Project: AHAP) among elderly women aged 60 years and above living in Amirkola, Northern Iran. Participant data were collected from the databank related to the second phase of the AHAP project [15].

Participants

All women aged ≥ 60 years living in this region were invited to participate in the AHAP cohort project. Eligible elderly adults who provided written informed consent for the study were recruited through census. Individuals with severe cognitive impairment that would have prevented them from recalling their menopause history, as well as women who did not have a natural menopause (e.g., menopause after ovarian surgery or after taking special medications) were excluded. The baseline characteristics of the participants are presented in *Table* 1.

Study variables and their measurement

Data were collected through direct interviews with eligible elderly women or their family members who had sufficient information about the participant's history. All relevant physical and laboratory examinations were performed at the Health Research Institute, Babol University of Medical Sciences, Iran.

Demographic information, history of harmful habits (smoking), menopause history, and self-reported age at menopause were collected via a study questionnaire. The most commonly known comorbidities, including diabetes mellitus, hypertension, cognitive decline, and depressive disorders, were assessed through direct interview, physical examination, review of the participant's medications, and laboratory tests whenever necessary.

The diagnosis of diabetes was confirmed by fasting blood sugar (two times FBS≥126 mg/dL) or the use of hypoglycemic agents with a previous diagnosis of diabetes.

Blood pressure was measured in the sitting position, and if the mean of the two measurements was greater than or equal to 140/90 mmHg or the participant was taking an antihypertensive drug as prescribed by the physician, she was considered hypertensive.

Body mass index (BMI) was calculated by measuring height and weight and dividing the weight by the square of the height.

Mini-Mental State Examination (MMSE) and Geriatric Depression Scale (GDS) were employed to assess cognitive impairment or depressive symptoms in the participants, respectively.

The 30-item MMSE questionnaire has been introduced as a reliable tool for assessing cognitive impairment in elderly adults. Women who scored less than 25 points were classified as patients with cognitive impairment. The validity and reliability of the Persian translation of this scale have been confirmed in a previous study [16].

Based on the 15-item GDS questionnaire, the participants were divided into two groups: without depressive disorder (scores ranging from 0 to 4) and with depressive disorders (scores of 5 and above). The validity and reliability of this questionnaire for assessing depressive symptoms in the elderly was assessed in the Iranian population [17].

The participants were divided into three groups based on the age at the onset of the menopause: Group 1 (normal menopause age: 45 to 54 years), Group 2 (early menopause: <45 years) and Group 3 (late menopause: ≥55 years). Also, the situation with chronic diseases including diabetes, hypertension, cognitive impairment and depression in these three menopause age groups was compared between the groups.

Statistical data processing

The data analysis was performed using the SPSS V.22 software package. The Kolmogorov-Smirnov test was employed to assess the normality of the data distribution. The chi-squared test and Pearson correlation coefficient were used to analyze the data.

Table 1. Baseline characteristics of study participants

Characteristics		*Number*	*Percent*
Age (years)	60-64	240	29.6
	65-69	252	31.1
	70-74	157	19.4
	75-79	96	11.8
	80-84	44	5.4
	85-99	22	2.7
Education level	Illiterate	548	67.6
	Primary school	169	20.8
	High school	80	9.9
	Academic education	14	1.7
Marital status	Married	591	72.9
	Single, divorced, or widowed	220	27.1
Current smoking or history of smoking	No	803	99.01
	Yes	8	0.99
Body mass index (kg/m^2)	<18.5	6	0.7
	18.5-24.9	126	15.5
	25-29.9	302	37.2
	≥30	377	46.5
Geriatric Depression Scale (GDS) score, pts: Mean ± SD		5.09 ± 3.74	
Mini-Mental State Examination (MMSE) score, pts: Mean ± SD		24.22 ± 4.42	

Table 2. Menopause age and comorbidities in elderly women, Northern Iran

Age at menopause	*Diabetes mellitus N (%)*		*P-value**	*Hypertension N (%)*		*P-value**	*Cognitive impairment N (%)*		*P-value**	*Depressive disorders N (%)*		*P-value**
(years)	Yes	No		Yes	No		Yes	No		Yes	No	
45-54	193 (68.0)	344 (65.3)		411 (65.3)	126 (69.2)		233 (64.0)	304 (68.0)		253 (64.0)	284 (68.4)	
<45	66 (23.2)	125 (23.7)	0.579	154 (24.4)	37 (20.3)	0.532	92 (25.2)	99 (22.1)	0.077	102 (25.7)	89 (21.4)	0.334
≥55	25 (8.8)	58 (11.0)		64 (10.3)	19 (10.4)		39 (10.7)	44 (9.8)		41 (10.3)	42 (10.1)	

*Chi-squared test.

