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Original Article

Risk Factors of Pregnancy Failure in Infertile Patients Undergoing Assisted Reproductive Technology

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Abstract

Background: Assisted Reproductive Technology (ART) represents a critical advancement in the treatment of infertility, providing hope to many couples struggling to conceive naturally. Despite its success, pregnancy failure remains a significant concern, influenced by various factors such as age, BMI, and underlying medical conditions.

Objective: The main objective of this study was to identify the risk factors associated with pregnancy failure in infertile patients undergoing ART treatments.

Methods: This clinical audit was conducted at Bahria International Hospital, Rawalpindi, from January 2023 to January 2024. Data were collected from 85 patients undergoing ART treatments, including In Vitro Fertilization (IVF) and Intracytoplasmic Sperm Injection (ICSI). The study included comprehensive demographic information, clinical history, ART cycle details, laboratory results, and lifestyle factors. Pregnancy failure was defined as either biochemical pregnancy loss or clinical pregnancy loss. Ethical approval was obtained, and data were analyzed using SPSS version 25. Descriptive statistics summarized patient characteristics, while comparative analysis and multivariate logistic regression were used to identify significant risk factors.

Results: The study included 85 patients with a mean age of 34.5 years. Those experiencing pregnancy failure had a higher mean age of 36.2 years compared to 33.2 years in those without pregnancy failure. The mean BMI was higher in the pregnancy failure group (26.0 kg/m²) versus the no pregnancy failure group (23.8 kg/m²). Significant risk factors for pregnancy failure included older age (OR=1.15, 95% CI 1.05-1.25, p=0.002), higher BMI (>25 kg/m²) (OR=2.45, 95% CI 1.10-5.47, p=0.03), and the presence of underlying medical conditions (OR=1.90, 95% CI 1.02-3.55, p=0.04).

Conclusion: Older age, higher BMI, and underlying medical conditions significantly increased the risk of pregnancy failure in infertile patients undergoing ART. Personalized treatment approaches addressing these risk factors could improve ART outcomes and enhance the chances of successful pregnancies.

1 Introduction

Infertility, defined as the inability of a couple to conceive after at least 12 months of regular unprotected intercourse, affects approximately 6.5 million individuals in the United States, representing about 10% of the reproductive-age population (1,2). In China, the rate of childlessness among couples of childbearing age is estimated to be around 25% (3). The etiology of infertility is multifactorial, encompassing both male and female factors, as well as psychosocial elements and the adverse effects of certain hormones and drugs used to enhance fertility (4). Assisted Reproductive Technology (ART) has emerged as a pivotal advancement in the treatment of infertility, providing a viable solution for many couples who face challenges in conceiving naturally. ART includes techniques such as In Vitro Fertilization (IVF) and Intracytoplasmic Sperm Injection (ICSI), which have become integral in reproductive medicine (5).

Despite the significant advancements in ART, pregnancy failure remains a critical concern, with various factors influencing the success rates of these technologies. The risk of miscarriage, encompassing both premature miscarriage and unrecognized embryo implantation failure, is influenced by a myriad of factors including the genetic makeup of the patients, their overall health, and specific ART procedures employed (6,7). Age, ovarian reserve, and comorbid conditions are notable factors that co-accelerate with the success rates of ART (8,9). Furthermore, lifestyle choices, such as diet and exposure to certain chemicals, can exacerbate the challenges faced during ART treatments. Consequently, it is imperative to identify and mitigate the determinants of clinical pregnancy rates post-ART to enhance its efficacy and accommodate the increasing demand for these services (10).

Infertility, which affects a substantial number of individuals globally, presents not only a medical challenge but also significant emotional and psychological burdens on couples. The ART procedures, while offering hope, also demand a thorough understanding of the associated risk factors that could lead to pregnancy failure. These include advanced maternal age, higher body mass index (BMI), and underlying medical conditions such as polycystic ovary syndrome (PCOS), endometriosis, and tubal factor infertility, all of which can adversely affect ovulation, fertilization, and implantation processes (11). For instance, PCOS is associated with anovulation and metabolic syndrome symptoms, whereas endometriosis can cause adhesions and inflammation, complicating the implantation process (12).

