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INFERTILITY AND OBESITY IN YOUNG ADULT WOMEN

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Abstract

Introduction: obesity has become a disease of concern worldwide, predominantly in women, due to the hormonal and environmental predisposition to which they are subjected during their childbearing age, therefore, being a multifactorial disease, it has an impact on the state of fertility in women, since it produces alterations in the menstrual cycle. These irregularities in the menstrual cycle secondary to the excess of adipose tissue also influence the development of other pathologies, so preventing obesity will allow us to counteract infertility in young adult women.

Methodology: A narrative literature review was carried out, the process of which includes informative material obtained from books and journals. Literature was excluded from reports, theses to obtain academic degrees or when access to them did not provide the full text, and review articles and clinical trials in English and Spanish, whose publication has been carried out in the last 5 years, obtained in databases: Scopus, Springer, Elsevier, Web of Science, PubMed, and Cochrane

Expected results: From the articles obtained on the subject, it was possible to know the epidemiological impact of obesity on infertility in young women, and the pathophysiological mechanisms determining infertility. Hence, women with abdominal obesity or higher body mass index have greater difficulty getting pregnant, both spontaneously and through assisted reproduction techniques.

Conclusion: obesity is a disease that causes several complications in women, due to its relationship with alterations in the menstrual cycle, ovarian and uterine failure, which result in problems in women's sexual function, mainly infertility. Therefore, taking preventive or corrective measures to control weight is advisable before trying to conceive spontaneously.

Key words: anovulation, infertility, obesity.

INTRODUCTION

The study of the effects of obesity on hormonal changes in young adult women is a very worrying issue, as it becomes one of the most common problems during childbearing age, with infertility due to anovulation being one of the main consequences (1,2) .

Women are the group with the highest risk and predisposition to suffer from obesity since the same genetic and social factors and hormonal changes determine its appearance, for this reason it is of great importance to prevent bad behavioral habits, such as: poor nutrition, lack of physical activity and

other risk factors. that predispose to the development of obesity at an early age, especially during a woman's reproductive age. (3,4)

It has been seen that obesity is more common in women of low socioeconomic status, associated with several factors such as: not having the habit of dieting or adapting to a healthy diet, since it requires a greater investment of resources, which cannot be afforded; in addition to the fact that changes in the food system have made processed foods more accessible for consumption by the population. (5,6) (5,7)

As obesity is a chronic multifactorial disease, more common in women, the prevalence in adult women is 59.5%, (1,2), becoming a health problem worldwide, as it is related to multiple diseases such as: ovarian or endometrial cancer, complex endocrinometabolic diseases, insulin resistance, alteration in gonadotropin secretion and changes in sex steroids. In addition to being the main cause of developing diseases with a negative impact on women's reproductive health, (6,9) obesity predisposes to diseases that interfere with embryonic development (1).

It is estimated that 35% of obese women have alterations in the menstrual cycle, either absence, delay or irregularity of the period or abnormal bleeding patterns, among which we have: oligomenorrhea or amenorrhea, which are usually evident as the body mass index (BMI) increases, or in women whose Adipose tissue distribution is greater in the upper body region, such that abdominal adiposity is a better predictor of ovulatory dysfunction. (4,8)

These gynecological and metabolic alterations such as hyperinsulinemia or insulin resistance and alterations in the menstrual cycle, raise the concentration of androgen levels and alter the release of female sex hormones, eventually leading to problems in ovulation. That is why obesity is related to long and irregular cycles, especially in the population whose BMI is greater than 35 kg/m2, since its incidence compared to women with BMI of 23 kg/m2 is five times higher. Epidemiological data show that, as the prevalence of obesity is higher in women under 35 years of age, the search for medical attention for infertility is higher than that of men. Therefore, the time to get pregnant spontaneously is prolonged in obese women, thus reducing the pregnancy rate. (8,11) (4,8) (8) (7,8)

Explaining the pathophysiological mechanisms of adipocytes over androgens will allow us to get to the basis of hormonal alterations related to infertility and thus know the effects of obesity that influence women's reproductive health, since there is a close relationship between excess adipose tissue and the appearance of amenorrhea that lead to infertility and spontaneous abortions. either due to the poor quality of the oocyte, embryonic or uterine alterations. (4,8)

METHODOLOGY

A narrative literature review was carried out, which included relevant information from reliable studies, whose research process has informative material obtained from articles of scientific contribution published in the last 5 years, open access, systematic or narrative review articles and clinical trials in English and Spanish. Scientific works were excluded, with information corresponding to the literature of reports, theses to obtain academic degrees or when access to them has not provided the full text.