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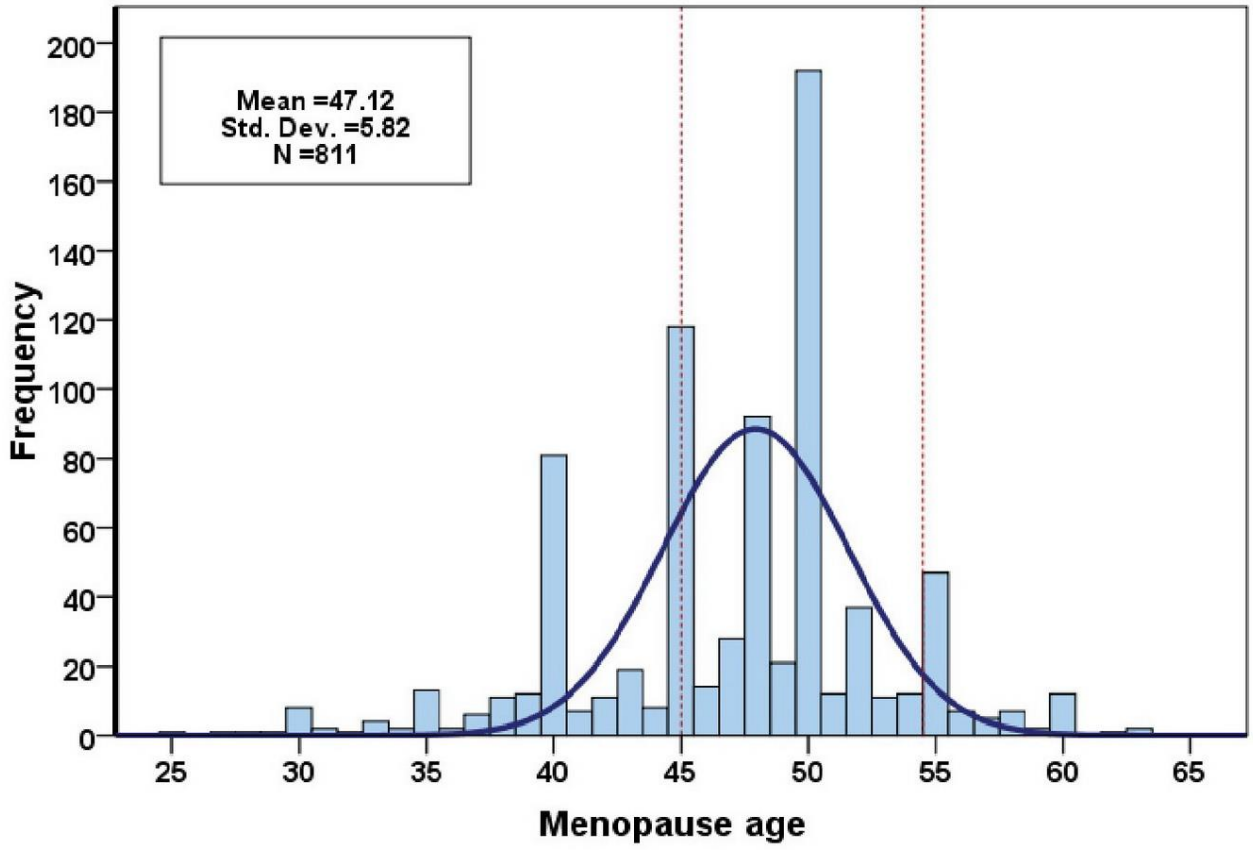

Figure 1. Reported age at menopause in elderly women of Northern Iran.

Results

A total of 811 eligible elderly women (mean age 68.93±6.72 years) for whom the required information was complete in the AHAP Cohort Project databank were included in our study. *Table 1* shows that almost one-third of the participants were in the 65-69 age group (252 subjects, 31.1%). Most of the study subjects were married (591 subjects, 72.9%), illiterate (548 subjects, 67.6%), and obese (377 subjects, 46.5%). Very few study participants were smokers (8 subjects, 0.99%).