A critical examination of ART outcomes reveals that advanced maternal age significantly correlates with reduced fertility and higher pregnancy failure rates due to diminished oocyte quality and quantity (13). This underscores the importance of personalized patient counseling and treatment planning, taking into account the patient's age and recommending appropriate interventions. Moreover, an elevated BMI has been linked to hormonal imbalances, poor oocyte quality, and inadequate endometrial lining, which collectively impair implantation and pregnancy success (14). Pre-ART weight management could thus play a crucial role in improving treatment outcomes.

The Vermont 2004 study indicated that the type of ART (IVF vs. ICSI) and the ovarian stimulation protocols might not significantly influence pregnancy failure rates, suggesting that individual patient characteristics might be more decisive in determining ART success (15-17). However, the quality of embryos transferred appears to be a critical factor, with higher quality embryos correlating with better pregnancy outcomes, though this study did not find a statistically significant difference in this aspect.

In conclusion, understanding the risk factors associated with pregnancy failure in ART is essential for developing effective prevention and treatment strategies. Advanced maternal age, higher BMI, and the presence of underlying medical conditions are significant risk factors that need to be addressed to improve ART outcomes. Personalized treatment approaches, including pre-ART weight management and tailored medical or surgical interventions for underlying conditions, could enhance the chances of successful pregnancies. The insights gained from this study are expected to contribute to better clinical practices and improved patient care in reproductive medicine.

2 Material and methods

This clinical audit was conducted at Bahria International Hospital, Rawalpindi, from January 2023 to January 2024. The study aimed to identify the risk factors associated with pregnancy failure in infertile patients undergoing Assisted Reproductive Technology (ART). The inclusion criteria encompassed patients undergoing ART treatments such as In Vitro Fertilization (IVF) and Intracytoplasmic Sperm Injection (ICSI), with complete medical records and follow-up data available up to the confirmation of pregnancy or pregnancy failure.

Data were collected from the patients' medical records, encompassing a wide range of demographic and clinical information. This included age, body mass index (BMI), clinical history detailing the duration and type of infertility, and records of any previous ART cycles and underlying medical conditions. Detailed ART cycle information was also gathered, such as the type of ART procedure used, ovarian stimulation protocols followed, the number and quality of embryos transferred, and luteal phase support administered. Additionally, laboratory results, particularly hormonal levels and ovarian reserve markers, were documented, alongside lifestyle factors such as smoking and alcohol consumption.

The primary outcome measure of the study was pregnancy failure, defined as either biochemical pregnancy loss, characterized by a positive pregnancy test followed by a decline in hCG levels, or clinical pregnancy loss, indicated by a confirmed gestational sac followed by miscarriage. Successful implantation and clinical pregnancy, confirmed by detecting a heartbeat on ultrasound, were also recorded.

Ethical approval for the study was obtained from the institutional review board of Bahria International Hospital, Rawalpindi. All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

Data analysis was conducted using the Statistical Package for Social Sciences (SPSS) version 25. Descriptive statistics were employed to summarize the demographic and clinical characteristics of the patients. Comparative analysis between groups experiencing pregnancy failure and those who did not was performed using the Chi-square test for categorical variables and the independent t-test for continuous variables. Multivariate logistic regression analysis was used to identify significant risk factors for pregnancy failure, with odds ratios (OR) and 95% confidence intervals (CI) calculated for each variable.

The rigorous data collection process ensured the inclusion of all relevant variables that could potentially influence ART outcomes. The study's comprehensive methodology, ethical considerations, and robust statistical analysis provide a solid foundation for understanding the risk factors associated with pregnancy failure in infertile patients undergoing ART.

3 Results

Data were collected from 85 patients undergoing Assisted Reproductive Technology (ART). The mean age of the patients was 34.5 years, with those experiencing pregnancy failure having a higher mean age of 36.2 years compared to 33.2 years in those who did not experience pregnancy failure. The mean BMI was also higher in the pregnancy failure group (26.0 kg/m²) versus the no pregnancy failure group (23.8 kg/m²). The duration of infertility averaged 5.2 years, with no significant difference between the groups. Primary infertility was slightly more common in the pregnancy failure group (57.1%) compared to the no pregnancy failure group (50.0%).

The demographic data of the participants are summarized in Table 1.

