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The influence of diet and oral supplementation on female infertility

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Key words: infertility, pregnancy, female infertility, diet, lifestyle

Abstract:

Infertility is an increasing concern among young couples attempting to conceive. Despite advances in medical treatments, including ovarian stimulation, intrauterine insemination, and in vitro fertilization, the prevalence of infertility remains high, suggesting that multiple factors may interfere with reproductive success. Recent research has highlighted the important role of dietary patterns and oral supplementation in fertility, influencing metabolic health, inflammation, ovulation, and oocyte quality. Modifiable risk factors such as stress, obesity, and unhealthy diet have been associated with reduced pregnancy success. Given their potential impact, further investigation into diet and lifestyle interventions is essential to improve reproductive outcomes.

Key words: infertility, pregnancy, female infertility

The aim of the work: The objective of this review is to evaluate the impact of diet and lifestyle factors in infertility by compiling evidence on the most frequently studied and utilized substances.

Materials and Methods:

This paper presents a narrative review of the scientific literature assessing the role of diet and nutrition in management of infertility. The aim of this work was to collect and analyze scientific data regarding diet and lifestyle factors that contribute to infertility. The literature is focused on the main nutrients and its impct on women’s fecundity. Scientific articles were retrieved from electronic databases, including PubMed and Google Scholar, as well as from publicly available websites dedicated to the dissemination of reliable medical and scientific information. The analysis included preclinical studies, clinical trials, systematic reviews, and meta-analyses. The literature review and article selection process were conducted in December 2025.

Introduction:

Infertility is defined as the failure to achieve a clinical pregnancy after at least 12 months of regular, unprotected sexual intercourse. It is recognized as a disease by the World Health Organization and affects approximately 15% of couples of reproductive age worldwide. Female infertility is a multifactorial condition influenced by genetic, hormonal, metabolic, environmental, and lifestyle-related factors. While advances in assisted reproductive technologies have significantly improved treatment outcomes, the persistently high prevalence of infertility underscores the importance of identifying modifiable determinants that may enhance reproductive success.

Among these determinants, diet and lifestyle have gained increasing attention due to their profound effects on metabolic health, endocrine regulation, inflammatory status, and oxidative balance—all of which play critical roles in reproductive physiology. Emerging evidence suggests that dietary patterns and nutrient intake before conception may influence ovulation, oocyte quality, implantation, and pregnancy maintenance. Understanding the role of nutrition in female fertility may therefore provide opportunities for preventive and adjunctive strategies in infertility management.

Diet and dietary pattern:

Dietary patterns may represent one of the most important modifiable factors influencing fertility, as individuals consume whole meals rather than isolated nutrients. While evidence on the role of pre-conception diet and fertility remains limited, available data consistently suggest a beneficial effect of overall healthy dietary patterns on reproductive outcomes.

Prospective cohort studies from the Nurses ’Health Study II (NHS-II) and the Seguimiento Universidad de Navarra (SUN) project have demonstrated that greater adherence to fertility-focused or Mediterranean-style dietary patterns prior to conception is associated with a lower risk of infertility. Similarly, studies conducted in populations undergoing assisted reproductive technologies (ART) have shown that higher adherence to the Mediterranean diet before treatment is associated with an increased likelihood of achieving pregnancy and live birth following in vitro fertilization (IVF).

The Mediterranean diet (MD) is widely regarded as one of the healthiest dietary patterns due to its emphasis on plant-based foods, including fruits, vegetables, legumes, whole grains, nuts, and seeds; its use of olive oil as the primary source of fat; regular consumption of fatty fish; limited intake of red and processed meats; minimal food processing; and low consumption of simple sugars. Adherence to this dietary pattern has been consistently associated with reduced risk of cardiovascular disease, insulin resistance, type 2 diabetes, and all-cause mortality, as well as improved pregnancy outcomes.

Although the precise contribution of individual food groups to fertility is not fully understood, inflammation is recognized as a key biological pathway linking diet to reproductive health. Chronic low-grade inflammation has been shown to disrupt hypothalamic–pituitary–ovarian axis function, impair follicular development and ovulation, alter endometrial receptivity, and increase the risk of implantation failure and miscarriage (Weiss et al., 2011). The Mediterranean diet exerts strong anti-inflammatory effects through multiple mechanisms, including high intake of antioxidants, polyphenols, omega-3 fatty acids, and monounsaturated fats, alongside reduced consumption of pro-inflammatory components such as trans fats and refined carbohydrates.

