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The relationship between recurrent pregnancy loss and obesity

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Abstract

Recurrent pregnancy loss (RPL) is a multifactorial condition, with approximately 50% of cases classified as unexplained recurrent pregnancy loss (URPL). This study investigates the association between body mass index (BMI) and RPL, focusing on gestational week at miscarriage, the number of pregnancy losses, and BMI as a predictive marker for RPL. This retrospective cohort study included 400 women aged 20–40 diagnosed with RPL who attended Şanlıurfa Training and Research Hospital between November 6, 2021, and November 6, 2023. Participants were classified into four groups based on BMI categories: underweight (<18.5 kg/m², n=50), normal weight (18.5–24.9 kg/m², n=150), overweight (25.0–29.9 kg/m², n=120), and obese (≥30.0 kg/m², n=80). Obese women had the earliest mean gestational week at miscarriage (6.8±1.3 weeks) and the highest average number of pregnancy losses (3.0±0.6). Obesity is a significant risk factor for RPL, leading to earlier pregnancy losses and increased miscarriage frequency. Weight management should be prioritized to improve pregnancy outcomes, and future research should explore additional obesity-related factors contributing to RPL.

Keywords: Body mass index, gestational week, obesity, pregnancy loss, recurrent pregnancy loss, reproductive health

Introduction

Recurrent pregnancy loss (RPL), defined as two or more consecutive pregnancy losses before 20 weeks of gestation, is a distressing condition that affects approximately 1–2% of couples trying to conceive [1,2]. The etiology of RPL is multifactorial, involving genetic, anatomical, immunological, and endocrine factors. However, in nearly half of the cases, no identifiable cause can be determined and these are classified as unexplained recurrent pregnancy loss (URPL) [3].

Obesity, as measured by body mass index (BMI), has been increasingly recognized as a modifiable risk factor for adverse reproductive outcomes, including RPL [4]. Obesity is associated with metabolic dysregulation, chronic inflammation, and hormonal imbalances, all of which can impair endometrial receptivity, placentation, and fetal development [5,6]. Studies have demonstrated that higher BMI levels are linked to an increased risk of early pregnancy loss, suggesting that obesity significantly impacts the success of conception and pregnancy maintenance [7].

Despite its widespread use, BMI has limitations in accurately reflecting body fat distribution and its associated risks. Central obesity, often assessed through waist circumference or waist-to-hip ratio, is more strongly correlated with adverse pregnancy outcomes than overall body mass [8]. Nevertheless, BMI remains a standard tool in clinical practice due to its simplicity and accessibility.

Understanding the relationship between BMI and RPL is critical for developing effective prevention and management strategies. Given the increasing global prevalence of obesity, identifying its role in pregnancy outcomes has significant clinical and

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public health implications [9]. This study aims to evaluate the association between BMI and RPL, focusing on the impact of obesity on gestational week at miscarriage and the frequency of pregnancy losses. By identifying obesity's role in RPL, this research seeks to provide insights into targeted interventions to improve reproductive outcomes and reduce miscarriage risk in obese individuals.

Material and Methods

Study Design and Setting

This retrospective cohort study was conducted at the Department of Obstetrics and Gynecology, Şanlıurfa Training and Research Hospital, between November 6, 2021, and November 6, 2023. The study aimed to investigate the relationship between BMI and RPL. The study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

Study Population

A total of 400 women aged 20–40 years, who presented with a history of RPL (defined as two or more consecutive pregnancy losses before 20 weeks of gestation), were included in the study. Patients with identifiable causes of RPL, such as uterine anomalies, chromosomal abnormalities, infections, or systemic diseases (e.g., diabetes, hypertension), were excluded. Only patients diagnosed with URPL were included in the study. Embryo-less pregnancy cases (anembryonic pregnancies) were also included in the analysis.

Data Collection

Demographic data, obstetric history, and anthropometric measurements were obtained from medical records. Height (cm) and weight (kg) were recorded, and BMI was calculated using the formula:

$$BMI=Weight\ (kg)/Height\ (m)^2$$

Participants were categorized into four BMI groups based on the World Health Organization (WHO) classification:

- Underweight: BMI<18.5
- Normal weight: BMI 18.5–24.9
- Overweight: BMI 25–29.9
- Obese: BMI≥30

