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Original article

Risk Factors of Early Menopause: A Descriptive Study

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Menopause is an inevitable physical change experienced by women during the aging process. As the production of female hormones decreases and ovulation stops alongside the aging of the ovaries, regular menstruation disappears. Although menopause itself is not a pathological condition, menopausal transition is accompanied by negative physical changes. With the increase in life expectancy, the proportion of postmenopausal life also increases. Thus, the impact of menopause on women's health has become more significant from both clinical and health perspectives. This study was conducted to identify the risk factors associated with early menopause in women in Tripoli. This was a retrospective case series study; it was conducted in Aljala maternity hospital, Tripoli, Libya, during the year 2017. Three hundred and thirty women who were diagnosed as cases of early menopause were randomly selected from the hospital files and from interviews with the women who attend the gynecology clinic. The following data were obtained from the files and the women: the age of menarche, menstrual cycle, marital state, education level, working status, smoking, parity, history of oral contraceptive, BMI, and history of pelvic surgery. Regarding the age of menarche, the mean age of menarche was 12 ± 1.14 years. The majority of the women had their menarche at age below 13 years (70.3%). Most of the women in the study had regular menstrual cycles (85.5%). Most of the women were educated, not working, and married. The current study showed that about 26% of the women who had early menopause had a history of passive smoking. Regarding the obstetric history, most of the women were multiparous, and most of them did not use contraceptive pills. The study concluded that the majority of the women who had early menopause had menarche at an early age, had regular cycles, were married, educated, not working, multiparous, and did not use oral contraceptives. Other factors, such as smoking, BMI, and history of pelvic surgery, showed lower percentages.

Introduction

As a woman approaches menopause, there is a gradual cessation of ovarian function, leading to estrogen deficiency and a reduction in fertility. This is associated with a rise in gonadotropin levels. The mean age for this natural phenomenon is 50 years (standard deviation ± 4 years) [1]. When the menopause occurs before the age of 40 years, it is considered premature and is known as premature ovarian failure (POF). A widely used definition of POF is ≥ 4 months of amenorrhea and two follicle-stimulating hormone levels ≥ 30 IU/ml at an interval of at least 1 month [2,3]. In a large cohort of women followed up prospectively, 0.9% experienced menopause before the age of 40 years, although in this study, amenorrhea for >12 months was considered as the menopause [4]. Steadily improving cure rates of cancer among children and young women are likely to increase the incidence of POF [5].

Premature ovarian failure is the most widely recognized term, but alternatives to this have been proposed, such as primary ovarian insufficiency and premature ovarian dysfunction [6,7]. The term premature ovarian failure suggests that the state of ovarian failure is irreversible, which is not strictly true. The ovarian follicular function fluctuates in about 50% of women with POF8, and 5–10% of women with the diagnosis may eventually conceive [8,9]. Moreover, the term 'failure' has a negative connotation and conveys a sense of hopelessness, which does not help when trying to counsel a woman and her family sensitively.

In the majority of women with POF, no cause is identified, but with advances in genetics and endocrinology, our understanding of the pathophysiology of this clinical entity is ever improving [10]. This study was carried out to identify the risk factors associated with early menopause in women in Tripoli.

Methods

Study design and setting
This was a retrospective case series study conducted in Aljala Maternity Hospital, Tripoli, Libya, during the year 2017.

Study population
330 women who were diagnosed as cases of early menopause were randomly selected from the hospital files and from interviews with the women who attend the gynecology clinic. The following data were obtained from the files and from the women: the age of menarche, menstrual cycle, marital state, education level, working status, smoking, parity, history of oral contraceptive, BMI, and history of pelvic surgery.

Statistical analysis
Statistical analysis was computerized using the Statistical Program for Social Sciences (SPSS version 24), that used for data entry and analysis. Descriptive statistics were used, and all results are presented as frequencies, means, standard ± deviation, and percentages.

Results

Age of menarche
Regarding the age of menarche, the mean age of menarche was 12 ± 1.14 years. The majority of the women had their menarche at age below 13 years (70.3%). About 29.1% had menarche between 13 and 15 years, and only 0.6% had menarche at age more than 15 years.

