

The Association of the Dietary Fat and Functional Ovarian Cysts in Women of Reproductive Age Referring to Three Hospitals in Mashhad, Iran, 2014

Mahin Tafazoli¹, MS; Elham Fazeli², PhD candidate; Salameh Dadgar⁴, MD; Mohsen Nematy⁴, PhD

¹Department of Midwifery, School of Nursing and Midwifery, Mashhad University of Medical Sciences, Mashhad, Iran;

²Department of Anatomy and Reproductive Biology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran;

³Ovulation Disorders Research Center, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran;

⁴Department of Nutrition, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

Corresponding author:

Elham Fazeli, PhD candidate, Department of Anatomy and Reproductive Biology, School of Medicine, Shahid Beheshti University of Medical Sciences, Postal Code: 4471113436, Langroud, Tehran, Iran
Tel: +98 911 2448530; Fax: +98 51 38597313; Email: elhamfazeli15@yahoo.com

Received: 6 September 2015 Revised: 5 December 2015 Accepted: 7 December 2015

ABSTRACT

Background: Functional ovarian cysts (FOC) are one of the most common gynecological problems among women of reproductive age. Some studies have shown that diet may affect the function of the ovaries, so this study was performed to determine the association between the amount of dietary fat and functional ovarian cysts.

Methods: This case-control study was performed on 264 female patients (132 with cyst in the case group and 132 in the control group) aged 13 to 49. The case group had ovarian cyst with a size of less than 8 cm and the control group didn't have any ovarian cyst. Data were collected by questionnaires including a demographic questionnaire, and medical and midwifery characteristics questionnaire; the amount of fat in the diet was measured using food frequency questionnaire (FFQ). Data were analyzed using SPSS software. $P < 0.05$ was considered significant.

Results: The mean of fat consumption in the case group was 119.84 ± 103.09 g and in the control group it was 109.90 ± 54.66 g. The result of data analysis showed that there was no statistically significant relationship between the amount of fat in the diet and FOC in confidence level of 95% ($P = 0.056$).

Conclusion: According to the findings of this study, the amount of fat consumption was higher in women with ovarian cysts; however, this difference was not statistically significant. In this regard, it is recommended that women of reproductive age should reduce their fat intake.

KEYWORDS: Diet; Fat; Ovarian cyst

Please cite this article as: Tafazoli M, Fazeli E, Dadgar S, Nematy M. The Association of the Dietary Fat and Functional Ovarian Cysts in Women of Reproductive Age Referring to Three Hospitals in Mashhad, Iran, 2014. IJCBNM. 2016;4(2):148-156.

INTRODUCTION

Functional ovarian cysts (follicular and luteal) are one of the most common gynecological problems among women of reproductive age worldwide. If the cyst is large, persistent and painful, surgery may be needed, and in some cases it leads to removal of the ovary.¹ The prevalence of benign ovarian cysts in women of reproductive age is reported as 7%.² In a cross-sectional study, about 4% to 7% of women who were examined by sonography had ovarian cysts larger than 30mm. While many of these ovarian cysts are spontaneously impoverished, some of them require surgical interventions, leading to discomfort, risks of performed interventions and treatment costs.¹

Nutrition and diet may affect sexual hormones and their binding proteins.³ Fat can affect the metabolism of prostaglandins, thereby having an impact on ovarian function.⁴ Furthermore, plasma levels of IGF1 are directly linked with the energy situation and IGF1 is also one of the factors affecting the production of estrogen from the dominant follicle and plasma estradiol level; it also affects the ovulation and development of follicles.⁵ Mice with high fat and high energy diet were insulin resistant, glucose tolerant, and had dyslipidemia; these factors can be due to oxidative stress, cytokines inflammatory effect, and other factors⁶ which may affect the function of the ovaries.

Some studies performed on animals have shown that the Dietary Unsaturated Fatty Acids are effective on the quality of the oocyte and follicular development.⁷ High levels of dietary fat are associated with insulin signaling on ovarian function, and insulin resistance also affects the ovarian function. In this regard, in a cohort study performed on female rats, the researchers reported that diets with high levels of fat lead to insulin resistance, hyperinsulinemia, increased levels of progesterone and serum LH, and change in ovarian morphology in female rats; also, the number of insulin, Phosphatidylinositol 3, AKT / 3-Kinas receptors in the ovaries is decreased.⁸

