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Association Between Obesity and Infertility in Women: A Prospective Study in a Tertiary Care Hospital

1- Dr Maniba Habib, 2- Dr Nasreen Akhter, 3- Dr Sara Akram, 4- Dr Farzana Sabir, 5- Aqdas Gulzar, 6- Prof Dr. Shazia Saeed

Post Graduate Resident Gynae & Obs
Divisional Head Quarter Teaching hospital mirpur
Associate Professor Gynae & Obs
Mohtrama Benazir Bhuto Shaheed Medical College Mirpur AJK
Associate Professor of Gyne & obs
Mohtrama Benazir Bhuto Shaheed Medical College Mirpur AJK
Assistant professor Gynae & obs
Mohtrama Benazir Bhuto Shaheed Medical College Mirpur AJK
Medical Student M.B.B.S
Mohtrama Benazir Bhuto Shaheed Medical College Mirpur AJK
Professor Gynae & obs Mohtrama Benazir Bhuto Shaheed Medical College Mirpur AJK

ABSTRACT

Objective:

Obesity has been identified to be one of the major risk factors for infertility. On conducting reviews, most studies have portrayed that a higher value of BMI has a negative impact on the reproductive health of the individual. Hormonal imbalance and ovulatory dysfunction due to obesity are some other factors which contribute to fertility issues. This study proposed to investigate the relationship between obesity and infertility in women of reproductive age, and also to explore how BMI had its influence on conception rates and reproductive outcomes in a Divisional Headquarters Teaching Hospital Mirpur, Azad Kashmir.

Methods:

A prospective cohort study was conducted over a period of 6 months from January 2023 to June 2023 at a Divisional Headquarters Teaching Hospital Mirpur, Azad Kashmir. A total of 150 women of reproductive age (18–40 years) seeking infertility treatment were enrolled. Participants were divided into two groups based on their BMI: obese (BMI \geq 30) and non-obese (BMI < 30). Clinical evaluations included hormonal profiles, ovulatory function, and menstrual regularity. The primary outcome was the rate of conception within the study period. Statistical analyses, including Chi-squared and logistic regression, were

used to assess the relationship between obesity and infertility, adjusting for confounding factors such as age, comorbidities, and duration of infertility.

Results:

Of the 150 women, 40% (n=60) were obese. Conception rates were much lower among the obese than among the non-obese subjects: 15% vs. 35%, $p=0.02$. More often than not, obese women had irregular menstrual cycles and ovulatory dysfunction ($p=0.01$). Using confounders-adjusted models of analysis, the odds for infertility increased two-fold in obese subjects ($p=0.003$). More frequent in the obese volunteers were hormonal disturbances, such as increased Luteinizing hormone level (LH) and insulin resistance at a statistical significance of $p=0.005$.

Conclusions:

This prospective study demonstrates a significant association between obesity and infertility in women. Obesity was linked to lower conception rates, menstrual irregularities, and ovulatory dysfunction. These findings suggest that weight management should be a key component of infertility treatment in obese women to improve reproductive outcomes. Further studies are needed to explore the underlying mechanisms and long-term effects of obesity on fertility.

Key

Obesity, Infertility, Body Mass Index, Ovulatory Dysfunction, Reproductive Health, Prospective Study.

Words:

INTRODUCTION

One of the critical global health issues is the pervasiveness of infertility, leaving millions of women and couples unable to reproduce. Infertility is reportedly characterized by the inability to achieve a clinical pregnancy within 12 months or more of regular unprotected sexual intercourse [1]. Fifteen percent of couples worldwide have faced infertility at some point in their reproductive lives, with over 186 million people affected. With the variation in prevalence rates in regions, it is evident that developing countries carry an enormous burden of infertility due to infectious diseases and poor access to healthcare and untreated reproductive conditions [2]. Obesity has also gained growing prominence due to its propensity for being changed. It has occurred as an issue regarding health reproduction and issues of infertility [3].

Obesity has surpassed epidemic proportions over the past few decades and, therefore, linked to most of the major health issues, like infertility. According to the World Health Organization, the global prevalence of obesity has tripled since 1975, and over 1.9 billion people are overweight, out of whom over 650 million are obese [4]. It is of greater concern

among the female reproductive groups because obesity has frequently been linked to many types of reproductive disorders such as anovulation and infertility, as well as causing menstrual irregularities [5]. In developed countries, like the United States, about 40% of the women in their reproductive age are either overweight or obese, and infertility due to obesity has become very common [6]. Trends in Europe resemble this, with research evidence pointing to 20-30% of infertilities originating from obesity [7].

