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СВЯЗЬ ОЖИРЕНИЯ С ЖЕНСКОЙ РЕПРОДУКЦИЕЙ

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ASSOCIATION OF OBESITY IN FEMALE REPRODUCTION

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Резюме. Очевидная, но прискорбная тенденция широко распространенной эпидемии ожирения представляет собой значительную угрозу для мирового общественного здравоохранения. Ожирение в настоящее время поражает более 21% женщин репродуктивного возраста во всем мире. Ожирение отрицательно влияет на многочисленные аспекты женского здоровья и вызывает осложнения беременности. Более того, ожирение препятствует репродуктивной способности женщин и связано с ановуляцией, синдромом поликистозных яичников (СПКЯ) и бесплодием.

Ключевые слова: ожирение, женская репродукция, механизмы, бесплодие, осложнения.

Resume. The evident yet regrettable trend of a widespread obesity epidemic has presented a significant threat to global public health. Obesity now affects more than 21% of women of reproductive age worldwide. Obesity adversely affects numerous facets of women's health and causes pregnancy complications. Moreover, obesity impedes women's reproductive capacity and is linked to anovulation, polycystic ovarian syndrome (PCOS), and infertility.

Keywords: obesity, female reproduction, mechanisms, infertility, complications.

Actuality. Obesity diminishes fertility, presenting a 2.7-fold heightened chance of infertility in women with a BMI exceeding 30 kg/m² and a 25-37% elevated risk of miscarriage in pregnant women relative to their normal-weight contemporaries, which emphasizes the necessity of the current study.

Purpose: to analyze and summarize materials from scientific publications and papers concerning obesity as a risk factor in female reproduction, emphasizing its mechanisms and detrimental effects.

Objectives:

1. To examine the molecular relationship between obesity and its impact on the hypothalamic-pituitary-ovarian axis, oocyte quality, embryonic development, the endometrium, and fetal growth.

2. To assess the implications of maternal obesity on pregnancy and childbirth.

3. To elucidate the ramifications of obesity on the efficacy of assisted reproductive technologies.

Materials and methods. This paper reviews all literature indexed in Google Scholar and PubMed about the impact of obesity on female fertility. The inquiry commenced in December 2024 utilizing the search term "Obesity as a risk factor in pregnancy," restricted to publications from 2010 onwards. Articles authored in English from the United States, China, Africa, and India were incorporated. A comprehensive review of the reference lists

of the selected papers was conducted to find any relevant articles related to the research. Only 43 articles, discovered by the search methodology, were included in this review. The predominant research encompassed in the analysis consisted of cohort studies, case series, and qualitative studies.

Results and their discussion. Obesity negatively impacts reproduction due to altered hypothalamic-pituitary-ovarian (HPO) axis function. In addition, obesity is characterized by adipocytes acting as endocrine organs. High insulin levels in obese women can lead to increased ovarian androgen production. Androgens aromatize to estrogen rapidly in the periphery due to increased adipose tissue, causing negative feedback on the HPO axis and impacting gonadotropin production. This condition causes menstruation irregularities and ovulatory dysfunction. Hyperinsulinemia plays a significant role in the development of polycystic ovarian syndrome (PCOS), identified by oligomenorrhea and hyperandrogenism. Obese women have higher leptin levels than normal-weight control subjects. Elevated leptin-BMI ratios lower IVF pregnancy rates. Studies also show decreased LH pulsatility in obese women. [1]

