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Original Article

# Age at Natural Menopause and Associated Influencing Factors: A Cross-Sectional Analysis From the Shahrekord Cohort Study

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**Abstract**

**Background and aims:** Menopause is a natural phase in a woman's life that is influenced by various factors. This study aimed to identify the age at natural menopause and its associated factors within a large-scale, population-based cohort in Iran.

**Methods:** A subset of data collected during the enrollment phase of the Shahrekord Cohort Study (SCS) was utilized in this study. General information, along with factors related to fertility and childbearing, was gathered using a structured questionnaire. The data were analyzed using independent t-tests, ANOVA, Pearson correlation tests, and a linear regression model.

**Results:** Among the participants of the SCS, 2,141 were menopausal women. The mean age at natural and unnatural menopause was 49.30±5.9 and 45.26±7 years, respectively. Based on the results, job status, body mass index, history of hypertension, ischemic heart disease, number of pregnancies and live births, breastfeeding history and duration (in months), history of infertility treatment, contraceptive use, use of contraceptive pills, use of hormone replacement therapy, and age at oophorectomy influenced the age of menopause. However, after adjusting for confounding variables, none of these factors were significantly associated with natural menopause.

**Conclusion:** Overall, the mean age at natural menopause was consistent with the findings of other studies conducted in Iran. Following adjustment for confounding variables, none of the examined factors were remarkably related to natural menopause.

**Keywords:** Menopause, Risk factor, Population-based cohort study, Shahrekord cohort study

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## Introduction

Menopause, also known as the climacteric, is defined as the permanent cessation of natural menstruation in women over the age of 40, resulting from the complete cessation of ovarian activity and changes in the hypothalamic-pituitary function, which lead to the cessation of estrogen and gonadotropin secretion. In addition, menopause is confirmed after 12 consecutive months of amenorrhea without any other apparent pathological or physiological cause (1-3). It can naturally occur as a biological phenomenon or can be artificially induced through the surgical removal of the uterus/ovaries and through gonadotoxic treatments, such as radiation therapy and chemotherapy (3, 4). According to the findings of existing studies, the average age range for menopause is between 45 and 55 years worldwide, with an estimated age of onset between 50 and 52 years, exhibiting slight variations among different countries (1, 2). It has been reported that women in developing countries experience menopause earlier than women in developed countries (5). A review study reported that the average age of menopause in Iran is 48.57 years, with a maximum age of 52 years and a minimum age of 46.34 years (6). However, comprehensive and population-based studies on the age of natural menopause and its determinants in different regions of Iran remain limited. To the best of

our knowledge, no study has systematically investigated women in Shahrekord, where cultural, environmental, and lifestyle factors may differ from other parts of the country (7).

Previous studies have indicated that menopause can be influenced by genetics, obesity, alcohol consumption, socioeconomic status, ethnicity, education, diet, exposure to pesticides, reproductive factors, and place of residence; however, the results of these studies are inconsistent (5, 8). The age at natural menopause has garnered significant attention, as menopause affects fertility and has considerable negative implications for health. Based on multiple studies, early menopause is associated with cardiovascular diseases, osteoporosis, type 2 diabetes, early cognitive dysfunction, reduced life expectancy, and increased mortality from all causes (8-12). Therefore, identifying factors related to menopause, particularly those that are modifiable, may be crucial for preventing these chronic diseases (13). According to some researchers, the age of menopause is considered an important health indicator (14). By addressing this gap, our study provides region-specific evidence that can be compared with national and international data. Such findings are important not only for confirming the generalizability of global evidence but also for informing local health policies and preventive strategies tailored to women in this community. This study aims to determine the average age of natural menopause and identify the associated factors in adult women in a cohort study conducted in Shahrekord, with the hope that its results will enhance our awareness of its risk factors.

## Materials and Methods

### *Participants*

This cross-sectional population-based study utilized data collected from the Shahrekord Cohort Study (SCS). The SCS is a population-based prospective study involving a cohort of individuals aged 35–70 years, which commenced in November 2015 in Iran. The original cohort comprises a sample size of at least 10,000 participants. Additional information can be found in the study protocol (14). This study was conducted on 2,141 women aged 35–70 years from the population registered at the Shahrekord cohort center.

### *Data Collection*

The required data were collected using a standardized self-reported questionnaire and by conducting face-to-face interviews. Although a questionnaire could collect these data, face-to-face interviews were employed to ensure higher accuracy and completeness. Trained interviewers could clarify questions, probe for detailed responses, and reduce missing or inconsistent data, especially for complex information on fertility and reproductive history.

