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## IMPACT OF OBESITY ON MALE FERTILITY AND ITS MANAGEMENT

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### ABSTRACT

Obesity significantly affects the fertility and sperm quality in men at reproductive ages through hormonal imbalances, increased scrotal temperatures, thus decreasing the concentration and motility of sperm, decreased total sperm count, increased DNA fragmentation index, decreased sperm movement and sperm quality. Obese men suffer from hormonal imbalances, increased oestrogen levels, and low levels of inhibin-B and androgen, which affect sperm production. The present review discusses how obesity affects male fertility and sperm quality, as well as various treatment options. The men infertility due to obesity can be treated by changing in lifestyle, increasing physical activity, and behavioral treatment; Pharmacological intervention such as medication and food supplements involving weight loss medicines, appetite suppressants, and aromatase inhibitors; Surgical treatment including scrotal lipectomy and bariatric surgery, Assisted reproductive technology (ART) including In vitro fertilization (IVF), Intrauterine insemination (IUI), and Intracytoplasmic sperm injection (ICSI).

**Keywords: Obesity, Men infertility, body mass index, Management, Assisted Reproductive Technology**

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## INTRODUCTION

In the medical community, obesity is defined as abnormal or excessive fat accumulation in the body that negatively impacts human health. It is measured through the concept of body mass index (BMI), which is a person's weight (in kilograms) divided by the square of their height (in meters) [1-4]. Over 30 BMI is considered obese while 25 to 30 BMI is considered overweight (Table 1). World Health Organization (WHO) reports that in 2016, more than 1.9 billion adults ages 18 years and older (39% of males and 40% of females) were overweight and more than 650 million adults were obese [5]. There are many factors that contribute to obesity, including inactive lifestyles, uncontrolled diets, reduction in physical activity, unhealthy nutritional habits, stress, junk food, and genetic factors [6]. Obesity alters physical appearance as well as disrupts the hormones balance within the human body. Overweight and obesity contribute to a variety of health issues, such as type 2 diabetes, coronary heart disease, and sleep apnoea. Numerous scientific studies have found that obesity significantly adversely affects fertility and sperm quality in men of reproductive age [7, 8]. Sallmen *et al.* reported that overweight and obesity of men have 1.5 to 2 times lower sperm counts when

compare to normal men of reproductive age [9]. The current scenario shows an increase in the use of artificial reproductive technologies (ART), primarily intracytoplasmic sperm injection (ICSI), among couples with evidence of declining fertility in males and females. The present review discusses how obesity affects male fertility and sperm quality, as well as various treatment options.

## CORRELATION OF MALE OBESITY AND INFERTILITY

Obesity has an impact on male infertility directly by contributing to hormonal imbalances and increased scrotal temperatures, and indirectly by contributing to sleep apnea and a reduction in physical activity. Obese men suffer from hormonal imbalances, increased estrogen levels, and low levels of inhibin-B and androgen, which affect sperm production. The elevated body temperature associated with obesity, particularly around the scrotum, decreases sperm concentration and motility, reduces total sperm count, and increases the fragmentation index of DNA [9, 10]. An increase in BMI decreases the movement and quality of sperm, thereby lowering the sperm count in men [11]. Adipocyte-derived leptin plays an important biological role in

regulating food intake, energy expenditure, and reproductive function. Human brains are programmed to reduce their food intake and increase energy expenditure, thus causing the amount of leptin in your body to decline, reducing intra testicular testosterone and having an adverse effect on sperm production [12]. There are a number of physiological abnormalities associated with metabolic syndromes, such as obesity, dyslipidemia, hypertension, and insulin resistance. As a result of the metabolic syndrome, the scrotal temperature increased, the sperm concentration and motility decreased, the biological activity of the sperm was compromised, and the genome of the sperm was damaged [13]. The psychological conditions of obese individuals are worsened by psychological factors such as decreased sex drive and increased sexual dysfunction, which might prevent obese people from having sexual contact as frequently as non-obese people do, even if they are in a relationship with a sexual partner. A person's obesity can therefore affect their sexuality, which impacts their fertility in the long run [11].

