Influence of Dietary Supplements on Female Fertility

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Abstract:

Infertility is defined as the failure to generate a clinical pregnancy after 12 months of regular and unprotected sexual contact. It is believed that 8-12% of reproductive-aged couples globally are affected by it. Female fertility decline begins around 25-30, and the median age at last birth is 40-41 years in most studied populations with natural fertility. Over the last decade, the literature on the relationship between nutrition and human fertility has grown significantly, culminating in identifying a few distinct patterns. Supplemental folic acid consumption, particularly at higher levels than those recommended for the protection of neural tube abnormalities, has been linked to a reduced frequency of infertility, a decreased risk of pregnancy loss, and greater success in infertility therapy. Vitamin D, on the other hand, is well-known for its role in calcium and phosphorus homeostasis and bone mineralization. There is some evidence that, in addition to the conventional regulators of human reproduction, sex steroid hormones, vitamin D regulates reproductive processes in both men and women. Melatonin supplementation has lately been suggested as a therapeutic method in gynaecological practice. According to present research, women attempting to conceive are advised to increase their intake of whole grains, omega-3 fatty acids, fish, and soy while decreasing their intake of trans fats and red meat. A diet high in omega-3 polyunsaturated fatty acids (3-PUFA) improves fertility by improving oocyte quality, embryo implantation, and menstrual cycle function. This study focuses on the evidence from epidemiology literature supporting the relationships between essential dietary variables and female reproductive capacity.

Keywords: Diet, nutrition, supplements, female fertility, omega 3, vitamin

Introduction

Many reproductive-aged couples pursuing pregnancy suffer from infertility, defined as failure to obtain pregnant after 12 months of unprotected and routine sexual intercourse [17]. Female infertility is defined as infertility caused predominantly by female causes such as ovulation abnormalities, decreased ovarian reserve, reproductive system illnesses, or chronic diseases [17]. According to the Centers for Disease Control and Prevention (CDC), 10-16% of couples have trouble conceiving, and this may be higher in first-time mothers and as they age [6]. Female infertility is most commonly caused by ovarian dysfunction. Ovulatory irregularities account for approximately 25% of infertility diagnoses; 70% of anovulant women have PCOS

[7]. Primary and secondary infertility are the two types of infertility. A main infertile female is a lady who has never had a clinical pregnancy and meets the infertility criteria. Secondary female infertility describes a woman who is unable to establish a clinical pregnancy but has previously been diagnosed with a clinical pregnancy [16]. However, female infertility accounts for only 35% of all infertility cases; 20% of cases involve both men and women; 30% involve mainly male difficulties; and 15% of infertility cases are unsolved. According to the WHO, 80 million women worldwide are affected by infertility [17]. Aside from organic disorders, lifestyle variables such as an unbalanced diet and an unhealthy diet can disrupt women's physiological reproductive systems. This review aims to summarize the epidemiologic literature on nutrition and fertility and provide practical dietary recommendations based on the best available data. Recent research has shown that women experiencing unexplained infertility may have unrecognized nutritional abnormalities that impair fertility [7]. Identifying modifiable lifestyle factors influencing human fertility, such as food, is critical for clinical and public health [1]. While there is a growing understanding that nutrition may be connected to reproductive performance in both men and women, there is still no formal advice for reproductive-aged couples [1]. Nutritional deficiencies during pregnancy can have major health effects, such as iron deficiency, which causes anemia in pregnant women, and folate insufficiency, which causes neural tube abnormalities (NTDs) in fetuses. In addition to enhancing pregnant women's dietary quality, taking dietary supplements has become a popular way to boost the intake of specific nutrients [10]. Although it is widely acknowledged that nutrition and lifestyle factors such as food, exercise, and obesity affect reproductive capacity, preconceptional nutritional treatment is frequently poor [7]. Dietary supplements play an essential role in promoting mother's health and birth outcomes. Due to the growth of maternal tissues and fetal development, pregnant women have increased nutritional needs that are difficult to meet through their everyday diets. Dietary supplements are oral products that contain dietary elements such as vitamins, minerals, amino acids, or other dietary substances that are used to complement one's nutritional inadequacies [10]. Dietary factors have been implicated in the pathogenesis of numerous illnesses, and the hypothesis that dietary adjustments may improve fertility appears promising [4].The rationale for using DS is to supplement the deficiency of those substances or to achieve the optimal dose (i.e., minerals, vitamins, carbohydrates, fatty acids, and proteins) that may have a potentially positive effect on various fertility targets such as hormonal balance, ovulation, oocyte quality, embryo quality, and hopefully the likelihood of achieving pregnancy. Many women seek treatment or self-medicate with a variety of adjuvant therapies, including dietary supplements (DS) with varying contents, to increase their odds of conception [7].

