International Journal of Natural Medicine and Health Sciences
ISSN (Online):2790-2471 ISSN(Print): 2790-2463
Volume 1, No.3, June 2022
Journal homepage: https://journals.iub.edu.pk/index.php/ijnms

Review

Impact of obesity on reproductive cycle: a leading cause towards infertility: A review

Hiba Zahid[a]

[a] University of Saskatchewan Canada

Article Info.

Received: 20-04-22
Revised: 26-04-22
Accepted: 28-04-22
Online: 30-04-22

Correspondence:
hiba.zaahid@gmail.com

Keywords: Obesity; Fertility; Body mass index; Reproductive cycle

Abstract

Infertility is a condition in which a couple fails to conceive after regular unprotected intercourse for a period of one year or more. It is a public health problem that is rising day by day not at the national but at global levels. There are different causes that lead to infertility. Some are anatomical problems that underlie infertility while others are functional or endocrinal problems. All these problems are treated accordingly. But one of the most rising causes of infertility nowadays is obesity. Obesity is a leading cause of infertility both in males and females. It causes infertility in many ways, by affecting the metabolic system as well as the endocrinal system of the body. Obesity is reaching alarming conditions not only in the reproductive age but also in the teenage. There is a need to control obesity from its very beginning to avoid its devastating outcomes in the form of male and female infertility in the future. The current review provides a look over the vicious cycle that how obesity leads to infertility and how it can be overcome.

Citation: Zahid H. Impact of obesity on reproductive cycle: a leading cause towards infertility: A review. IJNMS. 2022; 1(3):.42-46

Introduction

Infertility is a vast terminology with psychological, medical, social as well as personal impacts on the mind and overall health of the sufferer. It can be defined simply as a failure of the couple to conceive after regular unprotected intercourse for the period of one year or more. Making it more specified related to the ages of male and female partners it is defined as inability in conception by the couple after 12 months of intercourse without any contraception and with a desire to conceive in women less than 35 years old. And if the age of the woman is greater than 35 years the duration of regular intercourse is reduced to 6 months.[1]

Incidence of infertility

Infertility is rising globally. It is approximated that about 80 million people are affected by it throughout the world. Almost every couple out of ten couples is found affected by infertility. Although the incidence is different in different countries ranging from a minimum of 5% to a maximum rate of greater than 30%. It is found more prevalent in developing countries. In USA the affected couples are estimated to the 10% of the whole population.[2]

Obesity

Obesity is reaching to the levels of pandemic throughout the world affecting both males and females. It does not only affect the people of reproductive age but the people of all age groups are equally being affected by obesity. It can be found in infants, children, adults to overage persons. In each age group it leaves its devastating effects that affect the whole life of the sufferer. It is estimated that about prevalence of obesity will become up to 18% in men and 20 % in women by the year 2025.[3] Obesity serves as underlying cause of many systemic diseases including cardiovascular diseases, diabetes, cancer, coronary artery disease, hypertension, depression, stress as well as more importantly infertility.[4]

Obesity is affecting almost all the age groups. Initially it was considered as the disease of only young age but with time obesity has spread its wing over a larger age group. It is affecting not only the young population but also the children and infants. Old aged people are also not spared from obesity. Most of the deaths are now occurring because of the diseases caused by underlying obesity. Obesity is increasing the fatality and morbidity rate very fast.[5] It is estimated that there will be only 30-40% of the population worldwide that will not be affected by obesity throughout their life span.

Measurement of obesity

Visible accumulation and distribution of fat over different parts of body is not just sufficient to access either the person is obese or not. Obesity is measured in terms of body mass index (BMI). On predicting the devastating outcomes of obesity and its rapidly increasing incidence, world health organization has made a scale to measure the obesity in 2000. WHO has already alarmed the situation regarding the obesity by developing specific cut off levels so that obesity can be diagnosed and controlled in time. But sadly due to number of factors obesity remained uncontrolled and is now become the root cause of many diseases.[6]

BMI

BMI is a body mass index which is calculated by ones weight and height.[7] The formula for calculating BMI can be used in two forms depending upon the units of weight and height used. Given in Fig no 1. [8]

World health organization has made the cutoff values of body mass index through which a person can easily access either he is coming in the category of obesity, overweight, normal or underweight.[9]

Causes of obesity

Obesity is rising in uncontrolled manner. The causes of obesity that lie in the root are not unavoidable, instead they are under one's own control[10]. It is reaching to pandemic level due to negligence of population. Poor even bad habits of the people make them prone to move towards obesity. These habits include junk eating, over eating, lack of physical activity, stress, lack of proper exercise, high calorie intake, use of sweeteners and fizzy drinks and several other environmental factors [11] (Fig 1). Those who are involved in these poor habits usually suffer from it due to their genetic background because obesity also runs in families.