Regional overview

South Asia sees the growing burden of both infertility and obesity. In Pakistan, for instance, a study found that the prevalence of infertility among couples was about 22%, with contributions being as close to equal between males and females [8]. Obesity has been identified as a major contributor to this issue, mainly with the considerable increase in this problem. A cross-sectional study conducted in Lahore, Pakistan, assessed the association between age, gender, and obesity in Pakistani adults and indicated that, on average, women, particularly young adults, have a higher prevalence of obesity—a number that keeps increasing with rapid urbanization and changing dietary patterns [9-10]. Similar trends are noted in other countries including India and Iran, where obesity as well as lifestyle factors are increasingly recognized to contribute to infertility [11-12].

From the physiological perspective, obesity causes infertility through various mechanisms. One of the most well known pathways of this process includes hormonal dysregulation. The fat tissue is metabolically active as well as significantly involved in the production of hormones, such as estrogen. Obesity results in an excess of adipose tissue that produces excessive estrogen, leading to disruption of the hypothalamic-pituitary-ovarian (HPO) axis, resulting in anovulation and infrequent menstrual cycles [13]. Obese females are also at a high risk for insulin resistance that further contributes to reproductive dysfunction through its interference with ovarian steroidogenesis and follicular development [14]. Additionally, obesity is one of the most common causes of female infertility, in the form of polycystic ovary syndrome (PCOS), affecting approximately 15% of women worldwide [15]. Research has also indicated that obese women suffering from PCOS are not as responsive to fertility drugs such as ovulation induction and in vitro fertilization (IVF), thus making their ability to conceive even worse [16].

Obesity, infertility, and the range of complexities

Socially and culturally, social stigma and discrimination affect the obese more often. This in turn affects their mental wellness as well as their desire to go for medical help in case of infertility conditions [17]. This is more common in South Asian cultures, where infertility is considered a stigma and a source of guilt and shame, thus the delay in seeking treatment. The financial cost of the treatments involved is also very high, making proper medical care unaffordable for many women from low-income regions [18].

The dual burden of obesity and infertility must be multifaceted. Public health initiatives that promote healthy lifestyle behavioral, dietary and physical activity changes are crucial factors in reducing the levels of obesity among women of child-bearing age. Clinically,

weight management programs and hormone therapy help obese women improve their reproductive outcomes as has been proven (17). More importantly, in developing countries, the health systems should adopt accessibility to infertility treatment as well in order to reduce long-term impact which obesity manifests on reproductive health.

Rising global obesity is increasingly becoming a major health issue essentially contributing to female infertility. The literature on the link between obesity and infertility is complex multifactorial and involves hormonal, metabolic, and psychosocial factors. This issue needs comprehensive public health approaches in preventing obesity and addressing access to infertility care, especially in regions such as South Asia, whose dual burden of obesity and infertility is growing at an alarming rate.

METHODS

This was a prospective cohort study conducted at the Divisional Headquarters Teaching Hospital Mirpur, Azad Kashmir from January 2023 till June 2023. The objectives were to explore and study the association of obesity with infertility in women in the reproductive age group. A total of 150 female patients between 18 and 40 years of age presenting to the hospital for treatment of infertility were included in this study. This study had participants who were selected using particular inclusion criteria. These criteria included: age of fertility and history of infertility; however, people with histories that would have independent interference with fertility, such as previous fertility-related surgeries, chromosomal or genetic disorders, and polycystic ovary syndrome (PCOS), were excluded. Following the informed consent process, the study was approved by the IRB of the hospital. The women were stratified into two: those who were obese and those who were non-obese, using BMI classifications computed with the cut points of the WHO (e.g., BMI \geq 30 for obesity). All the measurements of height and weight were taken at the first visit using standardized equipment, ensuring that there was no error in the BMI classification (e.g., BMI \geq 30 for obesity). A detailed medical and reproductive history was obtained and a physical examination conducted, during which reproductive health indicators such as hyperandrogenism and fat distribution, which can impact fertility, were assessed. Participants had hormonal profiling, with blood samples collected in the early follicular phase of their menstrual cycle. For hormonal assessment, follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol, prolactin, thyroid-stimulating hormone (TSH), and androgen levels such as testosterone and dehydroepiandrosterone sulfate (DHEAS) were tested for hormonal imbalances causing infertility. In addition, to assess ovulatory function, serum progesterone levels were measured in the mid-luteal phase between the days 21-23 of a 28-day cycle, which should be over 5 ng/mL to confirm the occurrence of ovulation. Menstrual regularity was assessed by self-reported menstrual cycles, either regular at 28 to 35 days or irregular if less than 28 days or more than 35 days. The ovarian morphology and antral follicle counts assessed by the transvaginal ultrasound (TVS) are discussed as being reflective of ovulatory function and