Methods

Review of literature: Review of literature: To acquire a better understanding of the various diets and supplements needed to improve fertility in women, we evaluated previously published research papers on nutrition and human fertility in female patients.

Result

Dietary and supplements are discussed as a potential approach to improve fertility in women. The maximum number of articles was explored, and a literature review was done accordingly.

Vitamin D

Emerging evidence suggests that vitamin D is not only essential for bone health and calcium and phosphate homeostasis, but also has multisystem regulatory effects that influence general wellness and health. More preclinical and clinical research is needed to understand the role of vitamin D in reproductive regulation and if vitamin D insufficiency is linked to infertility. Given the diverse character of infertility, it is complicated to identify vitamin D insufficiency as the only cause of failed conception, whether spontaneous or assisted reproduction [18]. Vitamin D is a fat-soluble steroid hormone with autocrine, paracrine, and endocrine activities in the female reproductive system [7]. Vitamin D is well-known for its

role in calcium and phosphorus homeostasis and bone mineralization [3]. A minor portion of the body's total vitamin D is acquired from diet and/or supplementation [1]. It is a steroid hormone, and roughly 80-90% of vitamin D is generated in the skin following exposure to sunshine [5]. Vitamin D insufficiency is common among women of reproductive age. Obesity, lifestyle changes, and decreasing sun exposure are all contributing to the rising prevalence. There is some evidence that vitamin D, in addition to sex steroid hormones, affects reproductive processes in both men and women [5]. Indeed, multiple studies have found a link between vitamin D and human fertility [3]. The presence of vitamin D receptors (VDRs) in both male and female central and peripheral reproductive organs, tissues, and cells emphasizes the importance of vitamin D in fertility [2]. Vitamin D is most likely involved in the regulation of female reproductive processes. Vitamin D receptors are expressed in several tissues of the reproductive organs, including the ovaries, endometrium, placenta, pituitary gland, and hypothalamus. Furthermore, vitamin D influences several endocrine processes, including the steroidogenesis of sex hormones [17]. According to the available literature, vitamin D may influence reproductive processes. Vitamin D receptors are found throughout the reproductive system, including the ovaries, uterus, and endometrium [4]. In women taking clomiphene citrate (CC), serum 25 (OH)-D levels have been linked to ovarian response. Low levels of 25 (OH)-D and vitamin D insufficiency were observed to be linked with reduced rates of follicle formation and subsequent pregnancy in women given CC at a dose of 50 mg/day [11]. The role of vitamin D in IVF women has also been investigated. Ozkan et colleagues investigated follicular fluid 25 (OH)-D levels obtained during egg harvesting and linked them to treatment outcomes.40 Follicular fluid 25 (OH)-D levels were considerably greater in women who conceived than those who failed IVF treatment. Women with follicular fluid levels of 25 (OH)-D in the highest tertile (43.01 10.65 ng/mL) had higher implantation rates than those with follicular fluid levels in the lower tertile (P 14 0.041). However, one of the two other studies published failed to find such a connection, while the other found that high follicular fluid 25 (OH)-D levels had a negative influence on embryo quality [11].

