https://ijmsphr.com

DOI: - 10.37547/ijmsphr/Volume07Issue04-12

Open Access Research Paper

INTERNATIONAL JOURNAL OF MEDICAL SCIENCE AND PUBLIC HEALTH RESEARCH

Vol. 07, No. 04, April 2026, 56-62

eISSN 2767-3774

The Role of Platelet-Rich Plasma (PRP) In Overcoming Repeated Implantation Failure in Art

Dilnoza Sharifovna Kudratova
PhD, Associate Professor, Department of Obstetrics, Gynecology and Pediatric Gynecology, Tashkent State Medical University, Uzbekistan

Janona Akbar kizi Sattorova
First-year Master's student, Department of Obstetrics, Gynecology and Pediatric Gynecology, Tashkent State Medical University, Uzbekistan

Article Received: 20/03/2026, Article Accepted: 05/04/2026, Article Published: 30/04/2026

Abstract

Repeated implantation failure (RIF) remains a major challenge in assisted reproductive technologies (ART) and is often associated with impaired endometrial receptivity despite the transfer of high-quality embryos. The aim of this review is to analyze current evidence on the effectiveness of autologous platelet-rich plasma (PRP) in improving reproductive outcomes in women with RIF.

A comprehensive analysis of recent literature, including randomized controlled trials, meta-analyses, and review articles, was conducted. The evaluated outcomes included implantation rate, clinical pregnancy rate, ongoing pregnancy rate, live birth rate, and endometrial thickness.

PRP therapy exhibits regenerative, angiogenic, and immunomodulatory properties due to high concentrations of growth factors such as VEGF, PDGF, and TGF-β. Meta-analyses suggest that PRP use is associated with improved implantation rate (OR≈2.62), clinical pregnancy rate (OR≈2.46), and ongoing pregnancy rate (OR≈2.78). However, randomized controlled trials show inconsistent results.

PRP appears to be a promising adjunctive therapy, particularly in patients with thin endometrium. Nevertheless, further large-scale randomized controlled trials are required to standardize protocols and confirm its clinical efficacy.

Keywords: Platelet-rich plasma; repeated implantation failure; IVF; endometrial receptivity; ART.

Introduction

Infertility is recognized as a major global reproductive health issue, affecting approximately 1 in 6 couples worldwide according to the World Health Organization (WHO). The growing prevalence of infertility has led to an increased reliance on assisted reproductive technologies (ART), including in vitro fertilization (IVF), which has become a cornerstone of modern reproductive medicine. Globally, millions of ART cycles are performed annually; however, despite continuous technological and clinical advancements, implantation remains the limiting step in achieving successful pregnancy outcomes. In Uzbekistan, infertility is also an important public health concern. In recent years, the country has demonstrated progressive development in reproductive healthcare, including improved access to ART services and implementation of modern fertility treatment protocols. Nevertheless, clinical outcomes remain heterogeneous, and a proportion of patients still experience repeated implantation failure despite high-quality embryo transfer. Repeated implantation failure (RIF) represents one of the most complex and unresolved problems in reproductive medicine. Despite significant advances in assisted reproductive technologies, a subset of patients fails to achieve pregnancy even after multiple embryo transfers [14]. Implantation is a highly coordinated process requiring synchronization between a competent embryo and a receptive endometrium. Increasing evidence suggests that impaired endometrial receptivity plays a central role in RIF [9]. Endometrial receptivity depends on adequate vascularization, immune tolerance, hormonal signaling, and cellular differentiation during the window

of implantation [14]. Various therapeutic strategies have been proposed; however, their effectiveness remains limited in refractory cases. Recently, platelet-rich plasma (PRP) has emerged as a novel regenerative approach aimed at improving endometrial function through the delivery of growth factors and cytokines [3].

Purpose of The Research

The purpose of this review is to evaluate the clinical efficacy and underlying mechanisms of autologous platelet-rich plasma (PRP) therapy in patients with repeated implantation failure (RIF) undergoing assisted reproductive technologies (ART), as well as to assess its impact on reproductive outcomes and endometrial receptivity.