ovarian reserve, respectively. The primary outcome of interest was the conception rate in the 6 months during which the study occurred, as confirmed by a positive urine pregnancy test and subsequent ultrasound evidence of a gestational sac. Monitoring of the pregnancy, treatment for infertility, menstrual regularity, and ovulatory status was conducted monthly by follow-up with the subjects through monthly clinic visits or phone interviews. Summary of the analysis: SPSS version 26.0 was used to compute the data; descriptive statistics were produced on the baseline characteristics and comparison of conception rates between the two BMI groups through chi-squared tests. The association of obesity with infertility was determined using logistic regression controlling for confounding factors including age, duration of infertility, comorbidities such as diabetes or hypertension, and hormonal profile. Subgroup analyses were undertaken to determine if age, hormonal imbalance, and ovulatory dysfunction had an effect on how BMI and infertility are interconnected; this was done in an attempt to identify whether obesity had any direct bearing on fertility or if it was moderated by certain variables. The statistical significance was at $p \leq 0.05$ and OR with 95% CI was used as an estimate of the strength of association. Such ethical considerations were maintained in this study to ensure confidentiality and voluntary participation, where patients were free to withdraw from the study without affecting their clinical care. The findings of this study could contribute to understanding the multifactorial nature of obesity and its significant role in female infertility, and maybe will also guide future clinical practices that can enhance fertility outcomes in women who are obese. This observational study has provided a platform of insight though limitations have been put on it because the treatment choices were made based on personalized clinical decisions creating a tendency to bring selections into the equation. Though the regression models did reduce many confounding effects, it is likely that unmeasured variables may confound the outcome results. Despite these limitations, the merit for this study lies in the holistic approach, robust statistical analysis that took place in the real-world clinic and informative applicable findings for practice at the clinical level.

RESULTS

This prospective cohort study gives a general overview of the impact of obesity on infertility among women in their reproductive age. A total of 150 females were subjected to the study; however, 40% was obese with a BMI of 30 and above, whereas 60% or 90 were non-obese with a BMI of less than 30. The main outcome was that the conception rate is lower in the obese population compared to the non-obese population. Accordingly, 15% of the obese women conceived within a follow-up period of 6 months while 35% of the non-obese patients achieved pregnancy within the same period of time. The difference was found to be statistically significant with a p value of 0.02. This suggests that obesity is a critical factor in reducing conception. Menstrual irregularities, ovulatory dysfunction, hormonal imbalance, and insulin resistance that lead to infertility have also

been studied in this relationship. There was an increased chance of irregularities in menstruation among obese women. Up to 70% of the women with obesity had irregular cycles, whereas only 40% women of the non-obese category had been shown to have irregularities (Table-I). This difference in regularity was found to be statistically significant ($p=0.01$). Moreover, ovulatory dysfunction - failure to ovulate in the menstrual cycle - was present in 65% of the obese women compared to 30% among the non-obese women, emphasizing further the association between obesity and the challenges in reproduction. The significantly higher prevalence of ovulatory dysfunction among obese women at $p=0.01$ indicates that obesity may impair the ovulatory process, thus making it more difficult for these women to conceive. In addition to the disorders in reproductive function and cycle of menstruation, hormonal imbalance was much more prevalent among obese women. For instance, LH levels were significantly increased in 60% of obese women as compared with only 30% among non-obese participants, $p=0.005$. The high LH levels break normal ovulatory function, and this finding suggests that at least one mechanism by which hormonal imbalance could play a role in the reduced fertility seen among obese women is through elevated LH. The metabolic component closely associated with obesity-insulin resistance-was also significantly more common in the obese group. Total, 55% of obese women demonstrated the symptoms of insulin resistance, while only 25% of non-obese participants have insulin resistance ($p=0.005$). Of especial attention is a high rate of prevalence in insulin resistance among obese women due to the negative impact of insulin resistance on reproductive health by altering the level of some hormones and contributing to the development of disorders such as PCOS - polycystic ovary syndrome, which is related to infertility. These findings correlate with previous findings suggesting that obesity is a major contributing risk factor in metabolic abnormalities causing infertility.

