

# Menarche and menopausal age changes over 40 years and its effective factors in women studied in Cohort Fasa population

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## Research

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# Abstract

**Background:** Age at menarche and menopause is affected by various factors. A reduction has been observed in these ages over time. The present study aimed to determine the trend of changes in age at menarche and age at menopause among the women participating in Fasa Cohort Study over a 40-year period.

**Methods:** This cross-sectional, descriptive-analytical study was conducted on 5545 women aged over 35 years in Fasa cohort population as a branch of the Persian cohort study. The participants were selected via census. The study data were obtained from the information registered in Fasa Cohort Center. Then, they were entered into the SPSS 22 software and were analyzed using descriptive statistics, chi-square test, correlation coefficient, and linear regression analysis.

**Results:** The results showed that the mean age at menarche reduced from 14.66 to 13.40 years and the mean age at menopause decreased from 56.88 to 40.16 years over the 40-year period, and the reductions were statistically significant ( $p < 0.001$ ). Age at menarche was affected by body mass index and physical activity. Besides, age at menopause was affected by education level, marital status, diabetes, hypertension, cardiovascular diseases, cervical cancer, hysterectomy, and stillbirth ( $p < 0.001$ ).

**Conclusion:** The results showed a decrease in age at menarche and age at menopause over the 40-year period.

## Introduction

Menarche is an important stage in women's development. It is one of the main indicators of the beginning of reproductive ages whose increase or decrease has direct effects on the society's reproductive indices and, consequently, economic, social, and population variables. It is also among the determinants of women's health status and maturity(1, 2). Puberty is one of the most important stages of life, which is accompanied with numerous physical, mental, and emotional variations. Heredity has been introduced as the major determinant of the age of puberty. Studies on the relationship between age at puberty in mothers and daughters as well as in sisters have also confirmed the role of heredity in puberty(3-5). Age at menarche has been reported to be affected by environmental factors, family size, social status, Body Mass Index (BMI), and genetic factors(5).

A woman's reproductive age is ended by the incidence of menopause. Based on the World Health Organization (WHO), menopause has been defined as the cessation of menstrual cycles due to the end of ovarian follicles activity, indicating the end of women's reproductive ages. Accordingly, menopause can be defined as the cessation of menstrual cycles for at least 12 months, which is not associated with pregnancy, breastfeeding, or other hormonal disorders(6). Various studies in Iran and the world have indicated that menopause age can be potentially affected by race, genetic factors, socioeconomic status, reproductive status, physical activity, nutrition, sexual behaviors, diseases, etc. To date, considering the increase in life expectancy around the world, women spend nearly one-third of their lifetime (20-30 years)

after the incidence of menopause, and tend to experience major short- and long-term problems, including the cessation or reduction of estrogen level, vasomotor instability (hot flashing and sweating), osteoporosis, cardiovascular diseases, urogenital atrophy, and psychosocial disorders(7).

Up to now, few studies have been conducted on the changes in age at menarche and age at menopause over a long period of time. Therefore, the present study aims to investigate the changes in age at menarche and age at menopause and their effective factors among the women participating in Fasa Cohort study over a 40-year period.

## Materials And Methods

In this cross-sectional, descriptive-analytical study, self-report data were obtained from Fasa cohort population. Fasa Cohort Study was designed to evaluate the risk factors of non-communicable diseases in Fasa(8). The present study was conducted on 5545 females aged 35 years and above who had participated in the first phase of Fasa Cohort Study as a branch of the Persian Cohort Study. The participants were selected via census. The participants were divided into 10-year age ranges and changes in age at menarche and age at menopause as well as their effective factors were explored. Number of live births, education level, cigarette smoking, hookah smoking, physical activity, history of infertility, history of tubectomy and hysterectomy, history of diabetes, and BMI were evaluated as predictor variables. All analyses were performed using the SPSS 22 software. Quantitative variables were described using mean and standard deviation, while qualitative variables were described using frequency and percentage. Log-rank test and Cox regression analysis were used, as well.