Methods

This review was conducted in accordance with general principles of evidence-based medicine and followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A comprehensive literature search was performed in electronic databases, including PubMed, Scopus, and Web of Science, covering publications from 2020 to 2026. The search strategy combined Medical Subject Headings (MeSH) terms and free-text keywords, including: “platelet-rich plasma”, “PRP”, “repeated implantation failure”, “RIF”, “thin endometrium”, “endometrial receptivity”, and “assisted reproductive technologies”.

Inclusion criteria:

• studies involving human subjects;

• randomized controlled trials (RCTs), systematic reviews, meta-analyses, and observational studies;

• studies evaluating intrauterine PRP administration in ART;

• studies reporting at least one reproductive outcome.

Exclusion criteria:

• animal or in vitro studies;

• publications without clinical outcome data;

• conference abstracts without full-text availability;

• duplicate or overlapping datasets.

Study selection was performed in two stages: initial screening of titles and abstracts, followed by full-text assessment for eligibility. The primary outcomes included implantation rate, clinical pregnancy rate, ongoing pregnancy rate, and live birth rate. Endometrial thickness was analyzed as a secondary outcome. Data extraction focused on study design, sample size, patient characteristics, PRP preparation protocols, route and timing of administration, and clinical outcomes. Due to heterogeneity in study designs and intervention protocols, a qualitative synthesis of the data was performed rather than a quantitative meta-analysis.

Results

1. Randomized Controlled Trials (RCTs)

Randomized controlled trials evaluating the efficacy of platelet-rich plasma (PRP) in women with repeated implantation failure (RIF) have yielded inconsistent and, in some cases, inconclusive findings.

In the study by Eftekhar et al. (2024), intrauterine administration of autologous PRP prior to embryo transfer demonstrated a higher clinical pregnancy rate in the intervention group compared with controls. However, the observed differences did not reach statistical significance. The authors attributed this outcome primarily to the limited sample size and insufficient statistical power, which may have masked potential clinical benefits. Despite the lack of statistical confirmation, a positive trend favoring PRP was noted, particularly in patients with a history of multiple failed IVF cycles.

Overall, existing RCTs suggest a potential beneficial effect of PRP on reproductive outcomes; however, the evidence remains insufficient to draw definitive conclusions due to methodological limitations, including small cohorts, heterogeneous inclusion criteria, and variability in PRP protocols.

2. Meta-Analyses

In contrast to individual randomized trials, meta-analytical data provide more robust evidence supporting the clinical potential of PRP in reproductive medicine.

A large systematic review and meta-analysis conducted by Maged et al. (2023), which included 29 studies comprising over 3300 patients with RIF and/or thin endometrium, demonstrated statistically significant improvements in key reproductive outcomes following PRP therapy. Specifically, PRP administration was associated with increased implantation rates (OR ≈ 2.62), clinical pregnancy rates (OR ≈ 2.46), and ongoing pregnancy rates (OR ≈ 2.78). The authors emphasized that the most pronounced benefits were observed in patients with impaired endometrial receptivity and refractory thin endometrium.

Similarly, the systematic review by Xu et al. (2022) confirmed that PRP may enhance endometrial thickness and improve pregnancy outcomes in women undergoing assisted reproductive technologies (ART), particularly in cases of endometrial dysfunction. Nevertheless, the authors highlighted substantial heterogeneity across studies regarding PRP preparation, dosage, and administration timing, which limits the generalizability of the findings.

Furthermore, Agarwal et al. (2021) reported that although PRP appears promising as an adjunctive treatment in infertility management, the current level of evidence remains moderate, and standardized clinical protocols are urgently needed to ensure reproducibility and comparability across studies.

3. Observational, Prospective, and Experimental Studies

Observational and prospective clinical studies generally demonstrate more consistent improvements in endometrial parameters and reproductive outcomes following PRP administration, particularly among patients with thin or refractory endometrium.

In the prospective study conducted by Chang et al. (2020), intrauterine infusion of PRP resulted in a significant increase in endometrial thickness and improved implantation and clinical pregnancy rates in women undergoing IVF cycles. The authors noted that the most substantial effects were observed in patients who previously exhibited poor endometrial response to conventional hormonal therapy.