In some epidemiological and ecological studies, a positive association between dietary fat and calories with ovarian cancer has been reported and the results of some studies especially the case-control studies have hypothesized that the types of fats except monounsaturated fats are associated with an increased risk of ovarian cancer.⁹

Diet plays a role in the regulation level of testosterone in women with polycystic ovary syndrome (PCOs).¹⁰ The result of a study evaluating the serum lipid responses and insulin resistance to a high-fat diet in patients with PCOs showed that patients with PCOs have insulin resistance and prolonged lipid response to oral fat tolerance test.¹¹ But in some studies the central obesity and insulin resistance were not strictly associated with energy intake or dietary macronutrient composition in women with PCOs.¹² Low-carbohydrate ketogenic diet in women with obesity and PCOS led to improvement in weight, percentage of free testosterone, LH/FSH ratio, and fasting insulin.¹³ Comparison of hormonal and metabolic markers in women with PCOs showed that high-fat, Western meal affects testosterone, insulin, blood glucose, and cortisol level in this female.¹⁰

According to the performed studies, diet seems to be associated with ovarian cysts; consequently, with regard to the prevalence of ovarian cysts and their outcomes, this study was performed with the aim of determining the association between dietary fat and FOC in women of reproductive age.

MATERIALS AND METHODS

Study Design and Setting

This case-control study was performed on 264 women (132 with FOC and 132 in the control group) referring to Mashhad Ghaem, Imam Reza, and Omolbanin hospitals in Mashhad (north east of Iran) during February 2013 to November 2014.

Participants

Sampling was conducted after obtaining

approval from the ethics committee of Mashhad university of medical sciences (research project code: 920571). Study was performed after the patients signed informed consent form that allowed review of their medical records for research purposes and the study did not interfere with their treatment process.

Sampling was performed by convenience non-probable method and according to the inclusion and exclusion criteria of sampling the women referring to the gynecology clinic and radiology and sonography ward in Mashhad Ghaem, Imam Reza, and Omolbanin hospitals from January 2013 to December 2014.

The inclusion criteria were as follows: 1) Iranian nationality, 2) literacy, 3) fluency in Farsi, 4) reproductive age (13-49 years old), and 5) availability of ultrasound findings. On the other hand, women with acute gynecologic, hormonal, or neoplastic conditions (e.g. severe vaginal bleeding, acute pelvic pain, and polycystic ovary syndrome) were excluded from the study. Overall, 264 women voluntarily participated in this study after giving written informed consents. Participation in the study did not interfere with the subjects' treatment process.

In this study, women with acute gynecologic, hormonal and neoplastic situations (including severe vaginal bleeding, acute abdominal pain, and polycystic ovarian syndrome), pregnant women, history of infertility, and postmenopausal women were excluded.

The number of women participating in the study was calculated using the results of Chafarino's study (2003)³ entitled "Diet and risk of seromucinous benign ovarian cysts" and using the formula

$$N = \frac{(Z_{1-\frac{\alpha}{2}} + Z_{1-\frac{\beta}{2}})^2 * [P_1(1 - P_1) + P_2(1 - P_2)]}{(P_1 - P_2)^2}$$

and variable of meat consumption in Chafarino's study,³ according to Confidence Interval 95% ($\alpha=0.05$), Power 80% ($\beta=0.02$), $P_1=0.47$ and $P_2=0.31$, the total number of participants in both case and control groups

was calculated 140 persons. According to the sample loss due to failure to complete the questionnaire, 132 females participated in both case and control groups. Thus, 264 women who volunteered to participate in the study were enrolled in the study after completing the written informed consent. In this study, participating in the study did not cause a disorder in the treatment process of women participating in the study.

Measurements

Subjects were enrolled after obtaining an informed consent form from them. To collect the information, we conducted the interview in a two part questionnaire including demographic information (age, education level, employment status, income level, contraception method, using dietary supplements and medical and reproductive history) and the amount of fat in the diet was measured using a semi-quantitative food frequency questionnaire (FFQ).

Food frequency questionnaire (FFQ) is appropriate with the Iranian food intake and is a tool for the assessment of diet the information is collected in this questionnaire based on the way and amount of consumption; in fact, it is a retrospective study of food intake repetition.

In this study, using this questionnaire, usual food intake of women in the past year¹⁴ was obtained using a semi-quantitative food frequency questionnaire by interview. This questionnaire consists of 109 items or food components that might have been used by them in the last month and measured by 9-point Likert scale including "never or less than once a month", "1-3 times in a month", "once a week", "2-4 times a week", "5-6 times a week", "once a day", "2-3 times a day", "4-5 times a day" and "6 or more times per day".

