

## **Determinants and predictors of age at menopause among women in southeastern Iran: Zahedan PERSIAN cohort study**

### **Abstract**

**Background:** Menopause age is an important indicator that not only indicates the end of a woman's reproductive period but also increases the risk of various middle-aged diseases and complications that can be prevented with timely interventions. This study examines the age of menopause and factors affecting it among Iranian women in southeastern Iran.

**Methods:** This population-based study was conducted among 2,649 postmenopausal women aged 35–70 years who participated in the Zahedan Cohort Study (ZCS), a component of the Prospective Epidemiological Research Studies in Iran (PERSIAN), from October 2015 to January 2019 in Zahedan. Data were analyzed using t-tests, chi-square tests, ANOVA, and multivariable logistic regression. A significance level of  $p < 0.05$  was used.

**Results:** The average age at menopause was  $49.01 \pm 5.39$  years. Among these women, 225 (8.5%) experienced premature menopause, 198 (7.5%) experienced early menopause, and 2,226 (84%) experienced normal menopause. Results from multiple logistic regression show that marital status, physical activity, depression, diabetes, and stillbirth are associated with premature menopause. In addition, body mass index (BMI), physical activity, depression, infertility, and diabetes are key predictors of early menopause.

**Conclusions :** This study indicated that predictors of menopausal age differ between women with premature menopause and those with early menopause. Prospective research is needed to evaluate how these factors influence the timing of menopause.

**Keywords:** Menopause, Women, cohort.

### **PLAIN LANGUAGE SUMMARY**

This study aimed to determine the age of menopause and factors affecting it among Iranian women in southeastern Iran. A study with 2,649 postmenopausal women aged 35–70 years who participated in the Zahedan Cohort Study (ZCS), a component of the Prospective Epidemiological Research Studies in Iran (PERSIAN), from October 2015 to January 2019 in Zahedan. Statistical tests, such as the t-test, chi-square, ANOVA, and multivariate logistic regression, were used to determine factors associated with menopause age. Within the results, the mean age of menopausal women was  $49.01 \pm 5.39$  years. Among these women, 225 (8.5%) experienced premature menopause, 198 (7.5%) experienced early menopause, and 2,226 (84%) experienced normal menopause. The results showed that marital status, physical activity, depression, diabetes, and stillbirth are body mass index (BMI), physical activity, depression, infertility, and diabetes are key predictors of age at menopause. Genetic predisposition plays a significant role in determining the age of menopause onset, but social factors also have a substantial influence. For example, marital status has been associated with variations in the timing of menopause, possibly due to differences in lifestyle and psychosocial stress levels. Pregnancy history and number of births are also implicated. Physical activity levels can affect hormonal balance and subsequently affect the age of menopause. Underlying diseases, especially autoimmune and endocrine disorders, can impair ovarian function and accelerate the transition to menopause. Therefore, a comprehensive understanding of the timing of menopause requires consideration of diverse genetic and social factors.

## **Background**

Menopause marks the end of the monthly menstrual cycle in females and is characterized by amenorrhea for 12 consecutive months due to decreased ovarian follicular function<sup>[1]</sup>. This transition is accompanied by a reduction in estrogen levels, resulting in the cessation of menstruation and reproductive capability<sup>[2]</sup>. The natural age of menopause is typically defined as occurring after the age of 45<sup>[3,4]</sup>. Menopause may occur before the age of 40, known as premature ovarian failure<sup>[3]</sup>. Approximately 4% of females experience this transition before reaching 40 years of age<sup>[5]</sup>, or it may occur between the ages of 40 and 44, called early menopause<sup>[3]</sup>. The average age of menopause varies globally: Europe: 54 years, North America: 51.4 years, Latin America: 48.6 years, Asia: 51.1 years<sup>[6]</sup>, and Iran: 50.4 years<sup>[7]</sup>. The age of menopause serves as a predictor of mortality and disease risk in women's later life stages. Early menopause is associated with increased risks of cardiovascular diseases, osteoporosis, and type 2 diabetes<sup>[7-9]</sup>. Epidemiological studies suggest a 2% reduction in mortality rates with adjustments in menopausal age<sup>[10]</sup>, whereas late menopause is correlated with increased risks of endometrial and ovarian cancer<sup>[11-15]</sup>.