The survey questionnaire included sections on general demographic information (e.g., employment status, education level, marital status, type of residence, and ethnicity), a history of chronic diseases (diabetes, hypertension, ischemic heart disease, thyroid disease, kidney failure, and breast cancer), body mass index (BMI), physical activity, smoking habits, and factors related to fertility and childbearing. These factors encompassed the type and age of menopause, age at menarche, number of pregnancies and live births, age at first birth, number of abortions, breastfeeding history, duration of breastfeeding (in months), and history of primary infertility and its treatment. Other factors associated with fertility and childbearing were contraceptive use, hormone replacement therapy, and surgical history related to the ovaries, including the age at which ovaries were removed and any history of tubal ligation. The weight and height of participants were measured by trained nurses to calculate BMI, following the established SCS protocol (15).

Written informed consent was obtained from all participants prior to their inclusion in the evaluation. The data were confidentially collected by a trained interviewer in a private setting, utilizing both interviews and questionnaire completion. In addition, the data collection process was supervised by a quality control officer to ensure adherence to protocol and maintain data integrity. Furthermore, all study procedures received approval from the Ethics Committee of Shahrekord University of Medical Sciences (IR.SKUMS.REC.1400.069).

### *Statistical Analysis*

The obtained data were analyzed using SPSS, version 24 (IBM Corporation, Armonk, NY, USA). Descriptive statistics, including means (±standard deviation), as well as correlation coefficients, t-tests, and analysis of variance (ANOVA), were employed to determine relationships among variables. A *P*-value of less than 0.05 was considered statistically significant. A linear regression model was utilized to adjust for potential confounding variables, and only variables meeting pre-specified criteria were included in the model.

## Results

Among the 2,141 women participating in the study, 1,681 (78.5%) experienced natural menopause, while 460 (21.5%) underwent unnatural (induced) menopause. Our results indicated that the mean age at the onset of menopause for the 2,141 women examined in the cohort study of Shahrekord was 48.52±6.3 years. Moreover, the mean ages at the onset of natural and unnatural menopause were 49.30±5.9 years and 45.68±7.0 years, respectively. The mean ages for both natural and unnatural menopause, categorized by place of residence, are illustrated in Figure 1.

A statistically significant relationship was observed between age at natural menopause in women and the variables of occupation ($P=0.026$) and marital status ($P=0.05$). The mean physical activity among the study participants was 39.88±5.8 minutes per week. However, no statistically meaningful relationship was found between

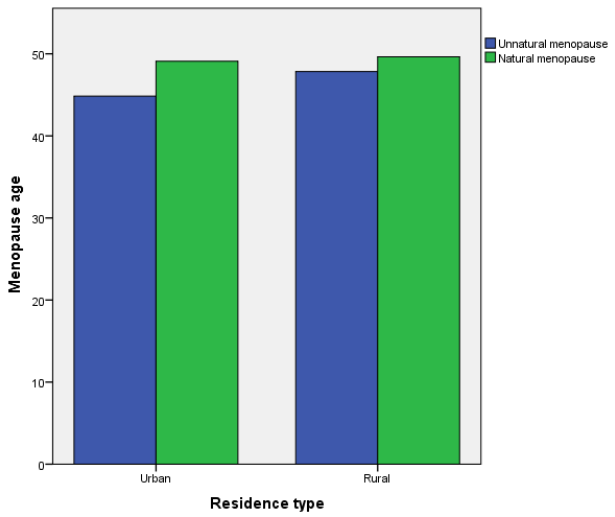


**Figure 1.** Age at the Onset of Natural and Unnatural Menopause by Type of Residence

the level of physical activity and natural menopause ($P=0.812$). Among these women, 22 individuals (1.3%) had a history of smoking; however, there was no statistically significant relationship between smoking and the age at natural menopause ($P=0.11$). Overall, 38.8% of the women were classified as having a high BMI or being obese. The results confirmed a noticeable relationship between BMI and the age at natural menopause ($P=0.024$). The results revealed a statistically significant relationship between a history of hypertension and ischemic heart disease and the age at natural menopause ($P=0.016$ and $P=0.047$, respectively; Table 1).

