Research Article

Gender Differences in the Effects of Obesity on Fertility: A Systematic Review

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Abstract

Background: The current paper focuses on obesity, a global concern to health that brings far-reaching implications, including high-impact effects on the state of reproductive health.

Aim of the study: This systematic review aims to synthesize current evidence on the relationship between obesity and fertility in males and females and its effects on conception, pregnancy and offspring health outcomes.

Material and Methods: A detailed literature search across various literature databases produced 12 good-quality studies published from 2010-2024.

Results: This review showed that obesity had a bad effect on male fertility through changes in sperm parameters and hormonal imbalance, probably due to epigenetic alterations. In females, it has been linked to ovulatory dysfunction, impaired quality of the oocyte and altered endometrial receptivity. Male and female obesity have been linked to poor success rates of assisted reproductive technologies. This review commented on the potential transgenerational effects of parental obesity on offspring health mediated by epigenetic mechanisms. The findings emphasized that strategies on reproductive health must therefore embody tackling obesity, including care of people planning a pregnancy and fertility treatments.

Conclusion: Future research directions should aim at clarifying the molecular mechanisms, developing targeted interventions and assessment of offspring health outcomes in long-term follow-up studies.

Keywords: Fertility; Gender; Obesity; Systematic

Introduction

Global health is seriously threatened by obesity, which has a significant impact on contemporary healthcare systems in a number of ways, including the creation of policies, financial strains and intervention tactics [1]. Numerous factors, such as governmental policies, economic situations, employment, educational background and individual behaviours and lifestyle choices, contribute to the complexity of obesity [2]. A Body Mass Index (BMI) of ≥ 25 kg/m² is considered overweight and ≥ 30 kg/m² is considered obese, according to the World Health Organisation [3].

Meanwhile, almost one in seven couples experience subfertility, which is characterised as the inability to conceive following a year of consistent, unprotected sexual activity [4]. Subfertility is caused by both male and female causes and research has progressively shown the molecular relationships between obesity and reproductive health, suggesting intricate interactions between metabolic dysfunction and fertility [5].

Alarmingly, obesity rates are rising worldwide. Obesity rates have more than doubled since 1975. Approximately 340 million children and adolescents and 650 million adults were categorised as overweight or obese by 2016 [2]. Significant ramifications flow from this increase for reproductive health in particular as well as public health.

The reproductive system is one of the endocrine systems that is affected by obesity. It is linked to ovulatory dysfunction and irregular menstruation in women. It lowers fertility in males by impairing sperm function and raising the likelihood of erectile dysfunction [6]. Additionally, the consequences of pregnancy are complicated by obesity; obese women are more likely to develop gestational diabetes, pre-eclampsia and gestational hypertension [7].

They are also more likely to experience labor induction, prolonged labor, cesarean delivery, postpartum hemorrhage, infections and premature birth [8]. Additionally, obesity is linked with increased rates of depression and anxiety during pregnancy and postpartum [9].

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Additionally, obesity has an impact on the health of foetuses and newborns, raising the risk of congenital defects, macrosomia and large-for-gestational-age babies. Complications such shoulder dystocia are more likely as a result and they can have detrimental effects on the mother and child [8].

Research on the significance of reaching a healthy body weight before to conception is noticeably lacking, despite the fact that the consequences of obesity on pregnancy and delivery are widely discussed in the literature. This disparity is alarming, according to Lindqvist et al., pregnancy frequently inspires women to adopt better lifestyles [10]. Studies show that pre-pregnancy BMI women frequently report worse dietary quality [11].

A thorough analysis of the research on the consequences of obesity on fertility is urgently needed, given the widespread prevalence of obesity and its significant implications on reproductive health and pregnancy outcomes. The purpose of this systematic review is to shed light on the connection between obesity and fertility as well as how it affects conception, pregnancy and the health of the children. In order to guide future research and improve clinical practice, the review will compile and critically assess the body of literature in order to design focused therapies to address these health issues.