Several factors may influence the age of menopause onset, such as the use of contraceptive medications, BMI, smoking and alcohol consumption, physical activity, socioeconomic status, genetic factors, education level, and environmental, socioeconomic, and lifestyle factors<sup>[16-18]</sup>. Identifying factors that determine menopausal age is highly important. Understanding the genetic aspects of this phenomenon can enhance our understanding of the causes of premature menopause, which in turn affects women's fertility<sup>[19]</sup>. Therefore, careful study and identification of factors affecting the age of menopause can help to predict and better manage the health risks associated with this period. This can improve the quality of life for postmenopausal women and enable them to approach this important stage of life with greater awareness and preparation. While some studies have been conducted on menopause in Iran. There is a lack of research specifically focused on the age of menopause and its influencing factors in a large population of women in Zahedan. Understanding these parameters can provide valuable insights into women's health in this region and public health strategies for them. To address these gaps, we conducted a cross-sectional study aimed at determining the age of menopause and identifying factors associated with it in women living in Zahedan, Iran.

## **Methods**

### **Participants and study design**

This cross-sectional study was carried out based on the data of the ZCS, as part of the Prospective Epidemiological Research Studies in Iran (PERSIAN), which was conducted in Zahedan, one of the cities located in the Southeastern part of Iran.

ZCS is a prospective, population-based study whose data collection was conducted between October 2015 to January 2019 in Zahedan, and a 15-year follow-up is planned.

The sampling method in the ZCS study was conducted via a multistage stratified method. In this approach, the city of Zahedan was divided into three areas (periphery, center, and upper city) based on municipal regions and socioeconomic class. A comprehensive health service center was randomly selected in each region, and all women who met the study eligibility criteria were enrolled at each center. The data collection tool used in this research was a questionnaire, the validity and reliability of which have been confirmed through Persian cohort studies<sup>[20, 21]</sup>. It was administered and completed by trained personnel who collected information from the study participants. This study's aims, foundation, and design have been previously published<sup>[22]</sup>. Trained interviewers used a laptop-based questionnaire to gather data on participants' socio-demographics, anthropometrics, medical history, lifestyle, nutrition, and reproductive characteristics. Data were collected after participants provided written informed consent. For this study, the research team received the data from the ZCS supervisor in coded, anonymous form, and the authors did not have access to participants' identification information.

Women with a history of cancer, hysterectomy, or oophorectomy (unilateral or bilateral) before menopause and those who had not experienced menopause were excluded from the study, of the 6099 women who participated in the study, 3450 were excluded, and 2649 were menopausal (lack of menstruation for at least 12 months). The menopausal status of women was identified as

(Premature menopause, Early menopause, Normal menopause). Premature menopause was classified as occurring before the age of 40, early menopause as occurring between the ages of 40 and 44, and normal menopause as occurring after the age of 45<sup>[3]</sup>.

### **Measurements**

Trained personnel utilized validated questionnaires to gather information on socio-demographic characteristics, substance use, medical history, family history, socioeconomic status, and physical activity. Marriage status was dichotomized as married and single status, including never married, divorced/ widowed. The level of physical activity was calculated based on metabolic equivalent task hours (MET-hours/day). Women who reported a diagnosis of diabetes, hypertension, infertility, cardiac disease, or depression by a physician before menopausal age were considered to have a positive history of these diseases. Socioeconomic status was measured according to the wealth score index (WSI), which considers various factors. These factors included access to facilities, travel status, homeownership, number of bedrooms, monthly household income, annual domestic and international trips, and the number of books read. WSI was calculated via multiple correspondence analysis (MCA). MCA is a widely used technique for analyzing categorical data; it aims to reduce large sets of variables into smaller sets of components that summarize the information contained in the data. MCA can be regarded as an adaptation of principal component analysis (PCA) for categorical data<sup>[22]</sup>. In this study, using the MAC method, the WSI was divided into three groups (poor, moderate, and rich) on the basis of the scoring of the mentioned variables. The level of physical activity was calculated based on metabolic equivalent task hours (MET-hours/day). We calculated the BMI of the participants by dividing their weight (kg) by their height (m<sup>2</sup>) and categorizing them accordingly: BMI < 18.5 as underweight, 18.5–24.9 as normal, 25–29.9 as overweight, and more than 30 as obese<sup>[23]</sup>. Triglyceride (TG) ≥150 mg/dl, Cholesterol (CHOL) ≥200 mg/dl<sup>[24]</sup>. Current cigarette smokers were defined as individuals who had smoked at least 100 cigarettes in their lifetime and currently smoked either every day or on some days<sup>[25]</sup>. In this study, stillbirth was defined as the death of the pregnancy product after the 20th gestational week<sup>[26]</sup>. Menarche age is the age at which a person experiences their first menstruation. In this study, menopause is defined as the passage of at least 12 months since the last menstruation<sup>[27]</sup>. To assess menopausal status, women were asked questions about their menopausal status (yes/no). Furthermore, among women who had menopause, the age of completion of menopause was then asked.