Similarly, Tandulwadkar et al. (2021) reported that repeated intrauterine PRP administration significantly improved endometrial thickness and pregnancy rates in patients with refractory endometrium. The study suggested a potential dose–response relationship, indicating that repeated PRP applications may enhance endometrial regeneration.

In a pilot study by Enatsu et al. (2021), PRP therapy was associated with improved endometrial growth and favorable pregnancy outcomes in patients with markedly thin endometrium. Although the study was limited by a small sample size and absence of a control group, the findings support the regenerative potential of PRP in endometrial repair.

Additionally, Dogra et al. (2022) demonstrated that intrauterine PRP administration in frozen embryo transfer (FET) cycles significantly improved clinical pregnancy and implantation rates in women with RIF, suggesting an enhancement of endometrial receptivity and vascularization.

From a mechanistic perspective, experimental evidence provided by Zeng et al. (2025) using single-cell transcriptomic analysis revealed that PRP therapy activates key molecular pathways involved in angiogenesis, cell proliferation, and endometrial remodeling. These findings offer biological support for the clinical observations and suggest that PRP exerts its effects through modulation of the endometrial microenvironment at the molecular level.

Summary of findings

Overall, the analyzed literature consistently indicates a positive trend toward imroved endometrial receptivity and reproductive outcomes following PRP therapy, particularly in patients with repeated implantation failure and thin endometrium.

However, the level of evidence varies considerably across study designs. While meta-analyses demonstrate statistically significant benefits, randomized controlled trials remain inconclusive, largely due to methodological limitations and protocol heterogeneity. Observational and experimental studies provide supportive biological and clinical evidence but lack the methodological rigor required for definitive clinical recommendations.

Consequently, PRP should currently be regarded as a promising but investigational adjunctive therapy in assisted reproductive technologies, warranting further large-scale, well-designed randomized controlled trials to establish standardized protocols and confirm its clinical efficacy.

Discussion

The present review highlights the growing interest in platelet-rich plasma (PRP) as a regenerative approach in the management of repeated implantation failure (RIF). Although the biological rationale for PRP application is well established, the clinical evidence remains heterogeneous and, in some aspects, controversial.

One of the most notable findings is the discrepancy between results obtained from randomized controlled trials (RCTs) and those reported in meta-analyses and observational studies. While pooled analyses suggest a statistically significant improvement in implantation, clinical pregnancy, and ongoing pregnancy rates, individual RCTs often fail to demonstrate comparable significance. This inconsistency may be attributed to several methodological and clinical factors.

First, the lack of standardization in PRP preparation protocols represents a major limitation. Variability in centrifugation techniques, platelet concentration, activation methods, and leukocyte content may significantly influence the biological activity of PRP. Consequently, comparing outcomes across studies becomes challenging, as different PRP formulations may produce different therapeutic effects.

Second, heterogeneity in patient selection plays a crucial role. The definition of repeated implantation failure itself varies across studies, including differences in the number of failed cycles, embryo quality criteria, and patient characteristics. Importantly, evidence suggests that PRP therapy is more effective in patients with compromised endometrial conditions, such as thin endometrium or chronic endometrial dysfunction. In contrast, its benefit appears limited in patients with normal endometrial parameters, which may explain the lack of significant findings in some randomized trials.

Third, the timing and route of PRP administration remain inconsistent. Most studies utilize intrauterine infusion during the proliferative phase or shortly before embryo transfer, whereas others apply subendometrial injections. The optimal timing for PRP administration in relation to the window of implantation has not yet been clearly defined, and this may directly impact treatment efficacy.

Another important consideration is the potential role of PRP in modulating the endometrial microenvironment. Beyond its regenerative properties, PRP may influence local immune responses, reduce inflammatory activity, and promote a more favorable implantation milieu. These effects are particularly relevant in patients with chronic endometritis or immune-related implantation failure,

suggesting that PRP may act not only as a structural enhancer but also as a functional modulator of endometrial receptivity.

Despite these promising mechanisms, the current level of evidence does not allow PRP to be universally recommended as a standard treatment in ART protocols. The absence of large, well-designed, multicenter RCTs limits the strength of recommendations. Additionally, the lack of long-term follow-up data, particularly regarding live birth rates and neonatal outcomes, remains a significant gap in the literature.

