

Correlates of age at natural menopause: a community-based study in Alexandria

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العوامل المرتبطة بسن اليأس (الإياس) الطبيعي: دراسة مجتمعية المراكز بالاسكندرية

نبيلة محمد هدايت وسامية عبد الفتاح شرف وسها راشد عارف وتوفيق عبد السلام توفيق وإيمان إبراهيم مبارك

خلاصة: تم بحث الاختلافات العمرية عند حدوث الإياس الطبيعي، حيث اختيرت لهذا الغرض عينة ارتجاعية بلغ عددها 289 سيدة بلغت سن اليأس (الإياس) الطبيعي. وتبين أن العمر الأوسط عند حدوث الإياس الطبيعي كان 46.70 ± 5.44 عاما. كما وجد أن الإياس قد حدث مبكرا بين السيدات المقيمت في مناطق شبه حضرية، وبين المطلقات والمنفصلات والأقل تعليما. وحدث الإياس المبكر أيضا بين النساء الأصغر سنا عند الزواج الأول أو عند الترمول أو الطلاق أو الانفصال، وكذلك عند أول أو آخر حمل مكتمل المدة. وحدث الإياس متأخرا لدى النساء اللاتي عانين من اضطراب الطمث قبل سن 25 عاما، أو من عسر الطمث أو من نزول بقع دموية بين دورات الحيض. وقد وجدت علاقة طردية جوهرية بين مدة تناول أقراص منع الحمل ووزن الجسم ومنسب كتلة الجسم وبين السن عند حدوث الإياس الطبيعي. وبإجراء تحليل الانحدار المتعدد، تبين أن العمر عند حدوث الحمل المكتمل الأخير ومحل الإقامة وغطاء انقطاع الطمث ومدة استعمال حبوب منع الحمل هي أهم عوامل التكهن بانتهاء الحيض.

ABSTRACT Differences in the age at natural menopause were examined using a retrospective population sample of 289 naturally menopausal women. The mean age at natural menopause was 46.70 ± 5.44 years. Earlier menopause occurred in women living in semiurban areas, divorced/separated and less educated women, and women who were younger at: first marriage, widowhood, divorce/separation and first or last full-term pregnancy. Later menopause occurred in women who had: irregular menstrual periods before 25 years, dysmenorrhoea and mid-cycle spotting. Duration of oral contraceptives use, weight and body mass index were significantly positively correlated with age at natural menopause. Multiple regression analyses indicated that age at last full-term pregnancy, residence, pattern of menstrual cessation and duration of oral contraceptive use were the significant predictors of the end of menstrual activity.

Les corrélats liés à l'âge au moment de la ménopause naturelle: étude communautaire à Alexandrie

RESUME Les différences d'âge au moment de la ménopause naturelle ont été examinées rétrospectivement au moyen d'un échantillon de population de 289 femmes ménopausées naturellement. L'âge moyen à la ménopause naturelle était $46,70 \text{ ans} \pm 5,44 \text{ ans}$. La ménopause précoce survient chez les femmes vivant en zone suburbaine, qui sont divorcées/séparées de leur conjoint et les femmes dont le niveau d'éducation est moindre ainsi que chez les femmes qui étaient très jeunes lors de leur premier mariage, veuvage, divorce/séparation et au moment de leur première ou dernière grossesse menée à terme. La ménopause tardive survient chez les femmes qui ont eu des menstruations irrégulières avant l'âge de 25 ans, une dysménorrhée et des saignements en milieu de cycle. La durée de l'utilisation des contraceptifs oraux, le poids et l'indice de masse corporelle étaient corrélés positivement à l'âge à la ménopause naturelle. Les analyses de régression multiple indiquaient que l'âge lors de la dernière grossesse menée à terme, le lieu de résidence, les caractéristiques de la cessation des règles et la durée de l'utilisation des contraceptifs oraux étaient des facteurs prédictifs de la fin de la fonction menstruelle.