The gestational week at miscarriage and the total number of pregnancy losses were recorded for each participant. The study specifically focused on URPL cases, ensuring that participants had no identifiable underlying causes for pregnancy loss. Patients with a history of recurrent miscarriages due to genetic, immunological, or uterine structural anomalies were excluded to maintain the study's focus on unexplained cases.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics (version 26.0). Normality of continuous variables was assessed using the Shapiro-Wilk test. Variables with normal distribution were compared across BMI groups using One-Way ANOVA with Tukey HSD or Games-Howell post-hoc tests, depending on variance homogeneity. Non-normally distributed variables were analyzed using the Kruskal-Wallis test, followed by Dunn-Bonferroni post-hoc analysis when significant. Categorical variables were assessed using the Chi-square test, and Fisher's exact test was applied when cell frequencies were <5.For continuous variables, normally distributed data were reported as mean±standard deviation (SD), whereas non-normally distributed data were presented as median (25th–75th percentile).A sample size calculation was performed to ensure adequate statistical power, and a P-value <0.05 was considered statistically significant after Bonferroni correction for multiple comparisons.

Ethical Considerations

The study was conducted in compliance with the Declaration of Helsinki. Ethical approval was obtained from the Clinical Research Ethics Committee of Harran University on November 13, 2023 (approval number: HRÜ/23.21.36). Written informed consent was waived due to the retrospective nature of the study.

Results

The mean gravidity (number of pregnancies) was 4.3±2.1, indicating a relatively high reproductive history among participants. The parity (number of births) averaged 2.7±1.3, suggesting that while most participants had multiple pregnancies, not all resulted in live births. The mean age was 29.4±4.8 years, reflecting a reproductive-age population. Anthropometric data showed an average height of 160.5±6.2 cm and a weight of 68.3±12.4 kg, which provides insight into the general physical characteristics of the participants. These baseline characteristics are crucial for understanding potential associations between maternal factors and pregnancy outcomes (Table 1).

Table 1. Gravidity, parity, age, height, and weight characteristics

Characteristic	Value (Mean±Standard deviation)
Gravidity (number of pregnancies)	4.3±2.1
Parity (number of births)	2.7±1.3
Age (years)	29.4±4.8
Height (cm)	160.5±6.2
Weight (kg)	68.3±12.4

cm: centimeters, kg: kilograms

Analysis revealed a significant association between BMI and both miscarriage count and gestational age at miscarriage. Specifically, women classified as obese exhibited the highest mean miscarriage count (3.0±0.6), with a statistically significant difference compared to the normal BMI group (p=0.01). Similarly, overweight women also demonstrated an increased miscarriage count (2.7±0.8) compared to the normal BMI group (p=0.03). In contrast, the underweight group did not show a statistically significant difference in miscarriage count when compared to the normal BMI group (p=0.15) (Table 2).

In terms of gestational age at miscarriage, both the obese and overweight groups experienced miscarriages at earlier gestational weeks, with mean values of 6.8±1.3 and 7.1±1.5 weeks, respectively. These differences were statistically significant when compared to the normal BMI group (p=0.01 and p=0.04, respectively). Conversely, the underweight group showed a later gestational age at miscarriage (7.5±1.2 weeks), though this difference was not statistically significant (p=0.12) (Table 2).

Table 2. Miscarriage count, gestational week at miscarriage, and pregnancy count by BMI categories

BMI category	Sample size (n)	Mean miscarriage count (±SD)	p-value (miscarriage count)	Mean gestational week (±SD)	p-value (gestational week)
Underweight	20	2.3±0.7	0.15	7.5±1.2	0.12
Normal	120	2.5±0.9	Reference	7.3±1.4	Reference
Overweight	150	2.7±0.8	0.03	7.1±1.5	0.04
Obese	110	3.0±0.6	0.01	6.8±1.3	0.01

BMI: body mass index, n: number of participants, SD: standard deviation, p-value <0.05 indicates statistical differences

These findings suggest that elevated BMI is associated with both an increased risk of miscarriage and an earlier gestational age at miscarriage. This highlights the importance of preconception weight management, particularly in overweight and obese women, to potentially reduce the risk of adverse pregnancy outcomes. Future studies with larger sample sizes and consideration of potential confounding factors, such as maternal age and comorbidities, are warranted to further explore these associations.

A flowchart has been added to illustrate participant distribution, providing a clearer overview of the study population (Figure 1).

