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Association between parity and ovarian reserve in reproductive age women

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ABSTRACT

Objective: A number of factors affect ovarian reserve. In this study, we investigate the association between parity and ovarian reserve in reproductive age women.
Materials and methods: This cross-sectional study was conducted on 186 women aged 20–35 years. The participants were divided into two main groups. Group A (n = 93) included women with at least one parity (pregnancy after 28 weeks), while group B (n = 93) included women with no history of pregnancy. We evaluated the following factors related to ovarian reserve: follicle-stimulating hormone (FSH), ovarian antral follicles, anti-Müllerian hormone (AMH), and ovarian volume.
Results: A total of 186 women with a mean age of 27.83 ± 4.49 years enrolled in this study. There was a difference in mean AMH between the nulliparous (2.53 ± 1.90 ng/ml) and multiparous (3.54 ± 1.42 ng/ml) groups ($p < 0.001$). FSH levels were from 5.27 ± 1.8 mIU/mL in nulliparous women to 5.01 ± 1.9 mIU/mL in multiparous women, which did not significantly differ ($p = 0.36$). Antral follicles and ovarian size in multiparous women increased significantly ($p < 0.001$).
Conclusion: Parity has a significant association with higher levels of ovarian reserve markers.

Introduction

Participation in social and economic activities, in addition to the desire to increase the level of education are important changes in a woman's life that contribute to the delay in childbearing or decision to remain childless. Our knowledge about female reproductive ageing assumes an age-dependent decline in both quantity and quality of the follicles. Concerns exist about the future fecundity of these women along with reports about the effect of reproductive characteristics, such as parity on ovarian reserve and menopausal age [1,2].

Many studies have reported associations between various demographic and medical factors with ovarian reserve and menopausal time [2–4]. However, only a few studies have focused on reproductive characteristics.

There are some reports of an association between higher parity and later menopause [5–7], which indicated that women with higher parity have higher ovarian reserve. Others, however, have reported contradictory results [8]. Many of these studies are based on FSH evaluation and this technique may have some limitations.

Understanding exact menopausal timing and ovarian reserve is relatively difficult. The recall method or laboratory tests such as follicular stimulating hormone (FSH) have some biases in their evaluations.

Anti-Müllerian hormone (AMH), a hormonal marker of ovarian reserve, helps overcome numerous methodological challenges in ovarian reserve evaluation [9–12].

AMH is secreted by granulosa cells in primary, secondary, and small antral ovarian follicles in females. The highest secretion is in the secondary and small antral stages. Its concentration reduces with further follicle growth [13,14]. AMH levels in women are low at birth, rise during early adulthood, and then decline gradually with age [10,15–17]. AMH is useful as a marker of ovarian reserve because it is produced in growing follicles; this hormone is believed to reflect the number of primordial follicles [18,19].

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Whether pregnancy during the early reproductive ages is an assurance for preservation of ovarian reserve remains unknown.

We gathered data from reproductive age women to investigate the association between parity and higher ovarian reserve.

Materials and methods

This cross-sectional study enrolled women aged 20–35 years who came to our clinic at Arash Women's Hospital, Tehran, Iran, from May 2012 to May 2013 for a check-up or other gynecologic conditions, such as vaginitis.

The study was approved by the Ethics Committee of Research at Tehran University of Medical Sciences, Tehran, Iran. A written informed consent was obtained from all individuals before they entered the study. The exclusion criteria are defined on the basis of the interview and constitute infertility, smoking, previous ovarian surgery, endometriosis, family history of premature ovarian failure, autoimmune diseases and history of hormone administration during the last 6 months. The patients were divided into the following two main groups: (i) group A (n = 93) comprised women who experienced at least one parity after 28 weeks and (ii) group B (n = 93) included women who were nulliparous. We controlled for age, as a potential confounder, by dividing the two main groups into three equal sub-groups as follows: 20–24, 25–29 and 30–35 years.

All patients completed a questioner for menarche age, duration and interval of menses.