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Received: 15/09/98; accepted: 12/01/99

Introduction

Numerous studies on the distribution of age at menopause have been published in the past 20 years [1,2]. These efforts have been motivated partly by interest in the natural history of ageing and more recently by evidence that the incidences of chronic diseases, such as osteoporosis, cardiovascular disease and, possibly, certain cancers vary with menstrual status [3,4]. Associations of disease incidence with menstrual status lead naturally to the idea that the lifetime risks of these diseases vary with age at menopause, which has further increased interest in identifying factors with which age at menopause varies [2].

One review of the data on natural menopause noted the prevailing view that menopause results from peripheral organ failure, namely of the ovaries, but that the mechanisms and the role of the pituitary gland remain unknown [1]. The median age of menopause, 50 years, has not changed in the past century according to some reports [5]. Although this would appear to support the notion that age at menopause is predetermined, a number of environmental factors have been shown to affect ovarian function [1].

There is considerable uncertainty as to what factors affect the timing of menopause. Genetic and racial factors have recently been proposed to be the most important determinants of age at natural menopause [2,6,7]. In addition to genetic factors, several behavioural (smoking, nutrition, and sociodemographic factors), reproductive and anthropometric factors are also associated with age at menopause [2,6,7].

Factors that affect menopause timing may have important clinical implications because early menopause is associated with

an increased risk of cardiovascular disease and osteoporosis, whereas delayed menopause has been associated with increased risk of breast cancer and endometrial cancer. These associations may result from the direct effect of menstrual function (or cessation of function) and the related hormone changes, or may be an indirect result of the other previously mentioned factors that are associated with age at menopause. The connection of menopausal age with risk factors for such medical conditions makes age at menopause an important epidemiological issue [6-8].

We aimed to study the distribution of age at natural menopause and then to explore the variation in this distribution in relation to sociodemographic, reproductive and other factors.

Subjects and methods

A retrospective, descriptive, epidemiological study was conducted. The target population was women with menopausal amenorrhoea for 1-5 years, who were aged 30 years and over and were living in Alexandria Governorate during the period from 1 November 1995 to 31 October 1996. Women who reported 12 continuous months of amenorrhoea (according to World Health Organization criteria) [5], without a hysterectomy or other procedure that would have stopped their menses, were classified as naturally menopausal. Age at natural menopause (NM) was defined as the age at last menstrual period.

Thirty clusters (geographic areas) within Alexandria Governorate were selected [out of the 127 *shiakhah* (small administrative units) according to the last available census at the beginning of the study]. The standard cluster sampling technique was

used as it allows a small number of the target population to be studied while providing statistically valid data. Ten menopausal women were obtained from each of chosen clusters. Thus the total number of menopausal women studied was 300. A school was identified at the centre of each of the chosen clusters and a direction was randomly chosen. Following that direction, the first house in the cluster was randomly selected. The second house was the one with the door nearest to the first. This was repeated until 10 menopausal women within each cluster were identified and interviewed.

Data were collected using a specially designed interviewing questionnaire. It was presented to the women as a survey on general health and menopause and included data on:

- Sociodemographic characteristics: age, place of residence, marital status, education, occupation and income.
- Menstrual and reproductive characteristics: age at menarche, gravidity, parity, abortions, age at first live birth, age at last delivery, duration and regularity of menstrual periods, dysmenorrhoea, midcycle spotting and pattern of menstrual cessation.
- The use of hormones for contraceptive purposes and hormone replacement therapy.
- Cigarette smoking: current smoker or non-smoker.
- Psychological condition: the standardized Arabic form of the Middle Sex Test [9] was used to assess the neurotic traits of the women. The test comprises 48 items, including scales for anxiety, phobia, obsession, depression, psychosomaticism and hysteria. Each scale was scored from 0–16. Women who scored

9–16 were considered to have the trait. The trait was considered absent in those who scored 0–8 [10].

- General health status: an inquiry about previously diagnosed morbid conditions was included in this section.

Height (in metres) and weight (in kilograms) were measured using the Harpenden stadiometer and the platform balance scale respectively [11]. Body mass index (BMI) was then calculated according to: $BMI = \text{weight}/\text{height}^2$ (kg/m^2) [12].

Clinical examination was carried out, if indicated, by the gynaecologist to exclude any pathological condition that could affect menopause.

