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Association between Obesity and Female Infertility

Review Article

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Abstract

Approximately one in every six people of reproductive age worldwide experience infertility in their lifetime (WHO, 2018) [1]. In general, infertility is defined as not being able to get pregnant (conceive) after one year (or longer) of unprotected sex .Obesity is always a risk factor for infertility. Abnormal or excessive fat accumulation that presents a risk to health. A body mass index (BMI) over 25 is considered overweight, and over 30 is obese. The quantity and distribution of body fat affect the menstrual cycle through a range of hormonal mechanisms. The more excess weight and the more abdominal fat, the greater the risk of fertility difficulties. Insulin resistance, which occurs when the body must produce more insulin to maintain normal blood sugar levels, and decreased levels of sex hormone-binding globulin (SHBG), a protein involved in the regulation of the sex hormones androgen and oestrogen, are both associated with excess weight, particularly excess abdominal fat. Even if the information about obesity and fertility may seem overwhelming, there is also some positive news. Weight-loss programmes, especially those that involve both nutrition and exercise, can encourage normal menstrual cycles and increase the likelihood of getting pregnant. Even a little weight decrease of 5–10% can enhance fertility in obese women with an ovulatory infertility and increase their chances of getting pregnant.

Keywords: Infertility Obesity; Ovulation; BMI; Pregnancy

Introduction

"Sometimes, struggles are exactly what we need in our life. If we were to go through our life without any obstacles, we would be crippled. We would not be as strong as what we could have been. Give every opportunity a chance, leave no room for regrets." — Friedrich Nietzsche

Friedrich Wilhelm Nietzsche was a German philosopher, prose poet, cultural critic, philologist, and musician. His works have had a significant impact on modern philosophy. As he said about infertility particularly that sometimes we need to struggle to know what our life really is. Otherwise we follow an ordinary life (Nietzsche). He also said that "Everything in woman hath a solution. It is called pregnancy". But unfortunately many of them are not gifted to have the privilege. That is they are infertile.

"Infertility is a disease of the male or female reproductive system defined by the failure to achieve a pregnancy after 12 months or more of regular unprotected sexual intercourse" (World Health Organization, 2018) [1]."In general, infertility is defined as not being able to get pregnant (conceive) after one year (or longer) of

unprotected sex" (CDS, 2023) [2]. "Infertility is defined as not being able to get pregnant despite having frequent, unprotected sex for at least a year for most couples" (Mayo Clinic, 2021) [3]. "Infertility is a disease of the male or female reproductive system defined by the failure to achieve a pregnancy after 12 months or more of regular unprotected sexual intercourse in women < 35 years of age or within 6 months in women > 35 years of age"(Indian council of medical research,2022) [4]. Globally, 48.5 million couples experience infertility. Approximately one in every six people of reproductive age worldwide experience infertility in their lifetime (WHO, 2018) [1]. The current fertility rate for India in 2023 is 2.139 births per woman (India infertility rate 1950-2023) [5]. Kerala is slightly ahead with a Total Fertility Rate of 1.5(Based on the Census 2011 data). If a woman keeps having miscarriages, it is also called infertility. Female infertility can result from age, physical problems, hormone problems, and lifestyle or environmental factors (Mediline Plus).Female infertility and obesity are related [6].

Weight gain that is abnormal or excessive and poses a risk to health is what is meant by the terms "overweight" and "obesity." Overweight is defined as a body mass index (BMI) of 25, and obesity

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as a BMI of greater than 30. According to the global burden of illness, the problem has reached epidemic proportions, with over 4 million people dying annually as a result of being overweight or obese in 2017. It's a medical problem that increases the risk of other diseases and health problems, such as heart disease, diabetes, infertility, high blood pressure and certain cancers the prevalence of overweight and obesity in both adults and children is rising. Globally, the incidence of overweight or obesity among children and adolescents aged 5 to 19 more than quadrupled from 4% to 18% between 1975 and 2016 (WHO,2022) [7]

Asians with a BMI of 23 or above may be more susceptible to health issues. The BMI offers a reliable assessment of body fat for the majority of people. BMI does not, however, directly measure body fat, therefore some persons, such as strong athletes, may have a BMI that falls into the category of obesity while having normal levels of body fat. Many medical professionals also take a patient's waist measurement to aid in treatment planning. Men with waist measurements above 40 inches (102 centimeters) and women with waist measurements over 35 inches (89 centimeters) are more likely to experience weightrelated health issues (Mayo Clinic).

