

Relationship between Dietary Fat Intake, Its Major Food Sources and Assisted Reproduction Parameters

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Abstract

Background: High dietary fat consumption may alter oocyte development and embryonic development. This prospective study was conducted to determine the relation between dietary fat consumption level, its food sources and the assisted reproduction parameters.

Methods: A prospective study was conducted on 240 infertile women. In assisted reproduction treatment cycle, fat consumption and major food sources over the previous three months were identified. The number of retrieved oocytes, metaphase II stage oocytes numbers, fertilization rate, embryo quality and clinical pregnancy rate were also determined. The data were analyzed using multiple regression, binary logistic regression, chi-square and t-test. The p-value of less than 0.05 was considered significant.

Results: Total fat intake adjusted for age, body mass index, physical activity and etiology of infertility was positively associated with the number of retrieved oocytes and inversely associated with the high embryo quality rate. An inverse association was observed between sausage and turkey ham intake and the number of retrieved oocytes. Also, oil intake level had an inverse association with good cleavage rate.

Conclusion: The results revealed that higher levels of fat consumption tend to increase the number of retrieved oocytes and were adversely related to embryonic development. Among food sources of fat, vegetable oil, sausage and turkey ham intake may adversely affect assisted reproduction parameters.

Keywords: Assisted reproduction, Dietary fats, Embryo quality, Pregnancy rate.

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Introduction

Lipids are rich sources of energy and the critical components of the physical and functional structure of oocytes (1). They play a vital role in development during and after fertilization (2).

Dietary fat intake can affect the fatty acids (FAs) composition in ovarian compartments (3). Some of these effects, such as lipid storage into lipid droplets in oocytes (4) could be altered by the type of eaten FAs (5). The increase in composition of free FAs may impair fertility by affecting

oocyte quality due to transport of FAs into the oocyte (4, 6, 7).

Eating high levels of fat may influence reproduction by affecting oocyte competence as defined the ability of oocyte to undergo fertilization and to reach specific cleavage stages at appropriate time intervals. It is known from animal models that fat consumption can affect the number of retrieved oocytes, zygote's developmental competence and quality of preimplantation embryo (6, 8). However, the effect of type and quantity of dietary fat on

human reproduction is unknown. In previous studies, the bovines were used for assessing the effect of nutrition on reproduction response. Despite many similarities between human and bovine ovarian function, oocytes and embryo features of bovine (9), it is difficult to generalize results of animal studies into human ones. In addition, the types of foods such as the ones containing fat are known to mediate the effect of susceptibility to oxidative injury (10, 11).

The beneficial effects of low calorie regimen on overweight women, attributed to the regulation of endocrine and metabolic environment (12-14) for improving assisted reproduction treatment were reported (15, 16). Also, the adverse effects of obesity on assisted reproduction outcome (17, 18) and the effect of fat rich diet on body mass index (19) were reported. But, to our knowledge, there is no study to evaluate the effects of fat source and level on assisted reproduction parameters in human. Therefore, the present study was designed to determine the effect of fat consumption and its major food sources on reproduction in infertile women who underwent assisted reproductive techniques.

Methods

A prospective study including 240 infertile Iranian women with a consecutive series of 240 non-donor in vitro fertilization (IVF) cycles from July 2010 to April 2011 was conducted at Isfahan Fertility and Infertility Center. The study was approved by Institutional Review Board and the Ethics Committee of Tehran University of Medical Science. The inclusion criterion was primary infertility of the subjects. Informed consent was obtained from all subjects. The criteria for exclusion were male factor infertility based on World Health Organization criteria (20) and considerable change in dietary regimen over the previous three months and during assisted reproduction cycle.

Measures: On day three of a spontaneous menstrual cycle, the heights and weights of all women were measured and then body mass index (BMI) was calculated.

A validated semi-quantitative food frequency questionnaire (FFQ) including 168 food items (21) was used to measure the calorie intake and total dietary fat and its components, namely saturated FA (SFA), mono-unsaturated FA (MUFA), poly-unsaturated FA (PUFA) and its major dietary sources over the previous three months. Oil, meat (red meat, fish, chicken), sausage and turkey ham

(as a subgroup of meat) and dairy foods as the major fat sources were focused on. Depending on the portion size, the frequency of food intake was recorded in times per day, week and month or as never. The portion size was estimated as median of each item.

For all the main food items in the FFQ, the frequency per day was multiplied by the amount consumed, depending on the portion size, to compute the total amount consumed per day. The USDA food composition table was used for most items (USDA, Release 11, 1994). For some items such as bread, vetch, green pepper, wild plum, mint, sweet canned cherry and sour cherry, the Iranian food composition table was consulted (22).