Statistical analysis

The following statistical measures were used:

- Descriptive statistics such as frequency distribution, mean and standard deviation were used to describe the different characteristics of the women.
- Different tests of significance (*t*-test and *F*-test) were used to test the difference in mean age at natural menopause between different groups.
- Correlation coefficient (*r*) was used to find the relationship between age at natural menopause (dependent) and different independent variables.
- Multiple regression analysis was used to study the partial effect of each independent variable after controlling for effects of the rest of the studied variables. Qualitative or categorical variables were recorded as: 0 (absent), and 1 (present).

Statistical analyses were considered significant when $P < 0.05$ (5% level of significance).

Results

Type and age at menopause

The majority (289, 96.33%) of the 300 menopausal women had reached their menopause spontaneously (i.e. natural menopause); only a minority (11, 3.67%) had experienced menopause after oophorectomy (i.e. surgical menopause) and were excluded from the study.

The age range of the women with NM ($n = 289$) was 30–59 years; the age range was 40–54 years in most of the cases (88.93%). Premature NM (at age 30–39 years) was experienced by 7.96%, while late NM (at age 55–59 years) was reported by 3.11% of the women. Distribution of the observed age at menopause was unimodal and a peak in the age group 45–49 years was noted. The median age at NM was 47.00 years, while the mean age was 46.70 ± 5.44 years.

Variables possibly influencing the age at natural menopause

Sociodemographic variables

Residence. Findings revealed that the semi-urban women reached NM significantly earlier than urban ones (41.22 ± 5.64 years compared with 47.25 ± 5.12 years) ($t = 7.66, P < 0.001$).

Marital status. NM occurred significantly earlier among divorced/separated women (40.67 ± 5.77 years) than among married (46.45 ± 5.17 years), widowed (47.69 ± 5.63 years) and single women (51.33 ± 2.08 years) ($F = 5.76, P < 0.001$). The age at NM was positively correlated with age at first marriage ($r = 0.18$), age at widowhood ($r = 0.51$) and age at divorce/separation ($r = 0.99, P = 0.001$).

Education. Age at NM was significantly higher among highly educated women (university graduates or higher, 49.46 ± 4.14 years) compared with those who were less educated (46.25 ± 4.39 years for those

with primary or preparatory certificates and 46.27 ± 5.60 years for those who were illiterate or could read and write) ($F = 3.79, P = 0.010$). A significant positive correlation was found between age at NM and years of education; the greater the number of years of education, the higher the age at NM ($r = 0.19, P = 0.001$).

Occupation. Working women experienced NM earlier (46.52 ± 5.52 years) than housewives (47.86 ± 4.79 years). However, the difference was not statistically significant ($t = 1.41, P = 1.160$).

Income. Women whose income was not enough for their basic needs reached NM earlier (45.96 ± 5.47 years) than those whose income was enough (47.15 ± 5.39 years). However, this difference was not statistically significant ($t = 1.81, P = 0.072$).

Reproductive characteristics

Age at menarche. Age at menarche among the women ranged from 9 years to 17 years with a mean age of 12.24 ± 1.32 years. Most of the women (83.04%) had menarche between 11 years and 13 years, while 12.46% had menarche at an older age (>13–17 years) and 4.50% at a younger age (9–<11 years). However, although age at menarche was positively associated with that of NM, the relationship was not statistically significant ($r = 0.03, P = 0.581$ and $F = 1.15, P = 0.318$).

Gravidity and parity. For the ever-married women, the number of conceptions ranged from 0 to 15 with a mean of 6.19 ± 3.29 pregnancies. The number of deliveries ranged from 0 to 10 with a mean of 5.09 ± 2.52 births. About two-thirds of these women (66.91%) had had five or more pregnancies and more than half of them (55.25%) had had five or more deliveries. Only a minority (2.80%) had never conceived or had a baby. The highest age at NM was found among those who had had

1-2 pregnancies or deliveries (47.94 ± 5.34 years and 47.64 ± 6.05 years respectively). There was a positive relationship between age at NM and both gravidity and parity ($r = 0.03$, $P = 0.579$ for each). However, all these relationships were not statistically significant.

