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Research Article

A Prospective Study of Factors Affecting Age at Menopause among the Bandar-E-Kong Cohort

Roozbeh N[1], Masoudi M[2], Moannaie M[3], Nejatizadeh A[4] and Kutenaee MA[3]*

[1]Mother and Child Welfare Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran

[2]Fatemiyeh Shiraz Institute of Higher Education, Shiraz, Iran

[3]Department of Gynecology and Obstetrics, School of Medicine, Fertility and Infertility Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran

[4]Molecular Medicine Research Center, Hormozgan Health Institute, Hormozgan University of Medical Sciences, Bandar Abbas, Iran

***Corresponding author:** Maryam Azizi Kutenaee, Department of Gynecology and Obstetrics, School of Medicine, Fertility and Infertility Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran

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Abstract

Menopause is a natural period of women's life and can be affected by several factors. This paper describes and identify the age of natural menopause and its associated factors based cohort study in Iran. In this study, we used data of Bandar-e-Kong study. This prospective cohort study includes 2,334 woman's aged between 18 to 70 years old, which was conducted from March 2016 to February 2019. All women completed data collection forms includes a validated questionnaire survey. Data were analyzed using chi-square test, independent t test, and ANOVA as well as a multivariate linear regression model. The total of participants with the age range of 18-70 years, 894 were menopause females. The mean age of menopause was 48.31 ± 6.34 years with a minimum of 20 and a maximum of 66 years. The number of pregnancies, duration of breastfeeding, level of education, residency, presence of thyroid disease, and body mass index affected the age of menopause. This study suggests that number of pregnancy was associated with menopausal age. According to the results of this study, the existence of appropriate educational programs to promote awareness and lifestyle in postmenopausal women is essential.

Keywords: Menopause; Menopausal age; Bandar-e- Kong Cohort Study; Healthcare policy

Introduction

Menopause is defined as a loss of menstruation for women and lead to transition process from reproductive to a non-reproductive state by ovarian failure in all women. Estrogen levels decrease and eventually lead to the menstrual cessation. This natural biological process usually occurs between 45 and 55 years [1]. Previous studies have reported that menopause can lead to influence on normal function of immune, cardiovascular, skeletal endocrine and genitourinary systems and will result in various diseases, such as high blood cholesterol, cardiovascular disease, osteoporosis, bone fractures and even Alzheimer's [2-5]. Based on WHO report by the year 2030, approximately 1.2 billion women of global population entered menopause and 47 million will be added every year [4]. One of the most important issues associated with menopause is early menopause. Early menopause is related to the decrease of hormonal secretion and ovarian estrogen deficiency over time [3]. Premature or early menopause can be characterized by several signs like as last menstruation between 40 to 44 years old, to consider that the median age of natural menopause is age 51 years [6]. Hyvärinen, Karvanen [5] reported that, common menopausal symptoms is including; joint pain, hot flushes, night sweats, headache, urinary tract and vaginal problems, osteoporosis, irritability or increased anxiety, pain during intercourse, cardiovascular diseases and finally amenorrhea and lack of estrogen [3]. Menopausal age varies in different geographical areas according to environmental and socio-economic variables, lifestyle and quality also, contraceptive pills, menarche age, calcium and vitamin D intake, genetic factors, diet, alcohol, obesity can be affected on it [2,4,7,8]. In studies about age at natural menopause, it is necessary to pay attention to the physical, behavioral characteristics and sociodemographic [5,9-12]. The average age of menopause is 51 years for US women [13]. For the majority of enrolled women in Europe the median age of natural menopause is 48 to 54 years [12,14,15], also, the age at menopause for Asian women reported 49 to 51 [16-20]. Several author's [16,21-23] have been reported the mean age at menopause 46.9 to 49.6 years for Iranian women in different part of Iran. One third of women's life spends in the postmenopausal period, it is useful to increase knowledge about the risk factors for onset of menopause across populations. One particular region where studies of menopause onset have been sparse is south of Iran. In the present large-scale population based cohort study we explore the relationship between ages of natural menopause with main associated factors in women who lived in south of Iran.

