Medical Science

Obesity and male infertility: Systematic review

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ABSTRACT

Introduction: Infertility is defined as the inability to conceive after a year of regular, unprotected intercourse. Male infertility is a major global health problem, and numerous studies have been conducted to determine the factors that influence it. Among the causes, obesity is often mentioned. The aim of our study was to analyze how obesity affects male infertility. *Methods*: A systematic literature search was conducted from 2015 to January 2025 via PubMed, Scopus and Google Scholar databases with the following keywords (Obesity OR Body mass index AND semen analysis OR male infertility). The main outcome of interest was the effect of obesity on male infertility and semen parameters. *Results*: Out of 1680 articles found in databases, only 21 met the criteria for inclusion in the final review. Most studies demonstrated that increased BMI is associated with reduced sperm quality parameters, more frequent sperm DNA fragmentation and adverse changes in hormonal profiles. Some researchers found minimal or no significant correlation between obesity and semen parameters. *Conclusion*: Our systematic review demonstrated increased body mass index is associated with reduced semen quality. We can assume that obesity is a significant factor that can cause male infertility.

Keywords: Obesity, body mass index, male infertility, semen analysis

1. INTRODUCTION

Obesity has become one of the most pressing health challenges of the modern world, reaching the scale of a global epidemic. According to the World Health Organization (WHO), the number of people with excess body weight is increasing at an alarming rate, affecting both adults and children. Adult obesity doubled between 1990 and 2022. In 2022, 43% of people aged 18 years or over were classified as overweight and 16% were living with obesity.

The World Health Organization (WHO) defines overweight people as those with a body mass index (BMI) of >25 kg/m2 and a BMI of >30 kg/m2 (Kluge, 2022). Even though BMI is not a perfect indicator of obesity, it is easy to calculate and in most groups of people correlates well with both the percentage of body fat and body fat mass. However, individuals with the same BMI may have differing amounts of body fat (Nuttall, 2015).

Measurements of waist circumference, including waist-to-hip ratio, act as a marker for abdominal fat mass and demonstrate a similar association with future morbidity and mortality as BMI. Changes in waist circumference correlate with changes in the risk of obesity-related comorbidities, particularly CVD, this association is independent of BMI (Elsayed et al., 2008).

Obesity is a significant public health challenge, because it significantly increases the risk of chronic diseases such as type-2 diabetes, cardiovascular diseases (e.g. coronary heart disease), hypertension and sleep disorders (Powell-Wiley et al., 2021). Obesity may also be associated with a wide range of psychological problems (Sarwer and Polonsky, 2016). On a societal level, obesity imposes significant direct and indirect costs, placing a heavy burden on healthcare systems and reducing overall productivity due to increased medical expenses and work absenteeism.

2. METHODOLOGY

2.1. Search strategy and study selection

The literature search was conducted using PubMed, Scopus and Google Scholar databases using keywords: Obesity, Body mass index, male infertility, Semen analysis. Boolean operators (OR and AND) were used to optimize the search results. The search was limited to articles published in English between January 2015 and January 2025. The process of identifying articles was conducted by two independent researchers. After an initial assessment of all potentially relevant articles by reviewing titles and abstracts, we excluded those not related to the research topic, as well as case reports, review articles, and meta-analyses. The article screening process adhered to the PRISMA guidelines (Figure 1).

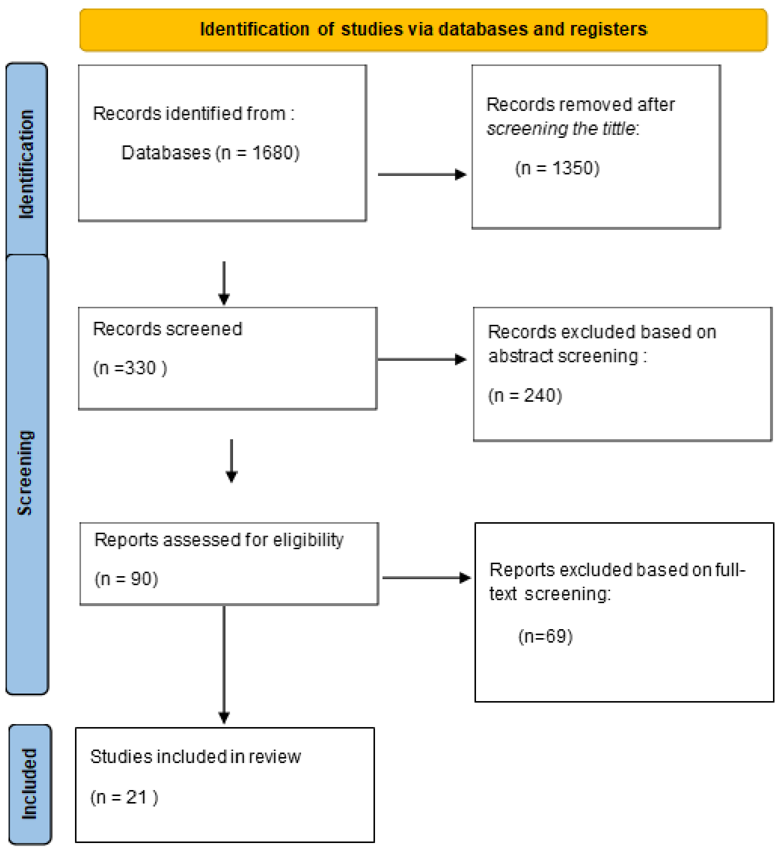

Figure 1 PRISMA flow diagram

2.2. Inclusion and Exclusion Criteria

Inclusion criteria

Articles published between January 2015 and January 2025

Studies in English language

Adult patients >18 years

Case-control or cohort study and cross-sectional study,

Exclusion criteria

Case reports, review articles and meta-analyses

Animal studies

Sexually immature male studies

2.3. Analysis

Due to the heterogeneous nature of the research, a narrative approach was used to analyze the data.