Age at first and last live birth. The women who had had children had their first live birth at a mean age of 20.53 ± 4.41 years and their last one at a mean age of 33.37 ± 6.26 years. Less than half of them (48.92%) had had their first child before the age of 20 years (14 < 20 years), while more than half (51.08%) had had the first child at the age of 20 years and over (20-29 years). On the other hand, more than two-thirds (68.35%) had delivered their last child between the age of 20 years and 35 years and less than one-third (30.93%) did so above the age of 35 years (> 35-53 years); only two women (0.72%) had their last child before the age of 20 years. The age at NM was significantly positively associated with both age at first live birth ($r = 0.19$, $P = 0.002$ and $t = 2.69$, $P = 0.008$) and age at last live birth ($r = 0.27$, $P = 0.001$ and $F = 4.92$, $P = 0.006$).

Previous abortions. Less than half (44.76%) of the married women had not had any abortions. More than half of them (55.24%) had a history of abortion. Of these, 45.80% had suffered spontaneous abortions 1-7 times with a mean of 2.12 ± 1.51 abortions. On the other hand, 9.44% had 1-6 induced abortions with a mean of 2.31 ± 1.61 abortions. NM occurred earlier among those who had a history of abortion (46.46 ± 5.59 years) and those who had experienced spontaneous abortion (46.42 ± 6.06 years) although the differences were not significant. Correlation analysis revealed a positive but non-significant relationship between the number of spontaneous abortions and age at NM ($r = 0.10$, $P = 0.243$).

Menstrual characteristics

Duration of menses. The duration of menstrual periods ranged from 3 days to 10 days with a mean of 5.15 ± 1.53 days. Correlation analysis revealed a negative but non-significant relationship between age at NM and duration of menses ($r = -0.10$, $P = 0.10$).

Regularity of menstrual periods. Menstrual periods were regular in 96.89% of the women before the age of 25 years and in 92.04% after that age. Having irregular periods before the age of 25 years was significantly associated with a higher age at NM (51.00 ± 3.12 years) compared with having regular ones (46.55 ± 5.45 years) ($t = 2.44$, $P = 0.015$). The same relationship was found after the age of 25 years, but it was not statistically significant ($t = 0.33$, $P = 0.745$).

Dysmenorrhoea. Half (50.17%) of the women had experienced their menstrual periods without pain, while 43.60% and 6.23% had suffered from spasmodic and congestive dysmenorrhoea respectively. It was found that both congestive and spasmodic dysmenorrhoea were significantly associated with a higher age at NM (48.67 ± 3.33 years and 47.30 ± 5.71 years respectively) compared with painless periods (45.91 ± 5.31 years) ($F = 3.53$, $P = 0.031$).

Midcycle spotting. The few women who reported midcycle spotting (2.77%) reached NM significantly later (48.37 ± 1.68 years) than those who did not (97.23%) (46.64 ± 5.50 years) ($t = 2.55$, $P = 0.026$).

Pattern of menstrual cessation. Two-fifths (39.79%) of the women had entered their NM abruptly, while the rest (60.21%) experienced a gradual cessation of menstruation over a mean transitional period of 16.84 ± 16.71 months. Sudden cessation of menstruation was significantly associated with lower age at NM (43.94 ± 5.30 years) compared with those with gradual cessation (48.51 ± 4.73 years) ($t = 7.47$, $P < 0.001$).

Exogenous hormonal use

The only form of hormones used by the women was contraceptive pills. Among the women, 59.44% had never used contraceptive pills, while 40.56% had used them at some time in their lives for a period that ranged from 0.25 years to 23 years with a mean of 7.43 ± 5.32 years. Although no significant difference could be detected among pill-users and non-users as regards age at NM, which was more or less similar in both groups, the duration of pill use was positively associated with the age at NM ($F = 4.49$, $P = 0.013$ and $r = 0.23$, $P = 0.012$).

Smoking

The majority (96.19%) of the women were non-smokers; only a minority (3.81%) were current cigarette smokers. The duration of smoking ranged from 10 years to 27 years with a mean of 18.86 ± 6.30 years. All the smokers smoked less than one packet a day. The mean age at NM was slightly lower among cigarette smokers (46.43 ± 3.23 years) than the non-smokers (46.70 ± 5.53 years). However, the difference was not significant ($t = 0.16$, $P = 0.84$).