The search was carried out in databases such as: Scopus, Springer, Elsevier, Web of Science, PubMed and Cochrane, whose keywords used during the search were: obesity, infertility, anovulation; In such a way, articles related to the topic were selected, which provide greater rigor to the research. Similarly, within the search strategy, Boolean operators "AND, NOT" were used.

Once the search was completed, the inclusion and exclusion criteria previously set out were applied. Once the articles were selected, they were analysed and relevant information extracted.

PUBLICATION BODY

1.1. Definition

Obesity is a chronic multifactorial disease, resulting from the imbalance between food consumption or intake and caloric expenditure, which produces alterations at the systemic level, being one of the main causes of the high morbidity and mortality rate worldwide. Factors involved in their development include: poor lifestyle, interactions with behavioral patterns, and psychological, genetic,

economic, political, and social components. Its diagnosis, according to the recommendation of the World Health Organization (WHO), is based on the use of BMI, calculated from the weight and height of the individual, considering obesity as a BMI greater than 30 kg/m2; However, this method has presented limitations when evaluating the percentage and distribution of body fat, so these data must be complemented with anthropometric measurements, such as abdominal circumference and subcutaneous folds, or through the use of multicompartmental techniques: electrical bioimpedance, magnetic resonance imaging and computed tomography. (13,14) (15) (15,16)
As mentioned above, obesity is the main cause of alterations at the systemic level, and one of them is infertility, which is defined as the inability to conceive by maintaining an active sexual life within a period of 12 months, without the use of contraceptive methods or after 6 months in those women whose age is over 35 years. in such a way that interventions are required to allow a pregnancy to take place. Age is considered to be closely related to fertility, since the risk of infertility increases in women from the age of 30 onwards. (2,15) (17)

Table 1. Classification of obesity according to the WHO

Weight Status	BMI (kg/m2)
Normal	18.5-24.9
Overweight	25-29.9
Grade I obesity	30-34.9
Grade II obesity	35-39.9
Grade III obesity	Greater than or equal to 40

Source: WHO, https://www.who.int/es/news-room/fact-sheets/detail/obesity-and-overweight

1.2. Epidemiology

Obesity has become a problem worldwide since its prevalence has been on the rise, as it is estimated that 609 million adults suffer from obesity globally, affecting men and women in equal proportion, however, it has been reported that the most severe forms of obesity are more common in women. associated in them with disorders in the menstrual cycle, with women's fertility being the most affected. Although it is mentioned that obesity affects men and women in equal proportions, Villanueva D, et al. demonstrated in a cross-sectional study, with 971 adults, of which 558 were women, that the percentage of obesity (18%) in them was higher, compared to men (16%). This is also evidenced in a cross-sectional study carried out by Lemamsha H, where 401 adults between the ages of 20-65 years were randomly selected, where the highest number of cases with obesity was the female sex with a percentage of 47%, compared to the male sex which was 33.8%; Women between the ages of 20-49 years of age are the most affected. (9) (12) (18) (13)
Latin America is one of the regions with a high proportion of adults with obesity, as is the Caribbean, whose proportion corresponds to 29%. In Ecuador, 62.8% of adults are overweight and obese, but in adults between the ages of 19 and 59 the prevalence is 64%, with the female population, the mestizo ethnic group and the urban area being again the most affected. (18) (19) (5,14,20)
According to the Pan American Health Association in Latin America, 12% of couples have problems conceiving, and according to the National Institute of Statistics and Census, 1 in 6 Ecuadorian couples between 18-35 years of age have this problem. In Ecuador, the results in relation to fertility are new, since the high birth rate that years ago has been replaced by a lower fertility; It is estimated that the fertility rate in Ecuador has been decreasing, in 2008 the fertility rate was 2.68 and for 2018-2019 it fell to 2.40. (21)