3. RESULTS

Fourteen of the analyzed studies found that obesity has an adverse effect on male fertility (Table 1). Over 20 000 patients were analyzed in large cross-section study based in Argentina. The researchers created 5 groups (underweight, normal weight, overweight, obese, and morbidly obese) and assigned participants to them based on BMI. They observed differences in semen parameters and some semen abnormalities between groups. They found that both morbidly obese and underweight experienced the highest decrease in semen quality. A BMI below 20 kg/m2 or above 32 kg/m2 is negatively associated with semen quality. These negative associations become more pronounced with increasing BMI, especially in men with a BMI of 37 kg/m2 and worsening further for BMI above 42 kg/m2 (Ramírez et al., 2020).

Another cross-section study showed that an increase in BMI was associated with decreased semen volume. Overweight and obese groups had lower sperm count than the normal BMI group. Researchers found an insignificant negative correlation between BMI and both semen volume and sperm count (Maskey and Rijal, 2022). A cohort study of male fertility and obesity (n = 4440 men) showed mild but significant relationships between serum hormone and semen parameters and BMI. Ejaculate volume, sperm concentration, motility, and morphology all showed significant negative correlations with BMI in univariate analyses. The strongest correlations with higher BMI values were observed for sperm concentration. When multiparametric models were applied, the negative associations between BMI and all semen parameters remained statistically significant, except for sperm motility, which lost significance (Bieniek et al., 2016).

In another study on this topic, Wang et al., (2017) analyzed sperm parameters of four groups of patients (2384 participants): underweight (68 participants), non-obese (1398 participants), overweight (620 participants) and obese (298 participants). They found that the sperm concentration, total sperm count, total motile sperm count, relative amount of progressive motility and the relative amount of type A motility (%) of overweight and obese men was lower than in the subjects with normal BMI. However, there was no difference in sperm morphology and sperm volume between the four groups. Engin-Ustun et al., (2018) conducted a study, in which they analyzed semen samples of 159 men, including 53 non-obese, 53 overweight and 53 obese. They found statistically significant differences in sperm volume, pH, progressive motility, postwash sperm count and Kruger morphology among three groups. These parameters were similar in the non-obese and overweight groups but were significantly worse in the obese group.

Based on body mass index and waist circumference (WC), Maghsoumi et al., (2020), Darand et al., (2023) and Ramaraju et al., (2018) showed that sperm motility and total sperm count were significantly lower in overweight and obese infertile men compared to infertile men of normal weight and those with WC <102 cm. Darand et al., (2023) additionally found that serum concentrations of hormones such as LH, FSH and leptin were significantly higher in overweight and obese infertile men compared to infertile men with normal weight and WC < 102 cm. An observational study conducted by Calderón et al., (2019a) investigated the topic at two levels: macro (blood plasma hormone levels) and molecular - the expression of lipid receptors/transporters and hormone-sensitive lipase (HSL) in human spermatozoa. The researchers found that plasma total testosterone and sex hormone–binding globulin (SHBG) were significantly decreased in adult obese patients compared with controls, whereas plasma estradiol was increased. Semen parameters of obese patients also showed a significant difference: total motility (%), spermatozoon concentration and progressive motility (%) of the spermatozoa were significantly decreased. When it comes to molecular differences, spermatozoids of obese patients had much lower expression of HSL and SR-BI/CLA-1, which may cause accumulation of cholesterol esters and decreased cholesterol excretion. This alteration in lipid homeostasis in obese patients' spermatozoa could induce lipotoxicity and infertility.

Another study focusing on both molecular and macro levels is a prospective study performed by Bibi et al., (2022). This study also assessed the results of assisted reproductive technology (ART) in both groups: those with normal BMI and those with elevated BMI. Researchers found that the patients with normal body weight had significantly higher levels of ROS and higher concentrations of motile spermatozoa in comparison to overweight patients. What's more, overweight men had a lower sperm chromatin integrity, higher percentage of DNA fragmentation and significantly higher levels of immature spermatozoids compared to men with normal BMI. In addition, stages and results of ART (fertilization, cleavage and cumulative birth rate) showed a significantly negative correlation with paternal BMI.