This article was extracted from a general medicine dissertation approved by Fasa University of Medical Sciences (code: 97143) and the University's Ethics Committee (IR.FUMS.REC.1397.131).

## Results

This study was conducted on 5545 participants, including 2199 menopausal women. The mean age at menarche was  $13.59 \pm 1.73$  years. The largest number of participants belonged to the 35-45 age group with the mean age at menarche of  $13.1 \pm 40.73$  years, while the lowest number was related to the >70 age group with the mean age at menarche of  $14.66 \pm 2.06$  years (Table 1). In addition, the majority of the participants' age at menarche was above 11 years, and most of them had experienced menarche after the age of 15 years (Tables 2 and 3). The results revealed that the mean age at menarche decreased from  $13.40 \pm 1.73$  years in the 35-year age group to  $14.66 \pm 2.06$  years in the >75 age group over the 40-year period. This indicated a significant decline in the mean age at menarche over time ( $p < 0.001$ ).

The results revealed no significant relationship between the age at menarche and number of pregnancies ( $r = 0.29$ ,  $p = 0.35$ ) and number of miscarriages ( $r = 0.01$ ,  $p = 0.45$ ). However, age at menarche was directly correlated to the number of children ( $r = 0.038$ ,  $p = 0.007$ ) and physical activity ( $r = 0.053$ ,  $p < 0.001$ ) and reversely associated with BMI ( $r = -0.071$ ,  $p < 0.001$ ). Accordingly, each unit increase in BMI caused a 0.71-

year decrease in the age at menarche. The results showed no significant relationships between age at menarche and the history of tubectomy, oophorectomy, infertility, and hysterectomy ( $p>0.05$ ) (Table 4). No significant relationship was also observed between the age at menarche and smoking cigarette and hookah (Table 8).

The mean age at menopause was  $49.22\pm 5.99$  years. The results showed a decline in the mean age at menopause from  $56.10\pm 86.06$  years in the 75-year age group to  $40.16\pm 3.86$  years in the 35-year age group. The largest number of menopausal women belonged to the 55-56 age group, while the lowest number was related to the  $>75$  age group (Table 1). In addition, most of the participants had experienced menopause at 40-55 followed by above 55 years of age, while the lowest number of participants had experienced the phenomenon at  $<40$  ages (Tables 2 and 3).

The results revealed no significant relationship between the age at menopause and history of tubectomy ( $p=0.15$ ), oophorectomy ( $p=0.428$ ), and infertility ( $p=0.032$ ). Nonetheless, the participants who had undergone hysterectomy had experienced menopause earlier compared to those who had not ( $p<0.001$ ). Moreover, age at menarche was higher among the menopausal participants ( $p<0.001$ ) (Table 4). Furthermore, increase in BMI was associated with a decrease in age at menopause, but the difference was not statistically significant ( $p=0.73$ ) (Table 5).

The results demonstrated that the number of pregnancies, deliveries, and miscarriages was significantly higher among the menopausal women with the history of cardiovascular diseases, hypertension, stillbirth, diabetes, and cervical cancer ( $p<0.001$ ). However, no significant relationship was observed between the age at menopause and cigarette smoking, hookah use, and education level (Tables 6-8).

## Discussion

Menarche is a critical stage during puberty, which represents a successful promotion in the process of maturity and the beginning of the reproductive ability for most girls(9). In the present study, the mean age at menarche was  $13.59\pm 1.73$  years. This measure was obtained as 12.6 (4) and 12.5 years(10) in other studies conducted on Iranian girls and 12.4 (11), 13(12), and 13.6 years(13) in those conducted in other countries. In the research conducted by Ali Kabir et al. on 629 girls from 24 provinces in Iran, the mean age at menarche was computed as 13.8 years(14). In another research performed by Bahrami et al. in Iran in 2013, the mean age at menarche was found to be 12.81 years (95% CI, 12.13-56.06) using the random model(15). The discrepancy among the results might be attributed to nutritional habits, different lifestyles in different countries, physical and mental stresses, and climatic conditions. Various studies have proved the impacts of genetic factors, nutritional status, obesity, environmental hormones, and stress on the age at menarche (14, 16, 17). Genetic factors are definitely the determinant of the beginning of puberty. Yet, other factors, including nutritional status, general health status, geographical location, exposure to light, and mental status could play a role in sexual development, as well(18).