The median age at menopause was 48 (interquartile range: 45-50) years. The distribution of age at menopause is presented in *Figure 1*. This figure shows that the lowest reported age at menopause in this study was 25 years, while the highest was 63 years, with a mean age at menopause of 47.12±5.82 years. Another notable point was the general preference of elderly women to round their age at menopause to a multiple of 5. In addition, the graph is relatively left-skewed, and self-reports of menopause at a younger age are much more common than late menopause.

Among these 811 participants, 537 individuals (66.2%) experienced menopause at the normal age (45–54 years); 83 individuals (10.2%) experienced late (≥55 years) menopause, and 191 individuals (23.6%) reported early menopause. The assessment of comorbidities showed that 284 subjects (35.0%) had diabetes, 629 (77.6%) experienced hypertension, 364 (44.9%) had cognitive impairment, and 396 (48.8%) had depressive disorders.

The association of these comorbidities with menopause age is shown in *Table 2*. No significant association was detected between the three menopause age groups and the occurrence of diabetes (P=0.579), hypertension (P=0.532), cognitive impairment (P=0.077), or depressive disorders (P=0.334).

The mean GDS score was 5.08±3.73 pts, while the mean MMSE score was 24.22±4.41 pts. Pearson correlation analysis revealed an inverse correlation between menopause age and GDS score; the younger the age at menopause, the higher the score for depressive symptoms (r=-0.093; P=0.008); however, no statistically significant correlation was revealed between the MMSE score and age at menopause (r=0.015; P=0.666).

Discussion

The goal of this study was to investigate the association of age at menopause with some important comorbidities in elderly women. We could not find a similar study that only included elderly women (≥60 years of age).

The self-reported age at menopause among elderly women living in the northern region of Iran ranged from 25 to 63 years, and their mean age at menopause was 47 years. Participants tended to report their age at menopause as a whole number multiple of five and report a younger age. A systematic review assessed the age at menopause in India and reported a mean age at menopause of 46.6 years [18]. A recent study reported that the mean age at menopause in Iranian women ranged from 46.9 to 49.6 years in different parts of this country [14]. The natural age at menopause among Asian women was reported as 49 to 51 years; Of course, age at menopause may be influenced by various factors such as age at menarche, genetic factors, medications, diet, smoking, alcohol and drug use, and BMI [14].

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We revealed no significant association between the three menopause age groups and the occurrence of diabetes, hypertension, depression or cognitive impairment, while the GDS score inversely correlated with menopause age. Contrary to our findings, a systematic review and meta-analysis investigated the association of menopause age with cardiovascular outcomes and reported a higher risk of coronary artery disease, cardiovascular mortality and all-cause mortality in women who experienced menopause before age of 45 years [19]. Another systematic review and meta-analysis reported a significant effect of menopausal age on frailty; a one-unit increase in menopause age was associated with a 2% reduction in the risk of frailty [20]. The independent effects of age and menopausal status on cardiovascular outcomes may justify our findings [21].

Regarding the association of GDS score with age at menopause, a nationwide study in Korea reported a higher prevalence of suicidal ideation in women who were younger than 45 years old at menopause [22]. A systematic review and meta-analysis demonstrated a 50% reduction in the risk of depression in women who were older at menopause vs. those who had a premature menopause; in addition, for every two years increase in age at menopause, there was a 5% reduction in the risk of major depression [23]. Menopause predisposes women to anxiety and depressive symptoms. Some evidence suggests the effect of estrogen decline on the neurotransmitters such as serotonin and GABA [24]. Especially in the early years after menopause, women are more vulnerable to developing depressive symptoms [25].

Contrary to our findings, a significant effect of menopause age on cognitive function has been noted in some previous studies. In a longitudinal study in India, cognitive function scores were significantly lower in women who experienced premature menopause [26]. In a study conducted in Japan, cognitive impairment was significantly less common in women who experienced menopause after age of 45 years vs. women who experienced early menopause [27]. The longer the exposure to endogenous estrogen, the lower the incidence of cognitive impairment is expected [23, 28]. However, different study designs and populations may explain differences in results across studies.

Strengths and limitations of the study

The most notable strength of this study is its large sample size. We considered diabetes, hypertension, depression and cognitive impairment among the study population, while other comorbidities were not considered. This can be mentioned as a limitation of this study. Besides that, the cross-sectional design of this study limited its capability to assess the incidence of comorbidities in the postmenopausal period.

Implications for future research

Further large-scale longitudinal studies are recommended to monitor the incidence of chronic diseases after menopause.