Similarly, in Taha et al., (2016) studies involving 165 fertile men, it turned out that in addition to the negative correlation between BMI and semen parameters, the DNA fragmentation of semen in obese men was much higher compared to fertile men. Oztekin et al., (2020) conducted a complex study about the impact of obesity on semen parameters and sex-hormone profile. They found that BMI is negatively correlated to serum testosterone (T) concentration and testosterone to estradiol ratio (T/E2), with no significant differences in serum FSH, LH, E2 and PRL concentration. BMI and semen parameters were negatively correlated, but the differences were not statistically significant. In a cohort study based in China involving 1684 couples, researchers found a significant correlation with higher BMI and longer time to pregnancy (Zhang et al., 2024). As for the time to get pregnant, Sundaram's study found that in couples with obese men, the time to get pregnant was longer compared to couples with men with a normal BMI (Sundaram et al., 2017).

Table 1. Characteristics of published studies evaluating the relationship between obesity and male fertility - studies that have shown the negative impact of obesity on male fertility.

Investigators	Study design	Participants	Main findings
(Ramírez et al., 2020)	Cross-sectional	20563 participants	Total sperm count was significantly higher in normal weight group than in obese, underweight and morbidly obese group. The lowest values was in MOB and underweight group. The worst score of motility and normal morphology was in the MOB group. Researchers found no significant differences in terms of sperm volume, viability, nuclear maturity, seminal citric acid content. Obese and overweight group had higher likelihood of oligozoospermia than normal weight group. Significant higher percentage of patients with teratozoospermia and asthenozoospermia was in MOB group.
(Maskey and Rijal, 2022)	Cross-sectional	249 participants	insignificant negative correlation of BMI with semen volume and sperm count
(Bieniek et al., 2016)	Retrospective multi-institutional cohort study	4440 men	Ejaculate volume, sperm concentration, motility, and morphology all showed significant negative correlations with BMI in univariate analyses.
(Wang et al., 2017)	Retrospective study	2384 men in couples with infertility (68 underweight, 1398 non-obese, 620 overweight, 298 obese)	The sperm concentration, total sperm count, total motile sperm count, relative amount of progressive motility and the relative amount of type A motility (%) of overweight and obese men was lower than in the subjects with normal BMI. There was no difference in sperm morphology and sperm volume between the four groups.
(Engin-Ustun et al., 2018)	Prospective, case control study.	159 men in couples with infertility (53 non-obese, 53 overweight, 53 obese)	The sperm volume, pH, progressive motility, postwash sperm count and Kruger morphology were similar in non-obese and overweight groups, but were statistically significantly worse in obese group.
(Maghsoumi-Norouzabad et	Cross-sectional	119 male patients who had lived as a partner	Based on BMI and WC, the sperm count, total motility and progressive sperm were significantly lower in overweight

al., 2020)		in an infertile couple for at least 1 year	and obese infertile males compared to that in normal weight infertile males and those with WC<102 cm. The fraction of sperm with abnormal morphology was significantly higher in infertile men with WC>102 cm compared to that in those with WC<102 cm. Serum levels of LH, FSH, and leptin were significantly higher in overweight and obese infertile males compared to that in normal weight infertile males and those with WC<102 cm..
(Darand et al., 2023)	Cross-sectional	218 infertile men aged 20–50	A high body mass index (BMI) has negative effects on sperm count, motility, morphology, and testosterone level. Overweight and obese men have lower sperm counts compared to their normal-weight counterparts. Abdominal obesity, and visceral fat had inverse associations with normal sperm morphology,
(Ramaraju et al., 2018)	Retrospective cohort	1285 male patients of infertility clinic	Obesity was associated with lower volume of semen, sperm count, concentration of spermatozoa, progressive motility, total motility. Obese men spermatozoids had higher head defects, thin heads and pyriform heads. Obese men were more likely to have oligospermia and asthenospermia
(Calderón et al., 2019a)	Observational study	20 obese men and 10 men in control group (non-obese)	Plasma total testosterone and sex hormone–binding globulin (SHBG) were significantly decreased in adult obese patients compared with controls, whereas plasma estradiol was increased. Semen parameters of obese patients also showed a significant difference: total motility (%), spermatozoon concentration and progressive motility (%) of the spermatozoa were significantly decreased. Spermatozoids of obese patients had much lower expression of HSL and SR-BI/CLA-1, what may cause accumulation of cholesterol esters and decreased cholesterol excretion. Described alteration in lipid homeostasis in obese patients' spermatozoa could induce lipotoxicity and infertility.
(Bibi et al., 2022)	Prospective study	750 men in couples with infertility	The patients with normal body weight had significantly higher levels of ROS and higher concentration of motile spermatozoa in comparison to overweight patients. Overweight men had a lower level of chromatin integrity of spermatozoa, higher percent of DNA fragmentation and significantly higher levels of immature spermatozoids. Stages and results of ART (fertilization, cleavage and cumulative birth rate) showed a significantly negative correlation with paternal BMI.
(Taha et al., 2016)	Case-controlled cohort	165 fertile men	Fertile obese men had significantly lower sperm concentration, progressive sperm motility, normal sperm morphology with significantly higher seminal ROS, and sperm DNA fragmentation compared with fertile normal-

			weight men. Fertile overweight men had significantly lower progressive sperm motility, normal sperm morphology with significantly higher seminal ROS, and sperm DNA fragmentation compared with fertile normal-weight men
(Oztekin et al., 2020)	Retrospective study	400 infertile men (274 primary and 126 secondary)	BMI is negatively correlated to serum testosterone (T) concentration and testosterone to estradiol ratio (T/E2), with no significant differences in terms of serum FSH, LH, E2 and PRL concentration. BMI and semen parameters were also negatively correlated, but the differences were not statistically significant.
(Zhang et al., 2024)	Cohort study	1684 couples	Increased Body mass index in both females and males is linked with higher likelihood of longer time to pregnancy.
(Sundaram et al., 2017)	Prospective cohort	501 couples trying for pregnancy	Extremes of BMI have been associated with a longer time-to-pregnancy and with less successful assisted reproductive technology (ART) outcomes. Obese couples were found to have approximately half the fecundability as couples with normal BMI.