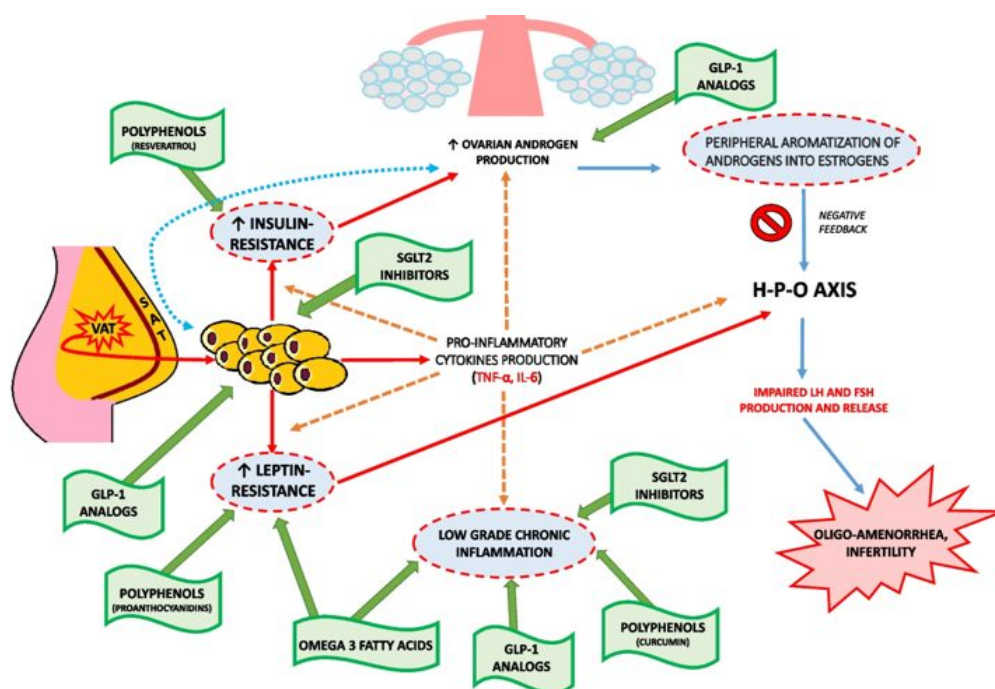


Fig. 1 – Impaired HPO axis and their consequences in obesity [1]

Obesity affects follicular environment in obese women undergoing IVF, leading to higher insulin, triglycerides, and inflammation markers. Obesity also affects the ovarian response to gonadotropin stimulation, resulting in lower oocyte yield and higher cycle cancellation rates. Obese women also exhibit more apoptotic follicles and smaller, less likely to be mature oocytes.[2] Mitochondria in obese mice have disrupted architecture, increased granulosa cell apoptosis, and increased endoplasmic reticulum (ER) stress. [3]. Obese women with polycystic ovary syndrome also have impaired oocyte competence. Obesity can lead to lipotoxicity, higher levels of circulating free fatty acids, which damage non adipose cells by increasing reactive oxygen species (ROS) that induce mitochondrial and ER stress leading to apoptosis, insulin resistance, and a chronic low-grade inflammation

state, affecting oocyte organelle damage. [2] These adverse effects of obesity on oocytes may subsequently influence endometrial receptivity and embryonic grade and development.

Tbl. 1. Comparing laboratory and clinical outcomes in 3 groups after IVF [4]

	Normal BMI	Overweight	Obese
No. of oocytes collected	586	771	338
Total fertilized oocytes. (%)	87.7	85.3	84
Good quality embryo at day 3 (%)	84	82.3	79.9
Good quality blastocyst (%)	92.9	91.5	88.7
Implantation rate (%)	53.7	31.8	28.2
Live birth rate (%)	89.6	52.3	39.5
Miscarriages (%)	2.2	2.7	6.7
Clinical pregnancy rate (%)	67.2	41.9	39.5