Psychological factors

The Middle Sex Test revealed that the most common neurotic traits were psychosomaticism (psychosomatic symptoms) (53.63%), followed by depression (49.13%) and obsession (46.37%). Anxiety was less common (31.14%), while phobia and hysteria were the least common (17.65% and 8.30% respectively).

When neurotic traits were considered as a factor in menopausal timing, symptoms of anxiety, phobia, obsession and hysteria were found to be associated with early NM. The reverse was found with psychosomaticism and depressive symptoms. However, the age differences were insignificant between those with and those without the

traits as shown by t -values. On the other hand, correlation analysis revealed that obsessive symptoms were significantly negatively correlated with age at NM ($r = -0.12$, $P = 0.035$).

General health status

Findings revealed that 34.95% of the women had hypertension, 23.53% had diabetes mellitus and 9.69% had ischaemic heart disease. Hypertensive women experienced NM at a significantly higher age (48.36 ± 5.55 years) than normotensive women (45.79 ± 5.18 years) ($t = 3.91$, $P = < 0.001$). Diabetics experienced NM at a higher age (47.74 ± 5.12 years) than the non-diabetics (46.37 ± 5.51 years), while women suffering from ischaemic heart disease experienced NM at an earlier age (44.89 ± 6.38 years) than the non-ischaemic women (46.88 ± 5.31 years). However, these differences were not significant ($t = 1.82$, $P = 0.070$ and $t = 1.85$, $P = 0.066$ respectively).

Anthropometric measurements

The weights of the women ranged from 48 kg to 143 kg with a mean of 81.39 ± 16.78 kg. Their heights ranged from 146 cm to 176 cm with a mean of 160.10 ± 5.79 cm. BMI ranged from 22.80 kg/m^2 to 68.00 kg/m^2 with a mean of $38.59 \pm 7.88 \text{ kg/m}^2$.

The majority (96.87%) of the women were obese as indicated by the BMI values; 57.29% and 31.94% were grade II and III respectively and only 7.64% were grade I. Only a minority (3.13%) were not obese or were of a normal weight.

Both weight and BMI were significantly positively correlated with the age at NM ($r = 0.21$, $P = < 0.001$ and $r = 0.20$, $P < 0.001$ respectively). A positive but non-significant correlation was found between height and age at NM ($r = 0.086$, $P = 0.086$).

Regression analysis

When factors associated with age at NM were related to each other in multiple linear regression analysis (Table 1), only four factors were found to be significant predictors of age at NM. They were: age at last delivery ($\beta = 0.449$), residence ($\beta = 0.306$), pattern of menstrual cessation ($\beta = 0.275$) and duration of pill use ($\beta = 0.261$). Age differences found for other independent variables were not significant. Thus it was revealed that a women with early NM (i.e. short fertile span) was one who had her last baby at an early age, lived in a semiurban area, abruptly ended her periods and had used contraceptive pills for a short period.

Discussion

Before discussing the results, attention should be given to some methodological limitations [12]. Because the diagnosis of menopause is often retrospective, most studies adopting this design, including the present one, have to rely on accurate knowledge and unbiased reporting of age [12], which is probably unreliable and liable to recall bias [2,6]. The accuracy of information depends on the period of time since menopause, alertness, motivation and educational level of the women studied, as well as on the availability of useful milestones (e.g. periods related to vital events,

Table 1 Correlation regression relationship between age at natural menopause and some independent variables

Independent variable	Regression coefficient	SE	β	P-value
Age at first marriage	-0.052	0.101	-0.516	0.610
Years of education	0.049	0.086	0.443	0.571
Age at first delivery	0.126	0.108	0.103	0.249
Age at last delivery	0.366	0.066	0.449	<0.001*
Duration of pill use	0.256	0.072	0.261	<0.001*
Obsession	0.442	0.833	-0.042	0.597
Weight	0.038	0.023	0.133	0.094
Residence (0 = urban; 1 = semiurban)	-5.220	0.189	-0.306	<0.001*
Marital status	1.615	0.961	0.131	0.096
Midcycle spotting	-5.664	2.918	-0.142	0.055
Dysmenorrhoea	-1.412	0.774	-0.135	0.71
Pattern of menstrual cessation (0 = abrupt; 1 = gradual)	2.915	0.774	0.275	<0.001*
Hypertension	-0.362	0.966	-0.030	0.708
Constant	39.447	6.123	-	<0.001*