Four teams of researchers have addressed the topic of "healthy obesity" (Table 2). This is a condition in which, despite increased body weight, no complications are observed or reflected in metabolic parameters. McPherson et al., (2020) performed a study in which they analyzed not only the semen parameters but also liver function and fasting blood glucose level. Based on this, they divide 84 participants into three groups: non-obese with normal blood parameters, overweight/obese "metabolic healthy" and overweight/obese "metabolically unhealthy" - this group included patients with obesity, abnormal liver function and elevated fasting glucose levels, understood as exceeding the upper reference limits of any of the parameters (ALP, ALT, AST, GTT, bilirubin, fasted glucose). They found that sperm count and total concentration were reduced in the "metabolically unhealthy" overweight/obese group. What's more, semen volume, total motile sperm per ejaculate, the percentage of sperm with normal morphology, and the proportion of men with normozoospermia were reduced in the "metabolically unhealthy" overweight/obese group compared with the "metabolically healthy" overweight/obese group. In contrast, the proportion of men with oligospermia was increased. Additionally, the authors conducted a regression analysis, which led to an interesting result: serum GTT concentrations were the most significant predictor of whether a patient would have a normal semen analysis or a reduced sperm count, with BMI having no effect.

Other studies on this topic, however, are not as clear. A cross–sectional study of 512 men showed that obesity alone, without metabolic complications, does not influence on semen parameters except for sperm DNA fragmentation. However, it increases the risk of primary and secondary hypogonadism, which may lead to infertility (Cazzaniga et al., 2020). A cohort study of 1231 infertile Chinese men populations showed that obesity-associated markers such as waist circumference, waist-to-hip ratio, waist-to-height ratio and BMI, could not predict semen quality. Obesity affects the hormonal profile, but this does not translate directly into deterioration of semen parameters. However, a study demonstrated that serum LH and FSH levels were negatively associated with sperm concentration and percent of normal sperm morphology (Lu et al., 2015).

In another study, Pini et al., (2020) conducted an analysis of the molecular composition of sperm received from obese men with no significant andrological diagnoses. They found that "healthy" obese men have normal semen parameters in basic examination, but at the molecular level, there are many abnormalities that may lead to infertility. One of the possible explanations for this phenomenon may be the increased level of pro-inflammatory cytokines and oxidative stress accompanying obesity, which appears earlier than its metabolic complications.

Table 2. Characteristics of published studies evaluating the relationship between obesity and male fertility - studies that have addressed the topic of "healthy obesity".

Investigators	Study design	Participants	Main findings
(McPherson and Tremellen, 2020)	Proof of concept retrospective study	84 men undergoing ART	The sperm count and total concentration was reduced in the "metabolically unhealthy" overweight/obese group. Semen volume, total motile sperm per ejaculate, percentage of sperm with normal morphology and proportion of men with normozoospermia was reduced in the "metabolically unhealthy" overweight/obese group compared with the "metabolically healthy" overweight/obese group, while the proportion of men with oligospermia was increased. The serum GTT concentrations were the biggest predictor of whether a patient would have a normal semen analysis or reduced sperm count, with BMI having no effect.
(Cazzaniga et al., 2020)	Cross-section study	512 primary infertile men	The obesity "alone", without its metabolic complications, doesn't influence semen parameters except sperm DNA fragmentation, but it causes a higher risk of primary and secondary hypogonadism, which may lead to infertility.
(Lu et al., 2015)	Cohort study	1132 subfertile men	Body mass index (BMI), waist circumference (WC), waist-to-hip ratio (WHR) and waist-to-height ratio (WHtR) could not predict semen quality
(Pini et al., 2020)	Prospective study	No information	"Healthy" obese men have normal semen parameters in basic examination, but at the molecular level, there are a lot of abnormalities that may lead to infertility.

Three of the analyzed studies showed little or no effect of obesity on male fertility (Table 3). In the study by Wang et al., (2023), which included 715 men who underwent fertility evaluation, researchers found that BMI was weakly associated with progressive sperm motility. Rufus et al., (2018) conducted a study on group of 206 men (110 with normal BMI and 96 with elevated BMI – obese and overweight), looking for correlation between BMI and semen parameters. They didn't find a statistically significant difference in the semen parameters (sperm count, motility and morphology) of samples received from participants belonging to both groups: with normal and elevated BMI. Similar results were given by the study conducted on 96 patients by Salas-Huetos et al., (2020). They investigated methylation of sperm DNA in obese and non-obese patients to find possible disorders. They identified no significant sperm DNA methylation alterations associated with BMI and reported that patterns of sperm DNA methylation aging have no statistically significant relationship with BMI.