#### **MECHANISMS OF OBESITY-INDUCED MALE INFERTILITY**

The obesity-induced male infertility can be used to explain by three main biological

mechanisms i.e., hypogonadism, testicular heat-stress-/hypoxia-induced apoptosis, and adipokines and metabolic hormones.

#### **Obesity may lead to hypogonadism**

Hypogonadism, or insufficient production of the male hormone testosterone, is a common symptom of obesity among men. The reproductive hormonal profiles of obese men are typically altered, i.e., estrogen and leptin levels are elevated, and testosterone levels, follicle-stimulating hormone (FSH), sex hormone-binding globulin (SHBG), ghrelin, and inhibin-B levels are decreased. In obese men, estrogen production is excessive because of the hyperactivity of aromatase (cytochrome P450 enzyme) in the redundant white adipose tissue. The hypothalamus and pituitary gland are impacted by feedback inhibition, causing a decrease in gonadotrophin secretion from the pituitary, which further results in a reduction in testosterone production via the fall of gonadotrophin-releasing hormone (GnRH)-luteinizing hormone (LH)/FSH pulses. Negative feedback loop disruption of the hypothalamic-pituitary-gonadal (HPG) axis is ultimately responsible for the significant decline in testosterone production. Thus, low testosterone levels and FSH levels in obese men are likely to result in impaired

spermatogenesis and reduced fertility [14-16].

### **Heat stress, hypoxia-induced testicular apoptosis**

During spermatogenesis, the scrotum temperature is approximately 3°C lower than the core body temperature, a condition critical for the efficiency of spermatogenesis. Obese males with adipose tissue combined with sedentary lifestyles have a higher scrotal temperature. Due to the fact that elevated scrotal temperatures are associated with impaired semen quality during sedentary activities, obese men will likely experience genital heat stress and infertility [17, 18].

### **Adipokines and metabolic hormones**

Adipose tissue is the body's main source of energy, and it also acts as an endocrine gland, increasing aromatase enzyme activities that convert testosterone to estrogen resulting in elevated estrogen levels and a surge of adipose tissue hormones, which can affect steroidogenesis and spermatogenesis. Adipose tissue hormones such as ghrelin, leptin, orexin, adiponectin, and obestatin are released under obesity conditions, and all of these hormones play a significant role in regulating male fertility levels [19, 20].

## **TREATMENT OF OBESITY-INDUCED MALE INFERTILITY**

The treatment of obesity-associated male infertility is a complex condition due to the intrinsic pathophysiology and allied comorbidities. Obesity-induced male infertility can be treated by changing lifestyle, taking medicine and food supplements, having surgery, as well Assisted Reproductive Technology (ART) (Figure 1) [21-25].

### **Lifestyle management**

The different exercise methods such as yoga, cardio, hit, pilates, and dance for the progress fitness, metabolic health, muscle strength, quality of life, and general wellbeing. The enhancement of physical activity might lower the chance of acquiring various diseases like coronary heart disease, stroke, hypertension, diabetes, cancer, and depression by enhancing our muscle fitness, cardio-respiratory system, bone, and functional health, blood circulation, and metabolism.

Behavioral therapy is monitored by the psychologist who analyzed the patient physical activity, thinking, and eating habits and according to the analysis set a proper treatment plan which includes stress management, exercise programs, and diet plan to control the obesity that combination of diet and exercise programs [23, 24].