*statistically significant

Multiple R = 0.78 $R^2 = 0.60$ $F = 11.75$ $P < 0.001$

The four variables: marital status, midcycle spotting, dysmenorrhoea, and hypertension were coded as follows: 0 = absent; 1 = present.

such as births, deaths, marriage) [2]. Comparison between different studies, as regards age and symptoms of menopause, is also difficult because of the differences in definitions, methodologies and populations (e.g. racial, environmental, sociodemographic, reproductive, health status, nutritional, psychological and cultural background, as well as the development level of a country).

Bearing in mind these limitations, a wide range for the age of NM has been reported in different countries. In our study, the mean age at NM was 46.70 ± 5.44 years; the median was 47 years. This mean is higher than those previously reported in different Egyptian governorates. Gadalla et al. [13] reported a mean age of 45.20 years for Sharkia Governorate in 1986. Es-hra et al. [14] found a mean age of 43.10 years for Menoufia in 1989. In Alexandria, Nasr [15] found a mean age of 45.80 years in 1988. On the other hand, a similar mean age to ours of 46.24 years was reported in Turkey in 1994 [16], while a higher one (50.60 years) was found in the USA in 1987 [17]. Higher figures were also observed in Thailand (50.13 years in 1997) [18] and (49.50 years in 1993) [19], in Russia (49.00 years in 1995) [20], in Spain (48.60 years in 1994) [21] and in Ghana (48.05 years in 1993) [22]. However, a lower mean age of 45.50 years was reported in Mexico in 1995 [23].

With regard to the median age, the reported figure in our study was lower than those reported in the USA (51.50 years in 1997) [24], Finland (51.00 years in 1994) [7], the UK (50.70 years in 1989) [2], Sweden (50.10 years in 1993) [25] and Ghana (48.00 years in 1993) [22].

The disparity of the observed ages could be attributed to the differences in definitions of menopause, research methodology and population discrepancies as mentioned

before [2,6,12], as well as the use of hormone replacement therapy in the perimenopausal period, which is an important determinant of delayed menopause [1,8].

Our study revealed that about 8% of the naturally menopausal women experienced premature menopause (before the age of 40 years). Premature menopause or premature ovarian failure is a condition which has been recognized for a considerable time [1,5]. Normally, human primordial germ cells separate from somatic cells at an early stage of embryogenesis. Some 1000–2000 cells migrate to the gonadal ridge from the dorsal aspect of the hind gut and yolk sac, where they multiply to a maximum of 5–7 million follicles around the fifth month of intrauterine life. Multiplication then stops and a steady loss of primordial follicles from the fetal ovary occurs, so that by the time a baby girl is born each ovary contains about 1 million follicles. This number continues to diminish after birth independent of the physiological state of the woman, and only about 500 ova ovulate throughout fertile life; the remaining ova degenerate [1,5].

Histopathologically, two types premature ovarian failure have been identified, namely follicular and afollicular. In follicular failure, an ample number of primordial follicles is present with elevated gonadotrophin levels, suggesting resistance to gonadotrophins and this is called resistant ovary syndrome [5]. The resistance is postulated to result from deficient follicle stimulating hormone (FSH) receptors within the follicles. In afollicular failure, it is not clear whether fewer primordial germ cells migrate to the gonadal ridge in fetal life, or if the rate of multiplication up to the fifth intrauterine month is reduced. It is also possible that the rate of follicular loss thereafter is greater than normal. It may be a combination of the three factors. However, radiotherapy, chemotherapy or viral infection

(mumps, oophoritis) can also result in premature ovarian failure. In addition, it has been associated with an autoimmune phenomenon in which ovarian antibodies were demonstrated, and in rare conditions, a genetic factor was identified. Intrinsic anomalies of the X chromosome which obstruct meiotic division are some of the factors known to interfere with oogenesis [26,27].

Although most of the results of our study concur with other research studies, there are some statistically significant differences. This might be partly due to the relatively small sample size and methodological differences, in addition to differences in nutritional status and other lifestyle practices not measured in our study. These factors will be highlighted during the discussion of the different variables.