Table 1: Age of menarche for the women

Age of menarche	No (%)
< 13 years	232 (70.3%)
13 – 15 years	96 (29.1%)
>15 years	2 (0.6%)
Mean age ± SD	12 ± 1.14

Menstrual pattern
With regards to the menstrual pattern, most of the women in the study had regular menstrual cycles (85.5%). Only 14.5% of the women had irregular menstrual cycles.
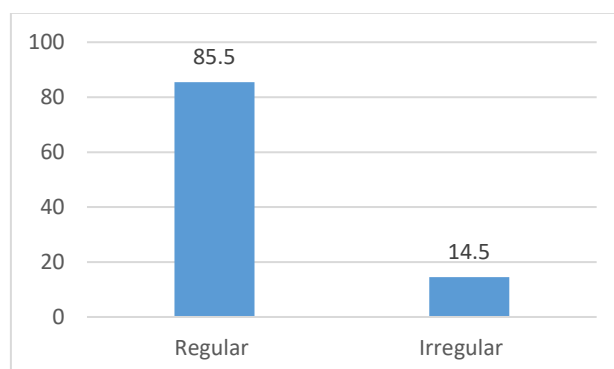
Figure 1. Menstrual pattern

Women's education level
About 22.7% of the women were illiterate or could only read and write, 9.4% had primary education, 44.8% had secondary education, and 23% had higher education level.

Table 2: Women's education level

| Women education	No (%)
Illiterate or can read and write	75 (22.7%)
Primary education	31 (9.4%)
Secondary education	148 (44.8%)
Higher education	76 (23%)

Marital status of the women

Concerning the marital state of the women, the majority of women were married (87.8%). About 5.5% of the women were single, 5.2% were divorced, and only 1.5% were widows.

Table 3: Marital status of the women

Marital state	No (%)
Single	18 (5.5%)
Married	290 (87.8%)
Divorced	17 (5.2%)
Widow	5 (1.5%)

### Working status of the women

Regarding the working status, more than two-thirds of the women were not working (68.8%), about 27.3% of the women were working, and only 3.9% were retired.
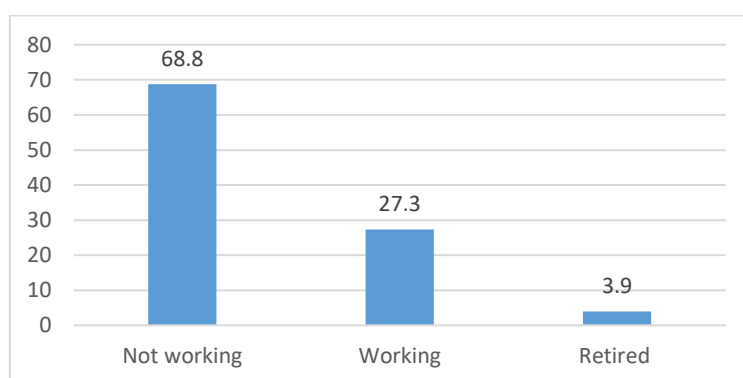
Figure 2. Working status of the women

History of passive smoking

The current study showed that about 26% of the women who had early menopause had a history of passive smoking, and about 74% had no history of passive smoking.
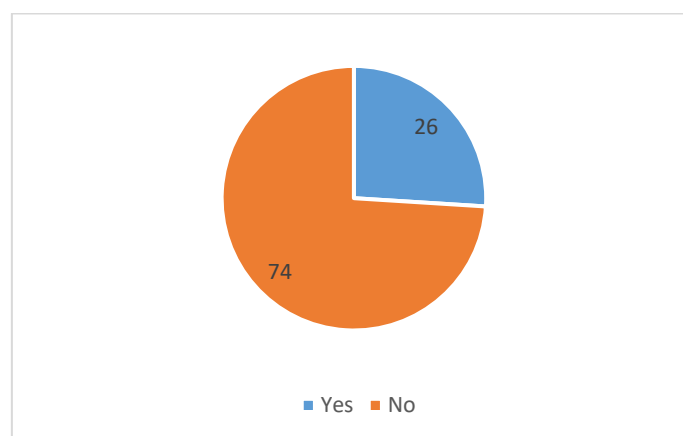
Figure 3. History of passive smoking

Number of deliveries

With regards to the previous deliveries, about 5.4% of the women reported no previous deliveries, 6.7% reported only 1 delivery, and the majority (87.9%) reported more than one delivery.

