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The relationship between the dietary protein intake and functional ovarian cysts

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Summary. *Objective:* Although ovarian cysts are of an unknown etiology, there is some information about the associated risk factors. To considering the high prevalence of ovarian cysts and the associated complications. This study aimed to assess the relationship between the dietary protein intake and the functional ovarian cysts in women at reproductive age. *Methods:* This case-control study was conducted on 264 women, aged 15-49 years. The case group consisted of women with the functional ovarian cysts (n=132) and the control group included the healthy individuals (n=132). The Pregnant women, females with a prior history of infertility, and the menopausal women were excluded in the study. A demographic questionnaire was used for collecting the patients' demographic information, medical and midwifery history. The dietary protein intake was measured using a Food Frequency Questionnaire. For the data analysis, t-test, χ^2, and regression analysis were performed, using SPSS version 16. *Results:* The mean levels of protein intake were 104.62±93.63 and 86.20±41.52 g in the case and control groups, respectively. A significant relationship was observed between the dietary protein intake and the functional ovarian cysts (P=0.04). *Conclusion:* To considering the direct relationship between high protein consumption and the functional ovarian cysts, appropriate educational programs are needed.

Key words: ???????

Introduction

The functional ovarian cysts are the most common problems among the women at reproductive age. These cysts are related to endogenous ovarian cycling and maybe resolved spontaneously without an intervention. The ovarian cysts may be associated with either the proliferative (follicular) or the secretary (luteal) phase of the normal menstrual cycle (1). But in some cases these cysts are large, persistent, or painful, and requiring surgical operation, which in some cases may be followed by the ovary removal (2). Although the ovarian cysts is an unknown etiology, there is some information about the associated risk factors such as menstrual irregularities and reproductive disorders (3).

Some studies on animals have shown that the nutritional status affects sex hormones and the binding proteins (4, 5). Nutrition has a direct impact on the ovarian function. In fact, nutrition can affect the hepatic function and ovarian follicles through affecting insulin-like growth factor 1 (IGF-I), systemic concentrations of IGF-I binding proteins (IGFBPs) and insulin hormone lead to reduce follicular responsiveness to luteinizing hormones (LH) and finally cause to reduce the follicular estradiol production. Moreover, nutrition indirectly affects the ovarian function by al-

tering the gonadotropin-releasing hormone (GnRH) pulse the generator while changing the secretion patterns of LH and the follicle-stimulating hormones (6). High levels of dietary protein seem to be associated with the increased IGF (7). Animal studies have shown that the production of IGFs and IGFBPs contributes to the control of the ovarian function. There is a clear evidence that distinct growth hormone receptors may express in follicles and corpus luteum (8). In fact, high levels of dietary protein lead to high levels of growth hormones (9), which may lead to the production of IGFs and IGFBPs and to contribute to the control of the ovarian function (8).

One of the important factors in the regulation of antral follicular development is the IGF system (10). IGF-I is the stimulator of progesterone and oxytocin release in granulosa cells. IGFBPs are extracted from follicular fluid or from the ovarian tissue itself. The highest expression of IGF-1 and mRNA occurs during the early luteal phase. Currently, GH, IGF, and IGFBP are considered to be effective in the development of follicles and corpus luteum (8).

Animal studies have shown that systematic changes in IGF-I level and the binding proteins can affect the follicular development and the amount of follicular fluid in some animals.(11) A study on the relationship between nutritional status, IGF-I level, and postpartum ovarian function in the dairy cows indicated a positive relationship between serum IGF-I and estradiol in the ovary of cows (12).

Animal studies have shown that high intake of dietary protein may result in an increase in the metabolic clearance of progesterone (13). Moreover, high levels of dietary protein increase ammonia, urea, or both (11). According to the results of some studies on animals; the intake of dietary protein is associated with the functional ovarian cysts.

Overall, a review of the exiting literature reveals that most studies on the relationships between functional ovarian cysts and protein intake have been conducted on animals. In fact, no previous study has focused on this topic in humans. Considering the high prevalence of ovarian cysts and their associated complications, the present study aimed was performed to investigate the relationships between functional ovarian cysts and protein intake in women of reproductive age.