Techniques and protocols

To gather and examine secondary data, a systematic review technique was used, with an emphasis on finding, picking, combining and evaluating pertinent research to offer proof of the influence of obesity on fertility and associated outcomes [12]. This approach is particularly effective for building a solid evidence base in reproductive health research [13].

The Cochrane handbook for systematic reviews of interventions and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement Page et al., quality criteria were followed in conducting the review. Following PRISMA rules makes reporting more transparent and thorough, which improves the review's dependability [12,13].

Inclusion criteria:

- Articles published from January, 2010 to March, 2024.
- Original research or review articles.
- Written in English.
- Examining the impact of increased BMI on fertility in both sexes.

Exclusion criteria:

- Articles published before January, 2010 or after March, 2024.
- Non-peer-reviewed articles, conference abstracts, or other non-scientific publications.
- Written in languages other than English.
- Focused solely on obesity during pregnancy without addressing preconception fertility.

Materials and Methods

In March, 2024 a thorough search of the literature was carried out using a number of electronic databases, including PubMed/MEDLINE, Embase and Web of Science. We also looked through the Cochrane library for pertinent systematic reviews and we used indexing sites to find any other papers. Controlled vocabulary and free-text phrases pertaining to BMI, obesity, fertility and reproductive health were incorporated into the search technique. To include the most recent research, the search was restricted to articles from January, 2010 to March, 2024.

Various combinations of "BMI", "overweight", "obese", "obesity", "fertility", "infertility", "subfertility", "reproductive health", "conception" and "preconception" were included in the search phrases. The search was narrowed down by using truncation symbols and the Boolean operators AND and OR. A manual search of pertinent review papers and reference lists was conducted to find further research and clinical trial registries were consulted for ongoing or recently completed research.

Search strategy

On 15 July, 2024, a search strategy was created and put into action. It combined free-text terms with regulated vocabulary (MeSH terms for MEDLINE and Emtree terms for Embase). The terms obesity/increased BMI, fertility/infertility and reproductive health were the main focus of the search. Only works published between 01 January, 2010 and 15 July, 2024 in the English language were included. The database searches were augmented with manual searches and clinical trial registration checks.

Procedure for gathering data

An altered standard sheet from Cochrane was used for data extraction. Five randomly chosen articles were used for a pilot test of the form and it was adjusted accordingly. The supervisor oversaw and verified the researcher's initial data extraction process using the improved form.

Data items

Data extracted included: The publication type, the author(s), the year of publication, the study design and the sample size. Participant characteristics, reproductive outcomes (such as time to conception, semen parameters and ovulatory function) and obesity measurements (such as BMI categories and waist circumference) were all taken into consideration. Confounding variables, significant findings, such as impact sizes and quantitative findings, weight-loss programs and how they affect reproductive outcomes. When appropriate, data were extracted independently for each sex and any reported interventions were documented.

Evaluation of quality: Using checklists from the Critical Appraisal Skills Programme (CASP) that were specific to the kind of study (qualitative, quantitative, or mixed-methods), quality was evaluated. With a maximum of 20 points per article, CASP checks have assessment questions with a scoring system: "Yes"=2 points, "Can't Tell"=1 point and "No"=0 points. Utilising the updated Cochrane risk-of-bias instrument, to evaluate bias risk, with independent review of grades to minimize bias.

Data synthesis

The results from the included research were integrated and analysed using a narrative synthesis technique. The association between obesity and fertility was explained through the development of themes that included qualitative and quantitative information. This method made it possible to examine in great depth the intricate relationships that exist between fat and fertility.