Materials and Methods

Patients and study design

We evaluated participants of the Bandar-e- Kong Cohort Study (KCS), KCS is part of the national cohort, a prospective, population-based cohort study in Iran, which has been previously described in detail [24]. This prospective cohort study includes 2,334 woman's aged between 18 to 70 years old, which was conducted from March 2016 to February 2019. All women completed data collection forms includes a validated questionnaire survey. All study procedures were approved by the Ethics Committee of the Hormozgan University of Medical Sciences (IR.HUMS.REC.1399.494).

Of 2,334 women who responded, decided to continue, and consented, 1440 were excluded based on the exclusion criteria. These criteria included several factors and medical conditions that could affect the timing of the final menstrual period or hinder the menopausal group definitions, such as severe obesity (body mass index more than 35), bilateral oophorectomy, women with surgical

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Table 1: Characteristic of study participants and its association with menopause age.

Variable	Total (n=894)		Premature Menopause (n=79)		Early Menopause (n=116)		Normal Menopause (n=699)		P-value*
	Mean ± SD	Correlation (P value)	Mean ± SD	Correlation (P value)	Mean ± SD	Correlation (P value)	Mean ± SD	Correlation (P value)	
Age of menarche (y)	13.75±1.530	0.049 0.143	13.71±1.46	0.187 0.102	13.51±1.42	0.11 0.24	13.80±1.55	0.002 0.953	0.165
Number of pregnancy	6.80±3.021	0.142 <0.001	6.19±3.035	0.405 <0.001	6.41±2.803	-0.085 0.369	6.93±3.04	0.12 0.002	0.045
Number of abortion	0.63±1.011	0.064 0.061	0.61±1.170	0.112 0.351	0.52±0.763	-0.103 0.284	0.65±1.02	0.074 0.054	0.423
Breastfeeding duration (mo)	107.96±64.71	0.077 0.024	100.63±59.74	0.236 0.046	112.35±61.17	0.049 0.612	108.03±65.79	0.113 0.003	0.489
Age of the first marriage (y)	18.41±4.712	-0.054 0.112	18.61±5.73	-0.248 0.028	18.68±4.72	0.056 0.564	18.34±4.58	-0.046 0.231	0.728

*P-value for ANOVA to compare mean of premature age, early age and natural menopause age

Table 2: Frequency of categorical variables in three menopausal groups.

Variable	Total (n=894)		Premature Menopause Age (n=79)		Early Menopause Age (n=116)		Normal Menopause Age (n=699)	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Stillbirth	170	19	22	27.8	16	13.8	132	18.9
Tubectomy	265	29.6	22	27.8	28	24.1	215	30.8
Infertility	45	5	8	10.1	5	4.3	32	4.6
Diabetes	219	24.5	19	24.1	30	25.9	170	24.3
Hypertension	301	33.7	23	29.1	39	33.6	239	34.2
Thyroid Disease	126	14.1	15	19	16	13.8	95	13.6
Cardiac Disease	135	15.1	9	11.4	22	19	104	14.9
CVD history	147	16.4	9	11.4	24	20.7	114	16.3

menopause (hysterectomy), polycystic ovary syndrome, pregnancy and use of estrogen containing medications.

Finally, the sample of 894 women participate to this study. A validated research database was used containing questions consist of general information, physical activity, physical examination, physical disabilities, sleep status, oral health, drug use, familial history of diseases, type of fuel used, life style, history of chronic diseases, occupational history, characteristics of the habitat, socioeconomic status, personal habits (drinking and smoking), food supplements, food frequency, exposure to pesticides, water drink, dietary habits and history of fertility. To describe the reproductive section of the questionnaire in more details, we got some information about the age at menarche, number of pregnancy, number of abortion, breastfeeding duration (month), age of the first marriage (y). Also to explain the socioeconomic status of the questionnaire in more details, we asked women about the travelling (internal trip or abroad trip), reading the books, access to computer and internet, owning a car/motorcycle, household appliances such as washing machine, dishwasher, vacuum cleaner and freezer. All the variables mentioned are numbered and based on total number of the whole socio-economic status categorized in five levels; level 1, poorest, level 2, Poor, level 3, moderate, level 4, good and level 5 richest.

