Acta Scientific Women's Health (ISSN: 2582-3205)

Volume 8 Issue 7 July 2026

Research Article

Intrauterine Infusion Versus Subendometrial Injection of Platelet Rich Plasma in Patients with

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Received: June 15, 2026

Published: July 03, 2026

Abstract

Aim: To investigate the effects of PRP on pregnancy rates and endometrial thickness by two different methods.

Patients and methods: Subjects were assigned to either hysteroscopic PRP group where PRP was injected subendometrially under hysteroscopic guidance (n = 50) or intrauterine PRP group where PRP was infused intra-cavitary by ET catheter (n = 73). Clinical pregnancy rates and endometrial thickness were recorded.

Results: Between the two groups, baseline demographic information and cycle features were similar, indicating well-balanced study cohorts. Clinical pregnancy rate was lower in the intrauterine PRP group compared with the Hysteroscopic PRP group (30.1% vs. 60.0%) indicating a superior outcome with the Hysteroscopic approach. BMI remained the only significant predictor of endometrial thickness (95% CI: -0.19 to -0.01, β = -0.10, p = 0.03). Estradiol dose (Dose E2) was not significantly associated with endometrial thickness (95% CI: -0.18 to 0.20, β = 0.01, p = 0.935), nor were PRP route, age, number of embryos transferred, or duration of infertility.

Conclusion: Both routes thickened the endometrium similarly, but hysteroscopic subendometrial injection achieved clinical pregnancy at roughly twice the rate of intrauterine infusion, and the difference held after adjustment.

Keywords: Endometrial Thickness; PRP; Hysteroscopy; Intrauterine Infusion; Pregnancy Rate

Introduction

A healthy communication between the endometrium and embryo is necessary for the complex process of implantation, which involves a variety of parameters. Achieving the parameters necessary for successful implantation is a task that is rife with controversies and is inadequately defined, and Assisted Reproductive Technology (ART) practitioners have frequently encountered difficulty in defining an optimal endometrium prior to embryo transfer. A variety of therapeutic approaches have been proposed and tested to address inadequate endometrial growth [1,2].

A predictive factor of implantation has been postulated in the past few years through the determination of endometrial volume. Nevertheless, empirical evidence suggests that the majority of clinicians favor endometrial thickness (ET) to exceed 7 mm in practice. Endometria ranging from 5 to 15 mm have been documented to produce pregnancies with comparable success rates, and the existing data does not advocate for any specific thickness [3]. In order to evaluate the most suitable ET requirements for implantation, Kasius., *et al*. conducted a meta-analysis in 2014. The chances of clinical pregnancy were substantially lower for

ETs of less than 7 mm than for ETs of 7 mm or more [23.3 versus 48.1%]. 48 and 77% were the negative and positive values that are predictive for the prognosis of clinical pregnancy, respectively [4].

In the plane through the central longitudinal axis of the uterine body, the endometrial thickness (ET) is the maximum distance between the echogenic interfaces of the myometrium and the endometrium, determined using transvaginal ultrasound technique. Vascularity is a critical factor in the prediction of implantation, surpassing the girth or pattern of the endometrium, according to multiple studies [4,5]. The lack of blood circulation in the subendometrial and endometrial zones has been linked to the failure of implantation, according to studies conducted. When the blood circulation reached the third and fourth zones of Applebaum's grading, the pregnancy rates were doubled in comparison to the first and second zones [6].

In standard practice, several treatments have been implemented in patients who are incapable of attaining an optimal endometrial lining, including the administration of increased dosages or the prolonged use of Estradiol valerate, adding low dose aspirin, use of Sildenafil, intrauterine Granulocyte-colony stimulating factor (G-CSF) instillation, Human Chorionic Gonadotropin (hCG), and electroacupuncture. However, these treatments are inconsistent in their ability to produce results [7,8].

It is imperative to assess alternative methods in this context, as the patient may experience repeated cycle disruptions or repetitive failures of implantation as a result of suboptimal endometrial expansion or vascularity. This can have a financial and psychological burden on the person receiving the procedure. This compels patients to contemplate surrogacy as an alternative, which may not be feasible at this time due to the medicolegal consequences.

