International Journal of Nutrition Sciences

Journal Home Page: ijns.sums.ac.ir

Review Article

Is Western Diet Harmful for Male Fertility? A Review of Fact or Fiction

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ARTICLE INFO

Keywords:
Western diet
Male fertility
Reproduction
Obesity

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Received: January 5, 2025
Revised: March 30, 2025
Accepted: April 8, 2025

ABSTRACT

Diet plays a crucial role in male reproductive potential. The global fertility rate has been declining, and this may be partly attributed to the changes in diet worldwide. This article aims to provide a summary of the existing knowledge on the molecular mechanisms that contribute to male infertility and reproductive issues in men who follow a western diet. It also discusses the key effects of the western diet on fertility. In the western diet, there is an excessive intake of lipids that can lead to elevated levels of cholesterol and fatty acids. This lipid overload contributes to obesity, which in turn disrupts male fertility through mechanisms such as androgenesis disruption, inflammation, and increased temperature. Additionally, carbohydrates in the western diet, particularly those with high glycemic index, are primarily responsible for insulin resistance and hyperglycemia. Insulin resistance reduces the ability of sperm to absorb glucose, thereby impairing their motility and metabolism. In conclusion, the western diet is not an optimal nutritional pattern for male fertility potential; while a significant factor driving the increased adoption of the western diet can be the profit-driven practices of large food processing companies that heavily promote processed foods and sugary beverages. However, it is the responsibility of health authorities in developed and developing countries to educate society about the detrimental effect of an unhealthy diet on fertility in order to prevent a decline in the fertility among younger population.

Please cite this article as: Pourmasumi S, Heydari Khoormizi SM, Mehrabian M. Is Western Diet Harmful for Male Fertility? A Review of Fact or Fiction. Int J Nutr Sci. 2025;10(3):doi:

Introduction

The Western diet (WD) is characterized by the consumption of processed, fried, and packaged foods, as well as processed red meat and animal products such as sausage and hamburger. It also includes high-sugar drinks, sweets, candies, and high-fat dairy products like butter, cream, whole milk, and ice cream. Moreover, this diet lacks essential nutrients and healthy foods such as nuts, fresh fruits, and seafood proteins like fish and shrimp (1). In developed countries, particularly in the United States of America (USA), this diet is widely regarded as the predominant eating pattern (2). The WD has attracted considerable attention due to its deleterious effects on health status, particularly in risk of different diseases such as

metabolic syndrome, diabetes, cardiovascular diseases, etc. (3, 4). Nevertheless, despite its unhealthy profile, WD is becoming increasingly popular as more cultures abandon their usual cautious diets in favor of richer and fattier diets. The global fast food culture has increased access to high-calorie foods, which has changed the composition of diet-related morbidity and mortality in areas where nutrient-dense foods were previously scarce (5). Mohajan *et al.* reported worldwide deaths from obesity exceeded deaths due to hunger (6).

There is a strong connection between a person's nutritional status and reproductive health. In terms of physical activity, dietary intake, body weight and body composition, lifestyle appears to have a significant impact on reproductive health (7). Fertility is particularly influenced by quantitative and qualitative nutritional characteristics. Research shows that an excessively high or low calorie diet can lead to physiological disruptions in reproductive processes such as sperm capacity and ovulation, thereby increasing the risk of infertility (8, 9). Infertility is a common clinical issue affecting both genders, while about half of the infertility cases are male-related. Infertility is a condition characterized by the inability to achieve pregnancy after 12 months or more of regular unprotected sexual intercourse. It can result from factors related to either the male or female partner, or it may be due to unexplained reasons. Male infertility is divided into various categories including pretesticular and testicular (NOA), and obstructive azoospermia (OA, post-testicular). Many factors can impact spermatogenesis (10-12).

The question of whether nutrients can actively inhibit fertility is an important scientific issue that show the impact of diet on reproductive health (9). Reproductive processes can be influenced by the amount and type of carbohydrates consumed. An association between decreased insulin sensitivity (13) and decreased of sex hormone binding globulin (SHBG) levels (14) as well as reduced androgen synthesis (8) that has been observed in infertile and diabetic patients. Consuming high glycemic products, on the other hand, can lead to increased insulin defects, blood lipids and reactive oxygen species (ROS), all of which are associated with lower reproduction potential (8, 9). Consuming proteins in the diet may have varying effects on reproductive health based on the source of protein. Plant proteins have been found to enhance reproductive potential, while other protein sources (such as red and animal meat) have been linked to decreased fertility in both males and females (15).