### **Medicine and food supplements**

The weight loss medicines and food supplements reduce or control body weight

based on reducing the appetite, altering the absorbability of nutrients, such as fat in the human body, and increasing the consumption of energy or accelerating fat burn. The appetite suppressant drugs or food supplements act on the neurochemical transmitters of the central nervous system (CNS) to reduce food intake. The Appetite suppressants reduce hunger block the absorption of certain nutrients or increase the consumption of calories. Examples of appetite suppressants drugs are benzphetamine, diethylpropion, mazindol, and phentermine. Examples of food supplements are green tea, bitter orange, yohimbine, caffeine found in coffee, tea, and dark chocolate. Appetite suppressants are only taken with concern with the doctor for a prescribed short-term treatment for patients with obesity due to side effects. The appetite suppressants are useful to control diet and increased physical activity to achieve significant weight loss [23, 24].

Obesity can be reduced by the choice of healthier foods i.e., increasing consumption of fruit and vegetables, legumes, whole grains, and nuts while limiting energy intake from fat, carbohydrates (especially those with a high glycaemic index), protein, or alcohol intake. The balanced diet contains all the essential proteins, vitamins, and trace

elements. The dietary control is based on the principle i.e. total intake of calories (energy) should be greater than total calories (energy) consumed. The rate of weight loss is increased when the difference between the total intake of calories and total calories consumed is more [21-23].

### **Surgery**

Obese men's excess fat accumulation causes infertility due to increased scrotal temperature or toxin buildup. A surgical technique called a scrotal lipectomy is used to remove extra fat from the scrotum. About one-fifth of female patients who underwent lipectomy for the removal of excess fat and were previously infertile were successful in getting pregnant [24].

In the treatment of obesity, bariatric surgery is a useful method for losing weight by reducing or bypassing parts of the small intestine or stomach. Patients with severe obesity and a BMI of 40 or higher, as well as those between 35 and 40 who have diabetes, high blood pressure, high cholesterol, fatty liver disease, or sleep apnea, and who have not been able to successfully lose enough weight despite dietary changes and pharmaceutical treatment, are candidates for bariatric surgery. Based on the different types of surgeries, bariatric surgery can be divided into three categories: (i) laparoscopic

adjustable gastric band (ii) gastric sleeve surgery, also called sleeve gastrectomy (iii) gastric bypass. The treatments for morbid obesity and associated concomitant problems, such as the laparoscopic adjustable gastric band and gastric bypass, are very successful. Patients who underwent vertical banded gastroplasty experienced a considerable decline in oestrogen level, an increase in testosterone level, a normalization of other hormones, and adipokine levels, according to the scientific study on bariatric surgery [25-27].

### **Assisted Reproductive Techniques**

Assisted reproductive treatment (ART) helps to achieve a pregnancy involves the management of eggs and sperm and/or embryos. The ART covers a wide spectrum of treatments such as *in-vitro* fertilization (IVF), Intrauterine insemination (IUI) Intracytoplasmic sperm injection (ICSI) gamete intrafallopian transfer (GIFT), pronuclear stage tubal transfer (PROST), tubal embryo transfer (TET), and zygote intrafallopian transfer (ZIFT). In-vitro fertilization (IVF) for male infertility includes the collection of sperm from the male partner or donor along with the

woman's eggs. The sperm and egg are incubated in a culture dish in the laboratory to allow the egg to be fertilized. If fertilization occurs and an embryo develops, the embryo is then placed into the woman's uterus in a procedure called an embryo transfer [28]. Sometimes multiple embryos may develop, and they can be frozen for use in later transfer procedures. IUI for male infertility is the process of injecting washed and prepared sperm into the female partner's uterus beyond the cervix, at the time of ovulation using a catheter (a thin tube). The placement of sperm with IUI is deeper into the female reproductive tract than sperm are normally placed with intercourse. Intracytoplasmic sperm injection (ICSI) for male infertility is similar to IVF specially designed for men with very low sperm counts. The embryologist isolates a single healthy appearing sperm and then injects one sperm into each egg to achieve fertilization. This is an excellent treatment option, and it has enabled thousands of men with sperm counts far too low for a successful natural conception to conceive healthy babies [29-31].