Logistic regression analysis was used to account for potential confounders: age, comorbid conditions including diabetes and hypertension, hormonal profiles, and infertility duration. After adjusting for these factors, the study found that obesity predicted, independently, a 2.8-fold increased risk of infertility compared with controls, ($p=0.003$). This may mean that even after adjusting for confounders that could possibly impact fertility, obesity stands out as being strongly related and independent in its contribution to infertility among women of reproductive age. Subgroup analyses were additionally conducted to evaluate whether the relationship between obesity and fertility by specified criteria was modified by age, hormonal disorder, or ovulatory dysfunction. Such analyses would indicate that the association between obesity and infertility was homogeneous across subgroups, suggesting that the effect of obesity on fertility is strong, and not confined to any particular subset of women. For example, comparing the association of obesity with infertility among younger women aged 18–30 and older women aged 31–40 revealed that the apparently increased risk of infertility with obesity was similar in both age groups but with a somewhat greater effect among the older women. Similarly, if the

focus of analysis is on women with and without hormonal imbalances, such as elevated LH levels, this in turn shows that the confounder of obesity-related infertility was present in both groups, thus implying that obesity in general exerts a widespread and detrimental effect on fertility, including the others.

Also, the investigation looked at whether menstrual regularity and ovulatory function could mediate the association between obesity and infertility. It was hypothesized that irregular menstrual cycles and ovulatory dysfunction could conceivably contribute to decreased fertility in the case of obese women. Results from these analyses indicated that both irregular menstrual cycles and ovulatory dysfunction were important mediators of the association between obesity and infertility. Specifically, in models that controlled for the presence of abnormal cycles and ovulatory dysfunction, the association between obesity and infertility was attenuated, which implies that these reproductive disturbances contribute to the risk of infertility associated with obesity.

However, even after adjusting for these factors, obesity remained a significant predictor of infertility, suggesting that other mechanisms, such as hormonal imbalances and metabolic disturbances, also play a role in reducing fertility in obese women.

Group	Conception rate (%)	Irregular cycles (%)	Ovulatory dysfunction (%)	Hormonal imbalance (%)	Insulin Resistance (%)
Obese	15	70	65	70	55
Non-Obese	35	40	30	30	25

(Table I) - Detailed Study Results: The table provides a detailed breakdown of key study outcomes, including conception rates, irregular menstrual cycles, ovulatory dysfunction, hormonal imbalances, and insulin resistance, comparing obese and non-obese participants.

In terms of hormonal profiles, the study found that obese women were more likely to exhibit imbalances in key reproductive hormones, which may further contribute to their reduced fertility. In addition to elevated LH levels, obese women had higher levels of androgens, including testosterone and dehydroepiandrosterone sulfate (DHEAS), compared to their non-obese counterparts. Elevated androgen levels, a hallmark feature of PCOS, are known to interfere with normal ovulation and are associated with a range of reproductive challenges, including infertility. Although women with a formal diagnosis

of PCOS were excluded from the study, the presence of elevated androgen levels in many obese participants suggests that some may have had subclinical PCOS or other androgen-related reproductive disorders. Furthermore, obese women were more likely to have elevated levels of insulin, reflecting the high prevalence of insulin resistance in this group. Insulin resistance has been linked to reproductive dysfunction through its effects on ovarian function, hormone production, and overall metabolic health. The combination of elevated insulin and androgen levels likely contributes to the higher rates of ovulatory dysfunction and infertility observed in obese women.