### **Data Analysis**

Quantitative variables are expressed as the mean ± standard deviation (SD), and qualitative variables are expressed in terms of frequency and percentage. Individual characteristics were compared across menopausal age groups (premature, early, and normal) via the chi-square and Fisher's exact test for categorical variables and one-way analysis (ANOVA) and the independent sample t-test for quantitative variables. Multiple logistic regression analyses were used to assess the associations between independent variables and categorical dependent variables (premature menopause, early menopause, and normal menopause). The normal menopause category was set as a reference category in this model. Potential confounding variables were entered into the model in order of their hypothesized association strength with menopausal age. Variables with a P-value less than 0.2 were selected as confounders. The adjusted model included educational status (categorical), marital status (categorical), BMI (categorical), physical activity (categorical), socioeconomic status (categorical), depression (yes/no), diabetes (yes/no), hypertension (yes/no), smoking (yes/no), stillbirth (yes/no), and infertility (yes/no). All analyses were performed using SPSS software version 22. All p-values are two-sided, and p-values less than 0.05 with 95% confidence intervals were considered statistically significant.

### **Results**

A total of 2649 women with a mean age of 57.21±5.8 years (range: 35–70 years) were included. Among these women, 225 (8.5%) reported premature menopause, 198 (7.5%) reported early menopause, and 2226 (84%) reported normal menopause. The mean age at menopause was 49.01±5.39 years. Furthermore, 75.5% of the study participants were married. A total of 86.9% of the female participants were housekeepers, and 82.5% of the women in the study had (physical activity ≥41). Participants with a history of smoking (3.4%), depression (21.7%), infertility (9.2%), hypertension (46.4%), diabetes (29.6%), stillbirth (13.1%), cardiac disease (14.9%), and 31.6% early menarche (age at menarche ≤13) were in the study. We observed significant differences among the

three menopausal age groups in terms of age, educational status, job status, cardiac disease, depression, infertility, and diabetes. (Table 1).