Results

15 July, 2024, saw the results of an advanced search across four databases: MEDLINE *via* PubMed (n=156), Embase (n=132), Web of Science (n=98) and Cochrane Library (n=41). After 37 duplicate entries were eliminated, 390 unique citations were left. After the title and abstract screening, 358 records were deemed irrelevant and were removed from the total of 390 records. 32 articles were then qualified for full-text screening. Following a thorough examination, twenty of them were eliminated on the grounds that the research did not specifically address obesity and fertility (n=8); there was insufficient data on BMI or reproductive outcomes (n=6); the study's design was flawed (n=4); and the language used was not English (n=2). Finally, 12 papers met the criteria to be part of this systematic review. A detailed summary of the study selection outcomes is shown in Table 1.

A healthy combination of in-depth reviews and original research papers comprised the 12 studies that made up this meta-analysis. They cover obesity in both sexes as well as its impact on several reproductive indicators. By investigating sperm parameters, IVF results and overall reproductive indicators with elevated BMI, they offered a fair-minded viewpoint on this subject (Figure 1).

Table 1: Systematic search results.

Database	Initial hits	Duplicates removed	Title/Abstract screening	Full-text review	Final inclusion
MEDLINE (PubMed)	156	14	131	11	5
Embase	132	12	112	8	3
Web of Science	98	8	85	5	2
Cochrane Library	41	3	30	8	2
Total	427	37	358	32	12

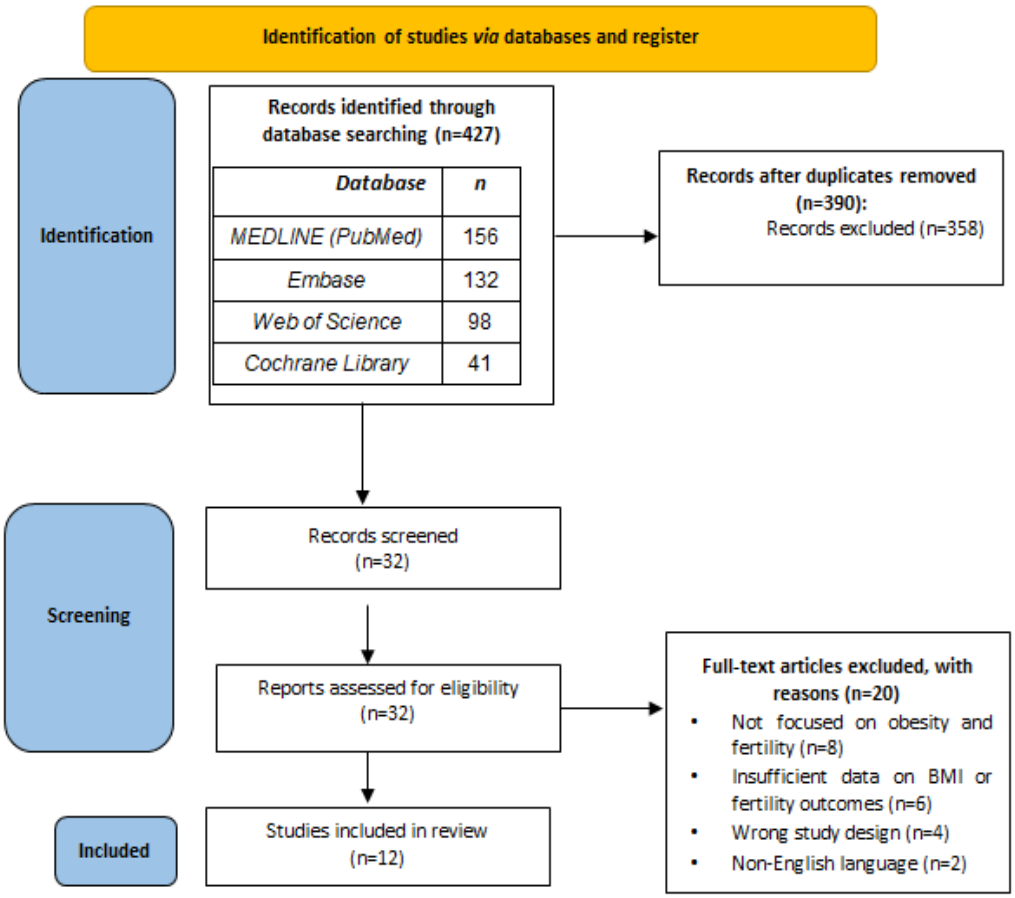

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Results flow chart.