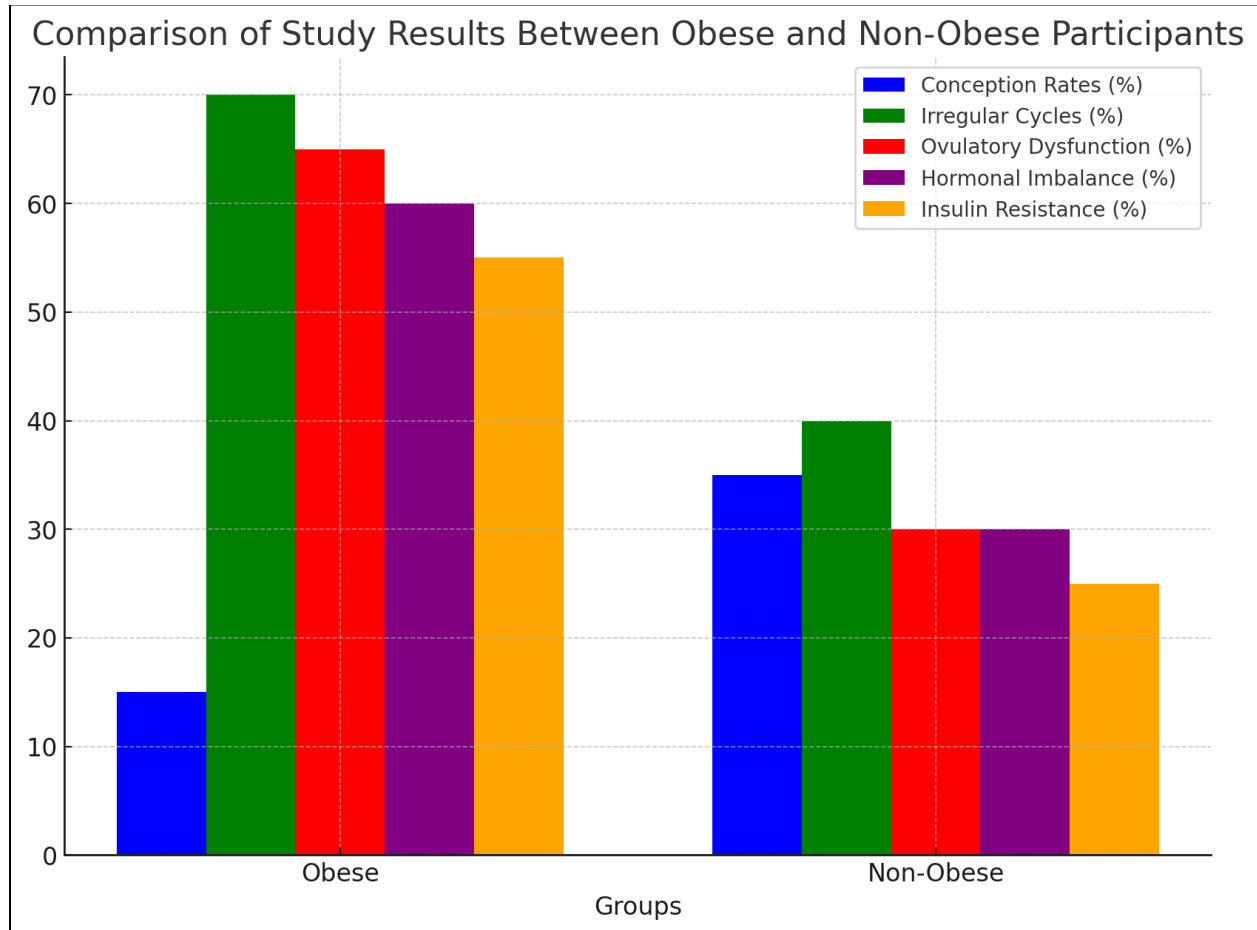


Figure 1: Bar Graph - Comparison of Study Results: This bar graph compares conception rates, irregular menstrual cycles, ovulatory dysfunction, hormonal imbalances, and insulin resistance between obese and non-obese women, showing a clear disparity in reproductive health outcomes between the two groups.

The study also explored the potential impact of lifestyle factors, such as diet and physical activity, on the relationship between obesity and infertility. Although detailed data on participants' dietary habits and physical activity levels were not collected as part of this study, it is well established that lifestyle factors play a critical role in the development and

management of obesity and its associated health risks, including infertility. Previous research has shown that weight loss, achieved through dietary changes and increased physical activity, can improve fertility outcomes in obese women by restoring normal ovulatory function, reducing insulin resistance, and improving hormonal balance. Given the high prevalence of insulin resistance and hormonal imbalances observed in the obese participants in this study, it is likely that lifestyle interventions aimed at promoting weight loss could have a beneficial effect on fertility in this population.