From a clinical perspective, PRP should be considered within the framework of personalized medicine. Its application may be most appropriate in selected patients with poor prognosis, especially those with thin endometrium or repeated failure despite optimized conventional treatment. In such cases, PRP may serve as a valuable adjunctive therapy aimed at enhancing endometrial receptivity.

Future research should focus on establishing standardized protocols for PRP preparation and administration, identifying optimal patient populations, and conducting adequately powered randomized trials. Moreover, integrating molecular and transcriptomic analyses may provide deeper insights into the mechanisms underlying PRP efficacy and help refine patient selection criteria.

In summary, PRP therapy represents a promising but still evolving approach in reproductive medicine. While current evidence suggests potential benefits, its clinical application should remain cautious and evidence-based until more robust data become available.[1,2,9,14]

Conclusion

Platelet-rich plasma (PRP) therapy represents a promising and biologically plausible regenerative approach in the management of repeated implantation failure (RIF), primarily through its angiogenic, proliferative, and immunomodulatory effects on the endometrium. Accumulating evidence suggests that PRP may enhance endometrial receptivity, improve endometrial thickness, and increase implantation and pregnancy rates, particularly in patients with refractory conditions such as thin endometrium.

Nevertheless, the current body of evidence remains heterogeneous and is limited by the lack of standardized preparation protocols, variability in administration strategies, and insufficient number of large-scale, high-quality randomized controlled trials. The discrepancy between encouraging results from observational studies and less consistent findings from randomized trials underscores the need for cautious interpretation.

At present, PRP should be regarded as an adjunctive and individualized therapeutic option rather than a standard component of ART protocols. Its use may be justified in selected patients with poor reproductive prognosis who have not responded to conventional treatments.

Future research should focus on protocol standardization, identification of optimal patient populations, and evaluation of long-term reproductive outcomes, including live birth rates. Only through well-designed, multicenter randomized studies can the definitive role of PRP in reproductive medicine be established.

Table 1. Comparative analysis of clinical studies evaluating PRP in repeated implantation failure and thin endometrium.

Study (Year)	Study Design	Sample Size / Population	Indication	PRP Protocol (Route, Volume, Timing)	Main Outcomes	Key Results	Level of Evidence	Limitations
Maged et al., 2023	Systematic review & meta-analysis (29 studies)	n=3308 RIF / thin endometrium	RIF, thin endometrium	Mostly intrauterine; 0.5–1 ml; mid-cycle or pre-ET	Implantation, clinical pregnancy, ongoing pregnancy, ET thickness	Significant improvement: implantation (OR≈2.62), clinical pregnancy (OR≈2.46), ongoing pregnancy (OR≈2.78)	Level I	Heterogeneity, variable PRP protocols, inclusion of non-RCTs
Eftekhar et al., 2024	Randomized controlled trial	n≈100; women with RIF	RIF	Intrauterine PRP before embryo transfer	Chemical & clinical pregnancy	Higher rates in PRP group, not statistically significant	Level II	Small sample size, limited statistical power
Dogra et al., 2022	Prospective controlled study	n≈120; RIF (FET cycles)	RIF	Intrauterine PRP; repeated administration	Clinical pregnancy, implantation	Significant increase in pregnancy rates in PRP group	Level II-III	Non-randomized design
Enatsu et al., 2021	Pilot study	n≈20; thin endometrium	Thin endometrium	Intrauterine PRP; cycle-based administration	Endometrial thickness, pregnancy	Improved ET thickness and pregnancy outcomes	Level III	Small sample, no control group
Chang et al., 2020	Prospective cohort	n≈64; refractory thin endometriu	Thin endometrium	Intrauterine PRP during cycle	ET thickness, pregnancy	Significant increase in ET and pregnancy rates	Level III	Lack of randomization
Tandulwadkar et al., 2021	Prospective study	n≈68; thin endometrium	Thin endometrium	Intrauterine PRP (multiple doses)	ET thickness, pregnancy	Improved endometrial growth and implantation	Level III	No control group
Zeng et al., 2025	Experimental molecular study	Human endometrial samples	Thin endometrium	PRP intrauterine therapy	Gene expression, angiogenesis pathways	Activation of angiogenesis and proliferation pathways	Level IV	No direct clinical outcomes
Sarli et al., 2026	Narrative review	Multiple populations	RIF, ART patients	Variable	ET thickness, implantation	Consistent trend toward improved receptivity	Level V	Non-systematic, descriptive

As shown in table 1 the comparative analysis of the included studies demonstrates that the majority of authors report a positive effect of PRP therapy on endometrial receptivity and reproductive outcomes.