Description of included studies

Twelve papers examining the complex association between obesity and fertility in males and females are included in this systematic review. These studies use a variety of approaches and methodologies to give a thorough overview of what is currently known about the subject. Refer to Annexure 1 design and methodological approaches for comprehensive details on each study, including authors, publication years, research aims, methodology, study settings, demographic characteristics, data collecting and analysis techniques and major indings Annexure 2.

The diversity of designs shown in the evaluated research reflects the intricacy of the link between obesity and fertility. These, six are thorough reviews that provide a wide-ranging summary of the body of extant literature [14-19].

Three studies also make use of quantitative techniques: Hajshafiha et al., carried out cross-sectional research [20]. The retrospective analyses were also carried out [21,22]. These research provide data-driven insights into the processes behind obesity and reproductive outcomes.

Location and geographic range: The study' many foreign settings demonstrate how worldwide obesity and fertility problems are. Reviews of the literature typically have a global viewpoint, referencing work from throughout the world. On the other hand, the empirical research was carried out in certain places in Greece, Iran and USA [20-22]. The analysis of cultural variables, environmental factors and healthcare system variations that may effect the obesity-fertility association is made possible by this regional variety.

Participants and sampling

The empirical research focusses on many pertinent populations, including: 301 couples having *In Vitro* Fertilisation (IVF) were studied by Anifandis et al., who emphasised both male and female aspects in fertility therapy. 2013 saw 159 male companions of infertile couples, according to Hajshafiha et al., According to Souter et al., 477 women underwent intrauterine insemination or ovulation induction for 1,189 cycles [20,22].

Based on different Body Mass Indices (BMIs), these studies offer insights into difficulties related to male and female fertility. Since literature reviews synthesise several research, they inherently cover a wider range of populations.

Gathering, examining and analysing data

The examined studies used a range of techniques for gathering and analysing data:

Literature reviews: Narrative synthesis of findings was conducted after extensive search tactics using strict inclusion and exclusion criteria were applied across several databases.

Empirical research: Applied methods such as retrospective analysis of medical records, blood samples and semen analyses. Statistical analyses were used to explore associations between obesity measures and fertility outcomes.

Key themes and findings

Impact on sperm parameters and quality: Reduced sperm count, decreased motility and changed morphology are only a few of the negative effects of obesity on sperm parameters. These effects are highlighted in studies [23,19]. These alterations were linked to elevated scrotal temperature and oxidative stress [17]. Negative connections between sperm quality and BMI were verified by meta-analysis in 2021 [23].

Male obesity has an impact on both the quality of the embryo and the success of *in vitro* fertilisation. Anifandis et al., discovered that higher pregnancy rates and improved embryo quality were seen by couples in which both spouses had a BMI of <25 kg/m² [21].

The detrimental effects of paternal obesity on embryo development were verified by Nikolic et al., highlighted the need of preconception counselling [24].

Hormonal changes: Men who are obese experience hormonal abnormalities, including low testosterone and problems with the hypothalamic-pituitary-gonadal axis. The Researchers documented noteworthy alterations in hormone levels, such as modified ratios of testosterone to oestradiol [17,20]. Increased aromatase activity was identified by Rastrelli et al., as the mechanism behind these abnormalities [25].

Molecular and epigenetic modifications: Both molecular and epigenetic modifications are brought about in obese sperm. Changes in histone modifications and DNA methylation were evaluated emphasised the possible long-term impacts on child health [18,23]. The weight reduction can repair some epigenetic modifications [26].

Impact of obesity on female fertility

Menstrual irregularities and ovulatory dysfunction: Obesity throws off menstrual cycles and regularity. The researcher talked about how obesity impacts ovarian function and hormone control [14,15]. Folliculogenesis is hampered by inflammation in the ovarian microenvironment [27].