Methods

PubMed, Scopus, Web of Science, Embase, PsycINFO, IndMed, and Google Scholar were searched along with books to find out information about infertility and obesity. This study included the articles published after A.D.1990.

Discussion

According to Mayo clinic the risk factors for female infertility includes Age, Smoking, Sexual history alcohol along with important factor obesity. Worldwide obesity has nearly tripled since 1975. In 2016, more than 1.9 billion adults, 18 years and older, were overweight. Of these over 650 million were obese.39% of adults aged 18 years and over were overweight in 2016, and 13% were obese. Most of the world's population live in countries where overweight and obesity kills more people than underweight (WHO).

Numerous mechanisms, including ones that operate at the molecular level, have been used to link obesity to infertility. Obese people experience more difficulties getting fertility treatments and getting pregnant, which can add to their financial and psychological burdens. There is room for improvement in the compassionate care provided to persons who are dealing with obesity and infertility [8].

Women are slightly more likely (40%) than men (35%) to have obesity. Obesity specifically affects some different aspects of women's health. **The first position is Fertility.** Women who have obesity are more likely to have problems getting pregnant than are women who are at a healthy weight. Overweight women have a higher incidence of menstrual dysfunction and an ovulation. Overweight and obese women are at a high risk for reproductive health. The risk of sub fecundity and infertility, conception rates, miscarriage rates, and pregnancy complications are increased in these women. They have poor reproductive outcomes in natural as well as assisted conception. These poor reproductive outcomes include assisted reproduction such as ovulation induction, *in vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI), and ovum donation cycles [9]. Obesity causes Obesity changes reproductive hormone levels as women age. Polycystic ovary syndrome (PCOS), **one of the most common reason for infertility**, is the most common hormone disorder among women of childbearing age (between about age 15 and 45). Most women with PCOS also have obesity. **Other than this** Women with obesity are more likely to have heart disease, diabetes, and breast cancer than are women without obesity (overweight and obesity). Obesity has a negative impact on health and raises the possibility of difficulties during pregnancy and labour. Preterm delivery and birth of a baby who is larger than gestational age (greater than they should be at that week of pregnancy) are risks that can be increased by obesity before becoming pregnant or by acquiring too much weight while pregnant.

Pregnant obese women are more likely to have a number of health issues. When pregnant, they can lead to major difficulties.

Usually, gestational diabetes is discovered around 20 weeks of pregnancy or just before birth. The result is elevated blood glucose levels because it makes it difficult for our body to adequately digest and store energy from food. This may have an impact on both their and their unborn child. High blood pressure that develops during the second part of pregnancy is known as gestational hypertension. Preeclampsia is a condition that combines pregnancy-related high blood pressure with indicators that one's organs are not functioning properly, such as elevated levels of protein in their urine. Seizures that might be fatal are a possible result. The condition known as obstructive sleep apnea occurs when one's throat muscles momentarily. When throat muscles relax while sleeping and momentarily stop breathing, this is known as obstructive sleep apnea. This might because one to wake up weary since it interferes with one's brain's natural sleep routines. If it is severe and not treated, it may be deadly (Mayo Clinic Staff, 2021) [3].