Table 2 presents data on the relationship between age at natural menopause and categorical reproductive and contraceptive factors. A statistically significant association was found between age at natural menopause and the history of breastfeeding, history of infertility treatment, history of contraceptive use, oral contraceptive pill use, and hormone replacement therapy ($P=0.041$, $P=0.036$, $P=0.002$, $P=0.019$, and $P<0.001$, respectively). Conversely, there was no statistically significant relationship between age at natural menopause and other categorical variables, including history of infertility, history of oophorectomy (one-sided or two-sided), history of tubectomy, use of Norplant, long-acting injectable progesterone, or intrauterine device ($P>0.05$ for all).

The results related to the relationship between age at natural menopause and continuous reproductive factors are summarized in Table 3. Age at natural menopause showed a statistically significant correlation with the duration of breastfeeding, number of pregnancies, number of live births, and age at oophorectomy ($P<0.001$ for all). However, no statistically significant correlation was observed with age at menarche, age at first birth, or number of abortions ($P>0.05$ for all).

Based on the obtained data (Table 4), the linear regression analysis, adjusted for potential confounding variables, revealed that none of the studied variables were significantly associated with age at natural menopause ($P>0.05$). While some variables demonstrated trends, the 95% confidence intervals included zero, confirming the lack of statistically significant effects. Comparisons with Pearson correlation tests, t-tests, and ANOVA revealed that apparent associations in unadjusted analyses may have been influenced by confounding factors (Table 4).

## Discussion

Our results indicated that the mean age of onset of menopause in the overall population of women examined in the SCS was 48.52 ± 6.3 years. Moreover, the mean age of onset of natural and abnormal menopause was 49.30 ± 5.9 years and 45.68 ± 7 years, respectively.

In comparison to the results of the present study, a systematic review conducted on 27,250 individuals in Iran estimated the age at menopause to be 47.26 years (16). In other studies performed in Iran, the mean age at menopause was 48.31 ± 6.34 years in Bandare Kong and 49.6 ± 4.02 years in Hamadan (17, 18). In Astara and Isfahan, the mean age at natural menopause was 47.21 ± 4.15 years and 48.66 years, respectively (19, 20). Further, the mean age at natural menopause for women in the Tabriz cohort study was estimated at 49.2 ± 4.7 years (5), which is close to the mean age at natural menopause found in this study. Compared to other countries, the age at menopause in our study was lower than that reported in Taiwan (50.2 ± 4 years) but higher than that of Chinese women (47.7 ± 4.3 years) (21, 22). Although our findings regarding mean age at menopause and associated factors are consistent with those of previous studies, this consistency is valuable as it confirms the applicability of global evidence to the population of (region/country). In settings where local epidemiological data are limited, such confirmatory evidence strengthens the generalizability of findings and enhances understanding of women's health patterns in this community. It has been found that various factors, including environmental and genetic factors, influence the age at menopause (23). The results of our study indicated that employment status and BMI have an impact on the age at menopause; however, neither of these factors remained significant after adjusting for confounding variables.

Living in greener neighborhoods is associated with a later onset of menopause and may reduce the aging process of fertility (24). Conversely, exposure to airborne particulate matter and traffic is linked to an earlier onset of natural menopause (25). Similarly, a study conducted in Tehran demonstrated a relationship between air pollution and a decrease in the age at menopause; nonetheless, this relationship was not statistically significant (26). In this study, although the mean age at menopause was higher among individuals residing in rural areas, no statistically significant relationship was found between the age at menopause in women living in urban and rural areas.

Likewise, divorce can be a significant factor influencing the early onset of menopause in women due to the impact of various stressors on different aspects of an individual's