**Table 1. Baseline characteristics of menopausal women**

		Total	Early menopause	Late menopause		
<b>Quantitative variables</b>						
Age (years)		57.21±5.8	54.39±7.6	53.16±6.5	57.86±5.27	0.001*
Cholesterol (mg/dl)		193.49±42.7	188.26±40.7	195.08±42.57	193.87±42.92	0.14
Triglycerides (mg/dl)		152.83±92.3	148.59±93.38	142.2±79.48	154.2±93.29	0.16
<b>Qualitative variables</b>						
		<b>Number (%)</b>				
Educational status	<6(year)	2025(76.4%)	165(73.3%)	128(64.6%)	1732(77.8%)	0.001*
	6-12(year)	494(18.6%)	50(22.2%)	57(28.8%)	387(17.4%)	
	>12(year)	130(4.9%)	10(4.4%)	13(6.6%)	107(4.8%)	
Married status	single	20(0.8)	0	4(2%)	16(0.7%)	0.108
	Married	2001(75.5%)	177(78.7%)	152(76.8%)	1672(75.1%)	
	Divorced/widow	628(23.7%)	48(21.3%)	42(21.2%)	538(24.2%)	
job status	Housekeeper	2302(86.9%)	198(88%)	163(82.3%)	1941(87.2%)	0.028*
	Employee	288(10.9%)	18(8%)	27(13.6%)	243(10.9%)	
	Other jobs	59(2.2%)	9(4%)	8(4%)	42(1.9%)	
Physical activity	<41 (hours)	2185(82.5%)	189(84%)	165(83.3%)	1831(82.3%)	0.76
	>=41(hours)	464(17.5%)	36(16%)	33(16.7%)	395(17.7%)	
Body Mass Index	<18.5	48(1.8%)	5(2.3%)	4(2%)	39(1.8%)	0.67
	18.5-24.9	612(23.4%)	48(21.6%)	39(19.9%)	525(23.9%)	
	25-29.9	996(38.1%)	79(35.6%)	82(41.8%)	835(38.1%)	
	>=30	955(36.6%)	90(40.5%)	71(36.2%)	794(36.2%)	
Socioeconomic status	poor	915(34.5%)	71(3.6%)	60(30.3%)	784(35.2%)	0.18
	moderate	857(32.4%)	73(32.4%)	59(29.8%)	725(32.6%)	
	Rich	877(33.1%)	81(36%)	79(39.9%)	717(32.2%)	
Cardiac Disease	yes	394(14.9%)	46(20.4%)	29(14.6%)	319(14.3%)	0.049*
	No	2255(85.1%)	179(79.6%)	169(85.4%)	1907(85.7%)	
Depression	yes	576(21.7%)	63(28%)	50(25.3%)	463(20.8%)	0.021*
	No	2073(78.3%)	162(72%)	148(74.8%)	1763(79.2%)	
Infertility	yes	241(9.2%)	30(13.3%)	22(11.3%)	189(8.6%)	0.033*
	No	2388(90.8%)	195(86.7%)	172(88.7%)	2021(91.4%)	
Smoking	yes	90(3.4%)	6(2.7%)	7(3.5%)	77(3.5%)	0.81
	No	2558(96.6%)	219(97.3%)	191(96.5%)	2148(96.5%)	
Hypertension	yes	1229(46.4%)	97(43.1%)	81(40.9%)	1051(47.2%)	0.13
	No	1420(53.6%)	128(56.9%)	117(59.1%)	1175(52.8%)	

Diabetes	yes	784(29.6%)	59(26.2%)	44(22.2%)	681(30.6%)	0.024*
	No	1865(70.4%)	166(73.8%)	154(77.8%)	1545(69.4%)	
Stillbirth	yes	337(13.1%)	35(16.4%)	17(9%)	285(13.1%)	0.087
	No	2240(86.9%)	178(83.6%)	172(91%)	1890(86.9%)	
Age at menarche (years)	Early(<=13)	836(31.6%)	61(27.1%)	60(30.3%)	715(32.1%)	0.28
	Late(>13)	1813(68.4%)	164(72.9%)	138(69.7%)	1511(67.9%)	

\* Significant difference P < 0.05 chi-square and Fisher's exact tests for categorical variables, Anova test for quantitative variables.

Table 2 shows the associations between sociodemographic characteristics and different subgroups of menopausal status (premature, early, and normal). In general, menopausal age is associated with educational status, job status, BMI, socioeconomic status, depression, infertility, hypertension, diabetes, and age at menarche. In the premature menopause group, menopausal age was associated with body mass index. In the early menopause group, menopausal age was associated with marital status and infertility. During normal menopause, menopausal age is associated with educational status, marital status, physical activity, body mass index, hypertension, and age at menarche.

**Table 2. Mean menopausal age based on categorical variables**

characteristics	Total(n=2649)		Premature menopause age(n=225)		Early menopause age (n=198)		Normal menopause age(n=2226)	
	Mean±SD	P value	Mean±SD	P value	Mean±SD	P value	Mean±SD	P value
Educational status								
<6(year)	49.27±5.45	0.001*	36.79±4.56	0.49	42.71±1.16	0.23	50.94±3.44	0.001*
6-12(year)	48.14±5.27		37.16±3.06		42.7±1.06		50.36±3.04	
>12(year)	48.36±4.56		38.3±1.88		43±1.15		49.9±3.05	
Married status								
single	47.85±3.54	0.11	0	0.64	42.5±1.29	0.027*	49.19±2.45	0.04*
Married	48.9±5.41		36.86±4.34		42.84±1.043		50.74±3.3	
Divorced/widow	49.37±5.38		37.19±3.58		42.3±1.22		51.01±3.57	
job status								
housekeeper	49.06±5.42	0.01*	36.86±4.33	0.15	42.7±1.1	0.8	50.84±3.75	0.28
Employee	49.07±4.68		38.5±1.65		42.85±1.134		50.54±3.3	
Other jobs	46.9±6.42		35.44±3.84		42.6±1.06		50.17±3.41	
Physical activity								
<41 (hours)	48.92±5.4	0.058	37.19±4.16	0.68	42.72±1.12	0.73	50.72±3.35	0.03*
>=41(hours)	49.44±5.35		36.89±4.2		42.7±1.02		51.11±3.43	
Body Mass Index								
<18.5	49.1±4.56	0.014*	39.6±0.89	0.036*	43.25±0.95	0.47	50.9±2.58	0.001*
18.5-24.9	49.17±4.7		39.19±3.07		42.6±1.06		50.5±3.34	
25-29.9	49.54±4.82		39.9±3.84		42.8±1.065		51±3.26	
>=30	48.83±4.88		38.3±3.93		42.62±1.16		50.47±3.19	
socioeconomic status								
poor	49.12±5.45		36.66±4.5		42.53±1.11		50.75±3.57	