AMH and FSH levels were measured at the third day of menses. Morning blood samples were collected into ethylenediaminetetraacetic acid (EDTA)-coated tubes by venipuncture using a 2CC syringe. The samples were taken in our laboratory in the hospital. We used the AMH assay second generation and an additional predilution step. The AMH assay kits were opened weekly. Therefore, patients' blood samples were kept refrigerated after centrifugation if they were to be evaluated more than two hours and less than 48 h after preparation. For longer storage, samples were maintained at −40 °C according to the manufacturer's recommendation. Plasma AMH levels were measured using the enzyme-linked immunosorbent assay (ELISA; Beckman Coulter Inc., Switzerland) based on the manufacturer's protocol with an interassay coefficient of variation of 9.7%. The results norm according to company guidelines is 0.19–9.1 ng/ml for women at 20–40 years old.

FSH was measured by electrochemiluminescence (Roche, Germany).

Our laboratory held quality assurance certification from Tehran University of Medical Sciences.

All patients underwent transvaginal sonography on the second-third day of their spontaneous menstrual cycles. The evaluations were conducted by the same expert using an ultrasound device (Accuvix V20, Medison) with a 6.5 MHz and MCX vaginal probe (Livingstone, Scotland, UK). All follicles 2–10 mm in size were counted in each ovary. The sum of both ovarian counts was considered to be the AFC.

Statistical analysis

As an initial step, descriptive statistics for all variables were calculated. Results are presented as arithmetic mean ± standard deviation for continuous variables with normal distribution. Log-transformation was applied to variables with skewed distribution and geometric means were calculated. Proportions are presented for categorical data. The relationship between parity statues and the outcomes (ovarian reserve parameters) were analyzed by Spearman correlation. The influence of potential confounding factors was examined through multivariable regressions.

In all of our models, variables were assessed for controlling potential confounders of age, BMI, age at first menstruation, menses regularity, the average length of a menstrual cycle, and the duration of menstrual bleeding during a menstrual cycle. All variables were included in the initial models and selected as confounders if their exclusion modulated the regression coefficients by more than 10%. Correlation coefficients of the variables retained in the final models were also calculated in order to determine which of these explain the model's variance. Final models were analyzed to verify if the assumptions of linear regression were respected. Thus, linearity, normality and homoscedasticity (homogeneity of variance) of the residuals were examined using graphic plots of the jackknife residuals versus predicted values of the dependent and independent variables. Co-linearity between variables included in the final models was also analyzed to avoid their inclusion in the same model when two variables are highly correlated. $P < 0.05$ was statistically significant. All statistical analyses were performed using STATA version 11 (STATA Corp., TX, USA). Kolmogorov–Smirnov test was applied for determining the normality of distributions.

In terms of a study performed by Bragg et al. [8] and using the formula of sample size estimation for a difference in mean (equal sized groups), we determined the sample size to be at least 77 subjects in each group in order to detect a difference of 1 unit in AMH levels with a significance level of 0.05 and a power of 80% ($SD_1 = 2.2$, $SD_2 = 2.3$).

Results

Totally, we collected data from 186 patients with a mean age of 27.83 years. The patients were assigned into two main groups (n = 93 per group), with and without history of parity. The two main groups were equally sub-divided into three age groups (20–24, 25–29 and 30–35 years). Parity of the study participants chosen from our clinic was as follows: 93 patients had no children, 49 (26.3%) had one child, 24 (12.9%) had two children, 19 (10.2%) had three children, and one woman (0.5%) had four children.

Table 1
Demographic and *baseline characteristics* of the subjects according to parity group.

Variables	Nulliparous group N = 93; (Mean ± Sd)	Multiparous group N = 93; (Mean ± Sd)	P Value
Age	27.7 ± 4.5	27.96 ± 4.4	0.70
Body mass index (BMI)	25.2 ± 3.0	24.5 ± 2.5	0.08
First pregnancy age	–	20.6 ± 0.4	–
Menarche age	12.4 ± 1.2	11.9 ± 1.9	0.05
Menstrual duration	7.0 ± 3.9	6.0 ± 1.4	0.02
Menstrual interval	28.2 ± 4.8	26.7 ± 4.7	0.056
Parity	–	1.7 ± 0.9	–
Irregularity of menses	5(5.4%)	9(9.8%)	0.19