Mean share of each time of food consumption is also determined using a Likert scale of three degrees including "low", "moderate" and "high". Standard units and the cases which were reported based on house scale were changed to gr, using the guideline

of house scale and protein consumption per person was calculated as gram.¹⁴

Food frequency questionnaire was valid and reliable with a standard serving size for each nutrient and its validity and reliability have been confirmed by Nemati and colleagues (2012).¹⁰ In this study, its reliability coefficient was determined by the Cronbach's alpha of $\alpha=0.70$.

The women diagnosed with FOC (single room ovarian cysts, no septum and with a size less than 8 cm) were in the case group and those with no functional cysts were in the control group. Diagnostic criteria were the form of performing sonography of the uterus and appendages up to one month ago.

Data Collection

In order to collect the required data, the first author attended the mentioned gynecology clinics and identified the eligible women. After being explained about the study objectives, women who were willing to participate were asked to provide written informed consent and fill out the demographic questionnaire. The FFQ was also completed through interviews to assess food intake within the past month.

Dietary Intake Analysis

All pages of the completed FFQs were scanned and the selected choices were recognized and saved in a TXT file using a software package developed through Delphi 7 programming. A second software package was then used to analyze the obtained data and enter the required variables, e.g. food items eaten, the weight of each food item, and the amount of consumed energy, macronutrients, fiber, and some micronutrients, into an SPSS file. The dietary variables selected for the purpose of this study were crude.

Statistical Analysis

After recording the data in the form of data collection, data was analyzed using SPSS software version 11.5. Kolmogorov-Smirnov test measured the normality of the

data. Linear relationship of variables was calculated using Pearson and Spearman correlation coefficients. T-test and ANOVA analysis were used to compare the variables two by two, and Chi-square test was used for qualitative variables. $P<0.05$ was considered significant.

RESULTS

In this study, 264 women (132 in the case group and 132 in the control group) were studied.

Demographic characteristics of women as separated in two groups are reported in Table 1. T-test was used for analyses of age variable homogeneity between the two groups. Statistical analyses showed that the two groups were homogenous in age variable ($P=0.73$). The Chi-square test was used for analysis of Educational Status, Occupational status and Economic status variable homogeneity between the two groups. Statistical analyses showed that the two groups were homogenous in Educational Status ($P=0.35$), Occupational status ($P=0.86$) and Economic status ($P=0.66$) variable.

T-test was used for analysis of BMI variable between the two groups. Mean BMI in women with FOC was 23.78 ± 5.18 and in those in the control group it was 22.57 ± 3.48 . Statistical analyses showed that women with FOC have higher BMI than the control group and this different was statistically significant ($P=0.03$) (Table 2).

T-test was also used for analysis of the homogeneity of parity variable between the two groups. Mean parity in women with FOC was 3.21 ± 1.02 and in those of the control group it was 1.61 ± 1.69 . Statistical analysis showed that the two groups were homogenous in parity variable ($P=0.16$).

We also used t-test for analyses of the homogeneity of abortion variable between the two groups. Mean abortion in women with FOC was 0.12 ± 0.45 and in women of the control group it was 0.12 ± 0.47 . Statistical analyses showed that the two groups were homogenous in abortion variable ($P=0.84$).

Table 1: Distribution of demographic variables in the control and case groups

Variable	Case group		Control group	
	N	%	N	%
Age(year)				
20>	14	10.7	12	9
20-34	51	38.9	57	42.9
35≤	67	50.4	64	48.1
Educational Status				
Elementary	27	20.5	19	14.3
Diploma	43	32.6	51	38.3
University	61	47.0	63	47.4
Occupational status				
Housewife	52	40.2	52	39.1
Employee	79	59.8	81	60.9
Economic status				
Less than daily	36	27.3	34	26.6
In the daily	89	67.4	90	70.3
More than enough	7	5.3	4	3.1

Table 2: Comparison of BMI in the control and case groups

BMI	Case Group		Control Group		Total	
	N	%	N	%	N	%
>19.8	33	28.2	35	27.3	68	27.8
19.8-25	37	31.6	70	54.7	107	43.7
26-30	22	18.8	18	14.1	40	16.3
30<	25	21.4	5	3.9	30	12.2

Chi-square test was used for analysis of the history of medical illness variable homogeneity between the two groups. Statistical analyses showed the two groups were homogenous in the history of medical illness variable ($P=0.30$) (Table 3).