moderate	49.29±5.19	0.032*	37.5±3.27	0.32	42.78±1.13	0.25	51±3.2	0.095
Rich	48.63±5.51		36.67±4.61		42.84±1.06		50.62±3.28	
Cardiac Disease								
yes	48.75±5.83		37.11±4.01		42.83±1.1		50.76±3.35	
No	49.06±5.31	0.3	36.89±4.24	0.339	42.7±1.1	0.59	50.97±3.45	0.3
depression								
yes	49.17±5.27		37.07±4.27		42.69±1.1		50.46±3.21	
No	48.45±5.79	0.005*	36.5±3.97	0.43	42.83±1.09	0.4	51.16±3.49	0.41
infertility								
yes	48.11±6.08		36.73±4.44	0.77	42.23±1.19	0.02*	50.6±3.32	0.39
No	49.11±5.32	0.006*	36.97±4.16		42.8±1.07		50.82±3.35	
smoking								
yes	48.99±5.38	0.32	36.98±4.16	0.39	42.43±0.97	0.46	51.31±3.5	0.16
No	49.57±5.7		35.5±5.2		42.74±1.1		50.76±3.35	
Hypertension								
yes	48.61±5.31	0.001*	37.02±4.48	0.72	42.84±1.09	0.68	51.16±3.49	0.001*
No	49.48±5.45		36.82±3.78		42.69±1.1		50.46±3.29	
diabetes								
yes	49.47±5.32		36.93±4.47	0.95	42.66±1.14	0.64	50.9±3.57	0.06
No	48.82±5.41	0.005*	36.97±3.3		42.75±1.09		50.7±3.27	
stillbirth								
yes	49.08±6.017	0.97	36.26±5.4	0.24	42.53±0.97	0.39	51.05±3.5	0.19
No	49.08±5.23		37.13±3.73		42.77±1.09		50.77±3.33	
Age at menarche (years)								
Early(≤13)	48.84±5.36	0.014*	36.59±5.06	0.44	42.62±1.15	0.35	51.05±3.46	0.01*
Late(>13)	49.39±5.45		37.07±3.83		42.78±1.08		50.67±3.32	

An independent t-test was used to compare the mean age at menopause between two groups; The ANOVA test was used to compare the mean age at menopause in more than two groups. \*Significant difference  $P < 0.05$ .

Table 3 displays the relationships between premature and early menopause and the selected variables, as analyzed using a multiple logistic regression model. As shown in this table, single women had greater odds of premature menopause (OR: 2.48, 95% CI: (1.23, 5.1)). Women with physical activity <41 years had greater odds of premature and early menopause (OR: 1.23, 95% CI: (1.02, 1.63), OR: 1.25, 95% CI: (1.12, 2.35), respectively). Additionally, having diabetes increased the odds of premature and early menopause (OR: 1.51, 95% CI: (1.07, 2.13), OR: 1.23, 95% CI: (1.1, 2.53), respectively). Women with a history of stillbirth had greater odds of premature menopause (OR: 1.7, 95% CI: (1.2, 2.2)). Women with a history of depression had greater odds of premature and early menopause (OR: 1.3, 95% CI: (1.1, 1.84), OR: 1.23, 95% CI: (1.02, 2.3), respectively). Women with a high BMI (OR: 1.22, 95% CI: (1.1–1.62)) and a history of infertility had greater odds of early menopause (OR: 1.51, 95% CI: (1.09–2.1)).