1.3. Pathophysiological mechanisms of infertility and obesity in women of reproductive age

Obesity, in addition to being the main cause in the appearance of metabolic endocrine diseases such as diabetes, high blood pressure, myocardial infarction, is also responsible for reproductive disorders in the female sex, the same ones that in the long term increase the risk of spontaneous abortions and

infertility, either due to menstrual alterations, alterations in the quality of the oocyte or in embryonic implantation and development. (1,8)

1.3.1. Hyperinsulinemia and insulin resistance:

Insulin normally acts in different parts of the body, both ovarian and pituitary, allowing the production of steroid hormones and increasing the sensitivity of gonadotropin hormone receptors, present in theca and granulosa cells. However, when there is excess adipose tissue, the levels of the sex hormone-binding protein will be decreased, while the levels of androgens will be elevated, which will be subjected to the aromatization process, leading to the elevation of estradiol levels, which will be responsible for altering the function of follicle-stimulating hormone (FSH). blocking the production of gonadotropins. (10) (10) (3,8)

It has been shown that the distribution of fat at the central level in the female sex is closely related to insulin resistance, which in turn causes an increase in the production of ovarian androgens and a reduction in the hormone that transports sex hormones produced at the hepatic level. This causes the peripheral aromatization of androgens for their conversion to estrogen to increase and together with the levels of certain altered adipokines: leptin, insulin-like growth factor (IGF-BP) transporter protein; They allow disruption of the hypothalamic-pituitary-ovarian axis. Therefore, the main effect of insulin is to modulate the bioavailability of sex steroids, by inhibiting hepatic synthesis of the sex hormone carrier protein. (1) (1,3) (1)

1.3.2. Hyperleptinemia:

One of the main hormones affected is leptin, whose function is to stimulate folliculogenesis and the regulation of body weight by reducing appetite, therefore, the greater the amount of adipose tissue the higher the concentration of leptin, causing delay in the process of follicular maturation at the ovarian level; since when it is in normal values it stimulates folliculogenesis, but when its values are high, it has an inhibitory function; The consequences of which are: low antral follicle count, lengthening of the cycle or delay in m000enstruation and anovulatory cycles. Likewise, leptin produced by adipose tissue compromises the pulsatile secretion of (3,8) gonadotropin-releasing hormone, causing anovulatory infertility due to involvement of the hypothalamic-pituitary-ovarian axis. (3,10)

Leptin is responsible for the stimulation of gonadotropin-releasing hormone, and its prolonged stay will induce hypogonadism, reducing the secretion of gonadotropins (FSH, LH) and estrogens, altering fertility. (6)

Leptin receptors have been found at the hypothalamic and pituitary level, so this adipokine is related to the secretion of gonadotropins, such that leptin regulates folliculogenesis through the secretion of luteinizing hormone (LH) and follicle-stimulating hormone. It is also mentioned that follicular cells and the oocyte have leptin receptors, so it is considered that this hormone regulates follicular maturation and oocyte development, resulting in fewer mature oocytes. (22) (3,8)

1.3.3. Hyperandrogenism:

Another effect of obesity is hyperandrogenism, since adipocytes have the ability to produce steroid hormones from conserved inactive forms, thanks to enzymes expressed in adipocytes (17B-hydroxysteroid oxidoreductase and p450 cytochrome aromatase) in such a way that it allows the production of testosterone and estradiol. Estradiol will have some interference in the action of FSH, producing anovulatory cycles. (8,10,23) (8,10)

Therefore, anovulation sterility is more frequent as BMI increases, with abdominal adiposity being the main predictor of ovulatory dysfunction. However, obese women without ovulatory disorders suffer subclinical endocrinological changes that induce anovulatory cycles. (1,6) (1)

The alteration at the level of the hypothalamic-pituitary-ovarian axis results in the hypersecretion of LH, since the hypothalamic activity produces a greater number of pulsations of gonadotropin-releasing hormone, causing an excess of androgens and thus irregularity of menstrual cycles. In addition, the alteration of this axis is related to anovulation, characterized by amenorrhea present in

polycystic ovary syndrome, since the large amount of adipose tissue at the abdominal level is closely related to the production of androgens and high cardiovascular risk. (1,12) (3,24)