At the molecular level, adherence to the Mediterranean diet has been associated with lower circulating levels of inflammatory markers, including C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α). These anti-inflammatory effects may contribute to improved ovarian function, enhanced oocyte quality, and better embryo development. Furthermore, the diet's favorable effects on insulin sensitivity and lipid metabolism may reduce hyperinsulinemia and androgen excess—key factors implicated in ovulatory dysfunction and conditions such as polycystic ovary syndrome (PCOS). In addition, the Mediterranean diet provides key micronutrients involved in reproductive physiology, including folates, vitamin B12, vitamin D, iron, and zinc, which support steroidogenesis, DNA synthesis, epigenetic regulation, and early embryonic development. The synergistic effects of these nutrients, rather than isolated components, likely explain the observed benefits of dietary patterns over single-nutrient interventions.

In conclusion, although further research is needed to fully elucidate the specific dietary components and mechanisms involved, current evidence supports the Mediterranean diet as a favorable dietary pattern for women attempting to conceive. Its anti-inflammatory, insulin-sensitizing, and hormone-regulating properties suggest that it may play an important role in optimizing fertility and reproductive outcomes.

Protein:

Dietary protein represents a fundamental component of a healthy diet and plays an important role in female reproductive health. Adequate protein intake is essential for women of reproductive age, with recommended intakes generally ranging between 1.0 and 2.0 g/kg body weight per day. Optimal protein consumption supports carbohydrate metabolism and insulin homeostasis, thereby reducing the risk of metabolic disturbances that may adversely affect fertility.

Beyond total protein intake, the source of dietary protein appears to be particularly relevant for ovulatory function. Higher consumption of animal-derived protein has been associated with an increased risk of anovulatory infertility (Chavarro et al., 2008). In contrast, plant-based protein intake is associated with a more favorable metabolic profile, including a lower postprandial insulin response, which may contribute to improved reproductive outcomes.

Moreover, diets rich in animal protein are often accompanied by higher intakes of saturated fatty acids, which may further exacerbate metabolic and hormonal dysregulation.

Evidence from epidemiological studies supports these observations. In a study involving 2,217 women, including those with anovulatory polycystic ovary syndrome (PCOS) and women with normal ovulatory function, ovulating women were found to consume a lower proportion of meat compared with those who were anovulatory. Additionally, substituting approximately 5% of total daily energy intake from carbohydrates with plant-based protein was associated with a 43% reduction in the risk of ovulatory infertility (Chavarro et al., 2008).

Fish consumption represents a unique category of dietary protein. Although concerns have been raised regarding environmental contaminants in fish, current evidence suggests that the reproductive benefits of fish intake outweigh the potential risks. Studies have demonstrated that replacing other protein-rich foods such as eggs, legumes, soy, nuts, or other meats with fish is associated with higher odds of live birth, particularly when fish replaces processed meats.

Soy protein has long been a topic of debate due to its isoflavone content, which has been shown in animal studies to exert estrogenic effects and potentially disrupt endocrine function. However, findings from human studies do not support these concerns. On the contrary, some clinical studies suggest that soy isoflavones may improve reproductive outcomes. For example, increased intake of isoflavones has been associated with higher rates of positive pregnancy outcomes among women undergoing assisted reproductive technologies (ART) (Vanegas et al., 2015).

In summary, current evidence indicates that maintaining an adequate total protein intake is important for women attempting to conceive. Furthermore, emphasizing plant-based protein sources while limiting excessive intake of animal protein particularly processed meats may offer additional benefits for ovulatory function and overall fertility.

Carbohydrates:

When considering carbohydrate intake, the most relevant aspects in relation to female fertility are the glycemic index (GI) and glycemic load. Diets characterized by a high GI are associated with postprandial hyperglycemia and hyperinsulinemia, which may promote insulin resistance, type 2 diabetes, and increased oxidative stress mechanisms that can negatively affect reproductive function.