Anthropometric indices and blood pressure were measured for all participants. Based on PERSIAN protocol all anthropometric indices include height and weight and waist and hip circumferences were measured by trained nurses [25]. All data were analyzed by using IBM SPSS-23.0 (IBM Corp., Armonk, NY, USA). Variables were described using maximum, minimum, mean, standard deviation and percentage. Quantitative variable and categories were compared in to groups using chi-square and independent t test respectively. ANOVA was used to compare quantitative variables in more than two groups. For possible confounding variables, we used the multivariate linear regression models. Variables with P value less than 0.2 were considered in model, which include marital status, number of pregnancy, breastfeeding duration, educational level, BMI and residency thyroid diseases (participant who self-reported to clinically diagnosed with thyroid disease or receiving thyroid related medicine). A written informed consent form was obtained from all participants before inclusion in the evaluation.

Results

In this present we notice to women who menopause naturally and follow the analysis on its related factors, although we look at data for premature and early menopause. The total of participants with the age range of 18-70 years, 894 were menopause females. The mean age of menopause was 48.31 ± 6.34 years with a minimum of 20 and a maximum of 66 years. The prevalence of premature menopause, early menopause and normal menopause was 79 (8.8%), 116 (13.0%) and 699 (78.2%), respectively. The mean age of premature, early and natural menopause was 34.27 ± 3.52, 42.00 ± 1.55 and 50.95 ± 3.71, respectively ($P < 0.001$). Table1 shows characteristic of participants included age of menarche, number of pregnancy, number of abortion, breastfeeding and duration, age of the first marriage and its association with menopause age. By using ANOVA test, compared the mean age of menopause in different socio-economic levels. The mean age of menopause was 48.86 ± 6.13 for lowest and 48.30 ± 6.250 for highest socio-economic level ($P = 0.105$). The mean age of menopause in women with and without history of infertility was 46.56 ± 9.514 vs. 48.45 ± 6.114; $P = 0.051$ respectively. Moreover there was no significant difference between the mean age of menopause in women with different marital status (single, married and widow/divorced), (48.50 ± 5.663, 48.39 ± 6.205, 47.93 ± 7.080, $P = 0.722$).

The result of correlation coefficient between menopausal age

Table 3: Mean of menopause age based on categorical variables.