Subjects and Methods

Study and Setting

This case-control study was conducted from February 2013 to November 2014 in Mashhad-Iran. The study was done in three referral hospitals including Imam Reza Hospital, Ghaem Hospital, and Omolbanin Hospital.

Participants and Sampling

According Chiaffarino et.al. (14) , The sample size was estimated using sample size formula for comparison of two independent group, considering α=0.05 and β=0.2, 138 individuals in each group. A convenience sampling was conducted and 282 women, who referring the gynecology clinics of abovementioned hospitals were included. They were Iranians, between 15-49 years old and speek in Farsi. They didn't use hormonal contraception methods and did not have acute gynecologic, hormonal, or neoplastic disorders (e.g., severe vaginal bleeding, acute pelvic pain, and polycystic ovary syndrome). Also they were not on diet for weight loss. All of the participants have had an ultrasonography report within last month. Participants in case group were diagnosed with functional ovarian cysts (unilocular ovarian cysts without septum, less than 8 cm) in ultrasounography report but in the case group no ovarian cysts had reported. During the study, 18 women were excluded since completing the questionnaires was interfering with their treatment process or due to incomplete questionnaires.

Instruments

The demographic questionnaire and the Food Frequency Questionnaire (FFQ) was used for data collection. The demographic questionnaire was contained some variables including the age, education, employment status, income level, medical and reproductive history. FFQ assesses the Iranian diet and provides some information on the amount of food intake (i.e., food consumption within a week, month, or year). In fact, it is a retrospective scale which measures the frequency of food intake. FFQ includes 109 food ingredients (or food combinations) an individual may use during a month. The op-

tions were graded using a 9-point Likert scale: "never or less than once a month", "1-3 times a month", "once a week", "2-4 times a week", "5-6 times a week", "daily", "2-3 times a day", "4-5 times a day", and "6 times or more daily". The average intake of each food was determined using a 3-point Likert scale: "a little bit", "enough", and "too much". The values reported in domestic scale were converted into gram using the guide of domestic scale conversion. The intake of protein was also expressed in grams. Nematiy et al. confirmed the validity and reliability of FFQ (with a Standard Serving Size for each food group), with a Cronbach's alpha of α= 0.070 (15).

Data collection

For the data collection, first author went to gynecology clinics and invited the women who meet inclusion criteria to participate in the study. After the explanation about the aim of the study, whether women were willing to participate, they should signed to inform their consents. Then they were asked to fill out the demographic questionnaire and FFQ one. In this study, the food intake within the last month was measured using FFQ by conducting interviews.

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 programing. A second software package was then used to analyze the obtained data and to enter the required variables, e.g. food items eaten, weights 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

The data were analyzed with the help of SPSS version 16 using T-Test, χ^2, regression. $P<0.05$ were considered significant. The normality of the data was evaluated by Kolmogorov-Smirnov test.

Results

Of 282 women, 18 people left the study, 11 women from the case group and 9 from the control group. 132 women in the case group and 132 women in the control group completed the study and were analyzed. Some of the main demographic characteristics in both groups are presented in Table 1. There was no significant difference between the case and the control groups regarding age, education, parity and BMI.

Table 1. Socio-demographic characteristics of two groups

Variables	Case Group (n=132)	Control Group (n=132)	P-value
Age, Mean±SD	31.85±9.59	28.57±9.19	P=0.48*
Parity, Mean±SD	1.69±1.74	1.40±1.61	P=0.49*
Women Education, n (%)			
Elementary	13.6%	12.1%	P= 0.39**
Diploma	41.7%	47.7%	
College	44.7%	35.6%	
BMI, Mean±SD	23.77 ± 5.18	22.57±3.48	P=0.03*
Cigarette smoking, n (%)			
Yes	35 (30.2%)	23 (19%)	P= 0.04**
No	81(69.8%)	98 (81.0%)	
Hormonal contraceptive n (%)			
Yes	32 (25.2%)	31 (25.6%)	P= 0.93**
No	95 (74.8 %)	90 (74.4%)	

** Independent Sample T-test was used.*

*** Chi-square test was used*

The mean protein intake was 104.62±93.63gr and 86.41±41.44gr in the case and control groups, respectively. The mean protein intake was higher in the case group [mean difference= 18.21; 95% confidence interval (CI): 0.693-35.724], the difference between the two groups was significant (p = 0.042). However, Pearson's correlation analysis showed no significant relations between protein intake and either the size or the number of functional ovarian cysts (p= 0.483 and 0.158, respectively).