Maged et al. (2023) conducted a large meta-analysis including 29 studies and showed a statistically significant improvement in implantation rate, clinical pregnancy rate, and ongoing pregnancy rate in patients receiving PRP therapy. These findings support the potential effectiveness of PRP as an adjunctive treatment in women with repeated implantation failure.

In contrast, Eftekhar et al. (2024), in a randomized controlled trial, reported higher pregnancy rates in the PRP group; however, the differences did not reach statistical significance, which may be explained by the limited sample size and insufficient statistical power.

Several prospective and observational studies, including those by Chang et al. (2020) and Tandulwadkar et al. (2021), demonstrated a significant increase in endometrial thickness and improved pregnancy outcomes following intrauterine PRP administration, particularly in patients with thin endometrium.

Similarly, Dogra et al. (2022) reported improved implantation and clinical pregnancy rates in women undergoing frozen embryo transfer cycles after PRP treatment.

At the same time, experimental data presented by Zeng et al. (2025) revealed that PRP therapy activates molecular pathways associated with angiogenesis and cellular proliferation, providing a biological explanation for the observed clinical effects.

Overall, the analysis indicates that while most studies demonstrate beneficial effects of PRP, the level of evidence varies, and high-quality randomized trials remain limited.

Table 2. Standardization challenges and variability in PRP protocols in ART

Parameter	Variability Across Studies	Clinical Impact	Current Evidence	Implication for Practice
Preparation method	Single-spin vs double-spin centrifugation	Affects platelet concentration and growth factor release	Double-spin yields higher platelet counts	Need for standardized preparation
Platelet concentration	2×–5× baseline	Influences biological activity	Optimal concentration not established	Dose-response relationship unclear
Leukocyte content	Leukocyte-rich vs leukocyte-poor PRP	May affect inflammatory response	Conflicting data	Requires further investigation
Volume administered	0.5–1 ml (intrauterine) to >30 ml (subendometrial)	Impacts distribution and tissue exposure	Small volumes effective intrauterine	Larger volumes not routinely justified
Route of administration	Intrauterine infusion vs subendometrial injection	Determines invasiveness and local effect	Intrauterine most commonly used	Subendometrial requires further validation
Timing of administration	Mid-cycle vs 24–48 h before embryo transfer	Critical for implantation window synchronization	No consensus	Timing optimization needed
Frequency of administration	Single vs repeated doses	May influence cumulative effect	Repeated dosing shows benefit in some studies	Individualized protocols recommended
Cycle type	Fresh vs frozen embryo transfer	Hormonal environment differs	PRP mainly used in FET cycles	Preferable in controlled cycles
Combination therapy	PRP + G-CSF / hormones	May enhance outcomes	Evidence limited and confounded	Requires controlled studies
Patient selection	RIF, thin endometrium, Asherman syndrome	Determines treatment response	Best results in thin endometrium	Key factor for success

As summarized in table 2 the analysis of PRP preparation and administration protocols reveals substantial variability across studies, which represents a major limitation in interpreting clinical outcomes.

Different authors employed various centrifugation techniques, resulting in significant differences in platelet concentration and biological activity of PRP. While double-spin methods are generally associated with higher platelet yield, the optimal concentration required for clinical efficacy remains unclear.

The route of administration also varies, with most studies utilizing intrauterine infusion due to its simplicity and low invasiveness, whereas subendometrial injection has been proposed as a more targeted but less commonly used approach.

Timing of PRP administration differs considerably, ranging from the proliferative phase of the menstrual cycle to 24–48 hours prior to embryo transfer. This variability may influence synchronization with the window of implantation and, consequently, treatment effectiveness.