Insulin plays a central role not only in metabolic regulation but also in reproductive physiology. Elevated insulin levels are associated with increased concentrations of insulin-like growth factor I (IGF-I) and androgens, which may disrupt normal folliculogenesis and impair oocyte maturation. In addition, insulin regulates the hepatic production of sex hormone–binding globulin (SHBG), thereby influencing the bioavailability of circulating sex hormones. Alterations in these pathways may contribute to ovulatory dysfunction and reduced fertility.

Evidence from large epidemiological studies supports the adverse effects of high carbohydrate intake and high-GI diets on fertility outcomes. In a large prospective cohort study including 18,555 women without a prior history of infertility who either became pregnant or attempted to conceive during the study period, higher total carbohydrate intake and substitution of carbohydrates for dietary fats were associated with an increased risk of ovulatory infertility. Women in the highest quintile of total carbohydrate consumption had a 78% higher risk of infertility due to anovulation compared with those in the lowest quintile (Chavarro et al., 2009).

Subsequent studies have corroborated these findings, demonstrating that diets rich in high-GI foods and simple sugars are associated with lower chances of successful conception and pregnancy (Willis et al., 2020). Moreover, specific dietary sources of carbohydrates may further influence reproductive outcomes. Intake of carbonated, sugar-sweetened beverages independent of caffeine consumption has been shown to reduce the likelihood of successful outcomes following assisted reproductive technologies (ART) (Machtinger et al., 2017). Additionally, consumption of carbonated beverages has been linked to increased concentrations of free estradiol, which may contribute to hormonal imbalances affecting fertility (Shliep et al., 2013).

Overall, these findings suggest that both the quantity and quality of carbohydrate intake, particularly dietary GI and sources of simple sugars, play a significant role in female reproductive health. Emphasizing low-GI carbohydrate sources may therefore represent an important dietary strategy for improving fertility outcomes.

Fats:

Dietary fatty acids represent an important nutritional factor influencing female fertility. Fats constitute a heterogeneous group of nutrients, and it is essential to distinguish between saturated fatty acids (SFAs), trans fatty acids (TFAs), and unsaturated fatty acids, including monounsaturated and polyunsaturated fatty acids (PUFAs). Both excessive and insufficient fat intake may adversely affect reproductive function; however, accumulating evidence indicates that the quality and type of dietary fat are more important determinants of fertility than total fat intake alone.

Fatty acids play a critical role in reproductive physiology at the molecular level. They are integral components of cell membranes, where they influence membrane fluidity, receptor function, and signal transduction. In ovarian follicles, membrane lipid composition affects granulosa cell responsiveness to gonadotropins and regulates steroidogenic enzyme activity, which is essential for estrogen and progesterone synthesis. Fatty acids also serve as precursors for bioactive lipid mediators, including eicosanoids and prostaglandins, which regulate ovulation, luteal function, and endometrial receptivity.

Strong evidence demonstrates a detrimental effect of trans fatty acids on fertility. Even a modest increase in TFA intake approximately 2% of total energy intake has been associated with a significantly increased risk of ovulatory dysfunction and infertility (Chavarro et al., 2007). At the molecular level, TFAs promote chronic low-grade inflammation by activating nuclear factor kappa B (NF-κB) signaling pathways and increasing the production of pro-inflammatory cytokines. Additionally, TFAs impair insulin signaling by disrupting insulin receptor phosphorylation and downstream PI3K Akt pathways, leading to insulin resistance. These metabolic disturbances result in hyperinsulinemia, which stimulates ovarian androgen production and suppresses hepatic synthesis of sex hormone–binding globulin (SHBG), thereby increasing bioavailable androgens and impairing folliculogenesis. The main dietary sources of TFAs include fast food, processed red meat, salty snacks, sweets, and ultra-processed convenience foods.

In contrast, unsaturated fatty acids—particularly omega-3 PUFAs—exert anti-inflammatory and fertility-promoting effects. Omega-3 fatty acids, such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are essential for steroidogenesis and are incorporated into ovarian cell membranes, where they modulate membrane dynamics and receptor sensitivity. At the molecular level, omega-3 PUFAs serve as precursors for anti-inflammatory eicosanoids and specialized pro-resolving mediators, including resolvins and protectins, which counteract inflammatory signaling and reduce oxidative stress within the ovarian microenvironment.