Depending on the percentage of fat in total calorie intake (23), the subjects were divided in two groups: appropriate calorie intake as fat ($\leq 35\%$) and non-appropriate calorie intake as fat ($> 35\%$).

Also the long form of original International Physical Activity Questionnaires (IPAQ) was used to evaluate the physical activity levels of participants. The metabolic equivalent (MET) values and equation for the computation of MET-minutes were used in this research (24).

The etiology of infertility was divided into four groups including polycystic ovarian syndrome (PCOS), endometriosis, anovulation and others.

Assisted reproduction parameters comprised the number of retrieved oocytes, MII stage oocytes rate, fertilization rate, good cleavage rate, high embryo quality rate and clinical pregnancy rate.

The long protocol, involving GnRH agonist and hMG administration, was consistent and follicular maturation was monitored by ultrasound examination. In brief, daily subcutaneous GnRH agonist (Ferring, Germany) was started in the midluteal phase of the previous cycle and gonadotropin stimulation of the ovaries commenced 12-14 days later when transvaginal sonography showed an absence of follicles/cysts larger than 20 mm diameter in size. For all patients, gonadotropin therapy was initiated with a daily dose of 100-300 IU of either rFSH (Gonal F, USA; Organon, USA) or hMG (Repronex and Menopur, Ferring, Germany) and adjusted according to follicular response.

Ovulation was triggered with 10,000 IU hCG (Pregnyl, Organon) which was administered 36 h before oocyte retrieval. Oocytes were collected transvaginally and the follow-up IVF procedure was performed in accordance with the standard protocol. The oocytes were scored for presence or absence of germinal vesicle and first polar body.

Oocytes were considered fertilized when two pronuclei were observed 17-19 *hr* after insemination. Morphologically, 3 days after oocyte retrieval, high quality embryos were defined as grades 1 and 2 according to Veeck's criteria (25). Numbers of blastomers were defined and percentage of embryos without fragmentation was calculated. Embryos with more than 5 cells, 3 days after oocyte retrieval were considered as good quality cleaved embryos. In intracytoplasmic sperm insemination cycles, the percentages of metaphase II (MII) stage oocytes were calculated. Embryos with less than 5% fragmentation were considered as none fragmented and percentage of these embryos was calculated. After a positive pregnancy test, an ultrasound scan was performed 4 weeks later to verify the viability of pregnancy and confirmation clinical pregnancy. The pregnancy rate was calculated per embryo transfer.

Statistical Methods: The data were analyzed using commercially available statistical packages (SPSS 13.00. Chicago, IL, USA). The normality of the dietary intake variable distributions was assessed by Q-Q plots and found to be skewed. Log transformation improved normality and the values were used throughout the analysis. Descriptive analyses were performed using mean and standard deviation.

The data were analyzed using multiple linear regression adjusted for age, physical activity (MET/min/week), BMI and etiology of infertility; binary logistic regression, chi-square and t-test were the appropriate means of analysis for this research. The p-value of less than 0.05 was considered significant and p-value of less than 0.001 was considered highly significant.

Results

In total, 240 eligible women participated in the study. Four individuals were withdrawn from the treatment prior to completion of the study. The etiology of infertility was polycystic ovarian syndrome (PCOS) in 29.7%, endometriosis in 18.2%, anovulatory disorder in 15.3%, and other etiologies in 36.8% of participants.

The results of linear regression adjusted for age, BMI, physical activity and etiology of infertility (Table 1) showed that the number of retrieved oocytes was positively related to the total fat intake level ($p < 0.05$). The relationship between PUFA consumption level and good cleavage rate was significantly negative ($p < 0.01$). The increased fat consumption level, percentage of calories com-

ing from fat ($p < 0.01$) and PUFA consumption ($p < 0.01$) were also related to lower high embryo quality rate. The fertilization rate was not related to fat intake level (results were not shown).

The sausage and turkey ham consumption level was negatively related to the number of retrieved oocytes ($p < 0.05$) and MII stage oocytes ($p < 0.05$). The relationship between the vegetable oil consumption level and MII stage oocytes ($p < 0.05$) and good cleavage rate ($p < 0.05$) was significantly negative (Table 1).

A binary logistic regression analysis was used to study the relation among age, physical activity, BMI, calorie intake, fat component, food sources of fat and clinical pregnancy.

The high embryo quality rate in 71 women with oil consumption level greater than 50 *g/week* was lower than others who consumed oil less than 50 *g/week* (39.6 ± 34.9 versus 50.37 ± 38.77 , $p = 0.04$).