Effects of obesity

As obesity is reaching to its peak level it is becoming the cause of many metabolic, endocrinal, systemic and inflammatory diseases. Metabolic derangements include type 2 diabetes mellitus[12], systemic diseases involve cardiovascular disease, arteriosclerosis, hypertension etc. [13], endocrinal conditions include disturbed menstrual cycles, polycystic ovarian disease, hirsutism [14] (Fig 3). If remain unnoticed it can lead to multiple organ damage leading to other diseases. Obesity is affecting males and females equally to some extent causing infertility[15].

Types of obesity

Regarding infertility there are two types of obesity. One is peripheral obesity and other is central obesity. Peripheral obesity is also known as apple shaped body while central obesity is named as pear shaped body.[16] Obesity is divided into these two classes on the bases of waist hip ratio (WHR). WHR in peripheral obesity is 0.82 while in central obesity it is 0.85.[17] The impact of each type of obesity on infertility is different. Usually it is seen that central obesity is more well involved in causing infertility than peripheral obesity.

Obesity and infertility

Male infertility

Male infertility differs from that of female infertility. Male infertility independently is defined as a failure of the male partner to result conception in a fertile female partner[18]. It affects about 7% of males[19]. Male fertility majorly depends upon the composition of their semen, number of sperms per ml, their motility, live and dead sperms, structure of sperm either they are normal to penetrate the female ovum properly which results in fertilization and so on. The normal physiological parameters of healthy sperm are given in Table 1. Males usually suffer through medical conditions leading to infertility mentioned in Table 2 along with their causes. It is diagnosed by analyzing the semen quality in two samples taken 4 weeks apart[20]. There are also other several underlying factors that lead to male infertility. The other factors that become the cause of infertility in males may include bad dietary habits, poor physical

activity, alcoholism, any medication hormonal imbalance and the most important one obesity[21].

Obesity and male infertility

Obesity specially the central type of obesity generally known as abdominal obesity is associated with male infertility. Central obesity causes the imbalance in the endocrinal functions that regulate the normal cycles of good quality sperm production. Central obesity causes hyper testosteronemia in males[26] this decrease in testosterone levels greatly disturbs the hormonal control of sperm production leading to formation of sperms with poor quality. Hypotestosteronemia also develops a consequence towards some other systemic diseases like cardiovascular disease that in turn affect the blood supply and imparting the reproductive function of males[27].

Female infertility

Out of all cases of infertility one third cases are because of female infertility. Mostly the females get affected by infertility and there are so many reasons that underlie the condition. They include hormonal imbalance, poor dietary habits, lack of exercise, menstrual problems, polycystic ovarian disease, alcoholism and most importantly the rapidly rising obesity[28].

Obesity and reproductive cycle

Normal reproductive cycle is very much important for the health outcomes of life specially in females. Reproductive cycle is under the control of many hormones that must be regulated with in the proper range. Their surge and sequential decline are required at the different stages of reproductive cycle. Any imbalance and ups and downs of their levels can lead to changes in cycle and abnormalities in females. It has been seen that obese female have more menstrual abnormalities. It has been estimated that 45 % of females that have the problem of amenorrhea are obese. Reproductive hormones like FSH, LH, estrogen, progesterone and testosterone are significantly affected by the total body mass. Obese females have greater amount of adipose tissue distributed in their body. Adipose tissue is a site for the production and metabolism of these steroid hormones[29]. Females with high BMI are associated with conditions that indirectly lead towards infertility. These conditions include altered levels of insulin with raised insulin resistance, reduced sex hormone binding globulin, increased androgen levels in blood and altered gonadotrophin (FSH and LH) levels. These parameters lead to dysregulated hypothalamic pituitary gonadal axis which in turn causes menstrual irregularities[30].