According to current data, reproduction and metabolism are closely related (8, 16). The eating habits of industrialized nations today focus on consuming large amounts of unhealthy fats while consuming high energy intake, which promotes the formation of white adipose tissue (WAT) (1, 17). In addition, the high concentrations of obese toxins in WD accelerate obesity and increase the storage of fat-soluble toxins in the body (18). The molecular processes that regulate hunger and energy intake are then disrupted by unbalanced consumption of energy-dense foods. Fat and intestinal hormones mediate these processes (19). Adipose and intestinal tissues are excellent for detecting energy status, and certain hormones derived from these tissues that have been found to control reproduction-related processes (via the Hypothalamic-Pituitary-Gonadal (HPG) axis). Therefore, any changes to adipose and intestinal tissues endocrine secretion can potentially have an impact on reproduction potential in men (20).

Knowledge of the molecular causes of the poor reproductive outcomes of these people could enable better recommendations and advice on behavior modification of these people to reduce the influence of these factors (21). Next, novel interventions that specifically assess and identify the main molecular mechanisms could open new avenues for pharmaceutical treatment and prevention that would helpful to increase the fertility outcomes in infertile cases (21). So the main aim of this review was to summarize latest knowledge about molecular mechanisms underlying decreased reproductive potential in men following a WD, as well as the key effects of WD on fertility (Figure 1).

Materials and Methods

The aim of this study was to conduct a comprehensive review of the current literature on the WD and its impact on male fertility. We searched various scientific databases, including PubMed, Cochrane Library, Web of Science, and Scopus, using keywords such as male infertility, testis, obesity, adipose tissue, lipids, and Western diet. We carefully evaluated the results and selected relevant papers for inclusion. Our criteria encompassed full-text studies, cohort studies, clinical trials, reviews, and meta-analyses, while we excluded studies consisting solely of abstracts, in-press studies, other types of infertility (such as female infertility), and studies focused on diets unrelated to the WD. After screening the final selection of studies, we chose only those pertinent to our topics of interest for review. During the literature search, we observed that most existing researches primarily focused on obesity and adipose cells as sources of hormones.