Chi-square test was also used for analysis of the contraception method and using dietary supplements variable homogeneity between the two groups. Statistical analyses showed that the two groups were homogenous in contraception method ($P=0.19$) and using dietary supplements ($P=0.16$).

Kolmogorov-Smirnov test was used to evaluate the normality of data distribution; the results showed that the amount of fat in the diet of the case group ($P=0.69$) and in the

control group ($P=0.16$) there was a normal distribution.

Mean size of the cysts in women with FOC was 43.91 ± 12.91 mm (range 30-78 mm). 53 women (40.8%) had the cyst with 30-39 mm in size, and only 8 women (6.2%) had cysts with a size of 70-79 mm.

Mean fat consumption in women with FOC was 119.84 ± 103.09 g with a range of 31-880 g and in women of the control group it was 109.90 ± 54.66 g with a range of 29-306 g. Data analysis using t-test showed that there was no statistically significant relationship between the amount of fat in the diet and FOC in women at confidence level of 95% ($P=0.056$).

Descriptive statistics showed that 39.9% of the studied women had not used any of the

Table 3: Comparison of the history of medical illness in the control and case groups

History of medical illness	Case Group		Control Group		Total	
	N	%	N	%	N	%
Yes	6	4.5	3	2.3	9	3.4
No	126	95.5	129	97.7	255	96.6

seafood in the past month. The mean amount of seafood fat (including fried fish, grilled fish and tuna) in women with FOC was 0.82 ± 0.95 g and in those in the control group it was 0.75 ± 0.93 g. Data analysis using t-test showed that there was no statistically significant relationship between the amount of seafood fat in the diet and FOC in women ($P=0.42$).

The mean amount of fat in dairy products (including milk, chocolate milk, yoghurt, cheese, butter, cream and buttermilk) in women with FOC was 17.95 ± 10.06 g and in the women of the control group it was 14.75 ± 9.20 g.

Comparison of dairy fat in women of the case and control groups showed that the amount of dairy fat consumption was higher in women with functional ovarian cysts, but this difference was not statistically significant based on the analysis of the data using t-test ($P=0.18$).

The mean amount of meat fat (including red meat and white meat) in women with FOC was 24.48 ± 16.84 g and in those in the control group it was 21.83 ± 15.35 g. Comparison of meat fat in women of the case and control groups showed that the amount of meat fat consumption was higher in women with functional ovarian cysts, but this difference was not statistically significant based on the analysis of the data using t-test ($P=0.40$).

DISCUSSION

In the present study, the amount of fat consumption was higher in women with FOC than women in the control group, although this difference was not statistically significant. Also, in this study, no relationship was observed between the amounts of dietary fat with functional ovarian cysts.

Several studies have shown that no study was found about fat consumption and functional ovarian cysts, but in some studies, an increased risk of ovarian cancer with increased amount of fat are reported; of course, the results of these studies are different in relation to different types of fat.

In a case-control study performed on 17-74 year old women living in New York measured the relationship of total fat, vegetarian fat, saturated fat and multiple unsaturated fat, and unsaturated with a double bond with benign ovarian cysts including teratomas, endometriosis, serous, mucinous, Brenner and fibroma-thecoma; the results of this study showed that a high intake of vegetable oils and multiple unsaturated fats is associated with increased chance of multiple endometriosis, serous, and teratoma.⁴ Fats affecting the metabolism of prostaglandin and insulin and growth hormone related to insulin can have effects on ovarian function.⁴⁻⁶

In a case-control study performed in Italy, the findings showed that consumption of red meat and cheese was associated with an increased risk of seromucinous cysts, but no relationship was observed between the fat in the butter and margarine and oil with seromucinous cysts.³

In our study, although the amount of dairy fat was somewhat higher in women with functional ovarian cysts, the association was not statistically significant. This difference may be because of the differences in the study population and our study was conducted on ovarian cysts while the mentioned studies have been conducted on ovarian cancer and ovarian seromucinous cysts that were the types of neoplasm.