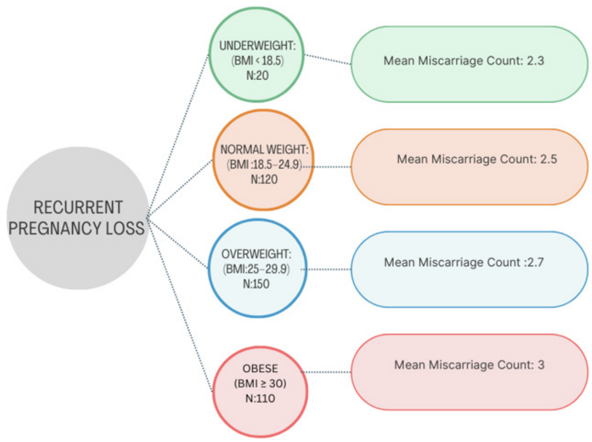

Figure 1. Association between BMI categories and recurrent pregnancy loss

Discussion

Summary of Findings

RPL is a multifaceted reproductive health issue with significant physical and psychological consequences [10]. This study establishes a significant association between obesity, as measured by BMI, and adverse pregnancy outcomes. Our findings reveal that higher BMI levels correlate with an increased number of miscarriages and earlier gestational losses. Specifically, obese participants exhibited the highest mean miscarriage count (3.0±0.6) and the earliest mean gestational week of miscarriage (6.8±1.3). These results are consistent with existing literature, including a 2017 systematic review and meta-analysis, which identified a significant increase in the risk of RPL among overweight and obese women [11]. Similarly, a 2021 meta-analysis found that women with a history of RPL had a mean BMI that was 0.7 kg/m² higher than that of women without such a history, supporting the observed association between elevated BMI and pregnancy loss [12].

Obesity and Mechanisms of Pregnancy Loss

The pathophysiological link between obesity and RPL can be attributed to chronic inflammation, insulin resistance, hormonal imbalances, and impaired endometrial receptivity. Our findings align with previous research indicating that visceral fat accumulation induces systemic inflammation and oxidative stress, which adversely affect placental development and increase the likelihood of pregnancy loss [13]. Studies have also highlighted how obesity-related hormonal alterations, such as changes in leptin and adiponectin levels, impair endometrial receptivity, thus heightening the risk of miscarriage [14]. These disruptions are further compounded by insulin resistance and hyperinsulinemia, which have been implicated in defective trophoblast invasion and abnormal placentation. This study reinforces the importance of incorporating metabolic markers alongside BMI in reproductive health evaluations, echoing recommendations from recent research on the role of metabolic dysfunction in RPL.

Clinical Implications and Future Research Directions

The findings of this study underscore the urgent need for targeted interventions addressing obesity in women at risk of RPL. While BMI remains a widely used clinical indicator, it should not serve as the sole parameter for risk assessment. Integrating additional metrics such as waist circumference and specific metabolic markers can provide a more nuanced understanding of an individual's reproductive risk profile. Evidence suggests that even modest weight loss prior to conception can significantly reduce the risk of miscarriage and improve pregnancy outcomes

[11,15]. This highlights the potential benefits of comprehensive weight management programs including lifestyle modifications, nutritional counseling, and, where appropriate, pharmacologic interventions for women with obesity who are planning pregnancies [16].

Future research should aim to investigate the role of obesity-related biomarkers, such as inflammatory cytokines and adipokines, in the pathogenesis of RPL [17]. Longitudinal studies examining the impact of preconception weight loss on reproductive outcomes would provide valuable insights into effective preventative strategies [18]. Additionally, exploring the combined influence of genetic predisposition and metabolic factors on RPL could pave the way for more personalized approaches to risk assessment and treatment [19].

Strengths and Limitations

One of the primary strengths of this study is its robust sample size, which allowed for detailed analysis of the relationship between BMI and RPL. The retrospective design enabled the inclusion of a broad dataset, enhancing the generalizability of the findings. However, this design also introduces inherent limitations in establishing causality. Furthermore, the exclusive reliance on BMI as an obesity measure may overlook the complex interplay between fat distribution, metabolic health, and reproductive outcomes. Future studies should incorporate alternative measures of adiposity, such as waist-to-hip ratio and body fat percentage, as well as longitudinal data to better elucidate the causal pathways linking obesity to RPL.

Conclusion

Obesity significantly increases the risk of recurrent pregnancy loss (RPL) beyond BMI alone. While BMI is a useful measure, it has limitations and should be considered alongside factors like inflammation, fat distribution, and metabolic dysfunction. Effective weight management and lifestyle interventions are crucial for reducing RPL risk. This study underscores the need for a comprehensive approach to obesity's impact on reproductive health, focusing on underlying mechanisms and targeted strategies to improve maternal and fetal outcomes.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
A small amount of the expenses was covered by the researchers.

Ethical Approval
The study was conducted in compliance with the Declaration of Helsinki. Ethical approval was obtained from the Clinical Research Ethics Committee of Harran University on November 13, 2023 (approval number: HRÜ/23.21.36).

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