Association of Dietary Factors With Male and Female Infertility: Review of Current Evidence

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Context: The aim of this study was to review research articles concerning association between dietary factors and infertility in males and females.

Evidence Acquisition: Literature review was performed on articles concerning male and female infertility and nutrition using the PubMed, EMBASE, and Scientific Information databases between January 1978 and July 2014. The bibliographies of included studies were searched for additional references.

Results: The effect of macronutrients (fat, carbohydrate, and protein) and food groups (dairy) on ovulatory infertility is related to their quality and quantity. High intake of antioxidants, fruits, vegetables, poultry, seafood, skim milk, and shellfish as well as low intake of full-fat dairy food intake, sweets, and processed meat with especially high-saturated fat foods were reported to have favorable association with sperm quality.

Conclusions: Studies revealed that nutritional factors play a substantial role in preventing or facilitating infertility.

Keywords: Dietary Supplements; Food; Ovulation; Spermatogenesis; Infertility

1. Context

Infertility is characterized by inability to conceive after 12 month of unprotected intercourse (1). The epidemiologic reports indicated that infertility prevalence rates range from 3.5% to 16.7% in developed countries and from 6.9% to 9.3% in developing countries (2). One of every six couples has been confronted with infertility during their reproductive lifetime (3). Despite many advances in treatment methods, the number of infertile couples has increased at latest decade (4). The global rates of infertility in male and female are equal (50%) (5). Although assisted-reproduction methods have been developed to overcome infertility, their expenses cannot be afforded by all couples (4). The etiology of infertility generally remains unexplained, although environmental, occupational, and lifestyle characteristics have been implicated (6). Nutritional status, as a major lifestyle factor, is crucial determinants of normal reproductive function (6-8).

The most common type of infertility is ovulatory infertility for females (9). The impact of macronutrients (fat, carbohydrate, and protein) and food groups (dairy) on ovulatory infertility is related to their quality and quantity. Intake of trans fatty acids (TFAs) rather than carbohydrate and polyunsaturated fatty acids (PUFAs) have been associated with greater insulin resistance and risk of infertility (10). Moreover, there is a positive association between total carbohydrate intake and ovulatory infertility in the models when this nutrient is endogenously converted to fat (11). The amount and sources of protein in diet can also affect the reproductive parameters (12). Dairy foods and lactose may impair fertility by affecting ovulatory function; however, few studies have been conducted in humans (13).

Male infertility is usually caused by testicular damage leading to inability to produce sperm; the damaged testicle will not usually regain its sperm-making abilities (14). Furthermore, dramatic changes in the semen quality has been seen during the past three decades (15). Male infertility is usually caused by testicular damage leading to inability to produce sperm; the damaged testicle will not usually regain its sperm-making abilities (14). Furthermore, dramatic changes in the semen quality has been seen during the past three decades (15). High intake of antioxidants, fruits, vegetables, poultry, seafood, skim milk, and shellfish as well as low intake of full-fat dairy, sweets, and processed meat, especially with high-saturated fat foods, have favorable association with sperm quality (9, 16, 17). In order to improve the understanding of the nutrition role in the etiology of infertility, we systematically review and summarize the evidence from research articles that have examined the association between nutritional factors and infertility in males and females.

2. Evidence Acquisition

The authors searched online databases including the PubMed, EMBASE, Scientific Information Database (SID). All of those searches were done between January 1978 and July 2014. Ongoing registered clinical trials were searched.
in the website of international clinical trial registry by the United States National Institutes of Health (http://clinicaltrials.gov). The following search terms were used individually or in combination according to the Medical Subject Heading (MeSH) terms: "male infertility", "female infertility", "human reproduction", "ovulation", "spermatogenesis", "sperm quality", "semen quality", "food groups", "dietary patterns", "nutrient", "antioxidants", "fatty acids", "vitamin", "mineral", "micronutrients", "macronutrients", and "dietary factors." The detailed search strategy of each database is available as supporting information. The bibliographies of included studies were searched for additional references. Experts in this field were contacted for additional references or unpublished studies. Two authors independently screened the titles, abstracts, and key words of each searched article for potentially eligible studies.