Folic Acid

Folic acid was the second most prevalent ingredient, appearing in 83.0% of the DS examined [7]. Folate, which is involved in DNA synthesis [7], is essential in gametogenesis, fertilization, and pregnancy. As a result, folate (a naturally occurring form of vitamin B9) or folic acid (a manufactured form of vitamin B9) may play a crucial role in human reproduction [4]. Folic acid supplementation (especially in larger doses than advised for the prevention of congenital abnormalities and mixed with vitamin B-12) in the time preceding pregnancy may increase the chances of becoming pregnant and ART success [17]. It is critical to remember that folic acid supplementation has been linked to a shortened menstrual cycle duration [17]. It has been demonstrated that taking a 400 g folic acid (vitamin B9) supplement daily before conception and during the first three months of pregnancy reduces the chance of neural tube abnormalities (such as spina bifida) in the fetus. Observational studies imply that a higher folic acid consumption may enhance a woman's chances of becoming pregnant. Given this information, it is recommended that women begin taking 400 g of folic acid daily for two months before trying to conceive to help avoid fetal neural tube abnormalities (NTDs) [8]. Nonetheless, folic acid supplementation during pregnancy has been proven to minimize the risk of non-NTD birth abnormalities such as cleft palates, upper limb reduction deficits, and genitourinary disorders. Thus, DS with low folic acid dosages (400 mcg) may be non-protective for both NTDs and non-NTD birth abnormalities [7]. According to one study, women who receive preconception counseling from their primary care physician are five times more likely to take folic acid prior to conception. Women who are taking folic acid antagonists or have carried a fetus with a neural tube defect or other birth defects associated with folic acid deficiency (e.g., oral facial cleft, structural heart disease, limb defect, urinary tract anomaly, hydrocephalus) should take 4 to 5 mg of folic acid daily beginning three months before conception and continuing until 12 weeks postconceptional. Women who have particular health risks (epilepsy, insulin-dependent diabetes mellitus, obesity with a BMI greater than 35 kg per m2, family history of a neural tube abnormality) should also take this higher dosage [9]. Natural folate consumption from daily foods with poor bioavailability is insufficient to meet the nutritional needs of pregnant women. Many nations have developed perinatal folic acid supplementation guidelines for

pregnant women [10]. However, our findings contradicted these guidelines because the existing folic acid dosage in the middle and late stages of pregnancy was unacceptably low. The majority of pregnant women were unaware of the long-term benefits [10]. Another source of worry was that more than 10% of pregnant women in their first trimester retook folic acid from individual micronutrient (IMN) and multivitamin (MMN), which could result in folic toxicity and increase the risk of colorectal neoplasia [10].

Melatonin

Melatonin is a low-molecular-weighted indoleamine that regulates biological rhythms, and reproductive, immunological, and metabolic processes in humans [7]. Melatonin is produced not only by the pineal gland, but also by glial cells, meningeal cells, and other peripheral organs, and its cyclical secretion pattern responds to zeitgebers [12]. Melatonin supplementation was found to have a favorable influence on oocyte quality, embryo quality, and luteal function in female fertility. As a result of these factors, it is currently seen as a promising EI for female infertility. Nonetheless, when melatonin was incorporated into supplements, its concentration was three times lower than mED (1 mg vs. 3 mg), according to our careful analysis. This decision is based on the fact that, according to EFSA, the Italian Ministry of Health reduced the permitted dose of melatonin in DS from 5 mg/day to 1 mg/day in 2013. This EFSA stance is based on data showing melatonin is beneficial in treating sleep problems at doses lower than 1 mg. There is currently no research on reproductive function with this low dose [7]. Melatonin's antioxidant capabilities on the HPG axis may reduce intra-follicular oxidative damage while also enhancing progesterone synthesis in the luteal phase and oocyte maturation. The ovary can absorb circulating melatonin, but the ovarian follicle can synthesize and produce its melatonin, indicating that melatonin plays an important paracrine role in the female reproductive system. Melatonin has been used as a beneficial clinical tool in the treatment of ovarian cancer due to its anti-proliferative, anti-inflammatory, anti-angiogenic, and immunomodulatory effects [12]. So far, the evidence suggests that melatonin supplementation has a good effect on regular gynecological treatment, not only enhancing general well-being but also improving reproductive parameters in women of childbearing age who want to become mothers. More data suggests that melatonin has musculoskeletal benefits, such as increased strength and bone health, in addition to psychological benefits [12].