Obesity and LH (luteinizing hormone)

Luteinizing hormone is a steroid hormone released from the pituitary gland and acts on the ovary. It is responsible for the maturation and release of the ova from ovary Fig 3. It has its role in the formation of corpus luteum after the ovulation. This corpus luteum develops to its maximum extent and then releases progesterone hormone that play very important role in the reproductive cycle of female. A timed surge of LH is required for healthy fruitful ovulation along with other hormones. Women suffering from central obesity have found to have raised levels of LH in their blood. This increased level of LH in reproductive cycle, significantly affect the ovulation, leading to menstrual disturbance. When ovulation does not occur at its regular time it easily moves the patient towards infertility[31]. In one of the studies carried out by Hartz and colleagues, they found that anovulation is powerfully associated with obesity. Obese females get affected by menstrual problems 3 times more frequently than males with BMI within normal ranges. Menstrual problems are not only associated with obese females of reproductive age, instead obesity in childhood also leads to menstrual cycle problems later during their reproductive age.

Obesity and estrogen

Estrogen is steroid hormone that is formed by cholesterol so rise in body mass leads to changes in its levels. Estrogen surge is required two times during the reproductive cycle. First surge is required in order to trigger the release of luteinizing hormone causing the release of ova. A second surge of estrogen is required for the growth of endometrium along with progesterone. Estrogen also plays its role in maturation of uterine lining before ovulation Fig 3. Adipose tissue is the site where androgens are converted in to estrogen. High levels of adipose tissue will lead to altered levels of estrogen in body and these altered estrogen levels affect the menstrual cycle and a female suffers from menstrual irregularities. This in turn leads to improper ovulation and most probably results in an ovulatory cycle that make a female unable to conceive leading to infertility.

Obesity and Poly Cystic Ovarian disease

PCO disease is a most prevalent endocrinal and metabolic disorder that prominently affect the females of reproductive age. PCO is considered as the traid of obesity, hirsutism and anovulation. In PCO there is marked dysregulation of hormones that leads to decreased ovulation as well as anovulation in most of the cases. The affected female very easily suffers from the fertility problems. If a female from PCO conceives, there are higher risks of developing pregnancy complications and outcome[33].

Obesity is associated with number of endocrinal and metabolic disorders and PCO is also a endocrine-metabolic disorders. It has been seen that females with high BMI are more suffered from PCO disease.

Effect of obesity on the treatment of infertility

When a couple fails to conceive even after a long period of regular efforts, then they are diagnosed as infertile. This news is itself very devastating and stressful for the couple. Almost more than 90% of the couples diagnosed with infertility move towards infertility treatment. It has been studied that the treatment methodologies that are followed most effective in couple that is not obese. Infertility treatment is found ineffective in couples in which one or both of the partners are obese. In more than 50% of cases an obese couple that is suffering from obesity just get conceived simply by reducing their weight. While in some other cases the medications become effective on the couple only after the reduction of significant weight. Increased weight and fat distribution in the body has direct or indirect effect over the endocrinal system of the body. In females the menstrual cycle is totally under hormonal control, therefore obese women have greater menstrual and ovulation problems than non-obese females. Reduction in body fat and controlling the body weight results in

regulation of menstrual cycles and regular ovulation in turn leads to conception.

Conclusion

Obesity and infertility both are public health problems and rising speedily. There are several undergoing mechanisms that make the obesity as a cause towards infertility. Obesity is becoming a pandemic and now it is becoming the top one cause of infertility that can be easily controlled by only changing one's personal habits. Modifying one's personal habits, like, eating habits, lack of exercise, oversleeping, no walking, junk food consumption, sleeping and immediately after eating. By overcoming these factors obesity and in turn the infertility can be controlled over remarkable levels.

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Table 1: The cutoff values of body mass index

Classification	BMI(kg/m²)	
	Principal cut-off points	Additional cut-off points
Underweight	<18.50	<18.50
Severe thinness	<16.00	<16.00
Moderate thinness	16.00 - 16.99	16.00 - 16. 99
Mild thinness	17.00 - 18.49	17.00 - 18. 49
Normal range	18.50 - 24.99	18.50 - 22.99
		23.00 - 24.99
Overweight	≥25.00	≥25.00
Pre-obese	25.00 - 29.99	25.00 - 27.49
		27.50 - 29.99
Obese	≥30.00	≥30.00
Obese class I	30.00 - 34.99	30.00 - 32.49
		32.50 - 34.99
Obese class II	35.00 - 39.99	35.00 - 37.49
		37.50 - 39.99
Obese class III	≥40.00	≥40.00

Table 2: parameters for Semen analysis

Areas of Review	Normal Semen Analysis Ranges
Total sperm count	39 – 928 million
Ejaculate Volume	1.5 – 7.6 mL
Sperm Concentration	15 – 259 million per mL
Total Motility (progressive and non progressive)	40% – 81%
Progressive Motility	32% – 75%
Sperm Morphology	4% – 48%