3. Results

3.1. Fatty Acid Intake and Ovulatory Infertility

A prospective cohort study identified that eating TFAs instead of mono-unsaturated fatty acids (MUFAs) was considerably associated with risk of ovulatory infertility (5). The substitution of 2% MUFAs energy with 2% TFAs energy was associated with twice as high as risk of ovulatory infertility. In the same way, the intake of 2% of trans fatty acid energy rather than from n-6 PUFAs was associated with the greater risk of ovulatory infertility. Surprisingly, consumption of PUFAs had no association with ovulatory infertility in the entire sample population. Nevertheless, a noticeable negative association was reported in female with high iron consumption. The function of ω-6 desaturase, an enzyme that catalyze the conversion of linoleic acid into arachidonic acid as well as α-linolenic acid into eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), is remarkably decreased in female who had low serum iron concentrations (18). Moreover, iron is an important practical constituent of α-6 desaturase (19). Since eicosapentaenoic acid and arachidonic acid bind peroxisome proliferators-activated receptor (PPAR-γ) with more affinity than do shorter chain lengths PUFAs (20), the observed interaction would be expected if females with low iron intakes had deflections in this metabolic pathway; however, females who had high iron intake could endogenously produce long-chain PUFAs more efficiently through this pathway. Pharmacologic activation of the PPAR-γ enhances ovulatory activity in females with polycystic ovary syndrome (PCOS) and can influence PPAR-γ function (21). Iron is a well-known oxidant. Oxidized metabolites of PUFAs are more influential ligands of PPAR-γ than are PUFAs themselves (22). It is crucial to conclude that the abovementioned mechanism explains the observed effect modification, especially after adjustment for the observed high prevalence of depleted iron stores (21%) among young female in national surveys (23). The intake of heme iron has been related to a greater risk of insulin resistance outcomes; therefore, this interaction should be interpreted with caution (24). In a Randomized trials of 782 females with PCOS, daily intake of 150, 300, or 600 mg/d troglitazone or placebo were studied in a period of 44 weeks and the dose-dependent improvements in signs of ovulatory dysfunction such as ovulation rate and pregnancy rates, clinical, and biochemical signs of hyperandrogenemia were observed (24). Moreover, replacing trans fats with non-hydrogenated vegetable oils may decrease risk of type 2 diabetes and coronary heart disease (25). Females who are planning pregnancy should consider this strategy, since it could also decline the risk of infertility.

3.2. Dietary Carbohydrate Quantity and Quality and Ovulatory Infertility

Chavarro et al. reported that high carbohydrate intake was associated with healthy life styles. Females in high-carbohydrate group, who took almost 60% of their calories from carbohydrates, consumed less fat and animal protein, alcohol, and coffee, and more plant protein and fiber than those in the low-carbohydrate group who took 42% of calories from carbohydrates. Females in the low-carbohydrate group also had less weight, were less likely to smoke, and were more physically active. Furthermore, the quantity of carbohydrate in the diet was not associated with ovulatory infertility. Females in high-carbohydrate group were just likely to develop ovulatory infertility as females in low-carbohydrate groups. After adjustment for age, smoking, quantity of animal and vegetable protein consumption, and other factors, which can also affect fertility, female in the highest glycemic load group were 92% more likely to have ovulatory infertility than female in the lowest group. Generally, foods with high glycemic index such as cold breakfast cereals, white rice, and potatoes were associated with a greater risk of ovulatory infertility. Foods with low glycemic index such as brown rice, pasta, and dark bread associated with higher pregnancy rates (11). Other researchers revealed that higher level of HbA1c was associated with decreased fertility rate and subclinical metabolic characteristics resembling PCOS in apparently healthy females. Furthermore, insulin sensitizers can enhance reproductive metabolic parameters and ovulatory function in female with PCOS (26). In a small feeding trial among females with PCOS, a low carbohydrate diet (43% vs. 56% of energy) was accompanied with changes that would be expected to result in improved reproductive and metabolic outcomes including significant reductions in fasting and post-glucose challenge insulin levels as well as a reduction in free testosterone levels with a borderline statistical significance. To conclude, since lower refined starch consumption is associated with reduced risks of major chronic diseases (27), diminishing intakes of carbohydrates from these sources is recommended for fe-
male who are attempting to conceive as it might enhance fertility as well (28).