The present study findings indicated that age at menarche was positively correlated to the number of children and physical activity and reversely associated with BMI. Farahmand et al. also reported that age

at menarche decreased with increase in weight, but increased with increase in height(4). Another research carried out in Zanjan demonstrated a significant relationship between age at menarche and higher BMI, frequency of fast food consumption in a week, and higher birth rank(19). A longitudinal study carried out in the U.S. also showed that BMI exerted a more significant effect on age at menarche compared to race and ethnicity(20). Overall, all studies have shown a relationship between high BMI and lower age at menarche. Early menarche has been defined as the occurrence of menarche prior to the age of 11 years. The prevalence of early menarche was 4.6% in the present study, which was mostly detected in the 35-45 age group. The results also revealed a decrease in age at menarche with increase in BMI. Other studies have also shown higher BMI among the girls experiencing early menarche. The impact of BMI on puberty has been attributed to changes in the regulation of leptin(21). According to Frisch's theory, menarche occurs when the amount of body fat increases from 16% to 23%, which represents an increase in BMI(19). The prevalence of early menarche was found to be 8.6% in the study conducted by Al-Awadhi et al.(22). Another study conducted in the U.S. also showed this measure to be 7.8% among Whites, 12.3% among Blacks, and 13.6% among Spanish Americans(23). The observed contradictory results might originate from differences in climatic conditions and lifestyles. On the other hand, late menarche has been defined as the occurrence of menarche later than 13 years of age. The prevalence of late menarche was 76.2% in the current study. This phenomenon was mostly detected among the participants in higher age groups who had experienced menopause later, as well.

Generally, age at menarche is effective in girls' health status(24). Akter et al. disclosed that age at menarche <12 years could enhance the risk of metabolic syndrome in comparison to late menarche after 13 years of age(25). However, contradictory results have been obtained in some other studies(26). For instance, it was reported that early menarche was associated with increased risk of cardiovascular diseases, breast cancer, endometrial cancer, ovarian cancer, and mortality, while late menarche was correlated to the incidence of asthma(27).

In the current study, the mean age at menarche has found to decrease from 14.66 years in the 75-year age group to 13.40 years in the 35-year age group. Accordingly, a 0.31-year decline was observed in the age at menarche per each 10-year period. In addition, the most significant reduction was related to 65-75 and >75 age groups (0.74 years), while the least significant decline was related to the 55-65 and 65-75 age groups (0.11 years). In Tehran Lipid and Glucose Study carried out by Ainy et al., two generations of women in Tehran were compared with respect to age at menarche. The results revealed that age at menarche was lower among girls compared to their mothers(5). Hozoori et al. also showed that age at menarche was significantly lower among girls in comparison to their mothers(28). In the same vein, Biro revealed a correlation between girls' age at menarche and that of their mothers. The results also showed a decline in age at menarche over 20 years(20). Urbanization and modernization have caused changes in lifestyle, eventually resulting in a decrease in age at menarche. As mentioned earlier, the current study was only conducted on the women aged above 35 years. Hence, age at menarche might have further declined in lower ages, manifesting an increase in the incidence of precocious puberty. Therefore, effective measures should be taken by the health system for training adolescents regarding lifestyle change and reducing the age at menarche.

In the present study, the mean age at menopause was  $49.21 \pm 5.99$  years. In a previous study conducted in Iran in 2013, the mean age at menopause was 50.4 years. In addition, this age was lower among rural women compared to urban ones and higher in industrialized communities compared to non-industrial ones(29). Esmaili et al. also computed the median age at menopause to be 52 years with the confidence interval of 51.9-52.5(7). This measure was also estimated as 52 years in the studies performed in Puerto Rico and the U.S.(7, 30). In the research carried out by Rajaeefard et al. the mean age at natural menopause was reported to be 48.183 years. It was also indicated that the mean age at natural menopause was desirable in Iran compared to other countries in the region, but was lower compared to developed countries(31). This implies that the mean age at menopause, as an important phenomenon in women's life, can be changed by changing lifestyle and social status.