Omega-3 fatty acids also influence reproductive hormone synthesis by regulating the expression and activity of key steroidogenic enzymes, including aromatase and 3β-hydroxysteroid dehydrogenase, thereby promoting adequate estrogen and progesterone production. Observational and clinical studies indicate that omega-3 intake is associated with improved oocyte maturation, enhanced embryo morphology, reduced risk of anovulation, and higher circulating progesterone concentrations. Consistent with these findings, fish consumption prior to in vitro fertilization (IVF) has been associated with improved embryo development and increased likelihood of pregnancy, whereas higher intake of red and processed meats shows an inverse association with fertility outcomes (Axmon et al., 2002).

Polyunsaturated fatty acids further contribute to fertility by modulating hypothalamic–pituitary–ovarian (HPO) axis function. PUFAs can influence the secretion and signaling of luteinizing hormone (LH) and follicle-stimulating hormone (FSH), thereby affecting follicular growth, oocyte quality, and ovulation induction. Moreover, PUFAs participate in intracellular signaling pathways involved in embryo implantation by regulating prostaglandin synthesis and integrin expression, which are crucial for endometrial receptivity and successful implantation.

In summary, dietary fatty acids influence female fertility through multiple molecular and physiological mechanisms. Limiting the intake of trans and saturated fats while increasing consumption of omega-3–rich foods, particularly oily fish, may promote hormonal balance, reduce inflammation, and support key reproductive processes such as ovulation, embryo development, and implantation.

Vitamin D:

Vitamin D deficiency has been associated with a wide range of diseases, including diabetes mellitus, multiple sclerosis, rheumatoid arthritis, and cardiovascular disease. In recent years, increasing attention has been paid to the role of vitamin D in human fertility. Both animal and human studies have demonstrated the presence of vitamin D receptors in reproductive tissues in both men and women, suggesting a direct role in reproductive function.

Recent research has focused particularly on the impact of vitamin D status in women undergoing assisted reproductive technologies (ART). A meta-analysis of 11 cohort studies involving approximately 2,700 women showed significantly higher live birth rates among vitamin D–sufficient women compared with those who were vitamin D–deficient or insufficient (odds ratio [OR]: 1.33; 95% CI: 1.08–1.65) (Chu et al., 2018).

Vitamin D may also influence fertility through its involvement in gynecological conditions such as polycystic ovary syndrome (PCOS) and endometriosis. In a cohort study of 49 women, higher serum levels of 25-

hydroxyvitamin D (25[OH]D) were moderately and inversely associated with the size of ovarian endometriomas ($r = -0.3$; $p = 0.03$), indicating that higher vitamin D levels were linked to smaller lesions (Ciavattini et al., 2017). Furthermore, a prospective comparative study including 135 women with endometriosis and 90 healthy controls found that vitamin D deficiency or insufficiency was significantly more prevalent in women with endometriosis than in controls (80% vs. 33.3%; $p < 0.001$) (Anastasi et al., 2017).

Vitamin D supplementation appears to have beneficial effects in women with PCOS. A meta-analysis reported that vitamin D supplementation, particularly when combined with metformin, improved menstrual cycle regulation compared with metformin alone (Fang et al., 2017). The same analysis demonstrated that vitamin D supplementation, administered in various doses, increased the number of dominant follicles (>14 mm) compared with placebo or metformin monotherapy.

Overall, vitamin D deficiency appears to be an independent factor contributing to female infertility. As evidence from human studies continues to grow, ensuring adequate vitamin D status in women with infertility may be an important component of clinical management. Nevertheless, further well-designed studies are required to fully clarify the underlying mechanisms and establish optimal supplementation strategies.

Antioxidants:

Antioxidants naturally present in colorful fruits and vegetables, nuts, seeds, cocoa, and green tea are well recognized for their role in neutralizing free radicals, delaying cellular aging, and supporting overall health. Despite these established benefits, current evidence does not conclusively support antioxidants as a key independent factor in improving female fertility or reducing infertility.