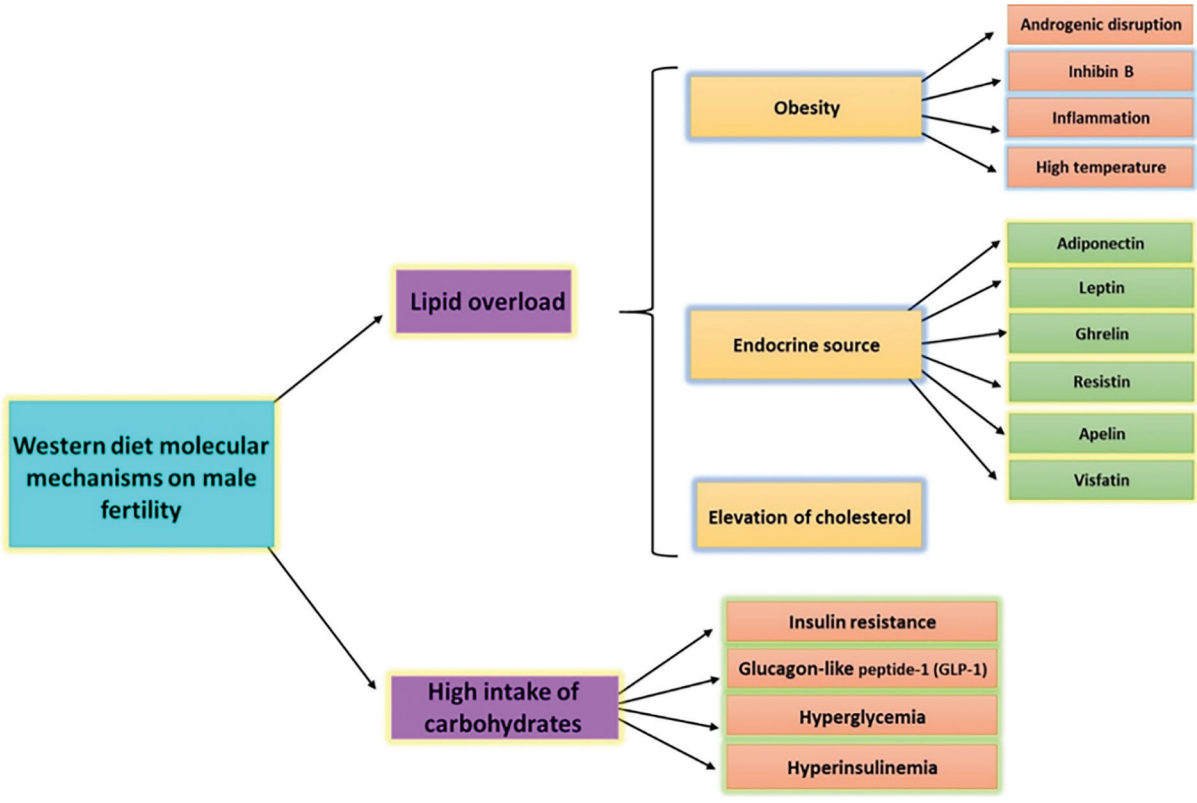

Figure 1: Structural and classification of Western diet molecular mechanisms in male infertility.

Therefore, after defining male fertility and the WD, we examined obesity as a major consequence of the WD and then explored the mechanisms through which the WD diet may impact fertility potential.

Male Fertility

Infertility affects 186 million individuals worldwide, with male partners accounting for nearly half of these cases (11, 12, 22). The undertaken researches indicate that male infertility impacts approximately 10% to 15% of men in the United States who are attempting to conceive (23). In-depth studies further reveal that male factors contribute to infertility in 40-60% of cases (11, 12). Currently, advancements in industry have led to an increase in andrological disorders and structural issues within the male reproductive system. The processes of spermatogenesis, fertility, and male infertility are complex, and any changes in the male reproductive system can significantly influence fertility. It was shown that both the quantity and quality of spermatogenesis in men of reproductive age have decreased by nearly 50%. Therefore, addressing the issue of male infertility is essential (11, 12). The roots of male infertility often trace back to childhood. Many issues affecting boys go unnoticed and untreated until they reach reproductive age. If identified at this stage, these conditions can become so severe that reversal is nearly impossible (11, 12). Additionally, male infertility can stem from reduced testosterone production in the testicles, decreased sperm production, irregular sperm function, or blockages obstructing sperm delivery. Factors such as diseases, injuries, chronic health issues, lifestyle choices, and environmental influences can all contribute to male infertility (23, 24).

Other contributing factors include overweight or obesity, being 40 years or older, exposure to radiation, environmental pollutants (like lead, calcium, pesticides, or mercury), and the use of tobacco, marijuana, or alcohol. Furthermore, varicoceles may also play a role in male infertility. Given these factors, assessing male reproductive health is a critical area of study. It is vital not only to monitor the reproductive well-being of the population but also for developing comprehensive strategies aimed at the early detection and management of male reproductive issues (24, 25).

Western Diet

The WD pattern represents a modern eating style characterized by a high intake of packaged foods, refined grains, red and processed meats, sugary beverages, sweets, fried foods, mass-produced animal products, butter and other rich dairy products, eggs, potatoes, and corn (including high-fructose corn syrup). This diet is typically high in added sugars, accounting for over 13% of daily caloric intake, and saturated fats. In contrast, it includes minimal consumption of fruits, vegetables, whole

grains, grass-fed animal products, fish, nuts, and seeds (1). Unlike the "prudent pattern diet," which emphasizes higher amounts of fruits, vegetables, whole grains, and poultry, the WD pattern is associated with increased risks of cardiovascular disease and obesity (26). The contemporary WD emerged after the industrial revolution, which introduced new food processing techniques. This led to the incorporation of cereals, refined sugars, and refined vegetable oils into the diet, alongside an increase in the fat content of domesticated meats. Recently, food manufacturers have also begun substituting sugar with high-fructose corn syrup (27). The WD significantly impacts health, particularly concerning obesity, inflammation, and chronic diseases. This eating pattern is increasingly prevalent around the world and is linked to numerous health issues, including metabolic syndrome, heart disease, and infertility (1, 28).