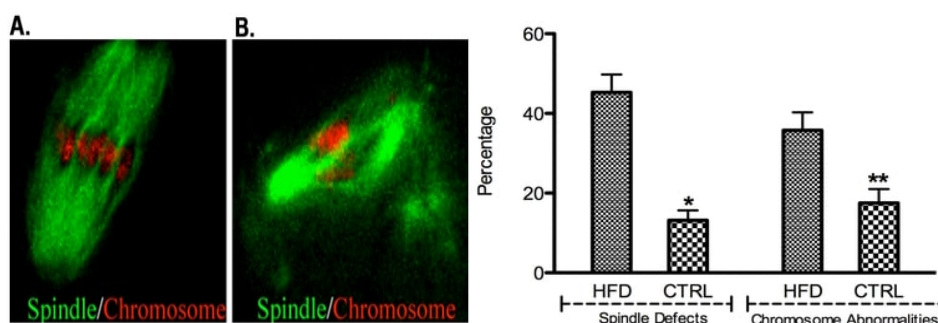
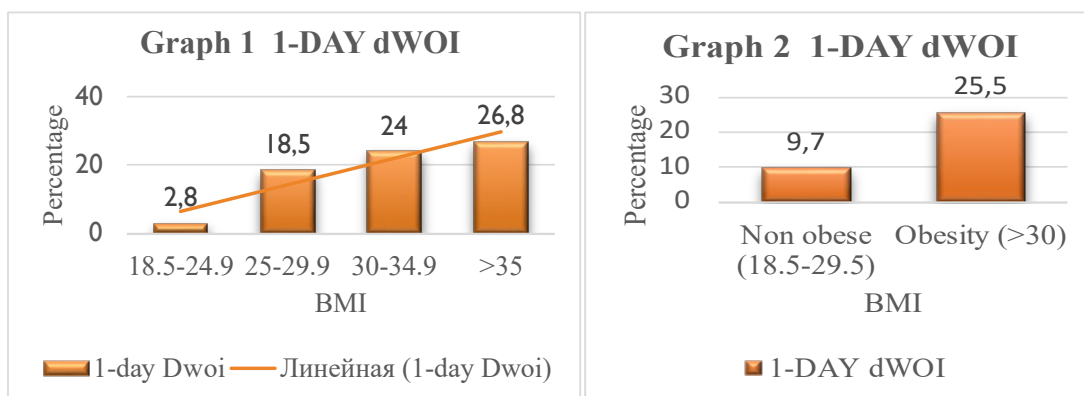


Fig. 2 – Oocyte MII spindles and chromosome alignment defects [3]

Aneuploidy in oocytes and embryos is a major cause of miscarriage, congenital disorders, and female infertility. Obese mice's oocytes show increased chromosomal abnormalities, affecting developmental competence and early embryonic death. [3]



Graph. 1 – Delay in window of implantation with BMI

Conflicting data exist about the significant impact of obesity on the endometrium. A recent study indicated that obesity adversely affects endometrial receptivity by prolonging the window of implantation, which correlates with an increase in body mass index and the patient's metabolic abnormalities. [5]

Obesity is also linked to over 50% of endometrial malignancies, with severe obesity increasing the risk of type 1 endometrial cancers by sevenfold, and overweight or obese individuals two to fourfold.

A recent study found that obese women with recurrent early pregnancy loss exhibit a heightened incidence of euploid miscarriage, a recognized risk factor for future miscarriage. The incidence of euploid miscarriage in obese women was 58%, whereas it was 37% in nonobese women. [2]

Obese women's cytokine profiles can affect fetal development outcomes. Metabolic variables like insulin, leptin, and IL-6 stimulate placental food transfer, while hypertension affects blood flow and restricts growth. Inadequate and excessive prenatal development can elevate risks of significant congenital malformations and even lead to long-term metabolic problems in offspring. [6]