Some researchers have referred to age at menopause as a health index. Therefore, better understanding of the effective factors in this age could provide the ground for clinical and epidemiological predictions. Delay in menopause age could increase the risk of endometrial cancer and breast cancer(32). On the other hand, early menopause could enhance the risk of cardiovascular diseases and osteoporosis. By determining the mean age at menopause as well as the differences related to individual, social, economic, and environmental factors, birth rate, consumption of oral contraceptives, obesity, nutritional status, and other factors, steps can be taken towards modification of the risks of the aforementioned disorders. The incidence of early and late menopause that are both accompanied with specific risks could be prevented, as well.

In the present study, the individuals who had undergone tubectomy and those who had the history of infertility had experienced menopause at earlier ages, but the difference was not statistically significant. The mean age at menopause was also significantly lower among the individuals who had undergone hysterectomy. In the same line, Ahn et al. revealed lower ages at menopause among the women who had undergone hysterectomy. The mechanism of effect of hysterectomy is not known yet, but it may increase ovarian dysfunction(33).

In the current study, the participants with lower ages at menarche had experienced menopause at lower ages. On the other hand, increase in age at menarche was accompanied with increase in age at menopause. In other words, early menarche was accompanied with early menopause and late menarche with late menopause, but the difference was not statistically significant. Farahmand et al. also disclosed that increase in age at menarche was associated with increase in age at menopause ( $p=0.04$ )(4). Consistently, Farjam et al. indicated that 10.6% of the women had experienced late menopause (after 55 years of age). The effective factors in age at menopause included being married, lower education level, consumption of oral contraceptives, and late menarche(34).

The current study findings revealed a significant relationship between BMI and age at menarche. Additionally, menopausal women had lower education levels and tended to smoke cigarettes and hookah more, but the difference was not statistically significant. This study was conducted in a rural area where smoking cigarettes and hookah was quite common among older women. This could justify the use of

cigarettes and hookah among the menopausal women who mainly belonged to >45 and 55-65 age groups. In the study conducted by Farahmand et al. also, menopause had occurred earlier among the women with the history of cigarette smoking ( $p=0.05$ ). However, no significant relationship was observed between the mean age at menopause, and education level and BMI(4). In the same vein, Morris et al. stated that increase in cigarette smoking was associated with a decrease in age at menopause(35). Cigarette smoking reduces the estrogen level and increases the androgen level, thereby decreasing the menopause age. Moreover, cigarette smoking has been mentioned to be a strong confounder due to its relationship with low BMI and early menopause(36).

The current study results revealed a significant increase in the number of pregnancies, deliveries, miscarriages, and stillbirths among the menopausal women. Since the non-menopausal participants belonged to the 35-45 age group and the fertility rate has decreased in Iran over time, this finding could be justified. These results were in agreement with those of other studies conducted on the issue (4, 34).

The present study results indicated that the menopause age was significantly lower among single women compared to married ones. This might be associated with the regular activity of ovaries and continuous stimulation of follicles under the influence of the pituitary hormones, causing menopause and ovarian failure to occur earlier(37).

The current study results revealed a significant increase in the incidence of diabetes, hypertension, cardiovascular diseases, and cervical cancer among the menopausal women. Similarly, Fu et al. demonstrated a decline in the menopause age with the incidence of diabetes(36). Furthermore, the mean age at menopause decreased from 56.88 years in the 75-year age group to 40.16 years in the 35-year age group, representing a significant decrease in the mean age at menopause. The researchers could find no studies on the effect of time on age at menopause.