Table 1: Demographic Data of Participants

Characteristic	Total (n=85)	Pregnancy Failure (n=35)	No Pregnancy Failure (n=50)
Age (years), mean (SD)	34.5 ± 4.5	36.2 ± 3.8	33.2 ± 4.6
BMI (kg/m²), mean (SD)	24.7 ± 3.0	26.0 ± 3.1	23.8 ± 2.8
Duration of infertility (years), mean	5.2 ± 2.1	5.5 ± 2.2	4.9 ± 2.0
Primary infertility, n (%)	45 (52.9%)	20 (57.1%)	25 (50.0%)
Secondary infertility, n (%)	40 (47.1%)	15 (42.9%)	25 (50.0%)
Underlying medical conditions, n (%)	30 (35.3%)	16 (53.3%)	14 (28.0%)

Both groups had similar distributions in terms of the type of ART used, with 82.9% of the pregnancy failure group and 82.0% of the no pregnancy failure group undergoing IVF, and 17.1% and 18.0% undergoing ICSI, respectively. Stimulation protocols were also comparable, with 68.6% of the pregnancy failure group and 72.0% of the no pregnancy failure group receiving a standard protocol, and 31.4% and 28.0% receiving a mild protocol, respectively. The mean number of embryos transferred did not differ significantly between the groups (2.0 vs. 2.1). Embryo quality was similar as well, with 57.1% of the pregnancy failure group and 70.0% of the no pregnancy failure group having good-quality embryos.

The ART cycle details are summarized in Table 2.

Table 2: ART Cycle Details

Variable	Pregnancy Failure (n=35)	No Pregnancy Failure (n=50)	p-value
Type of ART, n (%)			
- IVF	29 (82.9%)	41 (82.0%)	0.92
- ICSI	6 (17.1%)	9 (18.0%)	0.92
Stimulation protocol, n (%)			
- Standard	24 (68.6%)	36 (72.0%)	0.74
- Mild	11 (31.4%)	14 (28.0%)	0.74
Number of embryos transferred, mean	2.0 ± 0.5	2.1 ± 0.7	0.58
Embryo quality, n (%)			
- Good	20 (57.1%)	35 (70.0%)	0.23
- Fair	10 (28.6%)	10 (20.0%)	0.36
- Poor	5 (14.3%)	5 (10.0%)	0.54

Among the 35 cases where pregnancy failed, 57.1% experienced biochemical pregnancy loss, while 42.9% faced clinical pregnancy loss. Conversely, in the group of 50 without pregnancy failure, all experienced successful implantation (100%), and 90% achieved clinical pregnancy.

The primary and secondary outcomes are summarized in Table 3.

Table 3: Primary and Secondary Outcomes

Outcome	Pregnancy Failure (n=35)	No Pregnancy Failure (n=50)
Biochemical pregnancy loss, n (%)	20 (57.1%)	-
Clinical pregnancy loss, n (%)	15 (42.9%)	-
Successful implantation, n (%)	-	50 (100%)
Clinical pregnancy, n (%)	-	45 (90%)

Multivariate logistic regression analysis revealed that age showed a statistically significant association with pregnancy failure, with each year increase yielding an odds ratio (OR) of 1.15 (95% CI 1.05 - 1.25, p = 0.002), indicating a higher risk with advancing age. Elevated BMI (> 25 kg/m²) also demonstrated a significant association, with an OR of 2.45 (95% CI 1.10 - 5.47, p = 0.03), suggesting a 2.45-fold

higher risk compared to those with BMI ≤ 25 kg/m². Additionally, underlying medical conditions showed an OR of 1.90 (95% CI 1.02 - 3.55, p = 0.04).

The results of the multivariate logistic regression analysis are summarized in Table 4.

Table 4: Multivariate Logistic Regression Analysis

Risk Factor	OR	95% CI	p-value
Age (per year increase)	1.15	1.05 - 1.25	0.002
BMI (> 25 kg/m² vs. ≤ 25 kg/m²)	2.45	1.10 - 5.47	0.03
Underlying medical conditions	1.90	1.02 - 3.55	0.04

The analysis indicates that older age, higher BMI, and the presence of underlying medical conditions significantly increase the risk of pregnancy failure in infertile patients undergoing ART. These findings emphasize the importance of considering these factors when counseling patients and planning treatment protocols.