1.3.4. Polycystic ovary:

Among the pathologies related to metabolic syndrome we have polycystic ovary syndrome. This endocrinopathy is associated with abdominal obesity, insulin resistance, hyperandrogenism, and low adiponectin levels. Similarly, alterations in lipid metabolism during the gestation period damage the vascular endothelium, leading to poor placental perfusion, preeclampsia and premature birth, taking into account that insulin resistance that develops due to excess adipose tissue has negative effects on the endometrium and embryo implantation. (10) (10,25)

1.4. Causes of Infertility in Obese Women

Obesity is a health problem that mainly affects women of reproductive age, due to the alterations in the menstrual cycle already mentioned above, which make obese women three times more likely to be at risk of infertility, especially those with central obesity, whose negative aspects of obesity implicated in infertility are described in Figure 1. (6,8) (1,2)

Chaves B, et al. mention that the main alterations resulting from obesity are the alteration in the quality of the oocyte and low levels of the anti-Mullerian hormone, which is useful to assess the ovarian reserve or available follicles. (8,10)

Due to the low excretion of gonadotropin hormones and progesterone metabolites during the luteal phase, follicular dysfunction occurs due to the negative effect of obesity on the function of the corpus luteum. (10)

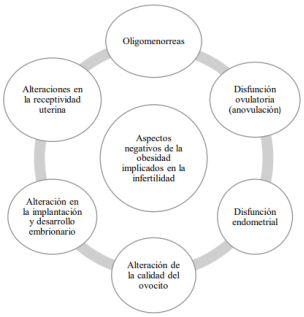

Figure 1. Negative aspects of obesity on fertility. Excerpted from "Obesity management in women of reproductive age" and written by Andreu A, Casals G, Vinagre I, Flores L. (1)

These effects, which lead to alterations in the menstrual cycle and, therefore, to an increased risk of infertility, are related to insulin resistance, since it increases the aromatization of sex hormones and the production of androgens. Therefore, the large conversion of estrogen from androgens in fat tissue increases its free levels, causing alteration in the hypothalamic-pituitary-gonadal axis. In addition, studies show that obese girls under 12 years of age have a higher risk of future infertility, since the development of the reproductive system has been affected by the early maturation of the hypothalamic-pituitary axis, due to its large production of estrogens, from the process of adrenal and ovarian androgenic aromatization, promoting the development of sexual characteristics. that lead to early adolescence, causing unfavorable effects on the reproductive stage, such as: ovarian dysfunction, poor oocyte quality, polycystic ovary development and risk of infertility. (3,8) (8) (2)

1.4.1. Menstrual cycle irregularities, ovulatory dysfunction

Menstrual anomalies such as oligomenorrhea (24% to 44.6%) and secondary amenorrhea (26.3%) have been more associated when adipose tissue is greater in the upper body portion than in the gluteofemoral portion; Since women whose body mass is greater in the lower body portion is metabolically healthy, because it acts in the release of insulin-sensitizing adipokin. (8,12)

Therefore, central obesity is closely related to insulin resistance, since, by increasing androgenic aromatization, the concentration of estrogen in adipose tissue and estradiol levels increases, which interferes with the synthesis of FSH, determining the prevalence of anovulatory cycles; In addition, together with the alterations of the adipokines involved, such as leptin and IGF-BP, they interrupt the hypothalamic-pituitary-ovarian axis, causing alterations in the menstrual cycle. Similarly, low levels of gonadotropin and progesterone hormones or decreased LH impulse prolong the follicular phase and shorten the luteal phase, respectively (3) (1,3) (1)

1.4.2. Endometrial dysfunction

One of the main risk factors for endometrial hyperplasia is obesity, since through histochemical studies it has been shown that, at a higher BMI, the expression of receptors for estrogen and progesterone at the glandular level is much lower compared to a normal-weight woman. In addition, at the molecular level there are also differences in gene expression in relation to embryo implantation (1,22) (1,22)