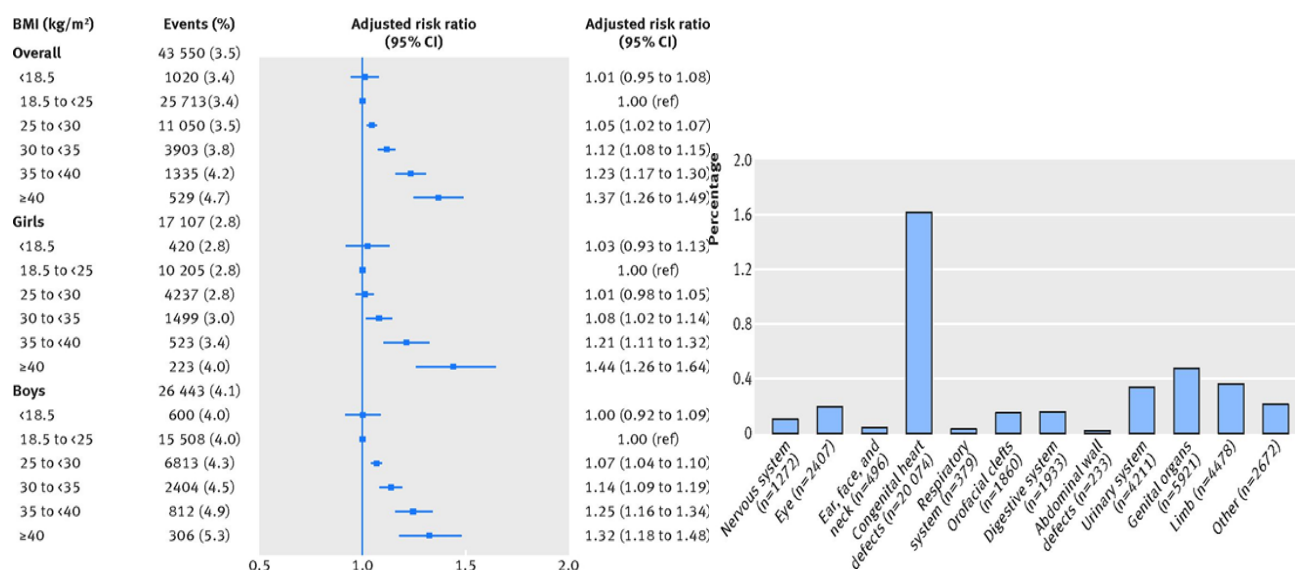
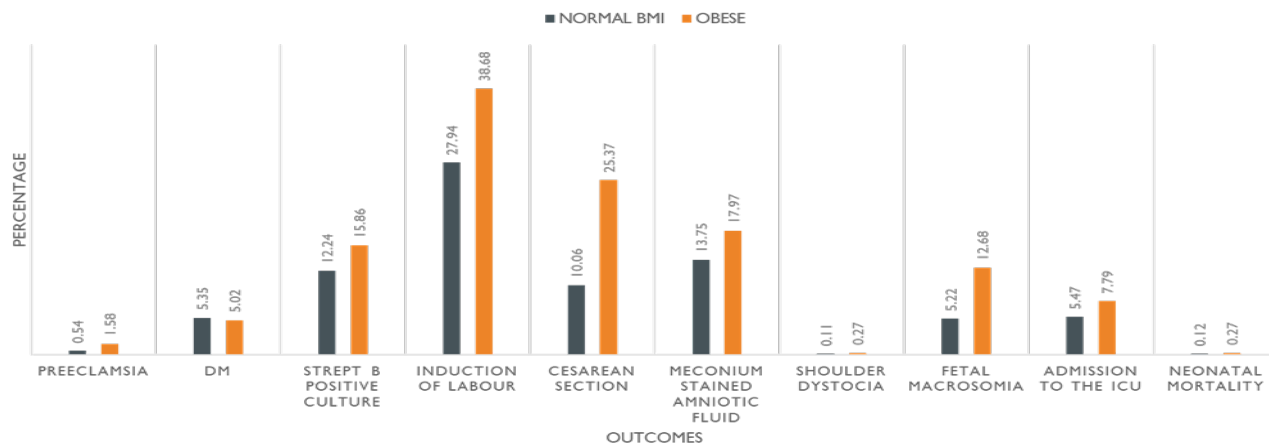


Fig. 4 – Major congenital malformations in liveborn singletons by maternal body mass index (BMI) [4]

Congenital heart defects represented the most common subtype of organ-specific malformation, with chances escalating in a dose-response manner correlated with maternal overweight and obesity. [6]

Numerous studies demonstrate that maternal obesity correlates with a heightened risk of negative maternal and fetal/neonatal complications. Pregnancy in this demographic of women should be regarded and handled as high risk. [5]



Graph. 2 – Effect of maternal obesity on pregnancy outcomes in women

As most studies have shown, obesity negatively impacts fertility and fertility treatments, reducing conception chances and affecting ovulation induction therapy efficacy. Obese women require higher gonadotropin dosages, exhibit suboptimal responses, and have lower retrieved oocytes. [3] Weight reduction in these women enhances their reproductive outcomes; nevertheless, for this process to be effective, it must be progressive and continuous.

Conclusions:

1. The systemic effects of obesity, such as hormonal imbalances and inflammation, disrupt the intricate processes of female fertility.
2. The effectiveness of assisted reproductive techniques, such as IVF, is influenced by obesity, highlighting the necessity of sustaining an ideal body mass index.
3. Consequently, tackling the relationship between obesity and infertility is crucial for improved reproductive outcomes worldwide.

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