Table 3. Characteristics of published studies evaluating the relationship between obesity and male fertility – studies that found little or no effect of obesity on male fertility.

Investigators	Study design	Participants	Main findings
(Wang et al., 2023)	Retrospective cohort	715 fertile men	BMI and WHR were significantly associated with semen parameters, while BMI was an independent risk factor for normal sperm progressive motility. Reproductive hormones, including FSH and testosterone, had a significant influence on sperm concentration and sperm morphology.
(Rufus et al., 2018)	Cross-section study	206 men attending the infertility clinic (110	There was no correlation between elevated BMI and semen parameters.

		with normal BMI and 96 with elevated BMI)	
(Salas-Huetos et al., 2020)	Prospective study	96 healthy men	The study identified no significant sperm DNA methylation alterations associated with BMI. Patterns of sperm DNA methylation aging have no statistically significant relationship with BMI.

4. DISCUSSION

4.1. Male infertility

Nowadays, infertility – understood as the inability to conceive after a year of regular intercourse - is becoming an increasingly serious health problem all over the globe. Currently, it affects approximately 10-15% of couples in reproductive age (Bibi et al., 2022; Punab et al., 2017), resulting in a significant increase in healthcare expenditures. According to De Jonge et al., (2022) 33 billion USD is spent annually worldwide on medically assisted reproduction (MAR), of which 10 billion USD is spent on procedures to treat infertility cases caused by male factor. It is believed that the pure male factor is responsible for about 20-30% of infertility cases (Agarwal et al., 2015; Rufus et al., 2018; Schlegel et al., 2021), but some studies suggest even up to 50% (Oztekin et al., 2020; Rafiee et al., 2016).

There is significant variation in the incidence of male infertility depending on the region of the world (Kumar and Singh, 2015). Some researchers claim that the percentage of infertility cases is higher among residents of developing countries than in developed ones (Bibi et al., 2022; Boivin et al., 2007). What could be caused by better availability of health care in developed countries and cultural differences? Rufus et al., (2018) suggested that in some countries, e.g. Nigeria, men often do not accept the fact that they may be responsible for couple infertility, which results in the inability of successful treatment. However, some studies show that the percentage of infertile men is higher in developed countries, which may be explained by greater willingness of patients in these countries to talk to the doctor about their problem, resulting in more cases being recorded in medical statistics (Agarwal et al., 2015).

There are several reasons for male infertility, e.g. environmental pollutants, industrial chemicals, genetic factors, unhealthy diet, reactive oxygen radicals and endocrine disorders (Kumar and Singh, 2022; Oztekin et al., 2020)The last three are directly related to obesity and all of them cause negative changes in both semen parameters and sex hormone profiles. This impact will be explained in detail later. It is also important to remember, that approximately 50% of male infertility cases are still considered idiopathic, which means that no etiological factor has been identified to cause them (Ghuman and Ramalingam, 2018).

4.2. How to measure male infertility?

Semen analysis is a fundamental and irreplaceable tool for assessing male infertility; therefore, precise thresholds are needed. It provides essential information regarding the contribution of the male factor to an infertile couple. The first guidelines for semen analysis were published by the World Health Organization (WHO) in 1980. However, the recent WHO guidelines on semen analysis have revised the interpretation of semen analysis compared to the previous guidelines in 2010 and 2021 (Table 4). This change has resulted in patients whose semen quality was considered abnormal according to the older classifications being considered normal under the new classification (Catanzariti et al., 2013; Chung et al., 2024).

Table 4. Comparison of the 2010 and 2021 reference ranges for semen analysis

Reference range for semen analysis		
Parameter	**Reference range (2010)**	**Reference range (2021)**
Semen volume (ml)	≥ 1,5	≥ 1,4
Sperm concentration (mln/ml)	≥ 15	≥ 16
Total sperm count (mln)	≥ 39	≥ 39

Total sperm motility	≥ 40%	≥ 42 %
Progressive sperm motility	≥ 32 %	≥ 30 %
Sperm normal morphology	≥ 4%	≥ 4%
Sperm vitality	≥ 58%	≥ 54 %

In addition to basic research focusing on semen parameters, WHO also took into account DNA damage in sperm. The completeness of the DNA structure in male semen has a positive effect on the chances of producing healthy offspring. Damage to sperm DNA can be defined as changes at the chemical level in the DNA structure. In addition to these changes, sperm DNA fragmentation (sDF) is one of the most common disorders affecting the genetic material in the form of single-strand and double-strand DNA breaks. sDF may be caused by various processes, such as oxidative stress, errors in DNA formation during spermatogenesis, in the processes of programmed cell death and various pathological external factors, including alcohol, tobacco smoke, and dangerous chemicals floating in the air (WHO, 2010).

Several tests have been developed to measure sperm DNA damage. We can distinguish two types of these tests. The first category is tests in which DNA fragmentation is measured directly by inserting probes at the site of damage that detect actual DNA strand breaks. Signals from these probes enable the quantification of DNA fragmentation in sperm. The second category briefly includes tests that use the property of fragmented DNA to be easily denatured under certain conditions (Shamsi et al., 2011). Increased sperm DNA fragmentation can lead to serious consequences such as impaired fertilization, altered embryo development, poorer implantation rates, higher incidence of spontaneous abortions, and reduced live births (Taha et al., 2016).