Obesity has a negative effect on ovarian and neuroendocrine function, as well as ovulatory problems, which are mostly caused by endocrine processes(American Society for Reproductive Medicine Practice Committee of [10] . which also lower ovulation omeostatic levels [11]. The enhanced peripheral aromatization of androgens to oestrogens in obese women affects gonadotropin production, and insulin resistance and hyperinsulinemia cause hyperandrogenemia. In addition, leptin (A fine hormonal balance regulates the menstrual cycle. Overweight and obese women have higher levels of a hormone called leptin, which is produced in fatty tissue. This can disrupt the hormone balance and lead to reduced fertility). levels rise while those of sex hormone-binding globulin (SHBG), growth hormone (GH), and insulin-like growth factor binding proteins (IGFBP) fall. As a result, the neuro regulation of the hypothalamic-pituitary-ovarian (HPO) axis may be seriously disturbed, and being fat further raises the risk of miscarriage, poor pregnancy outcomes, and compromised foetal health [12].

The molecular and endocrinological aspects of obesity, its effects and consequences on the reproductive system as well as benefits from modifying lifestyles improving the reproductive outcomes. The adipose tissue is considered an endocrine organ that plays important roles in the regulation of many physiological events, such as reproduction [13]. Based on the recently identified effects

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of adipokines, malfunction of the adipose tissue has been linked in recent years to the pathophysiology of infertility. The family of adipokines includes the adipose-specific cytokines, namely secreted by adipocytes, such as leptin, adiponectin (APN), resistin, visfatin and omentin, and the non adipose specific cytokines such as retinol binding protein-4 (RBP4), lipocalin-2 (LCN2), chemerin, interleukin 6 (IL6), interleukin 1 β (IL1 β), and tumor necrosis factor α (TNF α) are the panel of adipokines.

Obesity may impede the growth of ovarian follicles, cause qualitative and quantitative oocyte maturation problems, modify fertilisation, disturb meiosis, and cause aberrant mitochondrial dynamics leading to preimplantation of defective embryos [14]. In reproductive organs, an excess of free fatty acids may have a toxic impact that results in long-lasting cell damage and a persistent lowgrade inflammatory state. In this regard, a number of theories are connected to plasmatic levels of reproductive hormones and their metabolism, and a number of processes have been proposed to explain why obesity and/or being overweight impair the quality of female gametes.

The capacity of mature oocytes to sustain fertilisation and the development of the embryo [15]. Accordingly, the changed balance of driving hormones like SHBG with other soluble variables including insulin, glucose, lactate, triglycerides, and C reactive protein has a variety of effects on oocyte maturation depending on the systemic inflammatory state linked to obesity [16].

Numerous research on both naturally occurring and artificially inseminated pregnancies have examined the relationship between obesity and miscarriage. In these investigations, the risk of miscarriage was shown to be up to 40% in obese women, compared to less than 15% in women with a normal BMI. But despite these findings, there remains disagreement over the underlying causes of obesity in women [17].

The granulosa cells of tiny antral and pre-antral follicles produce anti-Mullerian hormone (AMH), which clinically may be indicative of the prediction of ovarian reserve in women undergoing fertility assessment and therapy [69]. Because of this, it's crucial to assess how the levels of AMH, a fertility parameter, alter in obese women with or without PCOS [18].

Overweight and obese women have lower outcomes following fertility treatments than normal population. They poorly respond to induction of ovulation, require higher doses of gonadotropins and longer treatment courses for follicular development and ovulatory cycles. In addition, the oocyte yield is lower in obese women resulting in a higher rate of cycle cancellation [19].

Weight loss has been shown to improve reproductive outcomes by ameliorating fertility, as well as by regularizing menstrual cycles and increasing the chance of spontaneous ovulation and conception in ovulatory overweight and obese women.

It has been demonstrated that losing weight helps with fertility, menstrual cycle regularity, and increases the likelihood of spontaneous ovulation and pregnancy in an ovulatory overweight and obese women [20].

Conclusion

Obesity has a definite effect on the probability of subfertility, according to clinical investigations. This goes beyond inadequate responses to ART and diminished fertility. Numerous pathways impacting the egg, endometrium, and preimplantation embryo have been linked through laboratory research. For obese people hoping to get pregnant, interventions like weight loss, exercise, dietary changes, and bariatric surgery show some promise. To better understand the relationship between obesity and reproduction and create healthy families, more translational research will be required.

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