Table 4: Number of deliveries

Number of deliveries	No (%)
0	18 (5.4%)
1	22 (6.7%)
> 1	290 (87.9)

Use of oral contraceptives

The study result showed that 33.1% of the women used oral contraceptive pills, and about 65.1% did not use oral contraceptive pills. Only 1.8% of the women were not sure if they used the contraceptive pills.

Table 5: Use of oral contraceptives

| Birth control	No (%)
Yes	109 (33.1%)
No	215 (65.1%)
Unknown	6 (1.8%)

Body mass index

Regarding the BMI, about 20% of the women had a BMI less than 18.5, 33% had a normal BMI (18.5-24.9), 31.8% had a BMI between 25 and 29.9, and about 15.2% had a BMI more than 30.

Table 6: Body mass index

BMI	No (%)
< 18.5	66 (20%)
18.5 – 24.9	109 (33%)
25 – 29.9	105 (31.8)
≥ 30	50 (15.2%)

History of pelvic surgery

Concerning previous pelvic surgeries, about 4.9% of the women had undergone pelvic surgery, and 95.1% had a negative history.
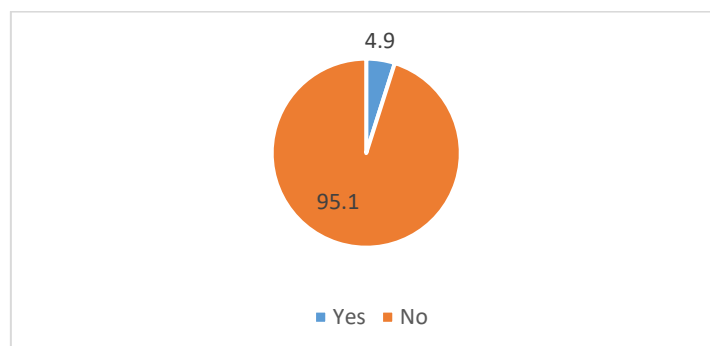
Figure 4: History of pelvic surgery

Discussion

The World Health Organization defines natural menopause as the permanent cessation of menstruation resulting from the loss of ovarian follicular activity or follicle depletion. Natural menopause is recognized to have occurred after 12 consecutive months of amenorrhea for which there is no other obvious pathologic or physiologic cause. early menopause (EM), which is characterized as the occurrence of menopause under 45 years of age, is also clinically important for women's health because of various diseases due to early deficiency of estrogen. Early age at menarche has been suggested as a risk factor for both POF and EM. However, the etiology of POF partly differs from that of EM since longer breastfeeding decreased the risk of POF and the use of oral contraceptives decreased the risk of EM. To the best of our knowledge, there has not been sufficient evidence regarding differences in factors associated with POF and EM [11-13].

The purpose of the current study was to identify the risk factors of early menopause. The result of the present study reported that the mean age of menarche of women who had early menopause was 12 ± 1.14 years. The majority of the women had their menarche at an age below 13 years. The Carmer DW study reported that most of the patients were ≤ 11 years. The same study reported that early menarche is associated with early or premature menopause because of more frequent ovulation among those women and the depletion of ova [14].

Regarding the menstrual pattern, most of the women in the study had a regular menstrual cycle. A study conducted by Whelan EA reported that shorter cycle lengths, particularly during early reproductive years, can decrease the age at natural menopause by 1 to 2 years [15]. Stanford et al speculated that the association between irregular cycles and later age at menopause could reflect the association between

anovulation and irregular cycles, which is compatible with the notion that menopause occurs after a certain degree of depletion of oocytes [16].

In respect of marital state, the study showed that the majority of the women were married, educated, and not working. Sievert LL reported that married and widowed women report a later mean age at natural menopause compared to single and divorced women [17].

With regards the smoking, the current study showed that about 26% of the women who had early menopause had a history of passive smoking. Studies showed that smokers reached menopause earlier than non-smokers, and their risk for experiencing early menopause was higher [18,19].

Regarding the past obstetric history, most of the patients who had early menopause were multipara, and only one-third of them used oral contraceptives between pregnancies. Many studies have found that nulliparous women are at greater risk of early natural menopause or have observed a trend of later menopause associated with increasing parity. Studies also showed that long-term use of OCs could postpone the onset of menopause by inhibiting follicle depletion [15,16,20].