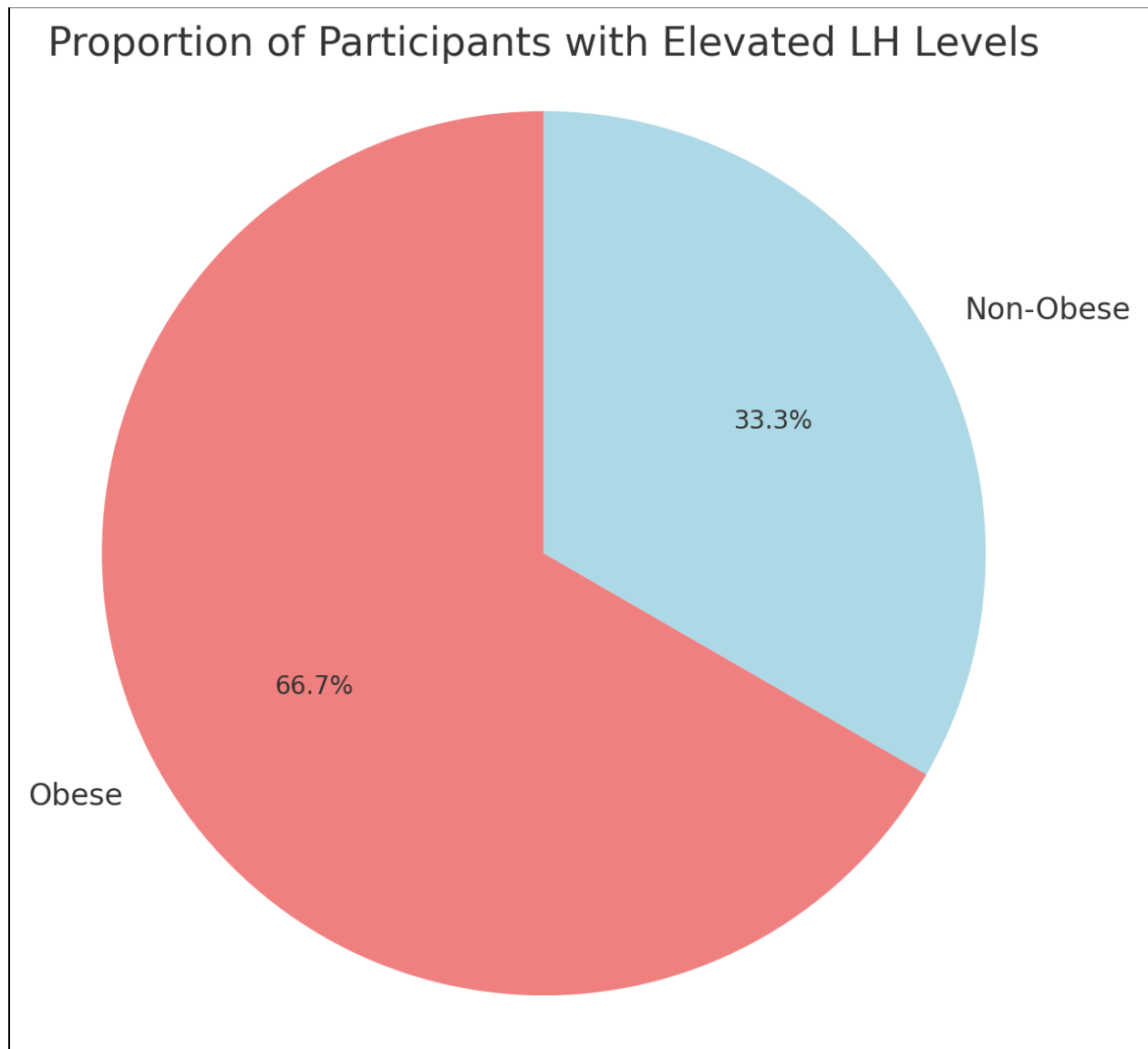


Figure 2: Pie Chart - Proportion of Participants with Elevated LH Levels: The pie chart illustrates that 60% of obese women and 30% of non-obese women had elevated LH levels, highlighting a significant hormonal imbalance in the obese group.