**Table 1.** Mean Age at Natural Menopause According to Demographic Characteristics

| Variable Frequency (%) / (Mean ± SD) | | | Age at Menopause | Statistical Test | *P* Value |
|---|---|---|---|---|---|
| Employment status (missing = 11) | Unemployed | 90 (5.4%) | 48.94 ± 5.5 | ANOVA | 0.026 [a] |
| | Employed | 172 (10.2%) | 48.08 ± 5 | | |
| | Retired | 90 (5.4%) | 49.26 ± 5 | | |
| | Homemaker | 1318 (78.4%) | 49.51 ± 6.1 | | |
| Educational level (missing = 7) | Elementary school | 196 (11.7%) | 49.44 ± 4.5 | ANOVA | 0.26 [a] |
| | Guidance school | 83 (4.9%) | 48.60 ± 6 | | |
| | Diploma | 111 (6.6%) | 49.56 ± 4.9 | | |
| | Associate degree | 46 (2.7%) | 48.24 ± 5.2 | | |
| | Bachelor's degree | 40 (2.4%) | 47.98 ± 4 | | |
| | Master's degree | 7 (0.4%) | 45.43 ± 4.7 | | |
| | Illiterate | 1191 (70.9%) | 49.42 ± 6.2 | | |
| Marital status | Single (never married) | 10 (0.6%) | 48.40 ± 3.9 | ANOVA | 0.05 [a] |
| | Married | 1413 (84.1%) | 49.22 ± 5.6 | | |
| | Widow | 246 (14.6%) | 49.99 ± 7.4 | | |
| | Divorced | 12 (0.7%) | 46 ± 6.6 | | |
| Type of residence | Urban | 1026 (61%) | 49.10 ± 5.4 | Independent t-test | 0.071 [b] |
| | Rural | 655 (39%) | 49.63 ± 6.6 | | |
| Ethnicity | Persian | 635 (37.8%) | 49.10 ± 5.2 | ANOVA | 0.076 [a] |
| | Turkish | 97 (5.8%) | 48.78 ± 6.2 | | |
| | Lor | 882 (52.5%) | 49.61 ± 6.3 | | |
| BMI (kg/m$^2$) (miss = 22) | Thin (18.5 >) | 10 (0.6%) | 45.50 ± 7.7 | ANOVA | 0.024 [a] |
| | Normal (18.5-24.9) | 350 (20.8%) | 48.87 ± 6.7 | | |
| | Overweight (25-29.9) | 646 (38.4%) | 49.21 ± 5.6 | | |
| | Obese (< 30) | 653 (38.8%) | 49.71 ± 5.6 | | |
| Smoking | Yes | 22 (1.3%) | 51.36 ± 5.8 | Independent t-test | 0.11 [b] |
| | No | 1659 (98.7%) | 49.28 ± 5.9 | | |
| Diabetes | Yes | 309 (18.4%) | 49.61 ± 6 | Independent t-test | 0.321 [b] |
| | No | 1372 (81.6%) | 49.24 ± 5.9 | | |
| Hypertension | Yes | 591 (35.2%) | 49.78 ± 9 | Independent t-test | 0.016 [b] |
| | No | 1090 (64.8%) | 49.05 ± 5.9 | | |
| Ischemic heart disease | Yes | 146 (8.7%) | 50.14 ± 5.2 | Independent t-test | 0.047 b |
| | No | 1535 (91.3%) | 49.22 ± 6 | | |
| Thyroid disease | Yes | 315 (18.7%) | 49.30 ± 5.4 | Independent t-test | 0.996 [b] |
| | No | 1366 (81.3%) | 49.30 ± 6 | | |
| Kidney failure disease | Yes | 15 (0.9%) | 49.07 ± 5.6 | Independent t-test | 0.872[b] |
| | No | 1666 (99.1%) | 49.31 ± 5.9 | | |
| Breast cancer | Yes | 18 (1.1%) | 48 ± 5.8 | Independent t-test | 0.348[b] |
| | No | 1663 (98.9%) | 49.32 ± 5.9 | | |
| Physical activity (MET) minutes/week | | 39.88 ± 5.8 | 49.30 ± 5.9 | Pearson correlation | 0.812[c] |

*Note*. BMI: Body mass index; ANOVA: Analysis of variance; MET: Metabolic equivalent of task.

life (27). In this study, the mean age at menopause was lower among divorced individuals. The results of a study performed in Fasa revealed that the age at menopause in single individuals was significantly lower compared to that of married individuals (28). This may be associated with regular ovarian activity and continuous follicle stimulation influenced by pituitary hormones, which could delay menopause (29). Consistent with the findings of the mentioned study, our results also showed that the age at menopause was higher in married individuals compared to single individuals.

The use of contraceptive pills reduces the rate of decline in ovarian follicle reserve, consequently leading to a decreased risk of early menopause (30). In the present study, a statistically significant relationship was also observed between the use of oral contraceptive pills and the age at menopause.