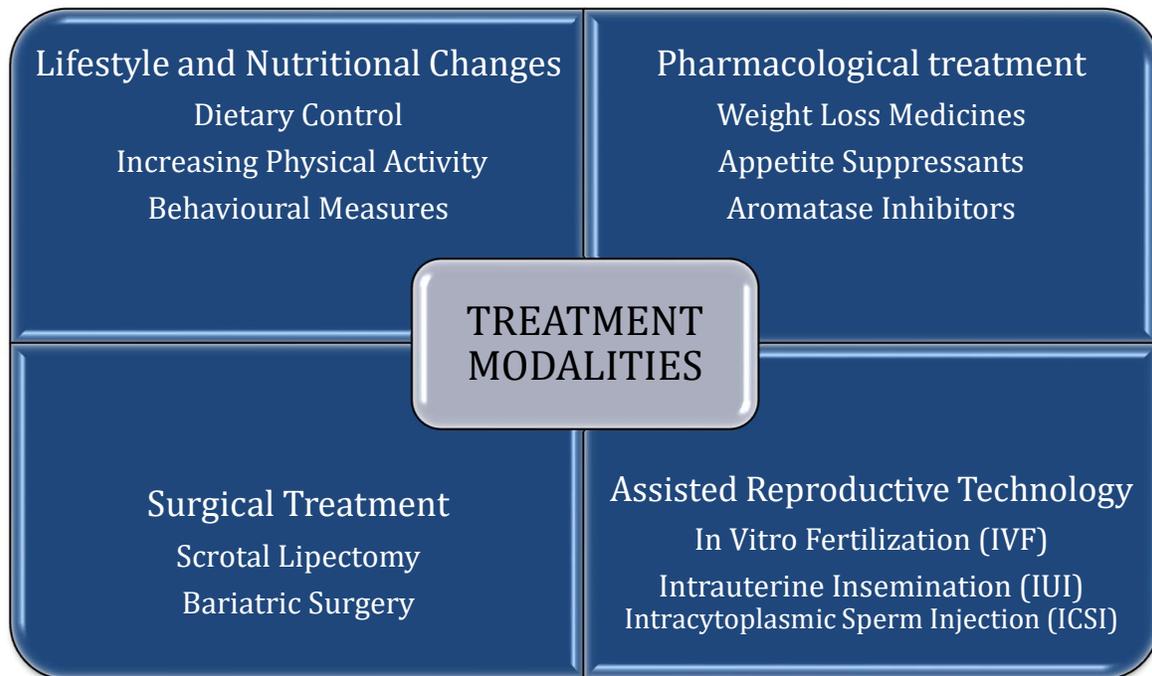


Figure 1: Treatment of obesity induced male infertility

Table 1: Body Mass Index (BMI) and health status.

BMI		Weight Status
Men	Women	
Under 20	Under 18.5	Underweight
20-24.9	18.5-24.9	Normal
25.0-29.9	25.0-29.9	Overweight
30.0-34.99	30.0-34.99	Obese Class-I
35-39.99	35-39.99	Obese Class-II
40	40	Extreme/ Morbidly obese

**CONCLUSION**

Overweight men experience hormonal imbalances, an increase in sperm temperature, decreased motility and concentration of sperm, a reduction of total sperm count, and decreased sperm quality, ultimately resulting in sperm count declines and infertility. Obesity results from a variety of factors, including sedentary lifestyles, uncontrolled diets, lack of physical activity, unhealthy nutritional habits, stress, junk food, and genetics. Obese men suffer from

hormonal imbalances, increased estrogen levels, and low levels of inhibin-B and androgen, what affects sperm production. The obesity induced male infertility can be used to explain by three main biological mechanisms i.e., Hypogonadism, Testicular heat-stress-/hypoxia-induced apoptosis, and Adipokines and metabolic hormones. A number of treatment options are available for men suffering from infertility due to obesity, changing lifestyle, taking medicine and food

supplements, having surgery, as well as Assisted Reproductive Technology (ART).

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