The biological rationale for studying antioxidants in the context of fertility is based on the role of oxidative stress in reproductive physiology. Reactive oxygen species (ROS) are produced during normal cellular metabolism and play essential physiological roles in follicular development, oocyte maturation, ovulation, and embryo implantation. However, excessive ROS production or inadequate antioxidant defense leads to oxidative stress, which can damage lipids, proteins, and DNA within reproductive tissues. In the ovarian microenvironment, oxidative stress may impair granulosa cell function, disrupt steroidogenesis, and compromise oocyte quality through mitochondrial dysfunction and DNA damage. During assisted reproductive technologies (ART), elevated oxidative stress in follicular fluid has been associated with reduced oocyte competence and impaired embryo development. Similarly, oxidative imbalance in the endometrium may interfere with implantation and early placentation.

Based on these mechanisms, antioxidant supplementation has been proposed as a potential strategy to improve reproductive outcomes. However, a comprehensive systematic review and meta-analysis published in 2013 evaluated the effects of antioxidant supplementation on women attempting to conceive and found no significant improvement in clinical pregnancy rates. This analysis included 13 randomized controlled trials involving 2,441 women and assessed various antioxidants, including pentoxifylline, L-arginine, melatonin, vitamin E, vitamin C, N-acetylcysteine (NAC), coenzyme Q10, and inositol. Antioxidant supplementation was not associated with increased clinical pregnancy rates compared with placebo or no/standard treatment (odds ratio [OR] 1.30; 95% CI 0.92–1.85; $p = 0.14$), with substantial heterogeneity between studies ($I^2 = 55\%$) and overall very low-quality evidence (Showell et al., 2013).

Nevertheless, several studies suggest that selected antioxidants may positively influence intermediate reproductive parameters. Melatonin has been associated with improved oocyte quality, likely due to its potent free radical–scavenging properties and its ability to protect oocytes from oxidative damage during follicular development (Espino et al., 2019). Improvements in embryo quality have also been reported with supplementation of melatonin and folic acid (Pacciarotti et al., 2016). Additionally, N-acetylcysteine has been shown to improve ovulation rates, particularly in women with polycystic ovary syndrome (PCOS) (Badawy et al., 2007), and increased pregnancy rates have been reported in selected populations receiving antioxidant supplementation (Ismail et al., 2014).

Importantly, the observed benefits of antioxidant supplementation appear to be dose-dependent and limited to minimal effective doses (mED). Many commercially available supplements marketed to women attempting to conceive fail to provide antioxidants at these effective concentrations, which may partly explain the inconsistent findings across studies. Moreover, excessive antioxidant intake may be counterproductive, as a certain level of ROS is required for normal reproductive signaling. Thus, maintaining redox balance rather than complete suppression of oxidative activity appears critical for optimal reproductive function.

In conclusion, while antioxidant supplementation alone does not appear to significantly improve clinical pregnancy rates, oxidative stress remains a relevant factor in female reproductive health. Further high-quality studies are needed to clarify which antioxidants, doses, and patient subgroups may benefit most. Regardless of supplementation, regular consumption of antioxidant-rich foods should be encouraged, as such dietary patterns support overall health and may indirectly contribute to reproductive well-being.

B Vitamins:

While the role of folate deficiency in the development of neural tube defects (NTDs) is well established, evidence regarding the effects of folate on female fertility is less consistent. Nevertheless, several observational and interventional studies suggest that adequate preconceptional folate intake may have a beneficial influence on reproductive outcomes.

At the molecular level, folate plays a critical role in one-carbon metabolism, which is essential for DNA synthesis, repair, and methylation. Adequate folate availability supports rapid cell division and genomic stability during folliculogenesis, oocyte maturation, and early embryonic development. Folate-dependent methylation reactions regulate gene expression through epigenetic mechanisms, including DNA methylation of genes involved in ovarian steroidogenesis, follicular development, and implantation. Folate deficiency may lead to aberrant DNA methylation patterns, impaired chromosomal segregation, and increased oxidative stress, thereby compromising oocyte quality and embryo viability.