The nutritional status was compared between two groups of healthy females with either hypothalamic amenorrhea (HA) or PCOS in a pilot study. Anthropometric measurements, body composition, and dietary intakes were evaluated through a food frequency questionnaire and a seven-day food dairy. Body mass index (BMI) and body fat were higher in PCOS group in comparison with HA group. Habitual intake assessment revealed the same macronutrient distribution between two groups (nearby 16% protein, 33% fat, and 52% carbohydrate) (29).

3.3. Protein Intake and Ovulatory Infertility

An interesting study categorized the participants by their average daily protein consumption (12). The lowest and highest protein group had an average of 77 and 115 g/d of protein intake. After justification for smoking, fat intake, weight, and other factors that might affect fertility, they found that females in the highest protein group were 41% more likely to have reported problems with ovulatory infertility than females in the lowest protein group. Ovulatory infertility was 39% more likely in females with the highest intake of animal protein than in those with the lowest. The reverse was observed for females with the highest intake of plant protein, who were strikingly less likely to have ovulatory infertility than females with the lowest plant protein intake. Moreover, adding a daily meal of red meat, chicken, or turkey had increased the risk of ovulatory infertility by 33%. In addition, adding a daily meal of fish or eggs did not affect ovulatory infertility. In addition, adding a daily meal of beans, peas, tofu or soybeans, peanuts, or other nuts were associated with modest protection against ovulatory infertility. It was also reported that adding animal protein instead of carbohydrate was associated with a greater risk of ovulatory infertility. Additionally, replacing 25 g of carbohydrate with 25 g of plant protein reduced the risk by 43%. Furthermore, replacing 25 g of animal protein with 25 g of plant protein was associated with 50% decrease in the risk of ovulatory infertility.

A small randomized trial compared the reproductive function effects of low-protein (15% of energy) with high-protein (30% of energy) diets for losing weight among overweight females with PCOS (30). Although here were an enhancement in menstrual cycles as well as reduction in circulating androgens as a result of improved insulin sensitivity due to weight loss, the protein content of diet had no association with the reproductive function (31). The findings are in accordance with previous studies measuring the effect of diet on ovulatory function in animals. Increasing vegetable (soy) protein consumption was associated with increase ovulation rates in pigs (32). Furthermore, protein intake may influence insulin and glucose response differently with respect to the protein source. In diabetics, the postprandial insulin response to vegetable (soy) protein and egg protein was lower than the response to red meat and turkey protein (33); similarly, the postprandial insulin response to vegetable protein is lower than response to animal protein in healthy subjects (34). Moreover, cod and soy protein were reported to improve insulin sensitivity in comparison with casein in rodent models (35). Another possible underlying mechanism of the observed associations could be a differential effect of animal and vegetable protein on circulating IGF-I levels. Elevations levels of free IGF-I may be involved in the development of PCOS (36, 37), the most common cause of anovulation. Holmes et al. reported that animal protein intake in females was positively associated with IGF-I levels whereas vegetable protein intake was not associated with this hormone (38). However, in a similar study in males, both animal and vegetable protein intake were positively associated with blood IGF-I levels and to the ratio of IGF-I to its binding protein (39).

3.4. Dairy Foods Intake and Ovulatory Infertility

Chavarrío et al. showed that females who reported having three or more servings of milk or other dairy foods per day and females who had one serving or fewer per week had equal rate of fertility problems. It was also reported that females at the highest extreme of the scale for both lactose and galactose, whose daily dairy intake was the equivalent of three glasses of milk, had similar rates of ovulatory infertility to females at the lowest extreme of the scale. Further, important constituents of milk such as calcium, vitamin D, and phosphorus did not influence fertility (13). There was also an inverse correlation between high-fat dairy intake and risk of developing ovulatory infertility. One serving of low-fat or no-fat dairy product per day increased the risk by 11%. Otherwise, one serving of whole milk per day was associated with 50% lower the risk of ovulatory infertility after adjusting for potential confounders (14). Cramer et al. showed that according to the age, fertility dropped faster in countries where female consumed more than three servings per week than it did in countries where they consumed less than three servings weekly (40). Following these findings, Greenlee et al. reported that females who consumed three glasses of milk a day were 70% less likely to have ovulatory infertility than females who rarely consumed milk (41). The association between low-fat (and high-fat) dairy foods intake and ovulatory infertility is stronger among females without some clinical manifestations of PCOS than among female with PCOS. Additionally, milk composition changes during the process in which fat is extracted; for example, the addition of some whey proteins such as α-lactalbumin has shown some androgenic effects in animals. Several of these mechanisms may be associated with ovulatory infertility, especially the increased IGF-I levels because of increased dairy intake, that may be justified by the consumption of low-fat dairy foods (42). Some data have suggested that IGF-I might participate in the developing PCOS as in human ovarian cells, IGF-I can induce theca cell function changes. In ad-
dition, exogenous IGF-I administration to females with specific endocrinopathies may be particularly relevant with clinical manifestations of PCOS (37).