The objective of the present investigation was to compare the effectiveness of intrauterine infusion of PRP and subendometrial injection on the thickness of the endometrium and the likelihood of pregnancy in patients who were undergoing frozen-thawed embryo transfer (FET) following prior implantation failure.

Patients and Methods

This cohort study was performed at 4 centers of ICSI in Egypt before frozen embryo transfer in prior implantation failure. The study started on March 2023 till September 2025.

Patients were selected according to inclusions criteria: (i) women aged <35 years (ii) prior implantation failure (iii) planned frozen embryo transfer (FET).The exclusion criteria were:(i) platelets < 150.000/mm^3, (ii) anticoagulant therapy, (iii) a ten-day period of NSAID administration preceding a surgical procedure, (iv) any significant psychiatric disorder or comorbidity that might conceivably compromise the patient's assent, (v) active uterine or cervical infection, (vi) poor embryo quality, Asherman's syndrome, or congenital uterine abnormalities.

Sample size calculation

Sample size estimation was performed using the (pwr.2p. test) function from the R-pwr package for comparison of two proportions based on the arcsine transformation of the binomial distribution. Based on effect estimates derived from previous research, an effect size (Cohen's h) of 0.60 was assumed. Using a two-sided significance level (α) of 0.05 and a statistical power of 80%, the required sample size was calculated to be 44 participants per group. After accounting for an anticipated dropout rate of 10%, the sample size was increased to 49 participants per group, resulting in a total sample size of 98 participants.

Allocations: Patients were allocated into two groups:

- **Hysteroscopic PRP group:** Where PRP was injected subendometrially under hysteroscopic guidance (n = 50).
- **Intrauterine PRP:** Where PRP was infused intra-caviatry by ET catheter (n = 73)

Interventions

PRP preparation

A venous blood sample of 15–50 mL was collected from the arm of a patient and placed in anticoagulant-containing sterile tubes at 21˚C–24˚C. The blood is subsequently centrifuged at 1,200 rpm for 12 minutes, resulting in three layers: a bottom layer that contains RBCs, an intermediate thin layer (the buffy coat) that is abundant in WBCs, and an upper layer that contains platelets and WBCs,. To assist in facilitating the growth of soft particles (platelets and erythrocytes) at the tube's base, the plasma undergoes centrifuge treatment once more at 3,300 rpm for 7 minutes. PRP is generated by homogenizing the granules in the lower third (5 mL) of the plasma. Magictube PRP tubes were employed as PRP special tubes.

PRP injection

Hysteroscopic PRP group

During the luteal phase of the preceding embryo transfer cycle, PRP was transvaginally injected into the subendometrial space. Under hysteroscopic guidance, the subendometrial region of all four walls of the cavity was injected with a total of 4 mL of PRP using an ovum collection catheter, with 1.0 mL for each wall. The beveled edge of the ovum pickup (OPU) needle was maintained in a slanting position toward the cavity to assure optimal instillation.

Intrauterine PRP group

The index FET cycle was conducted with PRP administration when the endometrium was less than 7 mm. One mm of PRP was injected by embryo transfer catheter under ultrasound guidance on day 11. One more infusion was repeated at day 13 if endometrial thickness is still < 7 mm.

Endometrial preparation

A quantity of 6 mg estradiol valerate pills was administered to women, and the dosage was gradually raised to 12 mg per daily schedule. A transvaginal ultrasonography was conducted on different days, with effect from day 6 onward to assess the thickening of the endometrium. The broadest section of the uterus in the longitudinal axis was measured by the same examiner to evaluate ET. Once the ET had attained an optimal thickness of over 7 mm, luteal phase support was initiated with vaginal progesterone supplement (400 mg).

The frozen-thawed embryo transfer was conducted according to the embryo's age and the date of initial progesterone administration (only embryos from day 5 were transferred). To maintain luteal support, the same dosage of progesterone and estradiol valerate was administered.