Variable		Total (n=894)		premature menopause age (n=79)		early menopause age (n=116)		normal menopause age (n=699)		P value*
		Mean ± SD	P value	Mean ± SD	P value	Mean ± SD	P value	Mean ± SD	P value	
Marital status	Single	48.50±5.663	0.722	34.10±3.198	0.639	41.71±1.496	0.701	51.67±3.658	0.423	<0.001
	Married	48.39±6.205		34.16±3.189		42.07±1.545		50.87±3.640		<0.001
	Widow/Divorce	47.93±7.080		34.61±4.578		41.81±1.662		51.28±4.055		<0.001
Soci-economic status	Poorest	48.86±6.13	0.105	34.80±3.688	<0.001	42.14±1.711	<0.001	51.5±3.860	<0.001	<0.001
	Poor	48.91±6.765		33.67±4.451		42.00±1.451		51.69±3.728		<0.001
	Moderate	48.19±6.250		34.40±2.746		41.70±1.589		50.96±3.600		<0.001
	Rich	47.34±6.212		34.71±3.327		42.15±1.523		50.38±3.580		<0.001
	Richest	48.30±6.250		33.46±4.701		42.00±1.604		50.55±3.604		<0.001
Job	No	48.37±6.405	0.516	34.20±3.624	0.68	41.92±1.548	0.167	51.03±3.721	0.132	<0.001
	Yes	47.96±5.916		34.70±2.869		42.50±1.549		50.40±3.585		<0.001
Thyroid disease	No	48.43±6.329	0.161	34.22±3.369	0.808	41.95±1.533	0.389	51.01±3.780	0.243	<0.001
	Yes	47.58±6.394		34.47±4.257		42.31±1.702		50.54±3.195		<0.001
Diabetes	No	48.27±6.429	0.684	33.82±3.061	0.043	41.95±1.571	0.588	50.93±3.685	0.803	<0.001
	Yes	48.47±6.078		35.68±2.926		42.13±1.525		51.01±3.787		<0.001
Cardiac Disease	No	48.30±6.343	0.83	34.37±3.564	0.461	41.99±1.548	0.88	50.93±3.662	0.727	<0.001
	Yes	48.42±6.355		33.44±3.283		42.05±1.618		51.07±3.976		<0.001
CVD history	No	48.28±6.374	0.724	34.37±3.564	0.461	41.97±1.551	0.66	50.94±3.671	0.853	<0.001
	Yes	48.48±6.195		33.44±3.283		42.13±1.597		51.01±3.907		<0.001
Body mass index (kg/m^2)	< 25	48.47±6.835	0.707	34.41±3.885	0.641	42.35±1.450	0.186	51.41±4.006	0.11	<0.001
	25–30	48.40±6.017		34.61±2.514		42.02±1.581		50.86±3.662		<0.001
	> 30	48.05±6.313		33.71±4.144		41.65±1.574		50.67±3.460		<0.001
Smoking	No	48.28±6.305	0.696	33.97±3.571	0.108	42.04±1.549	0.479	50.91±3.616	0.469	<0.001
	Yes	48.51±6.583		35.61±3.054		41.73±1.624		51.19±4.211		<0.001
Stillbirth	No	48.49±5.899	0.801	34.98±2.810	0.298	42.05±1.575	0.48	50.85±3.645	0.067	<0.001
	Yes	48.36±7.205		34.23±2.793		41.75±1.612		51.52±4.063		<0.001
Infertility	No	48.45±6.114	0.051	34.84±2.826	<0.001	42.00±1.581	1	50.94±3.712	0.306	<0.001
	Yes	46.56±9.514		29.13±5.222		42.00±1.225		51.61±3.722		<0.001
Tubectomy	No	48.31±6.600	0.948	33.82±3.616	0.073	42.02±1.576	0.782	51.15±3.822	0.03	<0.001
	Yes	48.34±5.695		35.41±3.065		41.93±1.514		50.49±3.401		<0.001

*P-value for ANOVA to compare mean of premature age, early age and natural menopause age

with abortion, breastfeeding duration and age at the first pregnancy, number of pregnancies, age at the first marriage, and age of menarche was calculated in Table 4. Based on Table 4, by adjusting the effect of other variables, for one unit of increase in the number of pregnancies, the mean of menopause age almost increased by 0.2 (P-value = 0.074). The mean menopause age was 0.92 less for people with the highest socio-economic status than the poor ones (P-value = 0.054). Also, for women with premature menopause, the mean menopause age for people with a history of infertility was 2.55 less than their counterparts (P-value = 0.092). Moreover, by controlling the effect of other variables, for women with normal menopause, the mean menopause age for women with a history of infertility was 1.36 less than their counterparts (P-value = 0.091) and menopause age was 0.89 less for people with the highest socio-economic status than the poor ones (P-value = 0.006).

The average age of the menarche, number of pregnancies, number of abortions, duration of breastfeeding, and the age at the first marriage of participants are presented in Table 1. The correlation coefficient between variations that summarized in Table 1 was calculated, with increasing the number of pregnancy the age of menopause in premature menopause and normal menopause significantly increased (P < 0.001). The frequency of variable such as stillbirth, tubectomy, infertility, diabetes, hypertension, thyroid disease, cardiac disease and cardiovascular disease (CVD) are showed in Table 2. By information that presented in Table 2, as shown in that, it is most frequency among people with a history of hypertension and low frequency belong to infertility group.

Mean of menopause age based on marital status, socio-economic status, job, thyroid disease, diabetes, hypertension, cardiac disease, CVD history, body mass index, smoking, still birth, infertility and Tubectomy showed in Table 3. We compared the age of menopause in women with and without diabetes. Our results showed that the age

Table 4: The effect of selected variables on menopause age using multivariate linear regression.