4.3. How Obesity Impacts Male Fertility: Mechanisms

Studies on the male reproductive system have shown that for certain reasons, for example due to anatomical pathologies such as obstruction of the genital tract, ejaculation may be impossible. These pathologies may occur in the vas deferens, prostate gland and even in urethra. Other examples include abnormal sperm quality and function, mitochondrial dysfunction, and oxidative stress in sperm, which lead to DNA damage and apoptosis (Figure 2). These factors are associated with reduced pregnancy rates or disorders of the male hormonal axis. Obesity may affect male fertility directly or indirectly through several possible mechanisms (Maghsoumi-Norouzabad et al., 2020).

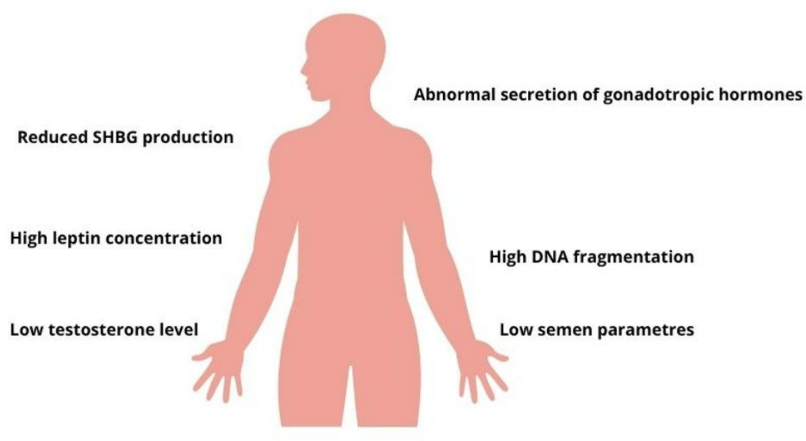

Figure 2 The mechanism by which obesity affects male fertility.

4.3.1. Obesity and hormones

Spermatogenesis is controlled by hormones such as androgens, estrogens and gonadotropins. These hormones are interrelated and play a key role in spermatogenesis and the development of secondary sexual characteristics. Obesity causes dysregulation of the hormonal axis, which contributes directly and indirectly to the reproductive hormonal profile and semen parameters. Testosterone is the primary male steroid sex hormone. It is produced by Leydig cells in the testicles. This hormone performs many functions in the male body, including the development of secondary sexual characteristics (body structure, voice, type of hair, facial hair, etc.), anabolic effect on the structure of muscle tissue by influencing spermatogenesis and increasing libido. Sex hormone-binding globulin (SHBG) is a protein that binds, among others, androgens. In male obesity, the production of SHBG in the liver is reduced (Rosenblatt et al., 2015).

According to (Fariello et al., 2021) the hormonal profile showed higher levels of sex hormone binding globulin (SHBG) and testosterone in obese men after metabolic surgery. Ramaraju et al., (2018) also showed that higher BMI reduces SHBG, which lowers testosterone levels. When it comes to gonadotropins - hormones produced in the pituitary gland that influence the function and development of the gonads, their reduced levels have been observed in obese men (Moreira et al., 2018). This is probably related to the abnormal secretion of gonadotropin-releasing hormone (GnRH) at the hypothalamic level, which contributes to the dysfunction of the hypothalamic-pituitary-adrenal axis in obese men. This may indicate a direct impact of obesity on male fertility, but further research is needed to find out the exact mechanisms behind it. When we talk about obesity we cannot forget about leptin, a hormone responsible for, among others: inhibition of gluconeogenesis in the liver, increased lipolysis in adipose tissue and, as a consequence, an increase in the level of free fatty acids in the blood, decreased lipogenesis, decreased insulin production, decreased glucose transport to adipocytes (Moreira et al., 2018).

Normally, leptin is secreted by fat cells and later enters the bloodstream. As a result, leptin levels indicate the amount of fat tissue in the body. This information reaches specific areas of the brain responsible for regulating energy in the human body. In summary, high levels of leptin in the blood signal the brain about high levels of stored body fat, which results in reduced food intake and increased energy expenditure. Overweight or obese people often have this mechanism dysregulated, which is characterized by leptin resistance. In these people, high leptin levels do not produce the desired effect. Leptin receptors are abundant in the gonads (Antinozzi et al., 2021; Moreira et al., 2018). Some studies have shown a negative relationship between leptin and testosterone levels in obese men (Antinozzi et al., 2021; Khodamoradi et al., 2020; Moreira et al., 2018). Moreover, leptin contributes to increased oxidative stress and uncontrolled production of reactive oxygen species (ROS). Physiologically, ROS plays a role in sperm maturation, including capacitation and the acrosome reaction. However, when their level exceeds the physiological concentration, ROS impairs sperm proliferation, which negatively affects the fluidity of their cell membrane, impairs their motility and increases DNA damage (Maghsoumi-Norouzabad et al., 2020).