Regarding the BMI, about 20% of the women had a BMI less than 18.5, 33% had a normal BMI (18.5-24.9), 31.8% had a BMI between 25 and 29.9, and about 15.2% had a BMI more than 30. Several epidemiologic studies have investigated the association between increasing body mass index and earlier menopause with mixed results. Beser et al. found that obese women (body mass index (BMI) > 25) had a significantly earlier menopause (about 1 year) than non-obese women. [21]. A published study by Bromberger et al. found no significant difference in the age of menopause of women below and above a BMI cutoff of 27.3 kg/m2, but did observe that women who were currently on a weight reduction diet or who gained at least 27 pounds after the age of 20 experienced menopauses about 1 year earlier than women with no such history, perhaps providing indirect evidence for the role of obesity in the determination of age of menopause [22].

Conclusion and Recommendation

The study concluded that the majority of the women who had early menopause had their menarche at an early age, had regular cycles, were married, educated, not working, multiparous, and did not use oral contraceptives. Other factors, such as smoking, BMI, and history of pelvic surgery, showed lower percentages. More studies with larger numbers of women need to be undertaken to determine the factors responsible for early and premature menopause.

Conflict of interest

Nil

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الملخص

انقطاع الطمث هو تغير جسـدي لا مفر منه تمر به النسـاء أثناء عملية الشـيخوخة. مع انخفاض إنتاج الهرمونات الأنثوية وتوقف الإباضـة إلى جانب شـــيخوخة المبايض، يختفي الحيض المنتظم. على الرغم من أن انقطاع الطمث في حد ذاته ليس حالة مرضـــية، إلا أن الانتقال إلى انقطاع الطمث يصاحبه تغيرات جسدية سلبية. مع زيادة متوسط العمر المتوقع، تزداد أيضًا نسبة الحياة بعد انقطاع الطمث. وبالتالي، أصبح تأثير انقطاع الطمث على صـحة المرأة أكثر أهمية من المنظورين السـريري والصـحي. أجريت هذه الدراسـة لتحديد عوامل الخطر المرتبطة بانقطاع الطمث المبكر لدى النسـاء في طرابلس. كانت هذه دراسـة حالة بأثر رجعي؛ وقد أجريت في مسـتشـفى الجلاء للولادة، طرابلس، ليبيا، خلال عام 2017. تم اختيار ثلاثمائة وثلاثين امرأة تم تشـــخيصـــهن على أنهن حالات انقطاع الطمث المبكر بشـــكل عشـــوائي من ملفات المستشفى ومن المقابلات مع النساء اللواتي يترددن على عيادة أمراض النساء. تم الحصول على البيانات التالية من الملفات والنساء: عمر بدء الحيض، الدورة الشـهرية، الحالة الاجتماعية، المسـتوى التعليمي، الوضـع الوظيفي، التدخين، عدد الولادات، تاريخ اسـتخدام موانع الحمل الفموية، مؤشر كتلة الجسم، وتاريخ جراحة الحوض. فيما يتعلق بعمر بدء الحيض، كان متوسـط عمر بدء الحيض 12 ± 1.14 سـنة. بدأت غالبية النساء حيضهن في سن أقل من 13 عامًا (70.3٪). كان لدى معظم النساء في الدراسة دورات شهرية منتظمة (85.5٪). كانت معظم النسـاء متعلمات وغير عاملات ومتزوجات. أظهرت الدراسـة الحالية أن حوالي 26٪ من النسـاء اللاتي تعرضـن لانقطاع الطمث المبكر لديهن تاريخ من التدخين السـلبي. فيما يتعلق بالتاريخ التوليدي، كانت معظم النسـاء متعددات الولادات، ومعظمهن لم يسـتخدمن حبوب منع الحمل. خلصـت الدراسـة إلى أن غالبية النسـاء اللواتي انقطع لديهن الطمث المبكر بدأن الحيض في سـن مبكرة، وكانت دوراتهن الشـهرية منتظمة، ومتزوجات، ومتعلمات، ولا يعملن، وأنجبن أكثر من مرة، ولم يسـتخدمن موانع الحمل الفموية. وأظهرت عوامل أخرى، مثل التدخين، ومؤشر كتلة الجسم، وتاريخ جراحة الحوض، نسبًا أقل.