Selenium

Selenium (Se) is a trace element that is required for the maintenance of human body homeostasis. Se, in the form of the amino acid selenocysteine, is integrated into a huge number of proteins known as selenoproteins, which perform a variety of functions such as antioxidant defense, redox state management, and cancer prevention, as well as being engaged in a variety of metabolic processes. Because of these characteristics, various selenoproteins have emerged as possible biomarkers of disease as well as Se status. Se, in addition to potentially protecting against the effects of heavy metals, also preserves the appropriate functioning of the reproductive system [13]. When compared to those with tubal infertility or a recognized male-related cause of infertility, patients with unexplained infertility had considerably lower follicular selenium concentrations [11]. Zinc and selenium have been linked to improved male and female reproductive health. Research comparing selenium levels in follicular fluid in women with unexplained subfertility to those with tubal occlusion or male factor infertility found that they were considerably lower in women with unexplained subfertility [14]. When compared to those with tubal infertility or a recognized male-related cause of infertility, patients with unexplained infertility had considerably lower follicular selenium concentrations [11]. Zinc and selenium have been linked to improved male and female reproductive health. Research comparing selenium levels in follicular fluid in women with unexplained subfertility to those with tubal occlusion or male factor infertility found that they were considerably lower in women with unexplained subfertility [14]. Serum Se concentrations and GPX activity in human trough in the early follicular phase and peak in the preovulatory phase, followed by a decrease in the middle luteal phase [13]. Grieger et al. discovered that low serum zinc and selenium concentrations were associated with a 1-month longer interval before attaining pregnancy. Furthermore, a lack of selenium and copper, but not

zinc, was connected to an increased risk of infertility. The impact of zinc and copper concentrations on women's fertility remains unknown based on little data, and more research is needed. Selenium also has an impact on thyroid gland function. It is also an antioxidant that aids in the decrease of oxidative stress. Selenium may alter oocyte growth and maturation. As a result, an appropriate quantity of selenium is required [17]. During pregnancy, the recommended Se dietary allowance (RDA) varies from 55 to 60 g/d, which is greater than in nonpregnancy. One probable explanation for the increased Se need is the necessity for good antioxidant defense, as gestation is associated with increased oxidative stress, particularly during early pregnancy. Placental oxidative stress (OS) is present during all three trimesters of a normal pregnancy and is required for appropriate cell function because reactive oxygen species (ROS) and reactive nitrogen species (RNS) act as secondary messengers in many intracellular signaling cascades. However, over a certain level, OS might harm pregnancy and lead to major difficulties. Higher maternal Se levels have been linked to a lower risk of miscarriage, premature birth, pre-eclampsia, and autoimmune thyroid disease. Se insufficiency may thus have negative consequences on both the male and female reproductive systems [13].

Omega-3 Fatty Acid

Saturated (SFA), monounsaturated (MUFA), and polyunsaturated (PUFA; including -3 PUFA and -6 PUFA) fatty acids may play essential roles in reproductive function via a variety of routes [4]. According to animal and human studies, a diet high in omega-3 polyunsaturated fatty acids (3-PUFA) has a positive effect on fertility, affecting oocyte quality, embryo implantation, and menstrual cycle function [15], whereas trans fatty acids may promote greater insulin resistance, which may impair ovulatory function [1]. Several studies have demonstrated that eating more omega-3 fatty acids is connected with better health and a lower risk of chronic disorders [6]. Fatty acids have been established in vitro to be key substrates in early reproductive events such as oocyte maturation and embryo implantation [1].

Dairy

Although studies on the effect of dairy-derived lipids on fertility are intriguing, the results are sometimes conflicting. On the one hand, low-fat dairy consumption—including low-fat milk, yogurt, and cottage cheese—increased the chance of infertility due to anovulation, whereas high-fat dairy consumption enhanced fertility. This could be due to greater levels of estrogen and fat-soluble vitamins in high-fat dairy. Furthermore, the favorable effect of dairy-derived fat may be related to the presence of trans-palmitoleic acid, which appears to improve insulin sensitivity. Wise et al., on the other hand, did not demonstrate that high-fat dairy consumption is associated with enhanced fecundity, but they did establish that lactose and low-fat dairy consumption did not negatively affect fertility. It is important to remember that eating more than three servings of dairy per day reduces the probability of endometriosis diagnosis by 18% when compared to eating two servings. Furthermore, women who consumed >4 portions of dairy daily during adolescence had a 32% decreased incidence of endometriosis in maturity than those who consumed 1 part. Furthermore, total dairy intake was related to live births among 35-year-old women [17].

