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Risks associated with premature ovarian failure in Han Chinese women

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Abstract   In this retrospective study, the relationship between demographic characteristics, past medical history, general lifestyle habits and susceptibility of premature ovarian failure (POF) in Han Chinese population was investigated. Five hundred and fifty-three patients with POF and 400 women with normal ovarian function were recruited. A questionnaire was designed to gather information from responders. Logistic regression was carried out to calculate odds ratios (OR), 95% confidence intervals (95% CI) and P-values. History of pelvic surgery, mumps, having relatives with menstrual abnormalities and exposure to chemical agents were significantly associated with increased risk of POF (OR 5.53 [2.15 to 14.23]; 3.26 [2.38 to 4.47]; 28.12 [8.84 to 89.46]; 4.47 [2.09 to 9.58]). Vegetarian diet, tea and mineral water consumption reduced the risk of POF (OR 0.27 [0.19 to 0.37]; 0.04 [0.03 to 0.07]; 0.63 [0.47 to 0.85], respectively). Heredity, pelvic surgery, mumps and exposure to chemical agents were identified as risk factors for POF, whereas vegetarian diet, tea consumption and mineral water drinking were protective. Therefore, genetic consultation could help those women whose relatives manifested an early or premature menopause to avoid the consequences of possible premature ovarian function cessation. Avoidance of exposure to endocrine disrupters and flavonoids intake should be considered.
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Introduction

Premature ovarian failure (POF), also known as premature menopause or primary ovarian insufficiency, affects 1–2% of women younger than 40 years of age (Coulam et al., 1986). It is characterized by primary or secondary amenorrhoea, infertility, oestrogen deficiency and elevated gonadotrophin (FSH > 40 IU/L) (Kalantaridou et al., 1998). Women with POF are now recognized to be at an increased risk for premature morbidity and mortality owing to experiencing oestrogen deficiency before the median age of natural menopause (Shuster et al., 2010). The physical consequences of premature hypo-oestrogen in women with POF include infertility, menopausal symptoms and higher risk of osteoporosis and cardiovascular disorders (Anasti, 1998; Sowers and La Pietra, 1995). In addition, POF also affects psychological health. The quality of life of women with POF as been evaluated with the World Health Organization Quality of Life-Brief (WHOQOL-BREF), and results have shown that patients score poorly in physical health and psychological states (Benetti-Pinto et al., 2011). Multiple causes of POF have been defined, such as genetic, autoimmune, infectious, environmental factors and iatrogenic agents (e.g. pelvic surgery, chemotherapy and radiations) (Nelson, 2009; Shelling, 2010; Simpson and Rajkovic, 1999). The underlying causes, however, remain unexplained in most cases. The complexity and heterogeneity of POF make diagnosis difficult before irreversible damage to the ovarian reserve. Therefore, identification of risk factors for ovarian damage is of great importance.

The prevalence of POF varies slightly among different populations. A cross-sectional survey of 15,605 women aged 40–55 years was conducted at seven sites in the USA, and the overall prevalence of POF was 1.1%. By ethnicity, 1.0% of white, 1.4% of African–American, 1.4% of Hispanic, 0.5% of Chinese and 0.1% of Japanese women experienced POF (Luborsky et al., 2003). Also, healthy conditions, such as osteoporosis, female hormone use (excluding oral contraceptive), body mass index and current smoking in women with POF are different across ethnic groups. It has also been suggested that lifestyle and environmental factors may contribute to the development of POF (Luborsky et al., 2003). The aim of the present study was to analyse the relationship between POF and health, reproductive, demographic and lifestyle factors to determine possible risk factors for POF in Han Chinese.

Materials and methods

In this case-control study, 553 patients with POF and 400 controls were recruited from the Center for Reproductive Medicine, Shandong Provincial Hospital Affiliated to Shandong University between January 2008 and October 2013. The case and control selection followed a pre-established protocol as below. All the patients and controls were Han Chinese. Inclusion criteria of POF consisted of cessation of menstrual cycles before age 40 years and at least two serum FSH measurements exceeding 40 IU/L. Age-matched women requesting treatment for infertility owing to their husbands' azoospermia, who had normal menstrual cycles, serum levels of FSH, LH and oestradiol, were included as controls. All patients and controls provided written informed consent for personal data collection and analysis. The study was approved by the Institutional Review Board of Reproductive Medicine of Shandong University on 3 February 2014 (Institutional Review Board reference number 17).

Information about participants was recorded on a pre-defined questionnaire. The questionnaire included demographic characteristics, gynaecological and obstetric data, past history, general lifestyle behaviour and environmental factors.

Data were analysed using the Statistical Package for Social Sciences (SPSS) version 16.0 (SPSS Inc., USA). The continuous variables were compared by t-test, and the categorical variables were compared by chi-squared test. The binary and categorical logistic regression was used to calculate odds ratios (OR), 95% confidence intervals (95% CI), and P-values for each risk factor. $P < 0.05$ was considered statistically significant.

Results

The clinical features of the 553 patients with POF are presented in Table 1. A total of 65 (11.95%) women presented with primary amenorrhoea, and 479 (88.05%) with secondary amenorrhoea. The menstrual cycle length before onset of premature ovarian failure in 328 (70.24%) patients was between 25 and 35 days, and longer than 35 days in 102 (21.84%) patients. The proportion of patients with secondary infertility was 113 (20.66%). Chromosomal abnormalities were present in 48 out of 553 (8.68%) POF cases, of which, 47 (97.92%) involved in the X chromosome and one (2.08%) was non-mosaic 46, XY. No autosome abnormalities were found.

Associations betweeen demographic characteristics and environmental exposure with POF are presented in Table 2. Housing renovation, exposure to agricultural chemicals and chemical agents were associated with an increased risk of POF (OR 4.76 [2.98 to 7.61]; 11.56 [5.51 to 24.25]; 4.47 [2.09 to 9.58]). Living in a suburb was a protective factor for POF (OR 0.38 [0.27 to 0.55]). Occupation and education showed no significant difference between POF and controls.

Medical history of the two cohorts were also compared (Table 3). A history of mumps and pelvic surgery, including ovarian cystectomy (e.g. endometrial, simple serous and teratoma cysts), unilateral oophorectomy and tubal ectopic pregnancy surgery (e.g. salpingectomy and salpingostomy) conferred a higher risk of POF (OR 3.26 [2.38 to 4.47]; OR 5.53 [2.15 to 14.23]). Ovarian surgery (e.g. ovarian cystectomy and unilateral oophorectomy) increased the risk of POF (OR 5.97 [1.78 to 20.02]). Women who had relatives with abnormal menstrual cycles had an increased risk for POF (OR 28.12 [8.84 to 89.46]). Compared with controls, allergy was a protective factor for POF (OR 0.62 [0.44 to 0.89]). No significant association was found between POF and menarche age, inter-menstrual bleeding and usage of diet pills ($P > 0.05$).

Univariate associations between lifestyle habits and POF are presented in Table 4. Tea consumption, vegetarian diet