Can Maternal Age at Menopause Predict Daughters Antimullerian Hormone in Babylon?

Hanan Abduljabbar Al-Taee

Department of Medical Physiology, College of Medicine, university of Babylon, Iraq. Hilla\Iraq.

Abstract

Objective: daughter fertility potential is possibly related to her mother fertility and age at menopause. This study aims to determine any relationship between maternal age at natural menopause with anti mullerian hormone of mid reproductive age daughters. Design: questionnaire survey and blood sample of women attending gynecology clinic in Babylon\ Iraq from June 2014 - July 2018 .Subjects and Methods: this cross sectional study, collected questionnaire data from 106 (N=106) mother daughter pairs who fulfilled the study inclusion criteria out of a random population. For this analysis, young women (daughters) between the ages of 16 and 35 years, who provided a blood sample for anti mullerian hormone and their mother's age at natural menopause were selected. Assessment of relationship between maternal age at menopause and their counterpart daughter anti mullerian hormone was done. Result: Person correlation for association of mother age at natural menopause with daughter anti mullerian hormone shows insignificant association. Conclusion: our selected mother-daughter pairs show no association between maternal age at natural menopause and serum anti mullerian hormone level.

Keywords: *Maternal menopause, Anti mullerian hormone (AMH), Fertility, Mid reproductive age women.*

Introduction

Reproductive organs of women is the first to age in humans, it starts in utero, pass through puberty, fertility, subfertility, the menopause transition and finally menopause [1].Women progress through these reproductive stages due to a decline in both the number and quality of ovarian oocytes and follicles which together contribute to increasing incidences of miscarriages, infertility, and birth defects [2]. To some extent this process is influenced by lifestyle factors like smoking and other social determinants [3], the use of oral contraceptives, genetic factors and events during intrauterine life probably play a more important role in the age-dependent decrease of female fertility [4].

Similarities in mother and daughter ages at menopause may be attributed to common habits such as smoking, education level, and diet/exercise resulting in similar body mass index (BMI) [5]. Many subtle changes in the endocrine regulation of ovarian function with advancing age may seem interesting but currently are not clinically useful as a predictive test. Examples are changes in concentrations of estradiol, progesterone, luteinizing hormone (LH) and Inhibin, as well as follicle dynamics. Other markers hold more promise; among these are chronological age, family history, anti-müllerian hormone (AMH), poor response to in vitro fertilization (IVF), basal follicle-stimulating hormone (FSH) and the antral follicle count for long term prediction. Anti-mullerian hormone (AMH), have been proved as valuable markers for predicting the size of the primordial follicle pool, i.e. the ovarian reserve [6],as such, AMH serves as an indicator for the number of follicles remaining in an individual's ovaries.

Since the exhaustion of the primordial follicle pool coincides with the age at natural menopause (ANM), AMH might constitute a marker for menopausal age as well [7]. Its value arises from the usefulness in women at different ages (very young or perimenopausal), and it may be an effective marker in the determination of the time of menopause even many years before its

occurrence [8]. Interestingly, mother's ANM has been found to be a determinant of AMH levels in the daughters [9]. Many epidemiological studies focus on the predictive power of mother age at natural menopause for daughter age to menopause, but how this marker play role in predicting fertility and AMH of daughters, few study have been done in this regard [10, 11].This paper aims to answer if mother age at natural menopause is a predictor of her daughter's AMH serum level in our selected population.

Subject and Methods

This is Cross-sectional study included 106 mother- daughter pairs; it was proved by the medical and research ethical committee of college of medicine-university of Babylon /Iraq. It was carried out from June2014- June 2018 in private gynecology clinic in Babylon. The young women (daughters) attended the clinic for fertility management or others. Verbal and written informed consent was obtained from all the participants prior to study inclusion declaring their will to participate in this work.

A detailed reproductive history and data was obtained through face to face pertained questionnaire; completed by all participants before the physical examination. Questions included: gynecological and reproductive history, including menstrual cycle characteristics; use of contraceptives; pregnancies and deliveries; socio-economic characteristics; smoking habits, including prenatal smoking exposure; physical activities; hereditary and chronic diseases and mothers' age at menopause.

With regard to records of age at maternal menopause, the participants were asked to obtain information about maternal ANM from their mothers. The definition of natural menopause was specified in the questionnaire as absence of menstrual bleeding for 12 months that was not related to oophorectomy or chemotherapy.