The oocyte recovery hypothesis suggests that the

**Table 2.** Mean Age at Natural Menopause by Categorical Variables

| Variable | Categories/Frequency (%) | Age at Menopause (Mean ± SD) | Statistical Test | *P* Value |
|---|---|---|---|---|
| Breastfeeding history | Yes: 1657 (97.6)<br>No: 24 (1.4) | 49.34 ± 5.9<br>46.67 ± 6.0 | Independent t-test | 0.041 |
| Infertility | Yes: 152 (9)<br>No: 1519 (90.4) | 48.54 ± 6.4<br>49.39 ± 5.9 | Independent t-test | 0.093 |
| History of infertility treatment | Yes: 88 (5.2)<br>No: 1583 (94.1) | 48.02 ± 6.2<br>49.38 ± 5.9 | Independent t-test | 0.036 |
| History of oophorectomy | One-sided: 28 (1.7)<br>Two-sided: 8 (0.5)<br>No: 1645 (97.9) | 48.14 ± 5.2<br>50.75 ± 6.5<br>49.32 ± 5.9 | ANOVA | 0.458 |
| History of tubectomy | Yes: 926 (55.1)<br>No: 755 (44.9) | 49.21 ± 5.9<br>49.42 ± 5.9 | Independent t-test | 0.451 |
| History of contraception | Yes: 879 (52.3)<br>No: 802 (47.7) | 48.88 ± 5.6<br>49.77 ± 6.2 | Independent t-test | 0.002 |
| Contraceptive pills | Yes: 775 (46.1)<br>No: 906 (53.9) | 48.94 ± 5.6<br>46.61 ± 6.1 | Independent t-test | 0.019 |
| Norplant | Yes: 7 (0.4)<br>No: 1674 (99.6) | 46.57 ± 5.2<br>49.31 ± 5.9 | Independent t-test | 0.215 |
| Long-acting injectable progesterone | Yes: 124 (7.4)<br>No: 1557 (92.6) | 48.32 ± 6.3<br>49.38 ± 5.9 | Independent t-test | 0.073 |
| Intrauterine device | Yes: 199 (11.8)<br>No: 1482 (88.2) | 48.92 ± 4.9<br>49.35 ± 6.0 | Independent t-test | 0.336 |
| Use of hormone replacement therapy | Yes: 94 (5.6)<br>No: 1458 (86.7)<br>I do not know: 129 (7.7) | 46.16 ± 6.2<br>49.67 ± 5.7<br>47.48 ± 7.2 | ANOVA | < 0.001 |

*Note*. SD: Standard deviation; ANOVA: Analysis of variance.

**Table 3.** Mean Age at Natural Menopause by Continuous Variables

| Variable | Mean ± SD | Age at Menopause (Mean ± SD) | Statistical Test | *P* value |
|---|---|---|---|---|
| Age at Menarche (years) | 13.88 ± 1.9 | 49.30 ± 5.9 | Pearson correlation | 0.149 |
| Age at first birth (years) | 19.26 ± 4.2 | 49.30 ± 5.9 | Pearson correlation | 0.079 |
| Duration of breastfeeding (months) | 102.34 ± 51.9 | 49.30 ± 5.9 | Pearson correlation | < 0.001 |
| Number of pregnancies | 0–>10 (grouped) | 46.67–51.88 ± 6.5 | ANOVA | < 0.001 |
| Number of live births | 0–>10 (grouped) | 47.55–52.25 ± 7.2 | ANOVA | < 0.001 |
| Number of abortions | 0–>6 (grouped) | 48.64–53.0 ± 5.6 | ANOVA | 0.643 |
| Age at oophorectomy (years) | 41.11 ± 13.8 | 49.30 ± 5.9 | Pearson correlation | < 0.001 |

*Note*. ANOVA: Analysis of variance; SD: Standard deviation.

absorption and atresia of ovarian follicles during pregnancy are suppressed, which helps preserve the ovarian follicle reserve, thereby contributing to delayed menopause (31). If this hypothesis holds true, the age at menopause would increase with the number of childbirths. The current study also supports the oocyte recovery hypothesis. Additionally, the age at menopause in women without children was lower compared to women with children, which aligns with the oocyte recovery theory. According to previous research, women who have never given birth or have given birth only once are at a higher risk of early menopause (8).

Langton et al examined the relationship between the age at menopause, number of childbirths, and breastfeeding in the United States (8) and concluded that the number of childbirths and breastfeeding are associated with a reduced risk of early menopause (8). In the present study, a statistically significant relationship was also found between the number of childbirths, the number of live births, breastfeeding, and the age at menopause. Similarly, a study conducted in Tabriz confirmed the relationship between breastfeeding and age at menopause (5).