The number of retrieved oocytes (12.3 ± 9.6 versus 9.8 ± 8.2) was significantly higher in 91 women with sausage and turkey ham consumption of equal and less than 50 *gr/week* than in 91 women with sausage and turkey ham consumption of over 50 *gr/week* ($p = 0.03$).

The high embryo quality rate in women whose calorie intake as fat was $\leq 35\%$ was higher than women whose calorie intake as fat was $> 35\%$ (Table 2).

Discussion

The objective of this study was to evaluate the relationship between fat consumption level and assisted reproduction parameters. Our findings revealed that higher fat consumption level tends to raise the number of retrieved oocytes.

The findings of dietary fat supplementation trials in animal models and ovarian response to gonadotropin and oocyte competence are contradictory (6, 8, 26, 27). The good effects of increased dietary fat at an appropriate level on ovarian function are supported by previous observations; supplementations of FAs in diets influence concentrations of prostaglandins, steroid hormones and growth factors (28-30).

One mechanism for the effect of fat on the number of retrieved oocytes could be related to a decrease in hepatic blood flow and hepatic extraction of gonadotropin after a high-fat meal (31). Most of human gonadotropin in circulation is metabolized by liver (32). Furthermore, previous studies have reported that there is a slower peak growth rate in mean velocity and volume flow in

Table 1. Results of multiple regression analysis adjusted for age, physical activity, BMI and etiology of infertility

Variables	Standardized Coefficient	95% Confidence Interval	
	Beta	Lower	Upper
Number of oocytes			
Total fat (g/d) *	12.5	0.18	25.1
Total fat (cal %)	10.37	-11.8	32.6
Sat. FA (g/d)	0.15	-11.2	11.5
Trans FA (g/d)	-0.15	-0.59	0.29
PUFA (g/d)	-1.76	-13.6	10.1
MUFA (g/d)	-6.71	-19.7	6.3
meat (g/w)	0.17	-1.65	1.97
Dairy (g/w)	-3.23	-6.61	0.16
Sausage & ham (g/w) *	-1.1	-2.08	-0.03
Oil (g/w)	0.44	-4.19	5.08
MII stage oocyte rate			
Total fat (g/d)	37.62	-2.39	77.62
Total fat (cal %)	-15.4	-84.1	53.41
Sat. FA (g/d)	31.71	-3.5	66.88
Trans FA (g/d)	-0.91	-0.49	0.31
PUFA (g/d)	-34.2	-70.8	2.5
MUFA (g/d)	-26.1	-66.4	14.14
meat (g/w)	3.51	-1.34	8.36
Dairy (g/w)	1.31	-9.79	12.4
Sausage & ham (g/w) *	-4.9	-11	-3.58
Oil (g/w) *	-5.9	-18.2	-4.34
Good cleavage rate			
Total fat (g/d)	33.16	-19.8	86.11
Total fat (cal %)	29.79	-61.2	120.8
Sat. FA (g/d)	21.19	-25.4	67.74
Trans FA (g/d)	0.61	-0.91	2.13
PUFA (g/d) **	-66	-115	-18.2
MUFA (g/d)	14.92	-38.4	68.22
meat (g/w)	3.99	-3.16	11.14
Dairy (g/w)	2.83	-12.6	18.21
Sausage & ham (g/w)	-1.51	-9.87	6.84
Oil (g/w) *	-21	-39.6	-2.85
High embryo quality rate			
Total fat (g/d) **	-0.30	-0.55	-0.01
Total fat (cal %)	-0.82	-1.4	-0.22
Sat. FA (g/d)	0.04	-0.1	0.17
Trans FA	0.47	-1.12	2.05
PUFA (g/d) **	-0.26	-0.49	-0.01
MUFA (g/d)	-0.22	-0.51	0.07
meat (g/w)	0.04	-0.03	0.11
Dairy (g/w)	-0.07	-0.06	1.02
Sausage & ham (g/w)	-0.01	-0.09	0.08
Oil (g/w)	-0.14	-0.32	0.04

* p<0.05; ** p<0.01

the superior mesenteric artery following a high-fat meal compared with a high-carbohydrate meal (33). The delayed increase in portal blood flow after the fat-rich meal (31) may reduce hepatic extraction of administered gonadotropin. Therefore, the ovaries may be stimulated by higher gonadotropin concentration. Also, provision of dietary fats could therefore influence ovarian response to administered gonadotropin via an endocrine or other route (28). In addition, increased availability of FAs precursors is accompanied by

Table 2. Comparison of assisted reproduction parameters between groups of calorie intake as fat

Calorie Intake as Fat	≤35 (n=182)	>35 (n=54)
	Mean±SD	
Number of retrieved oocytes	11.25±8.69	11.52±10.61
MII stage oocyte rate (%)	79.74±27.43	75.51±28.1
Fertilization rate (%)	62.82±29.79	61.79±31.21
Good cleavage rate (%)	72.96±36.36	66.61±5.09
High embryo quality rate * (%)	51.11±2.85	33.43±37.43
Clinical pregnancy rate (%)	30.79%	34.54%

* p<0.01

increased steroid and eicosanoid secretion, which can alter the ovarian function (34).