Obesity

Elevated blood levels of lipids and/or lipoproteins, which can lead to hyperlipidemia, indicate obesity (29). Tissue disorders and cell damage in obese men are mainly caused by lipotoxicity; while obesity is one of the main causes for several diseases such as diabetes, cancer, cardiovascular diseases and neurological disorders. It also occurs as a result of a combination of other risk factors (30). Other comorbidities associated with these diseases include hyperinsulinemia, dyslipidemia, hypercholesterolemia, hyperleptinemia, hypertension, hyperglycemia, chronic inflammation, and impaired reproductive abilities .(30)

To measure obesity, the body mass index (BMI) is used, which calculates body weight per height. Adults can be classified as overweight or obese based on their BMI. It is calculated by dividing the square of a person's height (measured in meters/m^2) by their body weight (measured in kilograms) (31).

Obesity is defined by the World Health Organization (WHO) as a BMI of 30 kg/m^2 or more, and overweight is defined as a BMI of 25 kg/m^2 or more. However, these limits may change depending on a person's race and ethnicity. Asians are considered obese if their BMI is 27.5 kg/m^2 or more. The aforementioned can be applied to non-Asians too (31). Nearly 2,000,000 adults (over the age of 18 years) worldwide or 39% of the adult population were classified as overweight or obese in 2016 according to WHO statistics and More than 650 million of them were classified as obese (6). Obese adult males have higher rates of poor reproductive outcomes, including infertility, in tandem with rising obesity prevalence. It was reported that the azoospermia and oligozoospermia risk in the obese men is higher compared to men of normal weight (32). Numerous variables have been proven to influence an obese person's ability to conceive. These include effects on intracellular enzymes, increased levels of oxidative stress or inflammatory mediators, endocrine factors, and genetic or epigenetic changes that affect spermatogenesis and sperm function (11, 12) (Figure 1).

Mechanisms

One of the risk factors for infertility is male obesity. In combination with other minor risk factors, it can affect fertility (32). Obesity can affect sexual performance or reduce libido, which can affect fertility too (7). Additionally, researches revealed a link between obesity and erectile dysfunction (33). The role of several hormones related to obesity has been discussed in next sections to provide readers with a better understanding of how obesity affects male fertility and semen quality. These hormones, which are essential for controlling male reproductive processes, include adiponectin, obestatin, ghrelin, leptin, etc.

Androgenic disruption

Obese men were found to have higher levels of estrogen and lower levels of SHBG and total testosterone (T) (34). Numerous studies have shown a positive correlation with estrogen and a negative correlation with testosterone in relation to obesity (12, 34). Levels of follicle stimulating hormone (FSH) and inhibin B are also lower in obese male populations (35). The overactivity of the cytochrome P450 enzyme aromatase in obese men could be a reason for these results (36). White adipose tissue produces this enzyme in excess, exceeding that of Leydig cells. It contributes to the high estrogen levels in overweight men by converting androgens into estrogens (37). Because estrogen has a stronger biological effect than testosterone, disruptions in sex hormones can affect male reproductive functions. Testicular functions can be significantly disrupted by even a small increase in plasma estrogen levels (38). On the other hand, normal spermatogenesis and steroidogenesis can also be impaired by a complete decrease in estrogen levels in the testes (39).

Because the male hypothalamus has estrogen receptors, it is possible that obese men's increased estrogen level can cause a negative feedback loop that lowers testosterone level. This prevents the release of luteinizing hormone (LH) and FSH following the release of pulsatile gonadotropin-releasing hormone (GnRH) (40). In addition to estrogen, inhibin B is another hormone that contributes to feedback

inhibition of FSH production. This growth-like factor not only stimulates testosterone synthesis by Leydig cells, but is also secreted by Sertoli cells. Obese men may have suppressed inhibin B production due to direct disruption of Sertoli cells through other mechanisms or increased estrogen levels (41) (Figure 1).

Inhibin B

Inhibin B is a protein composed of two subunits (alpha and beta) that is produced and secreted by Sertoli cells prior to puberty. Its exact location of secretion in adult men remains unknown (42). Both FSH and LH levels regulate inhibin B, which uses a negative feedback mechanism to control the production of FSH. Sperm production, testicular volume, and the amount of inhibin B in the bloodstream are all positively correlated. For this reason, inhibin B is a useful marker for the reproductive system in men (43). It is believed that Inhibin B is a molecular marker for Sertoli cells, which support spermatogenesis nutritional requirements and physical growth. It is a growth-like factor secreted by Sertoli cells that causes Leydig cells to secrete more testosterone and suppresses the secretion of FSH (44).