In several studies, rural-urban residence was investigated as a factor that can affect the timing of menopause [2,7,16,21]. However, results are inconsistent. In our study, a rural population was not represented in the sample. So, the effect of residence was studied only as regards urban and semiurban differences. Semiurban women were found to reach their menopause earlier than the urban ones. This difference may be explained by differences in socioeconomic and nutritional status, where menopause may be brought forward by low socioeconomic status [2,7,12,21,26] and malnutrition [12,26].

Single women have been found to experience earlier menopause than ever-married women [1]. However, several studies have indicated discrepancies regarding the effect of marital status on age at NM. [1,14,16]. Our study revealed that divorced/separated women had a significantly earlier menopause than married, widowed and single ones. This could be explained by the association of divorce/separation with social and psychological troubles, which can affect the

gonadal function [24,26]. In 1993, Vermeulen [26] reported that stress, via the release of corticotropin-releasing hormone, triggered by interleukin 1, inhibits the production of gonadotrophin releasing hormone resulting in anovulation or amenorrhoea. Earlier in 1992, Kirchengast [28] concluded that psychological stress may influence sex hormone levels in the climacteric period. On the other hand, in our study, age at NM was positively correlated with age at divorce/separation. Since the latter mean age was low, it seems logical to find a low age at NM among these women. However, such a correlation relationship may indicate a durational effect of marital life on age at NM.

Education is a strong socioeconomic indicator. We found that the age at NM was positively associated with both level and years of education. This finding is consistent with several earlier studies [2,7,16]. However, other investigators have failed to find such an association [14].

In agreement with Eshra et al. [14], the occupation of the women studied did not affect menopausal age. On the other hand, Luoto et al. [7] observed delayed menopause among working women.

In our study, women with sufficient income experienced slightly later menopause than those with insufficient income. This confirms the findings of other studies where higher income was significantly associated with later menopause [2].

Age at menopause may be a marker for hormonal status earlier in life [6]. The present findings indicated that women with irregular menstrual cycles before the age of 25 years experienced later menopause than those with regular cycles in the same period. This result is consistent with reports from earlier studies [6]. Irregular cycles reflect long ones, which have been found to be associated with anovulation and delayed

menopause. Anovulation delays or reduces the exhaustion of the available germ cells. This accords with the theory that menopause occurs after depletion of the available oocytes. If anovulation is the mechanism of late menopause, it would be expected that suppression of ovulation, either by use of oral contraceptives or pregnancy, would also postpone menopause [6]. However, in our study, oral contraceptive use was not associated with delayed menopause, while the duration of pill use was significantly positively correlated with age at NM, indicating that duration of use is the effective factor. Whelan et al. [6] pointed to the evidence that FSH influences the rate of follicular depletion in humans. Accordingly, it was hypothesized that the longer the suppression of FSH, the more the menopause is delayed. The present findings are consistent with that of prior studies regarding oral contraceptive use and duration of use [2,14]. On the other hand, and conforming with other studies, gravidity [21], parity [2] and age at menarche [6,14,21] in the present study were not significantly correlated with age at NM.

Dysmenorrhoea and midcycle spotting, which are indicators of ovulation, were significantly associated with later age at menopause and not earlier age. However, these findings cannot be explained on the basis of the oocyte depletion theory. Thus, it may be speculated that there is a non-linear relationship between number of oocytes and age at NM and that menopausal age is more sensitive to varying rates of atresia than to the ovulation process. Atresia is the degeneration and regression of an ovarian follicle before its maturation. However, the effect of alteration of the rate of atresia on age at NM is difficult to determine in humans. It is suggested that one or more pituitary hormones may be involved, or more likely, that certain aspects of the

neuroendocrine system, in particular the pituitary gland, may influence both the menstrual cycle and rate of atresia. These are in addition to the intragonadal factors, such as inhibin and other related hormones [6].

Contrary to other studies, age at menopause was positively correlated with both age at first live birth and age at last live birth [6,7]. However, the observation regarding age at last live birth is consistent with that of Brand et al. [29] and Whelan et al. [6], who attributed the association of later menopause with later age at last live birth to the longer fertile period in women who had late pregnancies. On the other hand, age at first live birth may be closely related to age at marriage, which was found to be positively correlated with menopausal age in this study.