Some studies showed that there was a relationship between the consumption of milk and dairy products with ovarian cancer, and they hypothesized that the association may be due to the presence of lactose in milk. A high galactose diet is toxic for the oocytes, and evidence showed that ovarian cancer may arise due to the premature depletion of the oocyte, and intake of dairy products is associated with a modest increase in the risk of ovarian cancer.^{15,16}

Relationship between milk consumption and ovarian cancer may be due to the presence of fat in milk.⁹ However, some studies hypothesize that the lactose present in milk and dairy products may increase the risk of

ovarian cancer.¹⁶ But in a study in Italy, the relationship of milk consumption and ovarian cancer was not reported.⁹ Cheese is also a source of animal's saturated fat.¹⁷ But in the mentioned study, cheese consumption was not associated with ovarian cancer.⁹ Previous studies have suggested that the lactose component of dairy foods may promote ovarian carcinogenesis via the accumulation of galactose (lactose metabolite) with potentially toxic effects on the oocytes and disruption of ovarian/pituitary feedback.¹⁵

In our study, although the amount of fat in white and red meat was somewhat higher in women with functional ovarian cysts, the association was not statistically significant. Some studies reported that there was a relationship between the consumption of the types of meat and ovarian cancer,⁹ because meat also contains saturated fat.¹⁸ They hypothesized that the association is probably because the animal fats present in meat are associated with ovarian cancer.⁴

In our study, there was no significant difference between marine consumption among women in the case and control groups. In some studies, fish had a protective effect on ovarian cancer and hypothesized that this effect can be due to the presence of omega-3 fatty acids in fish or low fat in fish meat than other meats;⁹ this finding in our study is likely due to the low consumption of marine products in the studied women.

Given that in most studies, the relationship between consumption of a fat-rich food such as milk, and meat with ovarian disease has been measured, one of the strengths of this study is that the amount of fat in food was evaluated separately with functional ovarian cysts; therefore confounding effects of other products in the food on the ovarian cysts are somewhat controlled.

In our study, there was a significant difference between BMI among the women in the case and control groups, and women with functional ovarian cyst had a higher BMI than the control group. There was a strong relationship between increasing BMI and

increasing morbidity and mortality.¹⁹ Obesity affects the insulin sensitivity and cause a reduction of the insulin concentration in the plasma.²⁰ Obese women have a higher extra gonadal estrogen production from steroid in the adipose tissue²¹ that has a positive effect on LH feedback and negative FSH feedback. The increased levels of LH can cause hyperplasia of the ovarian stroma and theca and increase in the production of androgens, which can increase the peripheral aromatization and cause anovulation cycle in women.²⁰ Studies showed that PCOs is associated with obesity.²¹ In a study performed in USA, the findings showed that obesity plays a role in paratubal cysts development in adolescents with PCOs.²² According to some studies, weight loss leads to improvements in the blood levels of insulin, insulin resistance, and decreases the androgenization, with consequent improvement of ovulation.²⁰

The limitations of this study are the difference in the accuracy of the women in answering the questions; also, the diagnosis of functional ovarian cyst in women was performed by different sonographers, so the researcher was not able to control it. Also, in this study Ultrasound was performed in multicenter and by different sonographers that might have affected the study result.

Because of the difficulty of access to people with functional ovarian cysts, the sampling of this study was a non-probable method; for this reason, generalization of the results is reduced. It is recommended that future studies should use random sampling methods to enhance the generalizability of their results.

CONCLUSION

According to the results of this case-control study, the amount of fat intake was higher in women with functional ovarian cysts. Also, consumption of dairy fat and meat fat was higher in women with functional ovarian cysts, although this difference was not statistically significant.

Dietary fats may affect the ovarian function. Meat and dairy production contain saturated fat that was probably associated with functional ovarian cysts. For this reason, a low risk diet for functional ovarian cyst in Iran should include limited fat intake and specially saturated fat, and use of meat and dairy products with less fat.

In this study, women with functional ovarian cyst had higher BMI. For this reason, it is recommended that women in reproductive age should lose their weight and/or reach a suitable BMI to improve their reproductive function. In this regard, appropriate educational programs are needed to modify the lifestyle patterns in reproductive age women.

ACKNOWLEDGEMENT

The present study was extracted from the research project approved by Mashhad University of Medical Sciences in 2013.10.14 which was performed by financial support of research faculty of the university. Therefore, the cooperation and assistance of the Deputy and also personnel of health centers and the women participating in this study would be appreciated.

Conflict of Interest: None declared.