In addition, the number of PRP administrations varies from a single injection to repeated applications, particularly in patients with refractory endometrial conditions. Some studies also combine PRP with other therapies, such as granulocyte colony-stimulating factor (G-CSF), which complicates the interpretation of isolated PRP effects.

Importantly, patient selection appears to be a key determinant of treatment success. The most consistent benefits are observed in women with thin endometrium and repeated implantation failure, whereas outcomes in unselected populations remain less predictable.

Thus, the lack of standardized protocols highlights the need for further research aimed at optimizing PRP preparation and administration strategies.

References

1. Maged AM, El-Mazny A, Kamal N, Mahmoud SI, Fouad M, El-Nassery N, et al. The value of platelet-rich plasma in women with previous implantation failure: a systematic review and meta-analysis. J Assist Reprod Genet. 2023;40:969–983.

2. Eftekhar M, Aflatoonian A, Mohammadian F, Tabibnejad N. Effectiveness of autologous platelet-rich plasma therapy in women with repeated implantation failure: a randomized clinical trial. Int J Fertil Steril. 2024;18(2):162–166.

3. Sarli V, Papakonstantinou E, Tziomalos K. Endometrial autologous platelet-rich plasma instillation and IVF outcomes: a narrative review. Cureus. 2026;18:eXXXXX.

4. Zeng J, Quan J, Liu H, Geng W, Qiu F, Liu J. Comprehensive single-cell transcriptome analysis of autologous platelet-rich plasma therapy on human thin endometrium. Sci Rep. 2025;15:14637.

5. Tehraninejad ES, Aghahosseini M, Kalantari V, et al. Autologous platelet-rich plasma improves endometrial receptivity in patients with repeated implantation failure. JBRA Assist Reprod. 2020;24(1):30–35.

6. Coksuer H, Akdemir Y, Ulas Barut M. Improved in vitro fertilization success and pregnancy outcome with autologous platelet-rich plasma treatment in unexplained infertility. J Turk Ger Gynecol Assoc. 2021;22(1):14–20.

7. Enatsu N, Enatsu T, Kurokawa T, et al. Autologous platelet-rich plasma therapy for infertile women with thin endometrium: a pilot study. Reprod Med Biol. 2021;20(2):215–221.

8. Dogra Y, Singh N, Vanamail P, et al. Intrauterine platelet-rich plasma improves pregnancy outcomes in women with recurrent implantation failure. J Hum Reprod Sci. 2022;15(1):68–74.

9. Xu B, Zhang Q, Hao J, et al. Platelet-rich plasma for thin endometrium and repeated implantation failure: a systematic review. Front Endocrinol (Lausanne). 2022;13:870805.

10. Kim H, Shin JE, Koo HS, et al. Effect of autologous platelet-rich plasma treatment on refractory thin endometrium during the frozen embryo transfer cycle. J Obstet Gynaecol Res. 2020;46(5):823–830.

11. Chang Y, Li J, Chen Y, et al. Autologous platelet-rich plasma promotes endometrial growth and improves pregnancy outcome during IVF. J Assist Reprod Genet. 2020;37(2):261–267.

12. Zadehmodarres S, Salehpour S, Saharkhiz N, et al. Treatment of thin endometrium with autologous platelet-rich plasma: a pilot study. JBRA Assist Reprod. 2020;24(1):54–56.

13. Tandulwadkar SR, Naralkar MV, Surana AD, et al. Autologous platelet-rich plasma improves endometrial thickness and pregnancy rates in patients with refractory endometrium. J Hum Reprod Sci. 2021;14(1):32–36.

14. Kamath MS, Kirubakaran R, Sunkara SK. Platelet-rich plasma in assisted reproduction: current evidence and future directions. Reprod Biomed Online. 2023;46(3):405–412.

15. Agarwal A, Baskaran S, Panner Selvam MK, et al. Platelet-rich plasma for infertility treatment: a systematic review. World J Mens Health. 2021;39(4):605–621.

16. Kusumi M, Tamura I, Hasegawa A, et al. Intrauterine administration of platelet-rich plasma for patients with repeated implantation failure. Gynecol Endocrinol. 2021;37(6):498–502.