Nowadays, with increase in the female population around the world, number of menopausal women has increased. It has also been estimated that nearly five million menopausal women will be living in Iran by 2021(9). Considering the increase in life expectancy, women have been expected to spend one-third of their lives after the incidence of menopause(38). In this period, women are exposed to cardiovascular diseases, osteoporosis, lipid disorders, and Alzheimer's disease and, as a result, they require a new range of healthcare services (39). Overall, considering the impact of chronic diseases on the reduction of age at menopause, effect of early menopause on the incidence of some diseases, and increase in life expectancy among women, women spend more years of their lives with chronic diseases. Therefore, health plans and beneficial interventions have to be carried out for increasing women's quality of life and reducing the burden of the diseases associated with increase in age.

## Conclusion

The results indicated that environmental factors, lifestyle change, and increase in BMI have caused a decline in age at menarche, which could be accompanied with numerous problems. In order to prevent the complications of this phenomenon, governmental institutions including the department of education are

recommended to begin the necessary trainings at lower ages and train children regarding the healthy lifestyle. Furthermore, the decreased age at menopause has led women to spend more than one-third of their lives after the incidence of menopause. Although genetic factors play a crucial role in menopause age, the role of other social factors should not be neglected. Overall, age at menopause is highly important in women's life, requiring important measures on the part of healthcare providers for improvement and clarification of women's and their own viewpoints regarding this period. Moreover, basic trainings have to be incorporated in health programs so as to help women spend their middle- and old-ages in relatively healthy and high-quality conditions.

## Abbreviations

WHO: World Health Organization

BMI: Body Mass Index.

## Declarations

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### Declarations:

Fasa University of Medical Sciences (code: 97143) and the University's Ethics Committee (IR.FUMS.REC.1397.131).

**Consent for publication:** Not applicable

**Availability of data and material:** This study is taken from Cohort information and all the information is available in Cohort Fasa Center in Fasa University of Medical Sciences.

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### Authors' contributions:

NB performed the thematic analysis and wrote the first draft of the manuscript as part of her masters project. AD and MF participated in the design of the study and performed the statistical analysis. ZM supervised the project and oversaw its delivery FM and AKJ conceived of the study, and participated in its design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

### Competing Interests:



The authors declare that they have no competing interests.

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## Tables

**Table1:Frequency distribution of study participants according to the mean variable of menstrual age and menopause**

	Number	Mean±SD Menopause age	Number	Mean±SD Menarche age
45-35	61	86/3± 16/40	2370	73/1±40/13
55-45	723	73/4± 28/47	1729	72/1±66/13
65-55	1135	02/6± 17/57	1167	73/1±81/13
75-65	271	55/5± 13/52	270	66/1±92/13
>75	9	06/10±86/56	9	06/2±66/14
Mean menstrual and menopausal age and total number	2199	99/5±21/49	5545	73/1±59/13

Table 2: Menopause and menarche pattern in women participating in the study

Number / percentage	
137(6/06%)	Premature menopause (under 40 years)
1734(76/79%)	Menopause between the ages of 40 and 55
387(17/6%)	Late menopause (age over 55)
255(4.6%)	Premature menarche (under 11 years)
5294(95.3%)	Menarche over 11 years

**Table3:Menarche age division**

<b>Number and percentage</b>	
255(4.6)	11<
255(4.6)	11-12
802(14.4)	12-13
1249(22.5)	13-14
1419(25.5)	15-14
1565(28.2)	>15
5545(100)	total

**Table 4: Relationship between gynecological surgery with menopausal age and menarche age**

P-value	Mean±SD Menarche age	P-value	Mean±SD Menopause age	Number and percentage	gynecological surgery and infertility	
0.15	1.73±13.95	0.948	5.71±49.00	1945(35%)	Yes	Tubectomy
	1.74±13.59		6.18±49.37	3609(65%)	No	
<0.001	1.67±13.47	0.26	6.74±44.91	222(4%)	Yes	Hysterectomy
	1.74±13.6		5.70±49.69	5332(96%)	No	
0.428	13.39±1.56	0.71	45.61±5.81	43(0/8%)	Yes	Oophorectomy
	13.52±1.85		46.81±7.02	5502(99.22%)	No	
<0.001	13.75±1.71			(6/39%)2199	Yes	Menopause
	13.49±1.74			3355(60.4%)	No	
0.032	13.6±1.81	0.97	48.84±6.31	1454(27.4%)	Yes	Infertility
	13.6±1.68		49.45±5.77	(72.6%)4100	No	
0.001	13.55±1.93	0.127	37.26±3.78	215(9.8)	<40	Menopausal age group
	13.76±1.69		49.41±3.68	1735(78.8)	41- 55	
	13.88±1.74		58.16±2.43	251(11.4)	>55	