Variable		Total (n=894)			premature menopause age (n=79)			early menopause age (n=116)			normal menopause age (n=699)		
		Unstandardized Beta	standardized Beta	*P value	Unstandardized Beta	standardized Beta	P value	Unstandardized Beta	standardized Beta	P value	Unstandardized Beta	standardized Beta	P value
age of menarche		0.093	0.023	0.508	0.194	0.103	0.414	0.182	0.159	0.119	-0.039	-0.016	0.676
Number of pregnancies		0.198	0.091	0.074	0.028	0.026	0.882	-0.128	-0.208	0.162	0.066	0.051	0.374
number of abortion		0.142	0.023	0.564	0.312	0.13	0.352	-0.162	-0.078	0.485	0.175	0.048	0.291
breastfeeding duration		0.001	0.007	0.871	0.011	0.231	0.17	0.002	0.09	0.507	0.004	0.068	0.176
Age of the first marriage		-0.003	-0.002	0.956	0.006	0.009	0.942	0.031	0.091	0.404	-0.019	-0.023	0.555
Infertility	No	Reference											
	Yes	-0.153	-0.005	0.894	-2.55	-0.25	0.092	-0.255	-0.031	0.772	-1.361	0.065	0.091
Socio-economic status	Poor	Reference											
	Moderate	-0.687	-0.044	0.24	0.512	0.071	0.613	0.021	0.006	0.961	-0.444	0.047	0.267
	Rich	-0.926	-0.073	0.054	0.04	0.007	0.957	0.04	0.012	0.914	-0.895	-0.117	0.006

* With a 90 percent level of confidence

of menopause in premature menopause age group with diabetes is significantly higher than women without diabetes (35.68 ± 2.92 *vs.* 33.82 ± 3.06; P = 0.043). Also, we found that the age of menopause in premature menopause age group with infertility is significantly lower than women without infertility (29.13 ± 5.22 *vs.* 34.84 ± 2.826; P < 0.001). On the other hand, the age of menopause in normal menopause age group with tubectomy is significantly higher than women without Tubectomy (34.84 ± 2.82 *vs.* 29.13 ± 5.22; P < 0.001). Association of natural menopausal age with selected variables using multivariate linear regression of participants are summarized in Table 4. Multivariable regression analysis showed that menopause age was 0.89 less for people with the highest socio-economic status than the poor ones (P-value = 0.006) Table 4.

Discussion

This paper is modest contribution to the ongoing discussions about factors affecting age at menopause among the Bandar-e-Kong cohort in south of Iran. In our study, mean age of menopause in total population was 48.31 ± 6.34 with a minimum of 20 and a maximum of 66 years. In Overall our findings about mean of menopause is similar to the other studies in Iran [16,26-31]. Although the mean age of natural menopause in Bandar-e-Kong cohort population is lower than Hamedan province (49.6 ± 4.0) [32]. In compare to other countries, age of menopause in our finding was less than western countries [33-35], but it is higher than Chines women (50.53 ± 6.57) and Panjabi women (47.9 ± 3.2) [36,37]. In many study noticed to genetic and environmental factors that affected on the age of menopause [38]. We found that number of pregnancy as one of the important reproductive variable is related to age of menopause. Age at monarch is one of the important factors to age at menopause [39], based our results we did not find any association with this factor to age at menopause. Association between age at monarch and menopausal age was inconsistent in previous studies [27]. In this study we did not find any association between marital status and menopausal age. This Association has not been reported consistently in previous studies. Unlike the previous studies, results of present study did not show any significant relationship between BMI and menopausal age. Some studies reported that no association between BMI and age of menopause [36]. In our plan study we compared age at menopause in women with and without some diseases. Among of listed disease in Table 3, diabetes was significantly related with menopausal age but hypertension and thyroid were not related with age at menopause. Cigarette smoking can lead to perimenopause and reached the menopause early than non-smokers [40]. In this study the number of smoker was low, so we find no association between smoking and menopausal age. Like the previous studies [13,41,42], our result showed that significant relationship between socio-economic level and menopausal age. Some limitation of the present study should be considered that, reproductive history of women was self-reported of events years back in their life which can be subject to recall bias, and moreover remembering the exact time of menopause might be subject to recall bias as well.

In conclusion, the study suggests that number of pregnancy was associated with menopausal age. According to the results of this study, the existence of appropriate educational programs to promote awareness and lifestyle in postmenopausal women is essential.

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