Clinical pregnancy

Measurements of serum beta-hCG levels were conducted 14 days following the transfer of embryos A clinical pregnancy was confirmed by performing a transvaginal sonography on women with positive beta-hCG levels 14 days later.

Outcomes of study

The primary outcomes: clinical pregnancy while secondary outcomes were achieving endometrial thickness > 7 mm, dose of estradiol valerate and any complications or cancellations of cycles.

Ethical issues

This study was approval from local ethical committee and privacy was maintained all through the study. Any expected risks were explained for patients managed immediately. Before the commencement of the investigation, all individuals receiving treatment were required to provide written consent.

Statistical methods

R software (version 4.5.0) was employed to conduct all statistical computations. The frequencies and percentages were used to express categorical parameters, while mean ± standard deviation (SD) was used to summarize variables that are continuous.

Utilizing the independent samples t-test for continuous parameters with a normal distribution and the Mann–Whitney U test for non-normal parameters, comparisons were conducted between the hysteroscopic PRP and intrauterine PRP groups. To compare categorical parameters, the Fisher's exact test or chi-square test was implemented, as necessary.

Univariate and multivariable logistic regression analyses were implemented to identify predictors of clinical pregnancy. The results were reported as odds ratios (OR) with 95% confidence intervals (CI). The adjusted model encompassed the following variables: age, BMI, number of embryos transferred, duration of infertility, thickness of the endometrium, estradiol dose, and PRP administration route.

Additionally, a multivariable linear regression model was implemented to evaluate determinants of endometrial thickness as a continuous outcome, with β coefficients and 95% CI reported. The cutoff point for statistically significant results has been specified to be a p-value of lower than 0.05.

Results

The included patients were allocate into either hysteroscopic PRP group (n = 50) or intrauterine PRP group (n = 73). In Table 1, demographic data are presented.

Variable	Overall (n = 123)	Hysteroscopic PRP (n = 50)	Intrauterine PRP (n = 73)	p-value
Age (years)	29.98 ± 3.29	30.07 ± 3.61	29.92 ± 3.08	0.805
BMI (kg/m^2)	22.01 ± 2.66	23.15 ± 2.94	22.22 ± 2.73	0.095
Duration of infertility (years)	4.19 ± 4.74	3.99 ± 1.98	4.32 ± 5.95	0.705
Estradiol dose (mg/day)	10.05 ± 1.24	10.37 ± 1.25	10.10 ± 1.19	0.640
Endometrial thickness (mm)	8.80 ± 1.26	8.72 ± 1.32	8.85 ± 1.22	0.558
Embryos transferred (n, %)				0.433
1 embryo	54 (43.9%)	19 (38.0%)	35 (47.9%)	
2 embryos	62 (50.4%)	27 (54.0%)	35 (47.9%)	
3 embryos	7 (5.7%)	4 (8.0%)	3 (4.1%)	

Table 1: Demographic data of enrolled patients (n = 123).

A mean age of 29.98 ± 3.29 years and a mean BMI of 22.01 ± 2.66 kg/m^2 were observed in the entire cohort population (n = 123). The mean duration of infertility was 4.19 ± 4.74 years. Cycle characteristics showed a mean estradiol dose of 10.05 ± 1.24 mg/day and a mean endometrial thickness of 8.80 ± 1.26 mm. Most patients received one or two embryos, with no significant difference in distribution between Hysteroscopic and intrauterine PRP groups (p = 0.433). Between the Hysteroscopic and intrauterine PRP groups, baseline demographic and cycle features were similar. Age, BMI, duration of infertility, estradiol dose, and endometrial thickness showed similar distributions across both groups, indicating well-balanced study cohorts.

The distribution of patients with repeated implantation failure is shown in table 2. The distribution of previous failed IVF cycles was similar between the Hysteroscopic and intrauterine PRP groups, with most patients having 4–6 prior failed cycles. No substantial disparity was identified between the two cohorts (p = 0.615), indicating comparable reproductive history.