Mothers who had been using hormone replacement therapy or oral contraceptives up to the last menstrual bleeding, or had had an hysterectomy or oophorectomy were not classified as natural menopausal .The young women mean age was 30 ± 7.7 (16-35) years, and the mean age of natural menopause of the mothers was 51.27 ± 5.2 years.

Anthropometric measurements were also done.

Inclusion Criteria

For the Mothers

Reached natural menopause.

Not smoker or ex- smoker.

For the Daughters

Midre productive age, fertile women. Regular menstrual cycles in the reference range (22–35 d for the previous three menstrual cycles) Exclusion criteria included current smoking, use of psychotropic or hormonal medications, including hormonal contraception and hormone therapies; pregnancy or breast feeding; serious health problems known to compromise ovarian function (e.g. diabetes mellitus, liver disease, breast or endometrial cancer).

Hormonal Analysis for the Young Women Were Done with Especial Emphasis on AMH

From each woman, about three milliliters of blood collected in plain tube using disposable syringes. These samples were left to stand at least 15 min at room temperature before centrifugation at 3000 round per minute (rpm) for 10 min to separate the serum, patient name was written on the plain plastic tube and kept it in the deep freeze at (-20 C) temperature till the time of the assay. Serum samples for AMH were examined by sensitive Enzyme Linked Immune Sorbent Assay (ELISA) method, and the kit used was Beckman coulter Inc, USA

Statistical Analysis

Statistical analysis of data was performed with Statistical Package for Social Science; SPSS, Inc., Chicago, IL) SPSS version 20 for Windows. Qualitative data were expressed as percentages, while quantitative data were expressed as mean ± standard deviation (SD). Pearson correlation was used for testing correlation between ANM with AMH [12].

Results

Demographic Data of Study Group

The mean age of young woman was 30 ± 7.7 (16-35) years and that of maternal (ANM) was 51.27 ± 5.2 (39-60) years, they young women had reached menarche at 11.76 ± 2.1 years, with mean BMI 27.34 ± 4.89 kg/m2.

Most of them gained college level of education (47%), as shown in Table (1).

Table 4.1: Demographic data of the study group (No. are mean± SD or percentages) N= 106

Parameter	Mean± SD
Daughter age(year)	30 ± 7.7
Mother age at menopause/ (year)	51.27 ± 5.2
Menarche/year	11.76± 2.1
BMI(kg/m2) (Body mass index)	27.34 ± 4.89
Education level (%) Illiterate Primary school Secondary school College	 13 20 18 47

Association of Maternal Age ANM with Daughter's AMH

Person correlation was done for association of mother age of menopause with daughter AMH which was insignificant, (Table2).

Table 4.2: Association of maternal age at natural menopause with daughters AMH

	AMH ng/ml
MAN(year)	r = - 0.143
	P > 0.05

MAN (maternal age at natural menopause), AMH: Antimullerian hormone, correlation was calculated using Pearson correlation, r: correlation coefficient, p: level of significance

Discussion

Table 4.1 shows that means age of young women was 30 ± 7.7 year, and their mean AMH serum level was 4.20-4.68 ng/ml. In our selected population, a non-significant effect of maternal age at natural menopause on AMH levels (P > 0.005) was observed (Table 4.2). When we revised the literature, few papers were found studying this association .A study published in 2013, in Human Reproduction by Bentzen and colleagues who found strong positive association between maternal age at menopause and AMH serum level in subset of healthcare midreproductive age women in Copenhagen [9].

The selected daughter -mother population are nearly comparable in our and their study regarding the age of daughters and menopausal age of mothers, but the results are different. This discrepancy in finding may be due to several factors; **first**, our study population consisted of general citizen of different life style, living areas and of different educational levels, all have potential impact on fertility and AMH serum levels [13].

In addition to the life forces in Iraq, which contributes to extensive psychological and environmental pollutions in the last 25 years to which our young women have faced during their puberty, adulthood or reproduction lifetime; all these have negative or can

change reproduction habits of our women, [14, 15].We didn't include any smokers in our study nor contraceptive uses as they did in their study which could impact the results [16].

Second the Danish population consisted of health care workers, who might be more aware of healthy living than the general population. Additionally, social class and environment may be more homogeneous among health care workers than in our general population [17].

Third both AMH serum level and BMI are lower in their study group, both have potential impact on the results [18].

Fourth and last their study population is larger in size.

Conclusion

Our selected mother-daughter pairs show no association between maternal age at natural menopause and serum anti mullerian hormone level. Larger, multi-centric study is needed to confirm our preliminary results

Acknowledgements

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