1.4.3. Oocyte quality

Normally, inflammatory cells play a certain role during the follicular and ovulatory phases, however, a greater production of this type of cells as a result of obesity, triggers an inflammatory state due to the lipotoxicity of adipose tissue and increased oxidative stress, which is detrimental to the meiotic and cytoplasmic maturation of the oocyte; This greater release of inflammatory markers, fatty acids and insulin, is concentrated at the intrafollicular level, whose negative effect on the cummulus oocyte complex, has an impact on ovarian function and embryonic development, so that the cytokines and chemokines located in the theca during the follicular phase will allow the increase of macrophages, neutrophils and dendritic cells. There is no alteration in the proportion of euploid embryos, but when the BMI is greater than 35 kg/m2, abnormalities may be found in the mitotic spindle and chromosomal alignment. (1,26) (26,27) (1,26)

1.4.4. Impaired uterine implantation and receptivity

The rate of spontaneous abortions in obese women has increased significantly, since the hormonal alterations that develop in them affect the invasion of trophoblastic cells and uterine receptivity; therefore, the higher the BMI, the higher the incidence of complications in uterine receptivity, due to a higher risk of infertility, adverse pregnancy events and unfavorable response in in vitro fertilization. (3,22)

It has been shown that the embryos of obese women have a lower quality compared to those of normal weight, since it has been shown that the success of fertilization techniques is lower, especially in women with morbid obesity, that is, that the pregnancy rate in obese women from donated eggs is lower in relation to normal weight women. especially when autologous oocytes are used, thus demonstrating that obesity is closely related to a reduced implantation rate. (3,22)

1.4.5. Miscarriages

Women whose BMI is greater than or equal to 30Kg/m2 have a higher risk of spontaneous miscarriages due to the effects of the inflammatory state that develops in obesity, the main negative effect being embryonic aneuploidy during the first trimester of gestation, since the excess of adipose tissue alters the meiotic and cytoplasmic maturation of the oocyte. resulting in chromosomally abnormal oocytes and embryos. In addition, studies suggest that an abnormal uterine environment is the main mechanism associated with miscarriages, especially due to an increased risk of congenital malformations, complications during pregnancy and the development of chronic diseases, in children whose mothers were obese. (7,28) (7,28)

1.5. Addressing Infertility in Obese Women

Obesity is a multifactorial disease that affects the quality of life of a large part of the adult population, therefore, the main objective of obesity management is to reduce the morbidity and mortality rate and

the risk of comorbidities. For a better approach to the complications of obesity, the therapeutic approach must be multidisciplinary, in such a way that the goals of the medical intervention are defined, considering that each patient has different comorbidities and risk factors, therefore, the treatment must be carried out in an individualized manner. (15) (1,15)

The initial treatment to avoid complications of obesity at a systemic level is the modification of different aspects of lifestyle, among which are: eating a healthy diet, reducing caloric intake and implementing physical exercise for 180 minutes a week, where any type of physical activity can be included, with aerobic activity being considered the best; in such a way that these aspects allow weight loss by 5% and with it the return of menstrual cyclicity and consequently the ovulatory cycle. (15,22)

Similarly, since obesity is a multifactorial disease, behavioral therapy is positive for treating negative behaviors that predispose to weight gain, especially in patients with a history or risk of developing mental disorders such as: depression, anxiety, eating disorders, among others. (7,29)

Once patients undergo behavioral changes in relation to diet and exercise recommended by the physician; the pharmacological part for the treatment of obesity will be applied to those patients with BMI greater than 30 kg/m2 or greater than 27 kg/m2 plus risk factors or associated comorbidities such as diabetes, hypertension and dyslipidemia; which will be used until the patient reduces 5% of body weight; However, if the patient does not adhere to this plan, treatment becomes ineffective. (15,30)

The drugs approved in Europe to treat obesity have action at the central level and in gastric emptying, among the most used we have semi-synthetic derivatives such as Orlistat, this drug acts at the gastrointestinal level, inhibiting gastric and pancreatic lipases; It is recommended for use in dyslipidemias, diabetes, when they do not tolerate centrally acting drugs or before undergoing bariatric surgery. Another medication used to treat overweight and obesity is Liraglutide, a glucagon receptor agonist, whose action is to suppress the glucagon response and appetite, by maintaining the feeling of fullness; It has been recommended for use in diabetic patients. (15,31) (15,30)