Another finding of this study revealed that embryonic development is adversely related to fat-rich diet. Previous report indicated that changes in dietary fat intake can alter oviductal luminal fluid lipids (35) affecting embryo development (36). Higher levels of dietary fat may influence either the FAs content of cell membranes or cytoplasm of oocytes, hence affecting their developmental competence. It was documented that excessive intracellular lipids storage was associated with suboptimal mitochondrial function, thus, hampering the quality and viability of the embryo (37, 38). Also, according to Jungheim et al., elevated levels of follicular fluid FAs were associated with poor cumulus oocyte complex morphology (39).

However, the relationship between fat consumption level and assisted reproduction parameters may be attributed to calorie intake level due to fat intake. Although total calorie intake did not affect the assisted reproduction parameters, an increased percentage of calories coming from fat decreased oocyte quality.

The adverse impact of PUFA consumption level on cleavage rate and the high embryo quality rate were noted as well. These findings are not in agreement with other studies on animal models showing a positive impact of PUFA consumption on increasing embryo developmental competence and follicular size (3, 27, 40). The proportions of different PUFAs in cell membranes reflect the amounts consumed in the diet (41). Furthermore, the PUFA composition of the cell membranes of the sperm and oocyte is important during fertilization (42).

However, some studies provide evidence for the adverse effects of linoleic acid on oocyte development (39, 43). Zeron et al. reported that diets containing a PUFA rich rumen-bypass dietary supplement had no effect on the abundance of key FAs within oocyte phospholipids (36). Bilby et al. reported that feeding dairy cow with polyunsaturated FAs, compared to mono-unsaturated FAs, failed to affect the oocyte quality, as supported by subsequent embryo development (44).

Our study revealed that oil intake has adverse effect on oocytes nuclear maturation and embryo cleavage. The PUFA is abundant in oil (45). There seems to be a relation between oil consumption and assisted reproduction parameters which can be linked to the effects of FAs on the assisted reproduction parameters.

In addition, negative correlation of sausage and turkey ham consumption with the number of retrieved oocytes and oocytes nuclear maturation was observed too. According to Krajcovicova-Kudlackova et al., the industrial foods (such as sausage and ham) are the substantial sources of plasma Advanced Glycation End-products (AGEs) (10). The adverse effects of AGEs on follicular development and developmental competence of the oocytes and embryos are well documented (46-48). AGEs which are products of non enzymatic glycation and oxidation of proteins and lipids, have been found to induce oxidative stress and conversely oxidative stress stimulates AGEs formation (49, 50), a major cause of macromolecular damage in follicles (50).

The adverse effects of oil may be explained by the fact that usually oil is used for frying and cooking foods quickly and by flash heating under high temperature, deep-frying can increase AGEs in foods (51).

Although the data from the present study revealed that some assisted reproduction parameters are related to dietary fat consumption level, these findings should be interpreted with caution, as reproductive tract fluids contain markedly different nutrient concentrations as compared with plasma (52). Follicular lipids appear to be of serum origin but according to Vignon et al. lipid composition of follicular fluid differs from those of blood plasma (53) so that the effects of dietary fat on oocytes microenvironment need to be further explored.

Our study had a number of limitations which would urge caution in interpreting the findings. The fat consumption in our subjects was not at a low intake level and the effects of low fat consumption could not be detected on assisted reproduction parameters. In addition, many of the subjects with previous poor assisted reproduction outcome may be recommended to consume PUFA-rich foods. Also other aspects of the diet such as consumption of vegetable/fruit, type of the meat, *etc.* may act as the confounders.

Conclusion

The fat consumption might tend to influence the number of retrieved oocytes and adversely affect the embryo quality. In addition, high-level PUFA consumption may affect oocyte competence for later development. The assisted reproduction outcome might be affected by excessive oil and sausage and turkey ham intake. However, in women

with fat rich diet, though higher number of retrieved oocytes was observed, there was lower developmental competence in oocytes. Therefore, embryos with high quality belonged to women with lower intake of fat. These findings suggest that fat rich diet does not impair the success of assisted reproduction treatment.

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Conflict of Interest

Authors declare that there is no conflict of interest.

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