Conclusion

Self-reported age at menopause was 47.12±5.82 years among elderly women living in the investigated region of Iran. None of the three groups of menopause age exhibited a significant association with occurrence of diabetes, hypertension, or cognitive disorders. However, an inverse correlation was detected between the score on geriatric depression scale and menopause age.

Ethical approval

All procedures performed in this study were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

All participants provided an informed consent regarding their participation in the study. The research protocol was approved by the Ethics Committee of Babol University of Medical Sciences, Iran, with identification number: IR.MUBABOL.HRI.REC.1400.050.

Conflict of Interest

The authors declare no conflicts of interest.

References

1. Carneiro MM. Women's health in 2024: Change now for tomorrow will be too late. *Women Health* 2024; 64(1): 1-4. https://doi.org/10.1080/03630242.2024.2292320.
2. Chikwati RP, Chikowore T, Mahyoodeen NG, Jaff NG, George JA, Crowther NJ. The association of menopause with cardiometabolic disease risk factors in low- and middle-income countries: A systematic review and meta-analyses. *Menopause* 2024; 31(1): 77-85. https://doi.org/10.1097/gme.0000000000002292.
3. World Health Organization. GHE: Life expectancy and healthy life expectancy. 2024. https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates/ghe-life-expectancy-and-healthy-life-expectancy.
4. Lobo RA, Gompel A. Management of menopause: A view towards prevention. *Lancet Diabetes Endocrinol* 2022; 10(6): 457-470. https://doi.org/10.1016/s2213-8587(21)00269-2.
5. Barati M, Akbari-Heidari H, Samadi-Yaghin E, Jenabi E, Jormand H, Kamyari N. The factors associated with the quality of life among postmenopausal women. *BMC Womens Health* 2021; 21(1): 208. https://doi.org/10.1186/s12905-021-01361-x.
6. Pertyńska-Marczewska M, Pertyński T. Postmenopausal women in gynecological care. *Prz Menopauzalny* 2021; 20(2): 88-98. https://doi.org/10.5114/pm.2021.107103.
7. Crimmins EM, Shim H, Zhang YS, Kim JK. Differences between men and women in mortality and the health dimensions of the morbidity process. *Clin Chem* 2019; 65(1): 135-145. https://doi.org/10.1373/clinchem.2018.288332.
8. Mouodi S, Bijani A, Hosseini SR, Hajian-Tilaki K. Gender differences in the health status of elderly living alone compared to those who are not alone: Evidence of the AHAP study, North of Iran. *Caspian J Intern Med* 2016; 7(2): 126-132. https://pubmed.ncbi.nlm.nih.gov/27386065.
9. Liao H, Cheng J, Pan D, Deng Z, Liu Y, Jiang J, Cai J, He B, Lei M, Li H, et al. Association of earlier age at menopause with risk of incident dementia, brain structural indices and the potential mediators: A prospective community-based cohort study. *EClinicalMedicine* 2023; 60: 102033. https://doi.org/10.1016/j.eclinm.2023.102033.
10. Osibogun O, Ogunmoroti O, Tibuakuu M, Benson EM, Michos ED. Sex differences in the association between ideal cardiovascular health and biomarkers of cardiovascular disease among adults in the United States: a cross-sectional analysis from the multiethnic study of atherosclerosis. *BMJ Open* 2019; 9(11): e031414. https://doi.org/10.1136/bmjopen-2019-031414.
11. Huo N, Vemuri P, Graff-Radford J, Syrjanen J, Machulda M, Knopman DS, et al. Sex differences in the association between midlife cardiovascular conditions or risk factors with midlife cognitive decline. *Neurology* 2022; 98(6): e623-e632. https://doi.org/10.1212/wnl.0000000000013174.
12. Simbar M, Nazarpour S, KhodaKarami N, Nasiri Z, Rashidi Fakari F, Kiani Z, et al. A situation analysis on postmenopausal women's self-care needs and priorities in Tehran: A population-based study. *BMC Public Health* 2023; 23(1): 104. https://doi.org/10.1186/s12889-023-15040-z.