**Table 3. A multiple logistic regression model to identify risk factors associated with the age of menopause**

variable	Premature menopause vs. Normal menopause	Early menopause vs. Normal menopause
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	Adjusted OR	95%CI	P value	Adjusted OR	95%CI	P value
<b>Educational status</b>						
<6(year)	Ref					
6-12 (year)	1.14	(0.78,1.66)	0.47	1.23	(0.74,2.04)	0.41
>12 (year)	0.97	(0.51,1.91)	0.95	0.95	(0.73,1.27)	0.83
<b>Married status</b>						
single	2.48	(1.23,5.1)	0.023*	1.33	(0.46,3.85)	0.59
Married	1.14	(0.71,1.45)	0.48	0.96	(0.73,1.24)	0.79
Divorced/widow	Ref					
<b>Body Mass Index</b>						
<18.2	1.132	(0.39-3.24)	0.81	0.87	(0.21-0.98)	0.36
18.5-24.9	0.84	(0.56-1.27)	0.42	1.05	(0.82-1.33)	0.68
25-29.9	1.17	(0.8-1.52)	0.51	1.22	(1.1-1.62)	0.016*
>=30	Ref					
<b>Physical activity</b>						
<41 (hours)	1.23	(1.02,1.63)	0.035*	1.25	(1.12,2.35)	0.04*
>=41(hours)	Ref					
<b>Socioeconomic status</b>						
poor	1.7	(0.51,2.23)	0.2	1.31	(0.98,1.74)	0.064
moderate	1.8	(0.57,2.17)	0.33	1.16	(0.88,1.51)	0.27
Rich	Ref					
<b>Depression</b>						
yes	1.3	(1.1,1.84)	0.012*	1.23	(1.02,2.3)	0.007*
No	Ref					
<b>Diabetes</b>						
yes	1.51	(1.07,2.13)	0.02*	1.23	(1.1,2.53)	0.036*
No	Ref					
<b>Hypertension</b>						
yes	0.786	(0.58-1.7)	0.1	1.18	(0.99-1.59)	0.053
No						
<b>Stillbirth</b>						
yes	1.7	(1.2,2.2)	0.03*	1.68	(0.62,2.13)	0.36
No	Ref					
<b>Smoking</b>						
yes	0.98	(0.43-2.09)	0.912	1.13	(0.48-1.58)	0.68
No	Ref					
<b>Infertility</b>						
yes	1.29	(0.81-2.06)	0.27	1.51	(1.09-2.1)	0.013*
No	Ref					

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\*Significant difference  $P < 0.05$ ; OR: odds ratio; CI: confidence interval.

## Discussion

This study aimed to explore the determinants and predictors of age at menopause among Iranian women in the Zahedan Adult Cohort Study in Southeastern Iran (PERSIAN). We investigated the risk factors for age at menopause in general and by classifying early, premature, and normal menopause. Our findings revealed that the mean age of menopause in our sample was  $49.01 \pm 5.39$  years, which aligns with previous research conducted in Iran, where the average age at menopause has been reported to range from 48.3–49.6 years [28–33]. Notably, Iranian women tend to experience menopause earlier than their counterparts in Europe, 50.1–52.8 years, and North America, 50.5–51.4 years. However, the menopausal age of our population was greater than that of the Middle East, 46.9–47.8 years, and Latin America, 45.9–41.6 years [6]. The observed differences in menopausal age across geographical regions may be attributed to a combination of genetic, social, economic, and lifestyle factors [34]. For example, premature menopause is often linked to genetic disorders, autoimmune conditions, and certain medical interventions [35]. Additionally, early menopause may be influenced by an accelerated aging process due to both genetic predispositions and environmental factors [36]. Our analysis revealed no significant correlation between education level and age at menopause, which is consistent with the findings of some studies [29, 37, 38] but contrasts with those of other studies that reported a significant relationship [38, 39].