Poor inhibin B blood levels are associated with defective spermatogenesis (45). It was shown that in men with cryptorchidism, the level of Inhibin B is lower than normal cases as the level of Inhibin B can be a good sign for diagnosis of testicular dysfunction and a decreases in fertility potential (46). In conclusion, Inhibin B is an effective sign of hypogonadotropic and relative hypogonadism. By the enzyme aromatase, which is present in increased fatty tissue, Inhibin B promotes the conversion of testosterone to estradiol (E2) (Figure 1).

Inflammation

The level of systemic inflammation is a crucial factor in the different mechanisms that harm sperm in obese men. Obesity plays a significant role in increasing the levels of ROS in the body, which is linked to elevated production of pro-inflammatory cytokines like tumor necrosis factor alpha (TNF-α) and interleukin-6 (IL-6). These cytokines can result in a chronic and mild inflammatory condition (16). Obese patients have hypertrophic adipocytes that secrete high levels of TNFα. This occurs because the adipocytes stimulate local macrophages that use the non-esterified fatty acids (NEFA) (47). As a result, the adipocytes produce more NEFA, acute phase proteins, pro-inflammatory cytokines [such as interleukin 1ß (IL1β) and IL6], and chemokines [such as monocyte attracting protein-1 (MCP-1) or C-C motif chemokine ligand-2 (CCL2)] (47). These chemokines attract additional monocytes and macrophages to the adipose tissue, and create a vicious cycle that increases inflammation in the adipose tissue and ultimately leads to a low-grade inflammatory state throughout the body (47) (Figure 1).

High Temperature

Aside from hormonal imbalances, there has been extensive discussion about the negative consequences of accumulating fat in the thigh and suprapubic area on spermatogenesis. This fat accumulation raises the temperature of the scrotum, which in turn affects sperm production (48) Obesity can lead to oxidative stress, resulting in damage or reduction of sperm, which ultimately contributes to male infertility (49). The accumulation of fat is closely associated with heightened levels of oxidative stress and increased lipid peroxidation (50) (Figure 1).

Endocrine Source

Currently, adipose tissue is acknowledged as an important hormonal secreted tissue that generates various peptide hormones known as adipokines. Examples of these adipokines include leptin, adiponectin, resistin, ghrelin, orexin, and obestatin (51). In addition, adipose tissue secretes other chemicals such as cytokines and chemokines (52). Under normal physiological conditions, adipose tissue produces molecules that help maintain body homeostasis and can also affect the immune system (53). In obese men, adipokines can disrupt normal hormone regulation related to reproduction (54). It has been suggested that adipokines, both directly and indirectly, may be responsible for decreased fertility potential in infertile men (51). Adipokines directly regulate the steroidogenic genes expression (51). Scientific studies have shown that the development of chronic low-grade inflammation is caused by adipokine and cytokine pathways, leading to various chronic complications (54). Hypertrophic adipocytes, which are enlarged fat cells, have the ability to trigger inflammation and contribute to insulin resistance (47) (Figure 1).

Adiponectin

The hormone adiponectin, secreted abundantly by adipose tissue, has important roles in regulating glucose and lipid metabolism. During starvation, adiponectin production increases, and in obese individuals, it is inversely related to visceral adiposity and BMI (55). Adiponectin also enhances insulin sensitivity, and lower levels of adiponectin are associated with higher insulin resistance (56). Circulating levels of adiponectin are inversely proportional to testosterone level (57). Interestingly, in obese males with low

serum testosterone concentrations, adiponectin level is paradoxically elevated (58). Recently, it was shown that GnRH level is affected by adiponectin in chickens through the AMP-activated protein kinase (AMPK) and phosphoinositide 3-kinases (PI3Ks) signaling pathways (59). This inhibition affects the reproductive axis and can lead to infertility.