4.3.2. Obesity and semen parameters

About 15% of couples of reproductive age do not achieve pregnancy within 12 months despite regular sexual intercourse. In 50% of childless couples, abnormal semen parameters are a male factor associated with infertility (Balawender and Orkisz, 2020; Darand et al., 2023; Punab et al., 2017; Ramaraju et al., 2018) showed a negative correlation between obesity and sperm concentration, sperm number and motility, and semen volume. Wang et al., (2023) also showed that BMI and WHR were considerably negatively associated with semen parameters, while BMI turned out to be an independent risk factor for normal, progressive sperm motility in fertile men. Maghsoumi-Norouzabad et al., (2020) found that sperm count, total sperm motility and sperm progression were significantly lower in overweight and obese infertile men compared to normal weight infertile men. Moreover, the percentage of sperm with abnormal morphology was significantly higher in infertile men with WC >102 cm compared to men with WC<102 cm (Antinozzi et al., 2021). However, they did not find a statistically significant correlation between semen parameters and BMI in their study.

4.3.3. Obesity and sperm DNA fragmentation

Increased sperm DNA fragmentation may contribute to impaired fertilization, impaired fetal and embryo development; couples with high sperm DNA fragmentation have a worse implantation rate and these couples also have a higher incidence of spontaneous live abortions. Taha et al., (2016) Showed that fertile obese men had significantly higher semen ROS and sperm DNA fragmentation compared with fertile normal-weight men. Fariello et al., (2021) Showed that the activity of sperm mitochondria and sperm DNA integrity improved, and the level of lipid peroxidation in semen decreased in men after metabolic surgery. In the study by Campbell et al., (2015), the results showed that the reproductive potential of obese men is reduced compared to men of normal body weight. The data suggest that this may be due to abnormal morphology and increased rates of DNA damage.

4.3.4. Obesity and sperm transcriptome

Human sperm contain, among other things, various types of RNA, including long non-coding RNA (lncRNA), messenger RNA (mRNA), microRNA (miRNA) and transfer small RNAs (tsRNA), all of which plays a role in spermatogenesis, fertilization and embryo development. Male obesity is associated with altered sperm DNA methylation profiles that appear to affect reprogramming fidelity in a subset of sperm, suggesting an influence on the spermatogonia (Cannarella et al., 2024; Keyhan et al., 2021) showed that mRNA expression of obesity-related genes in human spermatozoa was associated with sperm parameters, fertilization rate, embryo cleavage rate and high-quality embryos.

4.4. Treatment

There are several ways to treat obesity-caused male infertility. The first step should always be non-pharmacological treatment, including lifestyle changes such as increased energy expenditure and diet modification (Donkin et al., 2016). It seems that the type of physical exercise is less important than its regularity and intensity. According to Service et al., (2023) endurance exercise extending over 60 weeks negatively impacted sperm concentration, motility, and morphology compared with moderate exercise. When it comes to food, it is not only the number of calories consumed that is important, but also the chemical composition of the food consumed. We should eat a lot of whole grain carbohydrates, antioxidant rich vegetables, seafood, nuts, seeds, fiber, vegetable oils and omega-3 polyunsaturated fatty acids, while avoiding high energy sugars, saturated and trans-fatty acids, alongside excessive alcohol and tobacco smoking, which may increase levels of pro-inflammatory mediators (Leisegang et al., 2019). Special attention should be paid to antioxidants, which neutralize free oxygen radicals, preventing the sperm membrane from lipoperoxidation damage. They also protect sperm DNA from damage and mutation (Rafiee et al., 2016). A perfect source of vitamin C and other compounds with a beneficial action profile in the treatment of obesity, such as anthocyanins, flavonoids, polyphenols, carotenoids, minerals, fatty acids, melatonin and vitamins is mulberry fruit. Its elements have antioxidant, antidiabetic, neuroprotective, anticancer and anti-inflammatory properties, which have been described in detail in Adthapanyawanich's research (Adthapanyawanich et al., 2025).

Non-pharmacological treatment is supplemented and extended with drugs, such as orlistat, aromatase inhibitors, topiramate/phentermine, bupropion/naltrexone and GLP-1 agonists, e.g. semaglutide, dulaglutide, liraglutide (El Salam, 2018). The last group is now being considered as the golden standard for pharmacological obesity treatment, because of its beneficial effects not only in terms of weight loss but also increased levels of gonadotropins and associated testosterone increases(Donkin et al., 2016; Service et al., 2023). However, not all drugs that have a beneficial effect on blood sugar level and body weight may be helpful in the treatment of obesity-related infertility. The influence of metformin on male fertility remains unclear and the results of some of studies on this topic are conflicting. Zaidi et al., (2017) reported that metformin users had better sperm motility and morphology than patients taking insulin. On the other hand, a previous study showed a statistically significant decrease of sperm count and motility in patients taking metformin 850 mg twice a day for 3 months. Due to these reports and the fact that the mechanisms by which some weight loss medications affect fertility are not yet fully understood, caution should be exercised in their use, and further research should be conducted in this area.