3.5. Antioxidants and Female Infertility

Recent data, implicate that oxidative stress and low antioxidant status may lead to either known or unexplained infertility (43). Exceeding scavenging capacity has resulted in oxidative stress, which can be accompanied with either decreased antioxidant intake or increased antioxidant utilization. Additionally, characteristics related to decreased fertility such as obesity and advanced maternal age are associated with increased oxidative stress (44, 45). A controlled clinical study has shown that females PCOS, which is a risk factor for female infertility, had higher serum CRP and lower total antioxidant status than their healthy counterparts (46). Polak et al. reported that female with unexplained infertility had lower total antioxidant status in peritoneal fluid in comparison to fertile group (47). An interesting cohort examined the effects of increasing antioxidant intake on time to successful conceive among couples being treated for idio-pathic infertility. The study reported that for female who had a BMI < 25 kg/m², increased supplementary vitamin C was associated with a shorter time to successful conceive; however, the association between tertiles of total intake of vitamin C or dietary vitamin C intake were not statistically significant. Among female with BMI ≥ 25 kg/m², increased β-carotene intake in dietary supplements resulted in shorter time to successful conceive. In young female (< 35 years) supplementary β-carotene, vitamin C, and total vitamin C and β-carotene intake were associated with shorter time to successful conceive. Eventually, for older female (≥ 35 years) increased supplementary vitamin E and total vitamin E intakes led to shorter time to successful conceive (48).

3.6. Antioxidants and Male Infertility

Vitamin E is a well-documented antioxidant and has been shown to inhibit free radical-induced damage to sensitive cell membrane (49). Oral supplementation with vitamin E significantly decreased concentration of malondialdehyde, an indicator of lipid peroxidation, and improved sperm motility and count (50). The association between vitamin E intake and progressive motility was reported in Eskenazi et al. study (51). Suleiman et al. study determined that vitamin E improved sperm motility (52). Whereas there was no effect of even higher levels of vitamin E supplementation alone (53) or even in combination with other vitamins (54). A low intake of vitamin E was associated with poor sperm concentration and motility in Nadjarzadeh et al. study (55). After 90 days of treatment with beta-glucan, lactoferrin, papaya, and vitamins C and E, an increase in the percentage of morphologically normal sperm and total progressive motility were reported. Structural sperm characteristics as well as chromatin integrity were also improved after this treatment (56).

Studies have shown that low level of vitamin C lead to infertility and increased damage to sperm’s genetic material. Concentration of ascorbate in seminal plasma is ten times greater than in blood plasma (57). Dawson et al. studied effect of vitamin C on male infertility; they divided males in two groups: healthy males as placebo group, and infertile males as target group. The first group was given a placebo and second group was given either 200 or 1000 mg/d of Vitamin C. After one week, the sperm count was increased by 112% and 140% in those receiving 200 and 1000 mg/d, respectively, while there was no change in placebo group. However, one week was inadequate time to reassess semen analysis. Most importantly, every participant in vitamin C group had impregnated their partner while no pregnancy was reported in placebo group by two months of therapy (58). Eskenazi et al. reported positive association between vitamin C intake and sperm count (51). Verma and Kanwar demonstrated dose-dependent preservation of sperm motility by vitamin C. Motility was highest after six hours incubation in 800 µmol/L vitamin C. However reduction in motility was initiated with concentrations > 1000 µmol/L (59).

Glutathione is a vital factor for sperm antioxidative defenses (60). Both Glutathione and selenium are essential to form phospholipids hydroperoxide glutathione peroxidase, an enzyme present in spermatid. This is a structural protein of mitochondria in the middle part of mature spermatozoa. Deficiency of glutathione and selenium leads to instability of middle part that results in defective motility. Glutathione and selenium were used in double-blinded placebo-controlled, crossover trial on 20 infertile males. The researchers demonstrated a statistically significant effect on forward sperms motility after a two months trial (61). Some studies showed that combined vitamin E and selenium improved sperm motility (62-64).