Table 3: Conditions related to sperms leading to infertility in males

Terminology	Definition	Causes	References
Oligospermia	Low sperm count	Bad eating habits Infection obesity	[21]
Asthenospermia	Poor sperm motility	Mutation	[22]
Teratospermia	Abnormal morphology of sperm	Mutation	[23]
Azoospermia	No sperm in ejaculate	Obesity, personal habits, mutations	[24]
Aspermia	Absence of ejaculation	Obesity, mental health	[25]

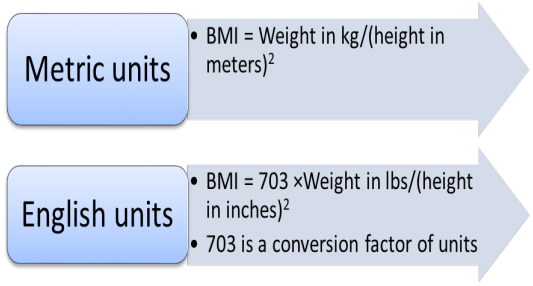

Figure 1: Formula for calculating BMI

Figure 2: Causes of obesity

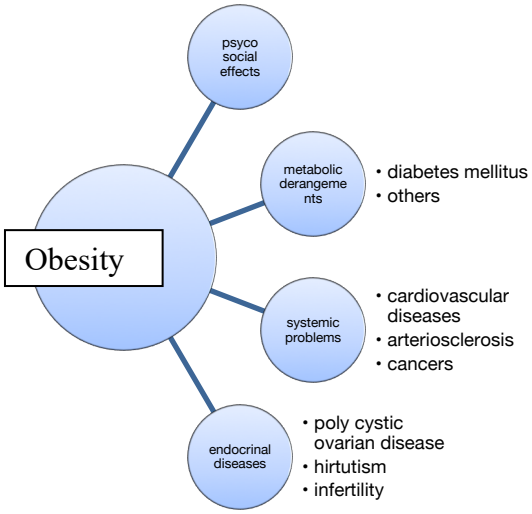

Figure 3: effects of obesity on different systems of body and their outcomes.

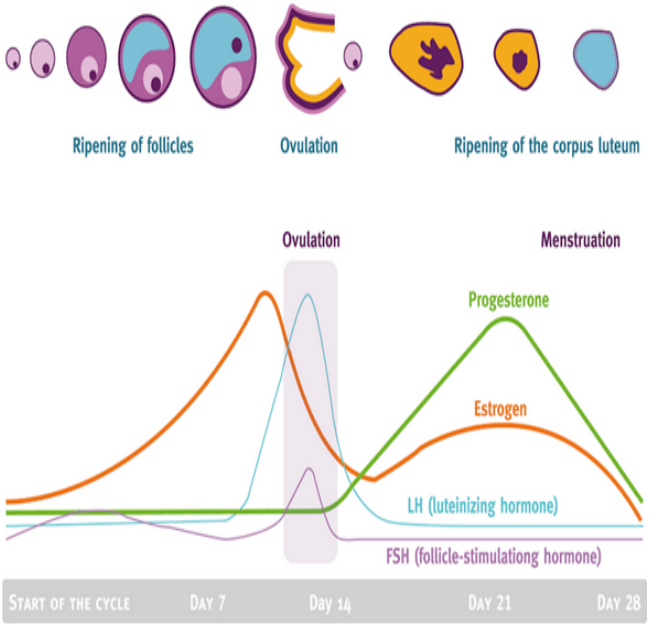

Figure 4: levels of different hormones during the reproductive cycle [32]

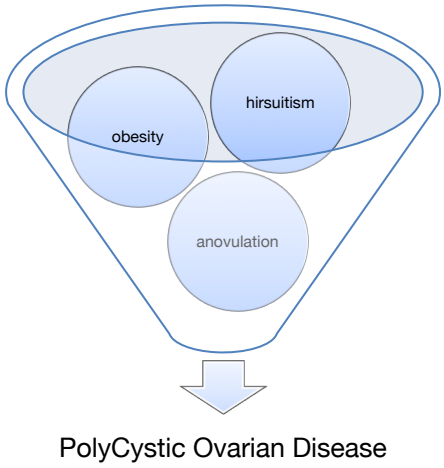

Figure 5: Poly Cystic Ovarian Disease