Variables with p < 0.2 in bivariate analysis were entered into multivariate logistic regression analysis (Enter" method) to calculate the adjusted odds ratios (12) and 95% CI. Multivariate logistic regression adjusted for other variables (BMI and protein) showed that only smoking significantly increased the odds of functional ovarian cysts (adjusted OR = 1.014; 95% CI: 1.001-1.028).

Discussion

In the present study, there was a relationship between the dietary intake of protein and the functional ovarian cysts. Moreover, the functional ovarian cysts were mostly diagnosed in the women with high levels of dietary protein.

The results of the current study were to some extent similar to a study by Chiaffarino et al., conducted in Italy in 2003. They performed a study on 250 women, aged 15-65 years with seromucinous cysts. High level of red meat intake was considered a risk factor for these cysts (14). Mori in Japan in 1988 also reported the increasing risk of red meat consumption (OR=3.1) (16). Similarly, Tavani (2000) (17) and Kushi (1999) (18) reported a relationship between ovarian cancer and red meat intake; these results were in agreement with the present findings.

Many effects of protein on reproduction may be explained by alterations in the hypothalamic-pituitary-ovarian axis (19). Bosetti et al. conducted a case-control study in Italy in 2001. Their results showed a relationship between meat dietary intake and the ovarian cysts. In fact, high consumption of meat resulted in higher risk of the ovarian cancer in women (20). Bosetti also reported a correlation between the ovarian cancer and the intake of red meat, pork, and processed meat. As it was indicated, any potential association between meat consumption and ovarian cancer may be due to the fat intake mostly from animal sources (20); however, in our study, no association was observed. Bosetti also showed that fish among other protein-rich foods seems to exert a protective effect on ovarian cancer. On the other hand, no association was found between ovarian cancer and the intake of milk, dairy products, or eggs (20). The inverse relation between fish consumption and the ovarian cysts may be explained by the potentially protective nutrients in fish such as omega-3 fatty acids. Some other studies have also indicated the protective effect of omega-3 fatty acids on the risk of developing various types of cancer. The lower fat content of some types of fish, compared with other protein-rich foods, may be responsible for its inverse relationship with the ovarian cancer.

Britton et al. in 2000 in USA in an analytical, mainly a case-control study were not able to find a relationship between the dietary protein intake and the benign ovarian tumors (21). These results were not in agreement with the findings of the present study, which could be explained by differences in the study populations. Moreover, Britton studied the relationship between the dietary protein intake and the benign ovarian tumors (including endometrioid, serous, teratoma, munic nous, Brenner, and fibroma-thecoma carcinomas) in women aged 17-74 years, who lived in New York City. The contrary, an attempt was made to evaluation the relationship between the dietary protein intake and the functional ovarian cysts in the women at reproductive age (14-49 years); these differences may have resulted in the observed discrepancy.

One of the limitations of this study was the differences in the women's accuracy in answering the questionnaires. Also, ultrasound is not a definitive diagnostic method for the functional cysts; however, it was not possible to use an alternative non-invasive method. It is recommended that further studies should be conducted in order to determine the impact of protein intake (e.g., red meat, fish, egg, and vegetables) on the ovarian cysts.

Conclusion

The results of this mainly retrospective case-control study indicated a positive relationship between the high levels of dietary protein and the functional ovarian cysts. Giving–the direct relationship between protein consumption and the functional ovarian cysts, the decrease

in the protein intake may prevent the occurrence of the functional ovarian cysts. In this regard, appropriate educational programs are needed to modify the protein intake patterns.

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