REFERENCES

- 1 Grimes DA, Jones LB, Lopez LM, Schulz KF. Oral contraceptives for functional ovarian cysts. *Cochrane Database Syst Rev.* 2009;15:CD006134.
- 2 Mimoun C, Fritel X, Fauconnier A, et al. [Epidemiology of presumed benign ovarian tumors]. *Journal de Gynecologie, Obstetrique et Biologie de la Reproduction.* 2013;42:722-9.
- 3 Chiaffarino F, Parazzini F, Surace M, et al. Diet and risk of seromucinous benign ovarian cysts. *European Journal of Obstetrics, Gynecology and Reproductive Biology.* 2003;110:196-200.
- 4 Britton JA, Westhoff C, Howe G, Gammon MD. Diet and benign ovarian tumors (United States). *Cancer Causes & Control.* 2000;11:389-401.
- 5 Butler W. Nutritional interactions with reproductive performance in dairy cattle. *Animal Reproduction Science.* 2000;60:449-57.
- 6 Yakar S, Nunez NP, Pennisi P, et al. Increased tumor growth in mice with diet-induced obesity: impact of ovarian hormones. *Endocrinology.* 2006;147:5826-34.
- 7 Bilby TR, Block J, do Amaral BC, et al. Effects of dietary unsaturated fatty acids on oocyte quality and follicular development in lactating dairy cows in summer. *Journal of Dairy Science.* 2006;89:3891-903.
- 8 Akamine EH, Marçal AC, Camporez JP, et al. Obesity induced by high-fat diet promotes insulin resistance in the ovary. *Journal of Endocrinology.* 2010;206:65-74.
- 9 Bosetti C, Negri E, Franceschi S, et al. Diet and ovarian cancer risk: A case-control study in Italy. *International Journal of Cancer.* 2001;93:911-5.
- 10 Katcher HI, Kunselman AR, Dmitrovic R, et al. Comparison of hormonal and metabolic markers after a high-fat, Western meal versus a low-fat, high-fiber meal in women with polycystic ovary syndrome. *Fertility and Sterility.* 2009;91:1175-82.
- 11 Bahceci M, Aydemir M, Tuzcu A. Effects of oral fat and glucose tolerance test on serum lipid profile, apolipoprotein, and CRP concentration, and insulin resistance in patients with polycystic ovary syndrome. *Fertility and Sterility.* 2007;87:1363-8.
- 12 Toscani MK, Mario FM, Radavelli-Bagatini S, Spritzer PM. Insulin resistance is not strictly associated with energy intake or dietary macronutrient composition in women with polycystic ovary syndrome. *Nutrition Research.* 2011;31:97-103.
- 13 Mavropoulos JC, Yancy WS, Hepburn J, Westman EC. The effects of a

- low-carbohydrate, ketogenic diet on the polycystic ovary syndrome: a pilot study. *Nutr Metab (Lond)*. 2005;2:35.
- 14 Mosalali Z, Nematy M, Safarian M, et al. Dietary intake and its relationship with non-alcoholic fatty liver disease (NAFLD). *Nutrition and Food Sciences Research*. 2014;1:175-6.
 - 15 Merritt MA, Cramer DW, Vitonis AF, et al. Dairy foods and nutrients in relation to risk of epithelial ovarian cancer. *Int J Cancer*. 2012;72:660-72.
 - 16 Faber MT, Jensen A, Søgaard M, et al. Use of dairy products, lactose, and calcium and risk of ovarian cancer-results from a Danish case-control study. *Acta Oncologica*. 2012;51:454-64.
 - 17 Mozaffarian D, Micha R, Wallace S. Effects on coronary heart disease of increasing polyunsaturated fat in place of saturated fat: a systematic review and meta-analysis of randomized controlled trials. *PLoS Medicine*. 2010;7:e1000252.
 - 18 Parazzini F, Viganò P, Candiani M, Fedele L. Diet and endometriosis risk: a literature review. *Reproductive Biomedicine Online*. 2013;26:323-36.
 - 19 Carmienke S, Freitag M, Pischon T, et al. General and abdominal obesity parameters and their combination in relation to mortality: a systematic review and meta-regression analysis. *European Journal of Clinical Nutrition*. 2013;67:573-85.
 - 20 Tolino A, Gambardella V, Caccavale C, et al. Evaluation of ovarian functionality after a dietary treatment in obese women with polycystic ovary syndrome. *European Journal of Obstetrics & Gynecology and Reproductive Biology*. 2005;119:87-93.
 - 21 Timberlake KS, Foley KL, Hurst BS, et al. Association of blood type and patient characteristics with ovarian reserve. *Fertility and Sterility*. 2013;100:1735-9.
 - 22 Muolokwu E, Sanchez J, Bercaw JL, et al. Paratubal cysts, obesity, and hyperandrogenism. *Journal of Pediatric Surgery*. 2011;46:2164-7.