Leptin

The significance role of leptin, on reproductive function in men was demonstrated before (60, 61). Leptin has multiple effects on the HPT axis. It influences the secretion rate of gonadotropins and control the steroidogenesis pathways by straight effects on Leydig cells (LCs) leptin receptors (61). A relationship was demonstrated between high levels of leptin and defects in the spermatogenesis process that, led to a decrease in fertility. It is possible that leptin is responsible for suppressing gonadotropin secretion, which in turn negatively affects sperm quality (62). Moreover, leptin resistance, exacerbated by intake of the unhealthy diet can contribute to dysfunction of the HPT axis and impairment of the LCs, leading to androgen deficiency (63). Interestingly, a deficiency of leptin can also have a detrimental effect on sperm quality; while it was shown that *in vitro* administration of physiological doses of leptin can stimulate the sperm motility (58, 64).

Although it has been documented that leptin plays an important role in regulating fertility in both males and females at physiological levels, while high levels of leptin have a negative impact on reproduction activity. During obesity, adipose tissue secretes excessive amounts of leptin, which leads to a lack of response from the HPT axis to leptin signals. This resistance is likely caused by the over-activation of several regulatory factors, including suppressor of cytokine signaling 3 (SOCS3), protein tyrosine phosphatase 1B (PTP1B), and T cell protein tyrosine phosphatase (TCPTP) (65).

Ghrelin

Ghrelin, like leptin, also has a major impact on male fertility. It influences reproductive processes through the HPT axis (66). Ghrelin was illustrated to have negative effect on secretion rate of GnRH as a hormone involved in reproduction (62, 67). Interestingly, ghrelin can also directly affect the testicular tissue. When injected into the testes, this hormone inhibits the growth of Leydig cells and reduces the level of stem cell factor mRNA (67).

Resistin

Resistin is a polypeptide that plays a role in the development of insulin resistance. It regulates insulin sensitivity and the differentiation of adipocytes. It is considered a hormone that connects obesity with insulin resistance (68). Recent studies have provided evidence supporting the relationship between resistin, obesity, insulin resistance, and type 2 diabetes (16, 58). Not only does resistin impair insulin functions, but it also exhibits increased levels in diet-induced obesity and insulin resistance. Furthermore, resistin gene expression is significantly reduced with anti-diabetic treatment (thiazolidinediones), which enhances tissue sensitivity to insulin (69). Resistin is also associated with elevated levels of cytokines such as interleukin-6 and elastase in seminal fluid, and it is implicated in the inflammation of reproductive organs in obese males (70). In addition to its effects on reproductive system, resistin has been found in the pituitary gland and hypothalamus in humans, indicating a potential in central action as well (71).

Apelin

The presence of apelin and its receptors has been identified in the hypothalamus, pituitary, and testis (72). It is known to have autocrine and/or paracrine effects on male reproductive control and physiology regulation (73). It was shown that in male cases, apelin has an inhibitory effect on LH and testosterone (74). There is clear documentation showing that apelin has a stimulating effect on steroidogenesis. Histological examination revealed that infusion of apelin-13 leads to a significant reduction in the number of Leydig cells, indicating that apelin may play a role in the central regulation of testosterone release by suppressing LH secretion (75).

Visfatin

Visfatin is a molecule derived from adipose tissue that increases in obesity. It plays prominent roles in obesity-induced insulin resistance and type-2 diabetes (76). Despite its contrasting effects on insulin sensitivity regulation, visfatin exhibits pro-inflammatory characteristics and is involved in regulating reproductive functions (76). In males, its high expression in testicular cells, including germ cells, as well as in hypothalamic areas related to energy and reproductive homeostasis, suggests that it may play significant roles in modulating male fertility during metabolic disorders (68). Most studies investigating the impact of visfatin on male reproductive functions are *in vitro* or *in vivo*, and they mostly demonstrate beneficial effects of visfatin molecules on testicular functions (77, 78). However, this adipokine is also reported to suppress gonadotropin secretion, negatively influence the HPG axis (74), and act as pro-inflammatory mediators in an obesogenic environment (51).