Effects on oocyte quality: Obesity has a detrimental effect on oocyte quality, which has an effect on embryo development and fertilisation. This decreased oocyte competency [15]. In oocytes from obese women, molecular alterations, such as changed gene expression linked to mitochondrial function [28].

Effect on results of ART: Obesity has an impact on ART results since it lowers ovarian response and necessitates larger gonadotropin dosages. This discovery lower IVF operation success rates for obese women [15,22]. It is confirmed that lower live birth rates and higher miscarriage rates in this population [29].

Overall quality of included studies

The CASP checklist, modified for different research designs, was used in the evaluation to evaluate the quality of the investigations. Most of the studies have a methodological quality score of 15 or above. The two studies with the highest ratings (19 out of 20) indicating their superior quality [20,22]. Because of the CASP tool's adaption, literature reviews often received lower scores-between 12 and 17 out of 18. Cekici less explicit study design earned it the lowest score (12 out of 18) [16] .

Despite these discrepancies, research generally provides

a solid foundation for understanding how obesity impacts fertility. Although there are biases and limits, the combination of empirical research and literature evaluations guarantees a thorough investigation of the subject.

Endometrial alterations

Impact of obesity on the endometrium: The endometrium is negatively impacted by obesity, which has an impact on early pregnancy maintenance and implantation. According to Moussa et al., endometrial alterations brought on by obesity can lower fertility and increase pregnancy problems [30].

Using cutting edge imaging, Shan et al., demonstrated how obesity modifies endometrial vascularity and diminishes important implantation indicators, potentially leading to a decrease in ART implantation rates [31]. Zheng et al., emphasised the way that chronic inflammation brought on by obesity impacts the immune milieu within the endometrium, compromising the immunological balance required for a successful implantation and continued pregnancy [14].

Obesity and results of art

Success rates for IVF: Numerous studies have demonstrated the detrimental effects of obesity on IVF success rates. According to Anifandis et al., the highest rates of pregnancy and embryo quality were observed in couples when both spouses had a BMI of less than 25 kg/m² [21]. Imterat et al. and associates observed decreased IVF success rates among obese women, attributing this to poor oocyte quality, altered endometrial receptivity and embryo developmental issues [15]. Sermondade et al., reported a 32% lower odds of live birth for obese women compared to those with normal BMI, based on a meta-analysis of over 120,000 IVF/ICSI cycles [32].

Gonadotropin responsiveness

The ovarian response to gonadotropins is impacted by obesity. According to Souter et al., obese women had lower ovarian responsiveness and needed larger dosages of gonadotropins [22]. They also generated fewer follicles. Obese women require specific stimulation regimens for ART since they have lower AMH levels, produce fewer oocytes, need more gonadotropins and have decreased ovarian blood flow [33,34].

Embryo calibre

BMI affects the quality of the embryo in both male and female couples. Male BMI has a major impact on embryo quality, as demonstrated by Anifandis et al., highlighted the need of taking male BMI into account while undergoing reproductive treatments [21]. According to Pandey et al., younger women who are obese have lower-quality embryos [33]. Advancements made recently by Hieronimus et al. and Bartolacci et al. have identified altered cleavage patterns and epigenetic changes in embryos from obese parents, which can impact embryo development and offspring health [35,36].

Pregnancy complications

Preterm birth, gestational diabetes, preeclampsia and other problems are increased when a pregnant woman is obese. According to Moussa et al., insulin resistance and impaired glucose metabolism in obesity increase the risk of gestational diabetes [30]. According to Zheng et al., obese women are also more likely to experience preeclampsia and other obstetric problems, such as protracted labour and postpartum haemorrhage [14].