Zinc is a trace mineral, which is essential for normal function of male reproductive system. More than 200 enzymes in various biochemical mechanisms of body are dependent to zinc (65). The zinc deficiency is associated with decreased testosterone level and sperm counts (66). In a trial, 24 mg of elemental zinc was supplemented in 37 males with idiopathic infertility for 45 to 50 days (67). The results showed a substantial increase in testosterone level and sperm count from eight million to 20 million/mL, leading to nine successful conceptions. However, Eskenazi et al. reported that zinc intake was not associated with improved semen quality (51). Nadjarzadeh et al. showed that males with asthenospermia/teratozoospermia had a significantly lower intake of zinc in comparison to control ones (55). Twice daily zinc therapy (250 mg) for three months improved the sperm quality, sperm count, progressive motility, and fertilizing capacity and reduced the incidence of antisperm antibodies (68).

In sperm cells, coenzyme Q10 (coQ10) is concentrated in mitochondria of middle part for energy production. It also works as an antioxidant, preventing lipid peroxi-
This association was significant at higher extremes of the pregnancy rate (72). Three-month supplementation with CoQ10 in Iranian males with astheno-teratozoospermia could attenuate oxidative stress in seminal plasma and antioxidant enzymes activity (73); however, it does not show any significant effects on sperm concentration, motility, and morphology (74). According to the recent meta-analysis, there is no evidence in the literature that CoQ10 might increase either live birth or pregnancy rates (75).

The main function of carnitine is to provide energetic substrate for spermatid as it is a necessary factor for transporting fatty acids to mitochondria. It helps directly in sperm motility and maturation (76). A multicenter trial among 124 infertile males receiving 3 gm/d of L-carnitine for four months assessed sperm parameters before, during, and after the study. The researchers reported increased total motility and rapid linear progressive movement. During four months of trial on 20 infertile male, 12 patients had significant improvement and five pregnancies were achieved during treatment. Two more pregnancies occurred during next four months following trial (77).

Carotenoid intake was associated with higher sperm motility and in the case of lycopene, better sperm morphology. Thus, dietary carotenoids may have a positive effect on semen quality in a population of healthy young males (78). Positive association was reported between beta-carotene intake and sperm concentration (51). There was a positive association between dietary intakes of lycopene and β-carotene and total motile sperm count (79).

### 3.7. Soy Food and Isoflavone Intake and Male Infertility

Xenoestrogens play an important role in a variety of male reproductive disorders including possible declines in sperm concentration (80). Isoflavones are plant-derived polyphenolic compounds with estrogenic activity and are found mainly in soy beans and soy-derived products (81). They are generally considered to have a weak estrogenic activity, being able to bind estrogen receptors with an affinity 100 to 1000 times as low as estradiol (54). In addition, isoflavones have been linked to male reproductive disorders in mammals, including impaired development of reproductive organs, especially following intrauterine exposure (82). In a cross-sectional study, dietary intake of soy food and isoflavones was reported in an inversely association with sperm concentration after adjustment for multiple potential confounders (83).

This association was significant at higher extremes of the sperm concentration distribution, proposing that soy food intake may have stronger associations among males with normal or high sperm concentrations than among males with low sperm concentration. Furthermore, consumption of soy food had a more significant inverse association with sperm concentration among overweight and obese males. Intake of soy foods or isoflavones was unassociated with the other examined semen analysis parameters. Studies by Chavarro et al. demonstrated that males in the highest group of soy food intake had 41 million sperm/ML less than males who did not consume soy foods (83). Mitchell et al. evaluated the reproductive effects of daily supplementation with 40 mg of isoflavones for two months among 14 young males. There were no dramatic changes in semen quality parameters or reproductive hormone levels in comparison with pretreatment levels. However, the lack of a control group and the small size of the study were limitations to make interpretation of their findings (84). In a study with a similar design, Song et al. investigated the association between isoflavone intake and semen quality in a group of 48 males with abnormal semen parameters and ten males with normal semen parameters. They reported that isoflavone intake was positively correlated to sperm count and motility and had an inverse association with sperm DNA damage (85). Rozati et al. have shown that the sperm motility is inversely associated with the proportion of xenobiotics in sperm membrane (86). Xia et al. study provided the evidence that phytoestrogens exposures were associated with the male reproductive function in China (87).