Elevation of Cholesterol

In both developed and developing nations, dyslipidemia is becoming more prevalent among young people. This increase is believed to be linked to the adoption of a Western diet and sedentary lifestyles (1). Dyslipidemia, also known as hyperlipidemia, can lead to various detrimental health effects, such as obesity, metabolic disorders, cardiovascular issues, and infertility (29). To prevent excessive accumulation of cholesterol in tissues, the body carefully regulates plasma and cellular cholesterol levels (79). Consuming a diet high in fat or cholesterol can lead to hyperlipidemia and hypercholesterolemia, which can negatively affect normal male reproductive functions and disrupt the cholesterol balance (8). Commonly consumed foods high in cholesterol include eggs, seafood, meat, and dairy products (15). When sperm leaves the testicle, they are initially infertile and immobile. As they pass through the epididymis, they undergo several physiological and biochemical changes. These changes include modification and rearrangement of sperm plasma membrane molecules as well as removal of seminal plasma proteins and glycoproteins from the surface of ejaculated sperm (80). Cholesterol and other phospholipid levels are changed during travel through the epididymis to improve membrane flexibility. Cholesterol is crucial for maintaining the integrity of membranes. Hypercholesterolemia impairs membrane flexibility, which is necessary for sperm motility and capacity (81).

The biochemical changes of sterols and fatty acids in the epididymis directly affect the structure and dynamics of the sperm plasma membrane (82). Furthermore, increased cholesterol level in testicular Leydig cells can lead to endoplasmic reticulum stress, which reduces testosterone production and downregulates steroidogenic enzymes (83). When testosterone level increases, sperm concentration decreases. Some studies in infertile men have shown a weak correlation between serum testosterone level and the total cholesterol level, but a significant negative correlation was noticed between serum total testosterone level and triglycerides (84, 85). Hypercholesterolemia was demonstrated to damage the testes and reproductive system by generating excessive free radicals and increasing oxidative stress, while both of which have deleterious effects on sperm activity (2, 25).

High Intake of Carbohydrates

Sweets, candy, french fries, and sugary drinks are examples of unhealthy foods in Western diet that contain carbohydrates (1). Fruit and vegetables, on the other hand, are considered healthy foods, but they also contain carbohydrates. In the Western diet, white bread, potatoes, sugar and white rice are common examples of simple carbohydrates with a high glycemic index (1). It has been observed that excessive consumption of these carbohydrates can lead to hyperinsulinemia and insulin resistance (86) (Figure 1).

Insulin Resistance

Insulin resistance is when a person's body is unable to effectively use insulin to process glucose, which can lead to inflammation, decreased release of male sex hormones, lower levels of sex hormone binding globulin, and worsened obesity (87). Capacitation is a process that freshly ejaculated sperm need to undergo before they can fertilize an oocyte. Insulin has been found to be secreted by sperm, and there is a notable difference in insulin release between capacitated and non-capacitated sperm, suggesting that insulin plays an active role in capacitation (58). Insulin resistance can impair the capacity and impair the effect of insulin secretion by sperm. Sperm cells have been shown to contain insulin receptors, which when activated improve sperm motility (13). The male germ cell line also has the ability to produce insulin. Increased steroidogenesis, altered LH/FSH ratio, and increased LH levels are associated with insulin resistance and hyperinsulinemia (16).

Insulin resistance reduces the amount of glucose that sperm can absorb, and decreases their motility and metabolism. Insulin also prevents the liver from producing SHBG (9). Lower sperm count and total testosterone level are associated with a reduced SHBG level (88). Sperm glucose metabolism is affected by hyperinsulinemia and hyperglycemia, which increases oxidative stress and weakens antioxidant defenses. For sperm, this disruption of glucose metabolism is an essential source of energy that can lead to increased sperm apoptosis and decreased sperm motility, both of which can worsen male infertility (89). Obesity-induced hypogonadism is caused by insulin resistance. It increases estrogen biological activity by reducing the production of SHBG in the liver (8).

Interestingly, obesity-induced insulin resistance decreases gonadotropin secretion at the hypothalamic-pituitary level, which in turn decreases testicular testosterone production (16). It has been found that glucose is also required for the production of testosterone, as the lack of this sugar prevents Leydig cells from producing testosterone. Therefore, poor testosterone production and spermatogenesis may be due to impaired glucose metabolism observed in people on a Western diet (90).