The use of bupropion-naltrexone has also been chosen, whose anorectic action is directly related to bupropion, by reducing appetite; while naltrexone prolongs its action. Its use is discontinued when the effects are not as expected, i.e. when the weight loss is less than 5%, or after the presence of adverse effects, such as: dizziness, insomnia and headache. Another combination of drugs approved by the European Food and Drug Administration (FDA) is phentermine-topiramate, whose effect is based on appetite control; This combination of both an appetite suppressant drug and an antiepileptic has allowed a weight reduction of up to 9%. Although there is evidence of the efficacy of these drugs in weight loss, their use in the preconception state is not fully recommended due to their teratogenic effect, however, phentermine is considered to have positive effects on weight loss and increase in the pregnancy rate. (30,31) (15) (29,31) (1)

These pharmacological and non-pharmacological measures will allow obese women to maintain an optimal weight, which allows them to conceive naturally. However, special techniques have been implemented that allow couples to reduce pregnancy attempts, through in vitro fertilization, whose recommendations are: not to be subjected to emotional or mental stress, to have medical advice, assessment of comorbidities and abdominal adiposity, in such a way that the possible negative consequences and safety of practicing this technique are known. Age is one of the limitations for this technique to be effective, as success rates have been shown to be lower in older women, as well as those with associated endocrinometabolic diseases such as diabetes or thyroid disease. (22) (1,22) (1,22)

In vitro fertilization, despite being a technique that increases the fertility rate in obese women, brings with it a high risk of preeclampsia, especially in the second and third trimesters of pregnancy, in addition to increasing caesarean section rates and the risk of death of the fetus and the mother; due to implantation defects and placental dysfunction. It is worth mentioning that this technique is recommended for women whose BMI is greater than 35kg/m2. (22) (22)

Bariatric surgery can be opted for when the BMI is greater than 40 kg/m2 or greater than 35 kg/m2 associated with comorbidities, especially it is considered as part of the treatment when the diabetic

patient has a BMI between 30-35 kg/m2. However, in 2022 the American Society for Bariatric and Metabolic Surgery, together with the Federation of Obesity and Metabolic Disorder Surgery, stated that bariatric surgery should be considered when the BMI is 35kg/m2, or otherwise when it is 30kg/m2 in the presence of type 2 diabetes mellitus. There are no conclusive studies where the fertility rate has improved after performing it, however, evidence has been found that bariatric surgery has improved hormonal imbalance and increased the rate of spontaneous pregnancy, as long as the nutritional status of the patient is assessed. (3,15,29) (32) (3,22)

2. RESULTS

A multicenter retrospective study conducted by Cozzolino M and collaborators, from 2016 to April 2019, based on data obtained in 7 clinics in Spain, applied ovarian stimulation to detect aneuploidy and euploid embryo transfer. The results were based on 3,480 cycles of in vitro fertilization, and BMI, allowing evidence that the rate of miscarriage in women with obesity was significantly higher, and the number of live births in those women was low. (28)

A descriptive study, conducted by Quintana A, Rivas E and Gonzáles J, included 137 women treated for fertility problems at the Territorial Center for Human Reproduction in Cienfuegos in 2012 and 2013. The pathological history in these women with the highest prevalence was obesity and thyroid dysfunction, whose predominant age range was 30 to 34 years of age. The results recorded in this study showed that 44.6% had oligomenorrhea and 27.7% had amenorrhea. Similarly, 66.4% were associated with secondary infertility, where 50.4% had an infertility time of less than 3 years. (12)

A descriptive cross-sectional study, conducted by Torres M and collaborators, included 88 couples with fertility problems, treated at the Guillermo Tejas Silva Teaching Polyclinic in the city of Las Tunas in Cuba, from 2017 to 2018. With respect to the data obtained from the female sex, it was determined that the majority of the population had a history of obesity and diabetes, whose predominant age was between 29 and 35 years of age, who also had a history of spontaneous abortions. Similarly, ovulatory disorders were determined to be the main cause of female infertility (17).