### 3.8. Fatty Acid Intakes and Seafood and Male Infertility

Afeiche et al. showed that consuming fish might have a positive effect on sperm counts and morphology, particularly when consumed instead of processed red meats (88). Furthermore, Conquer et al. showed lack of effect of DHA supplementation on sperm motility (89). However, Safarinejad showed a significant positive correlation between the EPA and DHA of seminal plasma and semen parameters (90). Intakes of flaxseed oil and walnuts contain α-linolenic acid is correlated with increased sperm quality (91, 92). Nissen et al. have illustrated a link between sperm motility and PUFAs (93). Jensen et al. showed a lower sperm concentration and total sperm count in males with a high intake of saturated fat (94). According to Eslamian et al. research, combined daily 465 mg of DHA and 600 IU of vitamin E led to increasing sperm concentration, sperm motility as well as DHA content of sperm (95).

Exposure to environmental toxins has been suggested as a potential cause of infertility (4). Mercury is one of the most potential reproductive toxins. Animal studies have revealed an adverse effect of mercury on spermatogenesis (96). In vitro studies have reported that mercury is able to perform sperm abnormality (97). Other in vivo studies failed to correlate mercury concentrations in blood or
semen with abnormal semen parameters; however, this studies suffered from the limitations of a small sample size, a narrow range of semen parameters, and a narrow range of mercury concentrations (98). In a pilot study involving 59 male partners of infertile couples in Hong Kong, 35% had abnormally high blood mercury concentrations although blood concentrations of lead, aluminum, selenium, and cadmium were normal. The result reported that this population may be at risk of mercury toxicity (99). Another case-control study demonstrated that infertile couples had higher blood mercury concentration than fertile couples (100). Infertile males with abnormal semen and infertile females with idiopathic infertility also had higher blood mercury concentration than fertile counterparts. Blood mercury concentrations were positively associated with the amount of seafood consumption. Infertile subjects with greater blood mercury concentrations had consumed a larger amount of seafood.

3.9. Food Group Intake and Male Infertility

Mendiola et al. demonstrated that normospermic controls had a higher intake of skimmed milk, shellfish, tomatoes, and lettuce and consumed less yogurt, meat products, and potatoes; in contrast, cases with poor semen quality had lower intake of lettuce, tomatoes, fruits (apricots and peaches) and significantly higher intake of dairy and meat processed products (101). Processed meat intake had unfavorable and consuming fish intake had favorable association with semen quality of young male in subfertile couples (88). Processed meat intake was related with lower total sperm count among young males (102). In healthy, young male, higher consumption of sugar-sweetened beverages was associated with lower sperm motility (102). The protective role of fruits, vegetables, poultry, skimmed milk, and sea foods and the increased risk of asthenozoospermia with meat processed foods, dairy products, and sweets consumption are supported in Eslamian et al. study (9). Afeiche et al. indicated that low-fat dairy intake, particularly low-fat milk, is associated with the higher sperm concentration and progressive motility whereas cheese intake is related to the lower sperm concentration among previously or current smokers (103). The prudent pattern, which was characterized by high intake of fish, chicken, fruit, vegetables, legumes, and whole grains, was positively correlated to the percentage of progressively motile sperms in multivariate models. Participants in the highest quartile of the prudent pattern had 11.3% higher progressively motile sperm in comparison with participants in the lowest quartile (103, 104).

4. Conclusions

Intake of TFAs, high-glycemic-load carbohydrate, animal protein, and low-fat dairy foods may be associated with ovulation infertility. Several micronutrients may improve reproductive outcome when administered to subfertile males. Furthermore, several investigators have demonstrated that higher intake of soy foods and soy isoflavones may be associated with lower sperm concentration and higher concentration of blood mercury might be associated with male and female infertility. There is a complete lack of appropriate randomized controlled trials that could correlate changes in diet with improvements of fertility. All of these studies lack control group and the interpretation of these data seems very hard. Hence, Future clinical trials in this field are needed. Overall, lifestyle and dietary choice may help to improve fertility in males and females.

Authors’ Contributions

Banafshe Hosseini and Ghazaleh Eslamian conceptualized the study; searched online databases, wrote the manuscript, and read and approved the final manuscript.

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