Glucagon-like Peptide-1 (GLP-1)

The distal ileum of humans contains entero-endocrine L-cells that secrete glucagon-like peptide-1 (GLP-1), a 29-amino acid peptide (91). It is worth noting that GLP-1 has an interesting effect on the brain, as it is able to cross the blood-brain barrier and increase satiety, leading to a reduction in food intake (92). The incretin hormone GLP-1 controls how much insulin is released by the pancreatic islets in response to glucose load and meal consumption and it is quickly removed by the kidneys (93). GLP-1 regulates energy intake and nutrient absorption through various mechanisms, including the promotion of insulin secretion (92), upregulation of genes associated with insulin synthesis (94), and initiation of pathways that elevate intracellular calcium level, both in response to and despite cyclic adenosine monophosphate (cAMP) (95). Testicular weight and the frequency of testosterone pulses were demonstrated to decrease with low GLP-1 level. Testicular weight and testosterone level were demonstrated to rise with the administration of GLP-1 receptor antagonists (96).

Hyperglycemia

Tsampoukas *et al.* in diabetic mice reported an increased testicular damage in comparison with the control group (97). Non-enzymatic glycosylation pathways lead to advanced glycosylation end products (AGEs) (58). Testicular tissue expresses AGE receptors at various locations. Perhaps the binding of AGE to these receptors in excessive amounts is potentially responsible for male infertility (98). The higher levels of inflammation factors, including interleukin-1 and TNF- α, in hyperglycemic conditions can also negative affect fertility potential (99).

Hyperinsulinemia

Insulin resistance-related hyperinsulinemia in obese individuals may lessen the liver's synthesis of SHBG. Furthermore, a substantial contributing factor to the decline in testosterone level in male patients with obesity elevates the serum SHBG level (9). Glycoprotein SHBG has the capacity to attach to sex hormones and obstruct their physiological effects (100). Estrogen consequently displays a greater degree of biological activity. Furthermore, spermatogenesis is negatively impacted by hyperinsulinemia, which also increases damage to mitochondrial and nuclear DNA (16, 69).

Conclusion

The increased rate of intake of unhealthy diets and lifestyle changes are the two main parameters contributing to the rise in obesity rates in developed countries. In addition, there has been a noticeable negative relationship between obesity and seminal parameters. Numerous scientific reports have demonstrated a strong link between diet and reproductive dysfunction. The Western diet was demonstrated to impair male reproductive potential through various known and complex molecular mechanisms. However, several mechanisms still remain not fully understood. A high intake of fats in a Western diet can lead to lipid overload and subsequently, the obesity that disrupts hormone secretion, impairs androgenesis, alters seminal analysis reports, stimulates inflammatory responses, increases the level of ROS, and raises body temperature.

Obesity can affect male reproduction through the intricate web of molecular mechanisms secreted from adipose tissue. Adiponectin, leptin, ghrelin, resistin, and other adipokines secreted by adipose tissue can significantly impact the hypothalamic-pituitary-gonadal (HPG) axis and male reproduction. In the western diet, there is an excessive intake of lipids, leading to elevated levels of cholesterol and fatty acids. This lipid overload contributes to obesity, which in turn disrupts male fertility through mechanisms such as androgenesis disruption, inflammation, and increased temperature. Additionally, the high carbohydrate intake in a Western diet, particularly those with a high glycemic index, is primarily responsible for insulin resistance and hyperglycemia. Insulin resistance reduces sperm's ability to absorb glucose, and impairs their motility and metabolism.

By uncovering the unknown molecular connections between unhealthy foods in a Western diet and male fertility potential, we could identify new targets for prevention and increase in the society's awareness about the effects of a Western diet on health status, particularly the fertility potential. In conclusion, the western diet is not an optimal nutritional pattern for male fertility potential. We believe that a significant factor that drives the increased adoption of the western diet is the profit-driven practices of large food processing companies that heavily promote processed foods and sugary beverages. However, it is the responsibility of health ministries in developed and developing countries to educate the society about the detrimental effects of an unhealthy diet on fertility in order to prevent a decline in the fertility of the younger population.

Acknowledgement

The authors would like to thanks research staffs (Miss Monavar Naderi and Zahra Ahmadi) for helpful comments.

Funding

The authors declared that this study received no financial support.

Authors' Contribution

S.PM conceived and designed the review, searched and selected the papers, and edited the manuscript. SM.H search and categorized the papers, revised final manuscript. M.M wrote, revised and edited the manuscript for submission.

Conflict of Interest

The authors declared no conflicts of interest.

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