Table 5: Relationship between body mass index and menopausal age and menarche age

Number and percentage of body mass profile groups	Mean±SD		P-value	Mean±SD		p-value
		Menopause age		Menarche age		
8/19 BMI<	319(5.7%)	49/5±5/21	0/733	1/83±13/90	<0/001	
8/19 <BMI<25	1682(30.5%)	49/28±5/96		1/71±13/64		
25<BMI<29	1879(39.1%)	49/23±6/05		69/1±13/63		
29 BMI>	1674(30.4%)	48/99±6/10		1/71±13/46		

Table 6: Relationship between menopausal age and female diseases

p-value	Number / Percent (in postmenopausal women)		Number / Percent (in non-menopausal women)		Menopause disease
	No	Yes	No	Yes	
001/0<	1730(78.67%)	469(21.32%)	3050(91.15%)	296(8.85%)	Stillbirth
001/0<	1659(75.44%)	540(24/55%)	2995(89.5%)	351(10.5%)	Diabetes
001/0<	1221(55.52%)	978(44.47%)	2817(84.2%)	529(15.8%)	High blood pressure
001/0<	1732(78.76%)	467(21.23%)	3117(93.15%)	229(6.84%)	Heart ischemia
001/0<	2144(97.49%)	55(2.50%)	3333(99.62%)	13(0.038%)	Myocardial infarction
0/36	2190(99.59%)	9(0.41%)	3337(99.74%)	9(0.26%)	Breast Cancer
0/005	2192(99.69%)	7(0.31%)	3345(99.98%)	1(0.02%)	Cervical cancer
0/78	2197(99.77%)	2(0.23%)	3346(100%)	0(0%)	ovarian cancer

Table 7: Relationship between midwifery history and physical activity with menopausal age

Variable	Mean±SD		Number		P_value
	Menopause age		Non-menopausal	Menopause	
physical activity	38.31±6.41	38.55±7.21	3355	2199	0.21
Gravida	3.68±1.99	7.47±3.26	3168	2160	<0.001
Parity	3.35±1.65	6.82±2.67	3044	2094	<0.001
Abortion	0.36±0.69	0.57±0.92	3041	2092	<0.001



**Table 8: Relationship between smoking, hookah, marital status and education level variables with menopausal age and menarche age**

		Number	Mean±SD Menopause age	P- value	Mean±SD Menarche age	P- value
cigarette smoking	<b>Yes</b>	<b>278</b>	<b>44.45±16.38</b>	<b>0.293</b>	<b>13.72±1.91</b>	<b>0.198</b>
	<b>No</b>	<b>5280</b>	<b>43.26±16.26</b>		<b>13.58±1.78</b>	
hookah use	<b>Yes</b>	<b>64</b>	<b>46.01±15.06</b>	<b>0.460</b>	<b>13.36±1.94</b>	<b>0.313</b>
	<b>No</b>	<b>5494</b>	<b>43.37±16.28</b>		<b>13.59±1.79</b>	
marital status	Single	281	46.326±7.8204	0.001	13.473±2.0425	0.182
	<b>Married</b>	4548	49.035±5.9826		13.587±1.7140	
	<b>Widow</b>	635	50.167±5.7104		13.707±1.7264	
	<b>divorced</b>	90	48.773±5.0703		13.756±1.9563	
education level	<b>Illiterate and elementary</b>	<b>4495</b>	<b>43.52±16.25</b>	<b>0.016</b>	<b>13.61±1.84</b>	<b>0.013</b>
	<b>Middle and high school</b>	<b>995</b>	<b>40.11±16.27</b>		<b>13.44±1.53</b>	
	<b>University</b>	<b>70</b>			<b>13.77±1.75</b>	