Moreover, folate interacts closely with vitamin B12 in homocysteine metabolism. Elevated homocysteine levels, which may result from inadequate folate or B12 status, have been associated with endothelial dysfunction, impaired ovarian blood flow, and reduced oocyte competence. By lowering homocysteine concentrations, adequate folate intake may improve the ovarian microenvironment and endometrial receptivity, thereby enhancing implantation and pregnancy outcomes.

Early evidence supporting this association comes from a large Hungarian randomized controlled trial, which demonstrated that 71.3% of women who used a multivitamin supplement containing 800 µg of folic acid before pregnancy conceived, compared with 67.9% of women receiving placebo (Czeizel et al., 1996). Similarly, a smaller study of subfertile women reported that supplementation with 400 µg of folic acid for three months resulted in a higher pregnancy rate compared with placebo (26% vs. 10%, respectively) (Westphal et al., 2006).

Further support is provided by data from a large prospective cohort study that observed an inverse association between multivitamin use and ovulatory infertility. After multivariate adjustment, the relative risk (RR; 95% confidence interval [CI]) of ovulatory infertility was 0.88 (0.60–1.28) among women consuming two or fewer multivitamin tablets per week, 0.69 (0.51–0.95) among those consuming three to five tablets per week, and 0.59 (0.46–0.75) among women consuming six or more tablets per week, compared with non-users. Folic acid intake appeared to explain a substantial portion of this association (Chavarro et al., 2008).

Evidence from assisted reproductive technology (ART) populations further supports a potential role for folate in fertility. A Polish cohort study reported that women receiving folic acid supplementation prior to in vitro fertilization (IVF) treatment had better oocyte quality and a higher proportion of mature oocytes compared with women who did not receive supplementation (Szymański et al., 2003). Similarly, a U.S.-based cohort study of women undergoing IVF found that the probability of live birth was approximately 20% higher among women consuming more than 800 µg/day of folate compared with those consuming less than 400 µg/day (Gaskins et al., 2014). In the same cohort, women in the highest quartiles of serum folate and vitamin B12 concentrations had higher probabilities of live birth compared with those in the lowest quartiles, with odds ratios of 1.62 (95% CI 0.99–2.65) for folate and 2.04 (95% CI 1.14–3.62) for vitamin B12 (Gaskins et al., 2015).

Overall, the majority of available evidence suggests that higher preconceptional folate intake, particularly through supplementation, may increase a woman's likelihood of conceiving and achieving a successful pregnancy. While the precise mechanisms underlying these associations require further clarification, ensuring adequate folate status before conception remains a key component of nutritional recommendations for women planning pregnancy.

Caffeine:

Caffeine is a widely consumed dietary component and has been extensively investigated in relation to female fertility and reproductive outcomes. Despite numerous studies, the evidence regarding its impact on fecundability and infertility remains inconsistent, suggesting a complex and potentially dose-dependent relationship.

Early prospective research involving 104 healthy women attempting to conceive over a three-month period reported that women consuming more than one cup of coffee per day were approximately half as likely to conceive compared with those who consumed less caffeine (Wilcox et al., 1988). Similarly, a multicenter European study observed that higher caffeine intake was associated with a longer time to achieve the first pregnancy, indicating reduced fecundability among women with higher caffeine consumption (Bolumar et al., 1997). In contrast, more recent studies have reported neutral or even potentially beneficial associations at moderate intake levels. A prospective cohort study demonstrated that moderate caffeine consumption (400–700 mg/day) was associated with higher fecundability compared with both lower intake levels and heavy consumption, whereas high caffeine intake (>700 mg/day), particularly among male partners, was associated with reduced fecundability (Florack et al., 1994). In women undergoing assisted reproductive technology (ART), low to moderate caffeine intake in the year preceding treatment was not associated with adverse reproductive outcomes, including implantation, clinical pregnancy, or live birth rates (Abadia et al., 2017).

Several biological mechanisms have been proposed to explain the potential effects of caffeine on female fertility. Caffeine readily crosses biological membranes and may influence reproductive physiology through its effects on the central nervous system, endocrine function, and uterine environment. At the molecular level, caffeine acts as a non-selective adenosine receptor antagonist, which may alter hypothalamic–pituitary–ovarian (HPO) axis signaling and subsequently affect gonadotropin release. Additionally, caffeine can increase circulating catecholamine levels and activate the hypothalamic–pituitary–adrenal (HPA) axis, potentially influencing cortisol secretion and disrupting reproductive hormone balance.