In agreement with earlier studies, we observed a non-significant positive correlation between age at NM and the number of spontaneous abortions [6,14]. Also, similar to Eshra et al [14], we found no significant correlation between menopausal age and duration of menses.

In the present study, three-fifths of the women experienced a gradual cessation of menstruation, a figure which is consistent with the finding of a previous study in Egypt in 1989 [14]. On the other hand, 40% of the women abruptly stopped menstruation compared with only 10% in the study of Whelan et al. [6]. Also, our study found that sudden cessation of menstruation was significantly associated with earlier menopause than gradual cessation. However, it is unusual for the menstrual cycle to stop abruptly at the time of menopause. Indeed, ovarian function declines gradually over several months to several years. During this period, production of ovarian estrogen fluctuates leading to menstrual irregularity. The amount and duration of menses decrease

gradually tapering to spotting and eventually to cessation [25]. However, abrupt cessation may accompany sudden psychological trauma (pituitary shock) [26,28] or may reflect abnormal or pathological ovarian failure that may occur at an earlier age.

Applying the Middle Sex Test in the present study, a mean score of less than nine for all the studied neurotic traits was found, indicating absence of these traits among the women as a whole. This result is consistent with Eshra et al. [14]. However, Seif El-Din et al. [30], applying the same psychometry, identified obsessive and depressive traits (score = 9) among postmenopausal women. This difference may be due to the fact that the whole sample of the latter study consisted of working women with possibly more responsibilities and stresses. In addition, our study did not show any difference in the menopausal age in those with or without the traits investigated, while in the study of Eshra et al., later menopause was seen in those with traits of obsession, depression and psychosomaticism. On the other hand, a negative correlation between obsessive trait and age at menopause was found in our study. This association may be explained by the fact that emotional state plays an important role in regulating gonadal function [24,26,28]. The discrepancy in results could be due to differences in cultural and socioeconomic characteristics of the studied population or due to differences in sample size or methodology as mentioned before.

Our study examined the effect of health status on the age at NM. We found that hypertensive women had a later menopause than normotensive ones. This is in agreement with Eshra et al. [14].

We found a positive correlation between menopausal age and both current weight and body mass index. However, the findings in other studies have been inconsistent.

While some investigators failed to find any effect for absolute or relative weight on age at menopause [2,7,29], others observed a positive effect, but only among smokers [1]. A third group reported a positive relation between absolute weight and menopausal age, but without control for the effect of smoking [14]. The effect of weight in such studies may be partly attributed to smoking. Earlier menopause in thinner women may be due in part to the tendency of smokers to be thin [2,7]. On the other hand, the association of obesity with later menopause may be due to the greater availability of endogenous estrogen produced in the adipose tissue from its androgenic precursor [12,31]. Current height was not associated with menopausal age in our study, which concurs with earlier ones [2,14].

With few exceptions [2,7], most studies describing factors associated with variations in the age at NM did not adjust for potential confounding effects [6,16,21,28]. Confounding with other covariates can explain some of the variations in outcome [2].

In summary, our study attempted to elucidate the factors which influence the timing of NM by employing multiple regression analysis. The analysis indicated that age at last live birth, residence, pattern of menstrual cessation and duration of pill use were the significant predictors of the end of menstrual activity in that order. The data provide evidence that women whose ovaries are ovulating during the reproductive years may experience early menopause, although the precise mechanisms are unclear. This accords with the notion that the exhaustion of available follicles causes natural menopause. If anovulation is the mechanism whereby irregular periods early in reproductive life and parity produce a delay in the age at menopause, one would expect that oral contraceptive use would also postpone menopause. Since the majority of

the women studied were of an older age when oral contraceptives became available, we could not properly evaluate the effects of oral contraceptive use. Additional research on the relationship between menopausal age and factors associated with anovulatory menstrual cycles during reproductive years seems warranted.

Acknowledgements

We would like to thank Professor Sanaa F. Abou El-Azm, Faculty of Dentistry, Alexandria University for her continuous help and support in supervising this study.

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