Conclusion

Over the last decade, the literature on the association between nutrition and human fertility has developed dramatically, revealing various distinct patterns. Vitamin D supplementation is a low-risk, low-cost medicine that may help with human fertility. A diet rich in omega-3 polyunsaturated fatty acids (3-PUFA) and melatonin increases fertility by altering oocyte quality, embryo implantation, and menstrual cycle function. Women should take 4 to 5 mg of folic acid daily beginning three months before conception and continuing for 12 weeks postconceptional. Taking folic acid supplements helps to avoid neural tube defects and other birth disorders associated with folic acid deficiency (e.g., oral-facial cleft, structural heart disease, limb defect, urinary tract anomaly, hydrocephalus). Low-fat dairy products such as low-fat milk, yogurt, and cottage cheese increased the likelihood of infertility due to anovulation, but high-fat dairy products boosted fertility. Selenium may influence oocyte growth and maturation. During pregnancy,

women require an adequate dosage of selenium; the recommended Se daily intake (RDA) ranges from 55 to 60 g/d, which is higher than in nonpregnancy. Aside from medications, eating and healthy lifestyle choices have been demonstrated to boost fertility. Finally, women who consume a well-balanced diet high in fish, poultry, complete grains, fruits, and vegetables have increased fertility.

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References:

1) Gaskins A.J., Chavarro JE(2018). Diet and fertility: a review. Am J Obstet Gynecol, 218(4):379-389.
2) Várbíró S., Takács I., Tűű L., Nas K., Sziva R.E., Hetthéssy J.R., Török M (2022). Effects of Vitamin D on Fertility, Pregnancy and Polycystic Ovary Syndrome-A Review. Nutrients, 14(8):1649.
3) Lerchbaum E., Obermayer-Pietsch B (2012). Vitamin D, and fertility: a systematic review. Eur J Endocrinol. 166(5):765-78.
4) Chiu Y.H., Chavarro J.E., Souter I (2018). Diet, and female fertility: doctor, what should I eat? Fertil Steril, 110(4):560-569.
5) Lerchbaum E., Rabe T (2014). Vitamin D and female fertility. Curr Opin Obstet Gynecol, 26(3):145-50.
6) Stanhiser J., Jukic AMZ., McConnaughey D.R., Steiner AZ (2022). Omega-3 fatty acid supplementation and fecundability. Hum Reprod, 37(5):1037-1046.
7) Vitagliano A., Petre G.C., Francini-Pesenti F., De Toni L., Di Nisio A., Grande G., Foresta C., Garolla A (2021). Dietary Supplements for Female Infertility: A Critical Review of Their Composition. Nutrients, 13(10):3552.
8) Boedt T., Vanhove AC., Vercoe MA., Matthys C., Dancet E., Lie Fong S (2021). Preconception lifestyle advice for people with infertility. Cochrane Database Syst Rev, 4(4):CD008189.
9) Farahi N., Zolotor A (2014). Recommendations for preconception counseling and care. Am Fam Physician. 2013 Oct 15;88(8):499-506. Erratum in: Am Fam Physician, 89(5):316.
10) Xiang C., Luo J., Yang G., Sun M., Liu H., Yang Q., Ouyang Y., Xi Y., Yong C., Khan M.J., Lin Q (2022). Dietary Supplement Use during Pregnancy: Perceptions versus Reality. Int J Environ Res Public Health, 19(7):4063.
11) Urman B., Oktem O (2014). Food and drug supplements to improve fertility outcomes. Semin Reprod Med, 32(4):245-52.
12) Genario R., Morello E., Bueno A.A., Santos HO (2019). The usefulness of melatonin in the field of obstetrics and gynecology. Pharmacol Res, 147:104337.
13) Mintziori G., Mousiolis A., Duntas L.H., Goulis DG (2020). Evidence for a manifold role of selenium in infertility. Hormones (Athens), 19(1):55-59.
14) Kermack A.J., Macklon NS (2015). Nutritional supplementation and artificial reproductive technique (ART) outcomes. Reprod Fertil Dev, 27(4):677-83.
15) Trop-Steinberg S., Heifetz EM., Azar Y., Kafka I., Weintraub A., Gal M (2023). Omega-3 Intake Improves Clinical Pregnancy Rate in Polycystic Ovary Syndrome Patients: A Double-Blind, Randomized Study. Isr Med Assoc J, 25(2):131-136.
16) Vander Borght M., Wyns C (2018). Fertility and infertility: Definition and epidemiology. Clin Biochem, 62:2-10.
17) Skoracka K., Ratajczak A.E., Rychter A.M., Dobrowolska A., Krela-Kaźmierczak I (2021). Female Fertility and the Nutritional Approach: The Most Essential Aspects. Adv Nutr, 12(6):2372-2386.
18) Luk J., Torrealday S., Neal Perry G., Pal L (2012). Relevance of vitamin D in reproduction. Hum Reprod, 27(10):3015-27.