The issue of the impact of bariatric surgery (BS) on male infertility deserves wider discussion. Currently, the most commonly performed surgeries in this area are sleeve gastrectomy and Roux-en-Y gastric bypass (English et al., 2020). Sleeve gastrectomy involves excision of part of the stomach along the greater curvature. Roux-en-Y gastric bypass is a more complex procedure, in which a small reservoir (volume 10–30 cm3) is first created from part of the stomach to digest food. The small intestine is then divided into two parts – a lower part (Roux loop), which is then pulled up and attached to the new stomach, and an upper part (enzymatic loop), which is attached to the distal end of the Roux loop (Akalestou et al., 2021). Both types of surgery lead to a stomach volume reduction and Roux-en-Y gastric bypass additionally leads to bypassing part of the small intestine, which allows for reduced food absorption. It all results in significant weight loss, on average by 55% EWL (percentage of excess weight loss) in one year after surgery (Bastos et al., 2024). It would seem that such significant weight loss would reverse the negative impact of obesity on fertility, making bariatric surgery (BS) an indirect method of treating obesity-related infertility. Moreover, scientists agree that BS improves sex hormones profile and sperm DNA fragmentation (sDF) (Bardisi et al., 2016; Calderón et al., 2019b; Carette et al., 2019; Samavat et al., 2018; Wood et al., 2020), but the matter turns out to be much complex when it comes to other semen parameters.

According to Samavat et al., (2018) BS improves almost all sperm parameters except sperm morphology. Bardisi et al., (2016) found that after BS there was an improvement in sperm concentration, but it was statistically significant only in patients with initial azoospermia and oligospermia. In this survey, the other semen parameters didn't change. Calderón et al., (2019b) conducted a study that gave similar results - they didn't find any statistically significant differences in semen parameters after BS. The most disturbing reports come from one of the latest studies on this topic, which found a deterioration in sperm quality. Carette et al., (2019) reported a decrease of total sperm count 12 months after BS with unchanged values of semen volume (mL), spermatozoa motility (%), and vitality

(%). Wood et al., (2020) found worsening of sperm concentration and total ejaculated sperm count, with two patients becoming even azoospermic after BS. It is worth noting that these two studies were conducted on larger groups than the others, except the study by (Bardisi et al., 2016).

These surprising observations can be attributed to systemic stress that accompanies any surgery, including bariatric operations. Sleeve gastrectomy and gastric bypass procedures, apart from positive results, may also be the cause of nutrient malabsorption from the GI tract, leading to electrolyte and metabolic disorders (Bardisi et al., 2016). An inherent element of the postoperative wound healing is also limited inflammation, which causes a temporary increase in reactive oxygen species (ROS) concentration, which, as we know, also can damage sperm. The other possible explanation is that, besides the postoperative recovery period, bariatric surgery doesn't have a direct influence on the different factors assessed with obesity and causing male infertility, such as elevated testis temperature or inflammatory responses of the testis and hypothalamus (Calderón et al., 2019b).

Due to conflicting research results, it is difficult to clearly state that BS can be a treatment for infertility related to obesity. Still, we cannot underestimate the positive results that it has on overall health, including reproductive health. It should be noted that to date, no long-term study has been conducted on patients undergoing bariatric surgery to assess the long-term effects of this procedure on semen parameters and, consequently, male fertility. This is undoubtedly an area for future research.

In patients in whom the methods described so far have not produced the expected result, assisted reproductive techniques (ART) can be used. These procedures aim to maximize the chance of having a child using sperm from a partner or a donor. The most commonly used methods are in vitro fertilization (IVF) and intracytoplasmic insemination (ICSI), where a morphologically normal motile spermatozoon is selected for microinjection into a mature oocyte (Raad et al., 2019). Unfortunately, both of these procedures have drawbacks. Normal sperm morphology doesn't exclude its damage at the molecular level. Injection of sperm in the ICSI technique circumvents the natural defense barriers and allows for fertilization with DNA-damaged sperm, which may cause lower pregnancy rates and a higher risk of pregnancy loss (Raad et al., 2019). That's why paternal obesity may lead to lower fertilization and clinical pregnancy rate also after the ART cycle (Bibi et al., 2022). To avoid this, donor sperm is sometimes used.

5. CONCLUSIONS

This systematic review indicates that obesity is a possible factor in male infertility. Most of the articles we analyzed showed that semen quality decreases with increasing BMI, while some studies have found a minimal or no link between obesity and male infertility. The mechanisms underlying these effects are multifactorial, involving hormonal dysregulation, oxidative stress, and molecular changes in sperm cells. Although interventions such as weight loss through lifestyle modification, pharmacotherapy, or bariatric surgery may improve certain aspects of reproductive health, the evidence is inconsistent and requires further investigation. Overall, these results provide further evidence of the importance of maintaining a healthy body weight for male fertility.

Author’s Contributions

Conceptualization, A.Z. and F.C.; Methodology, A.Z. and K.C.; Software, F.C. and M.W.; Validation: D.Z. and A.G.; Formal analysis: F.C. and K.C.; Investigation: A.G. and M.W.; Resources: D.Z. and A.Z.; Data curation: K.C. and M.W.; Writing- Original- draft preparation: F.C. and K.C Writing-review and editing: F.C. and A.Z.; Supervision: D.Z. and A.G.; Project administration: F.C., K.C., A.Z., M.W., D.Z., A.G.

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Conflict of interest

The authors declare that there is no conflict of interest.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

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