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13. Peycheva D, Sullivan A, Hardy R, Bryson A, Conti G, Ploubidis G. Risk factors for natural menopause before the age of 45: Evidence from two British population-based birth cohort studies. *BMC Womens Health* 2022; 22(1): 438. https://doi.org/10.1186/s12905-022-02021-4.
14. Kutenaee MA, Dashti S, Rafati S, Moannaei M, Masoudi M, Nejatizadeh A, et al. Factors predicting age at menopause among Iranian women in the Bandare-Kong cohort study (a cross-sectional survey of PERSIAN cohort study). *Womens Midlife Health* 2023; 9(1): 5. https://doi.org/10.1186/s40695-023-00088-z.
15. Bijani A, Ghadimi R, Mikaniki E, Kheirkhah F, Mozaffarpur SA, Motallebnejad M, et al. Cohort Profile Update. The Amirkola Health and Ageing Project (AHAP). *Caspian J Intern Med* 2017; 8(3): 205-212. https://doi.org/10.22088/cjim.8.3.205.
16. Malekian N, Hosseini SR, Moudi S, Bayani MA, Kheirkhah F, Bijani A, et al. Type 2 diabetes mellitus and cognitive function in the elderly. *Iran J Psychiatry Behav Sci* 2018; 12(2): e9494. https://doi.org/10.5812/ijpbs.9494.
17. Malakouti SK, Fatollahi P, Mirabzadeh A, Salavati M, Zandi T. Reliability, validity and factor structure of the GDS-15 in Iranian elderly. *Int J Geriatr Psychiatry* 2006; 21(6): 588-593. https://doi.org/10.1002/gps.1533.
18. Prasad JB, Tyagi NK, Verma P. Age at menopause in India: A systematic review. *Diabetes Metab Syndr* 2021; 15(1): 373-377. https://doi.org/10.1016/j.dsx.2021.01.013.
19. Muka T, Oliver-Williams C, Kunutsor S, Laven JS, Fauser BC, et al. 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 Cardiol* 2016; 1(7): 767-776. https://doi.org/10.1001/jamacardio.2016.2415.
20. Kojima G, Taniguchi Y, Ogawa K, Aoyama R, Urano T. Age at menopause is negatively associated with frailty: A systematic review and meta-analysis. *Maturitas* 2022; 165: 94-99. https://doi.org/10.1016/j.maturitas.2022.07.012.
21. de Kat AC, Dam V, Onland-Moret NC, Eijkemans MJC, Broekmans FJM, van der Schouw YT. Unraveling the associations of age and menopause with cardiovascular risk factors in a large population-based study. *BMC Med* 2017; 15(1): 2. https://doi.org/10.1186/s12916-016-0762-8.
22. Ryu KJ, Park H, Jeong Y, Nam S, Jeong HG, Kim T. Age at Menopause and suicidal ideation in menopausal women: A study of Korea National Health and Nutrition Examination Survey Data. *J Korean Med Sci* 2022; 37(45): e330. https://doi.org/10.3346/jkms.2022.37.e330.
23. Georgakis MK, Thomopoulos TP, Diamantaras AA, Kalogirou EI, Skalkidou A, Daskalopoulou SS, et al. Association of age at menopause and duration of reproductive period with depression after menopause: A systematic review and meta-analysis. *JAMA Psychiatry* 2016; 73(2): 139-149. https://doi.org/10.1001/jamapsychiatry.2015.2653.
24. Alblooshi S, Taylor M, Gill N. Does menopause elevate the risk for developing depression and anxiety? Results from a systematic review. *Australas Psychiatry* 2023; 31(2): 165-173. https://doi.org/10.1177/10398562231165439.
25. Campbell KE, Dennerstein L, Finch S, Szoeke CE. Impact of menopausal status on negative mood and depressive symptoms in a longitudinal sample spanning 20 years. *Menopause* 2017; 24(5): 490-496. https://doi.org/10.1097/gme.0000000000000805.
26. Kundu S, Acharya SS. Linkage of premature and early menopause with psychosocial well-being: A moderated multiple mediation approach. *BMC Psychol* 2023; 11(1): 228. https://doi.org/10.1186/s40359-023-01267-3.
27. Shimizu Y, Sawada N, Iwasaki M, Shikimoto R, Nozaki S, Mimura M, et al. Reproductive history and risk of cognitive impairment in Japanese women. *Maturitas* 2019; 128: 22-28. https://doi.org/10.1016/j.maturitas.2019.06.012.
28. Fu C, Hao W, Shrestha N, Virani SS, Mishra SR, Zhu D. Association of reproductive factors with dementia: A systematic review and dose-response meta-analyses of observational studies. *EClinicalMedicine* 2022; 43: 101236. https://doi.org/10.1016/j.eclinm.2021.101236.

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