Interestingly, single women were more likely to experience premature and early menopause than their married counterparts were, particularly in cases of premature menopause, which aligns with the findings of Farjami et al. [39]. This finding underscores the potential role of social support structures in influencing menopausal timing. The results of our study demonstrated that physical activity is a significant predictor of menopausal age; in this study, lower levels of physical activity were associated with increased odds of both premature and early menopause, which is consistent with some studies [40, 41] and contradicts others [42]. This aligns with the literature suggesting that active lifestyles may contribute positively to reproductive health outcomes in women. Our study revealed that a higher BMI was linked to increased odds of early menopause, corroborating findings from previous research indicating that obesity can adversely affect hormonal balance and reproductive function [43, 44]. Socioeconomic status plays a critical role in determining menopausal timing. Our results indicated that women from lower socioeconomic backgrounds had higher odds of experiencing premature and early menopause, although this relationship was not statistically significant in our analysis. However, several studies have reported a significant association between earlier age at normal menopause and lower social class [45–47]. A study by Golshiri (2015) indicated that women with lower socioeconomic status experience menopause at an earlier mean age, nearly three years earlier than those with moderate socioeconomic status. Additionally, women with moderate socioeconomic status have an earlier mean age at menopause, approximately four years earlier than women with high socioeconomic status [48]. Research has shown a link between early menopause and a heightened risk of cardiovascular disease and hypertension, highlighting the importance of monitoring health outcomes in this group. [49, 50].

In this study, we observed associations between a history of hypertension and early onset of menopause; however, these relationships were not statistically significant. Fertility history appears to affect the timing of menopause. Some studies indicate that women with a history of infertility or stillbirth experience menopause earlier than those without such a history. [35, 48]. In this study, a history of stillbirth increased the odds of premature menopause, and a history of infertility increased the odds of early menopause. These findings suggest that reproductive events may have lasting effects on women's health trajectories. Our study also revealed unexpected findings regarding smoking, while the literature often associates smoking with the earlier onset of menopause [51, 52]. Some studies have shown a statistically significant relationship between smoking and the age of menopause [53–55]. However, other studies, including the current one, did not find similar results [56]. This could be attributed to the small number of smokers in the cohort study or the absence of this habit among Iranian women. Evidence suggests that diabetes may contribute to the early onset of menopause. [57]. Specifically, women diagnosed with type 1 diabetes often experience menopause approximately five years earlier than their counterparts without diabetes do [58]. However, some studies have failed to corroborate these findings. For example, research conducted by Brand et al. revealed that women who developed diabetes before the age of 20 years experienced earlier menopausal onset. In contrast, those diagnosed after the age of 50 years experienced a delay in menopause [59]. Moreover, no significant correlation was found between diabetes onset between the

ages of 20 and 50 years and the age at which menopause began. In our study, women with a history of diabetes presented odds of experiencing premature and early menopause that were greater. Additionally, our findings suggest that women who began menstruating before the age of 13 years had elevated odds of both premature and early menopause. This observation aligns with certain studies but contradicts others in the literature [60-63]. The increased risk of depression during menopause has been attributed to biological vulnerability, with studies finding an association between greater variation in estradiol and follicle-stimulating hormone (FSH) levels and higher depressive symptoms [64]. Our findings revealed that a history of depression was also associated with increased odds of premature and early menopause, corroborating findings from Shea et al., which indicated a similar association between depression and menopausal timing [65].

#### **Strengths and limitations**

The strengths of our study include its large sample size and comprehensive evaluation of various factors influencing menopausal age among women. A significant advantage of our research is the adjustment for numerous potential confounders, such as demographic information and medical history. However, we acknowledge several limitations in our study. First, data regarding outcomes and exposures were primarily self-reported, which may introduce misclassification and recall bias among participants. Moreover, remembering the exact time of menopause might be subject to recall bias as well. Second, we excluded women over the age of 70 years, who might face more severe health challenges that could affect menopausal timing. Finally, the cross-sectional nature of our study limits our ability to establish causal relationships between various factors and age at menopause; thus, further longitudinal studies are warranted to elucidate these associations.

#### **Conclusion**

The findings of this study revealed that while genetic factors significantly influence the age at menopause, social factors such as marital status and pregnancy also play important roles.

The results of the study show that improving the health of premenopausal women requires a multidimensional approach that simultaneously includes regular physical activity, screening for mental disorders, healthy nutrition, diabetes prevention, and social support. Implementing community-based interventions and integrating screenings into primary care can lead to effective prevention of physical and psychological consequences of this period and sustainably improve women's quality of life. Menopause information relied on self-reports, potentially introducing reporting bias and misclassification of menopausal status.