4 Discussion

The results of this study indicated that older age, higher BMI, and the presence of underlying medical conditions significantly increased the risk of pregnancy failure in infertile patients undergoing Assisted Reproductive Technology (ART). These findings aligned with existing literature, which consistently demonstrated the negative impact of advanced maternal age on fertility and ART success rates. Previous studies have shown that advanced age is associated with decreased oocyte quality and quantity, leading to lower implantation rates and higher miscarriage rates (12). The observed increase in the odds ratio for each year of age underscores the importance of considering age as a critical factor in ART counseling and treatment planning.

Higher BMI was also found to be a significant risk factor for pregnancy failure. Patients with a BMI greater than 25 kg/m² had a 2.45-fold higher risk of pregnancy failure compared to those with a BMI of 25 kg/m² or less. This finding is consistent with prior research that highlighted the adverse effects of obesity on reproductive outcomes. Obesity has been associated with hormonal imbalances, poor oocyte quality, and inadequate endometrial lining, which collectively impair implantation and pregnancy success (12). The study emphasized the need for pre-ART weight management to improve treatment outcomes. Weight loss interventions prior to ART could enhance the efficacy of subsequent treatments by addressing these physiological impairments.

Underlying medical conditions, such as polycystic ovary syndrome (PCOS), endometriosis, and tubal factor infertility, were identified as significant contributors to pregnancy failure. These conditions can disrupt various stages of reproduction, including ovulation, fertilization, and implantation. For instance, PCOS is linked to anovulation and metabolic syndrome symptoms, while endometriosis can cause adhesions and inflammation that complicate implantation (15). Addressing these conditions with appropriate medical or surgical interventions prior to ART could potentially improve pregnancy outcomes. The study recommended individualized treatment plans that consider these underlying conditions to optimize ART success rates.

The study did not find significant differences in pregnancy failure rates based on the type of ART (IVF vs. ICSI) or the ovarian stimulation protocols used. This aligns with the findings of the Vermont 2004 study, which suggested that while procedural aspects are crucial, individual patient characteristics play a more pivotal role in determining ART outcomes (16). However, the quality of embryos transferred appeared to influence outcomes, with a higher proportion of good-quality embryos in the successful pregnancy group. Although this difference was not statistically significant in this study, it highlighted the importance of embryo quality in achieving successful pregnancies.

One of the strengths of this study was its comprehensive approach to data collection, encompassing a wide range of demographic, clinical, and lifestyle factors. The use of multivariate logistic regression analysis allowed for the identification of significant risk factors while controlling for potential confounders. Additionally, the study adhered to rigorous ethical standards, including obtaining informed consent and following the Helsinki Declaration, which ensured the integrity and ethical conduct of the research.

However, the study had several limitations. The sample size was relatively small, which may have limited the statistical power to detect certain associations. The study was also conducted at a single institution, which may limit the generalizability of the findings to other settings. Future research with larger sample sizes and multi-center designs would be beneficial to validate these findings and provide more robust evidence. Another limitation was the retrospective nature of the data collection, which relied on the accuracy and completeness of medical records. Prospective studies with standardized data collection protocols would help address this issue and provide more reliable data.

In conclusion, the study identified older age, higher BMI, and underlying medical conditions as significant risk factors for pregnancy failure in infertile patients undergoing ART. These findings underscore the importance of individualized treatment approaches that address these risk factors to improve ART outcomes. Pre-ART weight management and appropriate interventions for underlying medical conditions could enhance the chances of successful pregnancies. The study's comprehensive methodology and adherence to ethical standards provide a solid foundation for understanding the factors influencing ART success. Future research should aim to validate these findings in larger, multi-center studies and explore additional strategies to mitigate the identified risk factors.

5 Conclusion

In conclusion, Older age, higher BMI, and underlying medical conditions were found to significantly increase the risk of pregnancy failure in infertile patients undergoing Assisted Reproductive Technology (ART). These findings underscore the importance of personalized treatment approaches that specifically address these risk factors. Advanced maternal age is associated with diminished oocyte quality and quantity, which negatively impacts implantation and increases miscarriage rates. Similarly, a higher BMI is linked to hormonal imbalances, poor oocyte quality, and inadequate endometrial lining, all of which impair the success of ART. Underlying medical conditions, such as polycystic ovary syndrome (PCOS), endometriosis, and tubal factor infertility, can disrupt various stages of reproduction, including ovulation, fertilization, and implantation.

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Disclaimers	
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