Possible impacts on the health of offspring

Foetal programming may cause maternal fat to affect the health of her kids. The dangers of metabolic diseases and macrosomia in children of obese mothers were brought to light by Moussa et al., [30]. While Zheng et al., addressed how maternal obesity may change the foetal epigenome, resulting in long-term health consequences such obesity and cardiovascular disease in kids, Venigalla et al., proposed transgenerational impacts of parental obesity [14,23].

Discussion

The data from 12 research is compiled in this review to show the significant effects of obesity on fertility and reproductive health, from preconception to the health of the progeny. The results highlight the necessity for all-encompassing methods of reproductive treatment that take into account the systemic impacts of obesity as well as the BMIs of both couples. Research indicates that obesity impacts both male and female fertility. For males, it affects sperm characteristics and epigenetic modifications, while for females, it impairs ovulatory function, egg quality and endometrial receptivity. Obese individuals have much worse results with ART, requiring individualised treatment plans. The significance of preconception counselling and obesity treatment is underscored by the possibility of generational impacts resulting from parental obesity [37-39].

Impact of obesity on mental health and emotional well-being

Obesity also impacts on physical health; it also significantly affects mental health and emotional well-being, which can, in turn, influence fertility. Those struggling with obesity often deal with stigma, diminished self-esteem and depression, all of which can interfere with hormonal balance and menstrual regularity. The psychological stress and anxiety linked with obesity may hinder reproductive functions and lower the chances of conception. Addressing these mental health issues alongside physical health interventions offers a more comprehensive approach to enhancing reproductive outcomes. Future research should focus on incorporating mental health support within obesity management programs to better address the complex nature of infertility related to obesity.

Epigenetic mechanisms and intergenerational implications

Obesity can impact fertility not only through direct physical changes but also through epigenetic mechanisms. Epigenetic modifications, including DNA methylation and histone changes, can alter gene expression without modifying the DNA sequence itself, potentially affecting reproductive health and the development of offspring. These modifications can be influenced by environmental factors and lifestyle choices, making them important targets for intervention. Further research

should explore how obesity-induced epigenetic changes influence reproductive outcomes and whether these alterations can be inherited by future generations, potentially affecting intergenerational health. Understanding these processes could lead to new therapeutic approaches and preventive strategies for managing obesity-related reproductive issues.

Significance of early interventions and lifestyle changes

Implementing early interventions and lifestyle modifications is crucial for reducing the negative impact of obesity on fertility and reproductive health. Preventive measures, such as encouraging healthy eating, regular exercise and weight management prior to conception, can significantly lower the risk of fertility problems associated with obesity. Healthcare providers should emphasize lifestyle counseling as part of preconception care. Moreover, public health initiatives aimed at preventing obesity from an early age are vital for improving long-term reproductive health outcomes. Showcasing successful intervention programs and advocating for their wider adoption can help address the growing issue of obesity and its associated reproductive challenges.

Conclusion

The substantial and complex impact of obesity on fertility, including possible generational consequences, is confirmed by this research. For obesity treatment and BMI evaluation to be integrated into reproductive care, a paradigm shift is required. Preconception counselling and tailored ART treatments ought to be commonplace. Obesity should be a focus of public health programs in order to enhance reproductive health outcomes. Subsequent investigations have to examine molecular pathways, specific therapies and enduring consequences.

Limitations

Some of the limitations include the use of BMI as the only indicator of obesity, variations in methodology and variability in research designs and outcome measurements. Molecular processes influencing gamete quality and embryo development should be the main areas of future study. Focused measures to lessen the negative impact of obesity on conception. The long-term health consequences for children of fat parents. differences in the effects of obesity in various populations.

Author Contributions

All authors have accepted responsibility for the entire content of this manuscript and consented to its submission to the journal, reviewed all the results and approved the final version of the manuscript.

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Institutional Review Board (IRB)

Ethical review and approval were waived for this study due to secondary data analysis for the systematic review and meta-anlysis.

Data Availability

The Data will be available after writing correspondence to the author.

Conflict of Interest

The authors declare no conflict of interest.

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