Women with excess adipose tissue present alterations in the menstrual cycle, since the inflammatory state that it generates interferes with the correct functionality of the hypothalamic-pituitary-ovarian axis, this is the cause of amenorrhea or oligomenorrhea, which alters the ovulatory process. Therefore, based on the information obtained from different studies, it is possible to determine that obese women have greater difficulty in getting pregnant spontaneously or through the use of assisted reproduction techniques, especially those with a BMI above 35kg/m2, or greater disposition of adipose tissue at the abdominal level. Hence the importance of taking preventive measures.

3. DISCUSSION

Obesity is a disease that currently affects a large part of the general population, however, the most severe forms manifest themselves in the female sex, resulting in negative aspects in women's reproductive health. Andreu A et al. indicate that the negative effects on ovulation can be reversed as long as there is a weight loss of at least 5-10%, considering that weight loss should be individualized, however, Ramírez A, et al, indicate that, although weight loss is beneficial in a woman's fertility, The results are evident in women under 35 years of age. (12) (1,8)

For the treatment of obesity, Kaufer M and Pérez J indicate that the first line is based on the implementation of lifestyle changes, modifications in the diet and implementation of physical exercise, but when positive results are not obtained, long-term drugs such as orlistat and liraglutide or drugs for short periods such as phentermine phenylpropanolamine are chosen. Metherolin, chlorpheniramine and mazidol, however, when it comes to increasing the conception rate, Andreu A et al. indicate that the use of exenatide, or liraglutide combined with metformin, is more beneficial than phentermine compared to metformin alone, especially when a spontaneous pregnancy is intended. (1,33)

Obesity is not only associated with infertility, but also with a lower effectiveness of assisted reproduction procedures. Reyna N, et al, state that the chances of embryonic development are the

same as the embryos of normal-weight women after in vitro fertilization. However, Andreu A et al. reveal that the probability of live birth in vitro fertilization is lower compared to normal-weight women, due to the higher concentration of intrafollicular insulin and markers of inflammation, in addition to the fact that the oocytes of women with BMI above 35Kg/m2 present alterations of the meiotic spindle. (34) (1)

Bariatric surgery is a restrictive procedure that, according to Kaufer H, et al and Frigolet M, et al, has reduced the morbidity and mortality rate in a large part of the obese population, due to positive metabolic changes, hormonal balance and resolution of comorbidities associated with obesity such as: diabetes, steatosis and hypertension; even before weight loss. Therefore, through studies found by Enríquez R, the hormonal balance secondary to surgery has benefited the sexual function of the woman, increasing the probability of spontaneous pregnancy by 58%, assisted fertilization by requiring less ovarian stimulation, good quality of embryos and lower rate of miscarriages. (33,35) (3)

Despite the benefits of surgical procedures, used for weight reduction, Tan HS, et al; Andreu A, et al and Ramírez A, point out that women undergoing bariatric surgery have presented heavy menstrual bleeding, increased risk of premature births or small for gestational age, due to the nutritional or malabsorptive deficit that is exacerbated during pregnancy, so it is recommended to maintain close nutritional surveillance and delay conception for at least one year after performing this type of surgery. (1,8,11)

In addition, due to the nutritional deficit presented by obese women or after having undergone bariatric surgery, Pereira J, et al recommend supplementation with 400ug/day of folic acid, in the same way Andreu A et al. recommend its use during the preconception stage, but with a daily dose of 5mg/day; In this way, neural tube defects will be avoided. (1,2)

4. CONCLUSIONS

Alterations in the menstrual cycle, ovarian and uterine failure, or poor oocyte quality, are secondary conditions to the disorder of the hypothalamic-pituitary-ovarian axis that develop due to excess adipose tissue, and interfere with female sexual function, making it advisable to take preventive measures to reduce the rate of obesity.

These measures include maintaining a healthy diet and implementing aerobic exercises, in order to reduce weight and avoid the incorporation of pharmacological or surgical treatment. In this way, it will also be possible to increase the probability of pregnancy, reduce spontaneous abortions, in addition to increasing the effectiveness of pregnancy through assisted reproduction methods. It is worth mentioning that the treatment of obesity is multifactorial, since in addition to genetic and environmental factors, psychological disorders are a problem when trying to lose weight, so psychological help is very important when it comes to managing obesity, having an impact on the fertility of pregnant women.

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