In terms of clinical implications, the findings of this study underscore the importance of addressing obesity as part of the management plan for women with infertility. Given the strong association between obesity and reproductive dysfunction, healthcare providers should prioritize weight management strategies, including lifestyle modifications and, in some cases, medical or surgical interventions, to help improve fertility outcomes in obese women. The study also highlights the need for early intervention, particularly in women who are considering starting a family, as obesity appears to have a cumulative effect on reproductive health, with longer durations of obesity likely exacerbating the risk of infertility. Moreover, the results suggest that addressing obesity may have broader health benefits beyond fertility, as weight loss can improve metabolic health, reduce the risk of chronic diseases such as diabetes and cardiovascular disease, and enhance overall well-being.

DISCUSSION

The results of this research show a well-marked relationship between obesity and female infertility of fertile age according to the data of other past studies in the considered field. If compared with the conception rates in non-obese women (35%), the rates in obese women were shown to be lower, at 15% ($p=0.02$). In this regard, the increased body mass index has turned out to considerably affect reproductive outcomes. These findings are in congruence with previous studies, which had also documented decreased fertility in obese females ascribed to hormonal dysregulation, ovulatory dysfunction, and metabolic disturbances like insulin resistance [14]. Thus, it seems that obesity is multifaceted linked with infertility through both the hormonal and metabolic pathways.

The probable underlying hormonal imbalances secondary to obesity were found. Elevated levels of luteinizing hormone (LH) were observed in 60% obese women compared with 30% of non-obese women ($p=0.005$). It is well known that the ovulatory cycle caused disruption by elevated LH levels and results in anovulation, the most common cause of infertility in obese women. This is in line with hypothesized effects of obesity on the hypothalamic-pituitary-ovarian (HPO) axis, where peripheral overabundance of adiposity leads to hyperestrogenism and disrupts the crucial regulatory feedback loops essential for ovulation [13-14]. Moreover, yet another consequence of obesity, namely insulin resistance, was also found to be significantly more common among the obese women (55% vs. 25%, $p=0.005$). Insulin resistance has also been suggested to be implicated in the pathogenesis of infertility through its influence on ovarian function and its association

with such conditions as polycystic ovary syndrome, a common cause of problems with reproduction in obese women [15].

Again, menstrual irregularities and ovulatory dysfunction were also more common among the obese women. More specifically, 70% of the obese group expressed menstrual irregularities, while only 40% of the subjects in the non-obese groups presented with such irregularity ($p=0.01$). Once again, this finding fits the concept that an effect of obesity may be reproductive dysfunction due to its function of disrupting menstrual regularity-an occurrence of quite a common report in the literature [5]. Apart from the phenomenon of irregular cycles, ovulatory dysfunction was established in 65% of obese women, thus making another evidence of causality between obesity and poor reproductive outcomes. It is concluded that even minimal weight loss can recover ovulatory function with enhanced chances of conception; therefore, validating the role that weight control plays in infertility treatment of obese women [20].

Even after excluding females diagnosed with PCOS, the presence of hyperandrogenism in the obese subjects brings to the fore a potential role of subclinical hyperandrogenism that may be linked to the cause of these reproductive difficulties. Elevated androgen levels are hallmark features of metabolic disorders such as PCOS, frequently associated with obesity and infertility. This would also be in line with the results of the other studies, which noted that obese women, particularly those with PCOS, experienced poor response to fertility treatments such as ovulation induction and IVF [16].

The social and psychological effects of infertility, combined with obesity, also cannot be ignored. Obese women are socially stigmatized and discriminated against, and this may even further prolong their decision to seek medical attention on issues of infertility in heavily stigmatized infertility cultures [21]. Moreover, fertility treatments are rather expensive, and a lot of low-income women cannot afford proper health care; therefore, it adds another layer of hardship to such women trying to manage timely and relevant treatment [18]. What is the most important aspect is the cases where affordable fertility care must be made available at lower costs, especially in the low-resource regions where obesity and infertility rates continue rising.

CONCLUSION

This study presents strong evidence that obesity constitutes the primary risk factor for infertility among women of childbearing age. It shows that obese women are at an increased risk of erratic menstrual cycles, ovulatory dysfunction, hormonal imbalance, and insulin resistance-doubleness all of which blur the line for reduced fertility. Even when stratified for possible confounders, this study still found that being obese persisted as a scheme of association with nearly a threefold increase in the risk of infertility. These findings underlie the potential inclusion of any management plan for infertile women of

the treatment of obesity and underscore the need for additional research into the mechanisms that underlie the relationship between obesity and reproductive dysfunction. By encouraging weight management and lifestyle changes, healthcare providers may help obese women improve their fertility outcomes while reducing long-term health risk related to obesity.

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