Caffeine has also been shown to affect estrogen metabolism by inducing hepatic cytochrome P450 enzymes, particularly CYP1A2, which may alter the clearance and bioavailability of estrogens. Furthermore, caffeine may influence uterine and placental blood flow through its vasoconstrictive properties, potentially impairing endometrial receptivity and embryo implantation. Experimental studies suggest that high caffeine exposure may increase intracellular cyclic adenosine monophosphate (cAMP) levels and calcium signaling, which could affect oocyte maturation and early embryonic development.

Despite these plausible mechanisms, the inconsistent findings across epidemiological studies suggest that the effects of caffeine on fertility may depend on dosage, timing of exposure, individual metabolic differences, and interactions with other lifestyle factors. Moderate caffeine consumption may not exert clinically meaningful adverse effects, whereas excessive intake could disrupt hormonal and vascular processes critical for successful conception.

In summary, although biological mechanisms exist through which caffeine could influence female fertility, current human evidence remains inconclusive. Given widespread caffeine consumption and evolving dietary patterns, further well-designed prospective studies are warranted to clarify safe intake thresholds for women attempting to conceive.

Summary:

Infertility affects a significant proportion of couples of reproductive age and remains highly prevalent despite advances in medical and assisted reproductive treatments. Growing evidence indicates that diet and lifestyle factors play an important role in female fertility by influencing metabolic health, inflammation, hormonal regulation, ovulation, oocyte quality, implantation, and pregnancy outcomes.

Healthy dietary patterns, particularly the Mediterranean diet, are consistently associated with improved fertility and better outcomes in both natural conception and assisted reproductive technologies. These benefits are largely attributed to anti-inflammatory, antioxidant, and insulin-sensitizing effects, as well as adequate intake of key micronutrients involved in reproductive physiology.

Macronutrient quality appears more important than quantity. Plant-based protein sources are associated with a lower risk of ovulatory infertility compared with animal and processed meats. High–glycemic index carbohydrates and excessive intake of simple sugars are linked to insulin resistance, hormonal imbalance, and increased risk of anovulation, whereas low-GI carbohydrate sources are more favorable. Fat quality is critical: trans and saturated fats negatively affect fertility through inflammatory and metabolic pathways, while omega-3 polyunsaturated fatty acids support steroidogenesis, oocyte maturation, embryo development, and implantation.

Micronutrients also play a significant role. Adequate vitamin D status is associated with improved reproductive outcomes, particularly in women undergoing assisted reproduction and those with PCOS or endometriosis. B vitamins, especially folate and vitamin B12, support DNA synthesis, epigenetic regulation, and homocysteine metabolism, and higher preconceptional intake is linked to improved ovulatory function and higher pregnancy and live birth rates.

Although oxidative stress is implicated in infertility, evidence supporting routine antioxidant supplementation remains inconsistent, with benefits appearing limited to specific compounds, doses, and patient populations. Caffeine intake shows a dose-dependent and inconclusive relationship with fertility, with moderate consumption generally not associated with adverse outcomes.

Overall, current evidence supports the role of diet and lifestyle as modifiable factors in female fertility. Emphasizing healthy dietary patterns rather than isolated nutrients may represent an effective strategy to optimize reproductive health and improve fertility outcomes, although further high-quality research is needed to refine dietary recommendations.

AI

AI was utilized for two specific purposes in this research. Text analysis of clinical reasoning narratives to identify linguistic patterns associated with specific logical fallacies. Assistance in refining the academic English language of the manuscript, ensuring clarity, consistency and adherence to scientific writing standards. AI were used for additional linguistic refinement of the research manuscript, ensuring proper English grammar, style, and clarity in the presentation of results. It is important to emphasize that all AI tools were used strictly as assistive instruments under human supervision. The final interpretation of results, classification of errors, and conclusions were determined by human experts in clinical medicine and formal logic. The AI tools served primarily to enhance efficiency in data processing, pattern recognition, and linguistic refinement, rather than replacing human judgment in the analytical process.

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