In this study, a history of oophorectomy revealed no significant relationship with the age at menopause; however, the age at which the ovaries were removed was associated with the age at menopause. Although the mechanism by which hysterectomy affects menopause remains unclear, it may potentially increase ovarian dysfunction (32).

Changes in the concentration of sex hormones that occur after menopause can also affect the regulation of body fat deposition (33). A meta-analysis performed on Iranian women demonstrated that the average age at menopause is higher in obese individuals (6), which is consistent with the results of the present study.

The decrease in estrogen levels is the most significant physiological change during menopause. This reduction in estrogen affects various organs and systems in the body, including the cardiovascular and skeletal systems, thereby increasing the risks of metabolic syndrome, diabetes, cardiovascular diseases, osteoporosis, and fractures (34-

**Table 4.** Results of Multiple Linear Regression Analysis for Predicting Age at Natural Menopause

| Variable | β (Regression Coefficient) | SE | T-Value | 95% CI Lower | 95% CI Upper | *P* Value |
|---|---|---|---|---|---|---|
| Marital status | 0.09 | 0.439 | 0.205 | -0.77 | 0.95 | 0.84 |
| Employment status | -0.34 | 0.236 | -1.44 | -0.803 | 0.123 | 0.17 |
| Type of residence | -0.3 | 0.441 | -0.68 | -1.165 | 0.565 | 0.51 |
| Age at menarche | 0.19 | 0.202 | 0.94 | -0.206 | 0.586 | 0.36 |
| Age at first birth | 0.31 | 0.25 | 1.24 | -0.18 | 0.8 | 0.23 |
| Use of hormone replacement therapy | 0.16 | 0.219 | 0.73 | -0.269 | 0.589 | 0.48 |
| Duration of breastfeeding | 0.55 | 0.423 | 1.3 | -0.279 | 1.379 | 0.21 |
| Age at oophorectomy | 0.28 | 0.214 | 1.31 | -0.139 | 0.699 | 0.21 |
| Hypertension | 0.07 | 0.233 | 0.3 | -0.387 | 0.527 | 0.77 |
| Ischemic heart disease | -0.07 | 0.219 | -0.32 | -0.499 | 0.359 | 0.75 |
| Ethnicity | -0.2 | 0.26 | -0.77 | -0.71 | 0.31 | 0.46 |
| Infertility | -0.05 | 0.556 | -0.09 | -1.14 | 1.04 | 0.93 |
| History of infertility treatment | -0.11 | 0.5 | -0.22 | -1.09 | 0.87 | 0.83 |
| History of contraception | -0.05 | 0.5 | -0.1 | -1.03 | 0.93 | 0.92 |
| Contraceptive pills | -0.3 | 0.423 | -0.71 | -1.129 | 0.529 | 0.49 |
| Long-acting injectable progesterone | 0.122 | 0.182 | 0.67 | -0.235 | 0.479 | 0.52 |
| Number of pregnancies | -0.06 | 0.316 | -0.19 | -0.679 | 0.559 | 0.85 |

*Note*. β: Regression coefficient; SE: Standard error; CI: Confidence interval.

38). In this study, there was a statistically significant relationship between a history of hypertension and ischemic heart disease with the age at natural menopause.

Among the strengths of this study was the use of a large sample size, which consequently provides a high statistical power for the tests applied. However, one of the limitations of this study was the collection of data through self-reporting, which may introduce recall bias. Another limitation was the lack of genetic data, which are known to play a key role in the timing of menopause (39-40), potentially limiting the scope of our findings. Accordingly, future studies should incorporate genetic data to provide a more comprehensive understanding of menopausal timing. It is also recommended that future studies adopt a prospective design to examine the incidence of certain diseases, mortality, and their specific causes in relation to the onset of natural menopause.

## Conclusion

In our study, the average age at natural menopause was similar to the findings of other Iranian studies but lower than the global average. After adjustment for confounding variables, none of the variables under investigation were associated with the age at menopause. Thus, further research is needed to investigate the physiological mechanisms of factors related to the age at menopause and their effects on ovarian follicles.

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### Authors' Contribution

**Data curation:** Elham Amini, Ali Ahmadi.
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### Competing Interests

The authors declare that there is no conflict of interests regarding the publication of this article.

### Ethical Approval

The study received approval from the Ethics Committee of Shahrekord University of Medical Sciences (IR.SKUMS.REC.1400.069).

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