Failed cycles	Overall	Hysteroscopic PRP	Intrauterine PRP	p-value
3	8 (6.5%)	2 (4.0%)	6 (8.2%)	0.615
4	27 (22.0%)	10 (20.0%)	17 (23.3%)	
5	44 (35.8%)	21 (42.0%)	23 (31.5%)	
6	30 (24.4%)	11 (22.0%)	19 (26.0%)	
7	13 (10.6%)	5 (10.0%)	8 (11.0%)	
8	1 (0.8%)	1 (2.0%)	0 (0.0%)	

Table 2: Distribution of Previous implantation failure.

The primary outcome was displayed in table 3. Comparing the Hysteroscopic PRP group to the intrauterine PRP group, the clinical pregnancy rate was significantly higher in the former (60.0% vs. 30.1%). The odds of achieving clinical pregnancy were significantly lower in the intrauterine PRP group (OR = 0.29, 95% CI: 0.13–0.62, p < 0.01), indicating a superior outcome with the Hysteroscopic approach. The adjusted logistic regression was displayed in table 4.

The adjusted predictors of clinical pregnancy were displayed in figure 1. After adjustment for potential confounders, the PRP route remained a significant predictor of clinical pregnancy. Intrauterine PRP was associated with significantly lower odds of clinical pregnancy compared to Hysteroscopic PRP (adjusted OR = 0.33, 95% CI: 0.15–0.74, p < 0.01). No significant associations were observed for age, BMI, duration of infertility, endometrial thickness, or number of embryos transferred.

Outcome	Hysteroscopic PRP (n = 50)	Intrauterine PRP (n = 73)	Effect size (Unadjusted)	95% CI	p-value
Clinical pregnancy, n (%)	30 (60.0%)	22 (30.1%)	OR = 0.29	0.13 – 0.62	<0.01
Non-pregnant, n (%)	20 (40.0%)	51 (69.9%)			

Table 3: Primary Outcome Analysis according to PRP route.

Variable	Adjusted OR	95% CI	p-value
PRP route: Intrauterine vs. Hysteroscopic	0.33	[0.15; 0.74]	<0.01
Age (years)	0.99	[0.88; 1.12]	0.87
BMI (kg/m^2)	1.07	[0.91; 1.26]	0.40
Duration of infertility (years)	1.00	[0.92; 1.08]	0.93
Endometrial thickness (mm)	1.16	[0.85; 1.59]	0.36
Embryos transferred: 2 vs 1	1.75	[0.78; 3.92]	0.17
Embryos transferred: 3 vs 1	2.00	[0.36; 10.97]	0.42

Table 4: Adjusted Logistic regression model (Outcome: Clinical pregnancy).

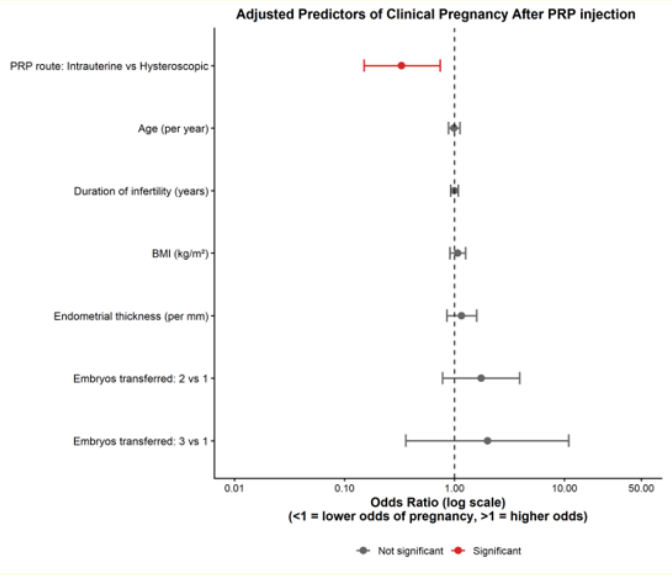

Figure 1: Adjusted predictors of clinical pregnancy.

Model performance and diagnostics

The logistic regression model showed good calibration, as the Hosmer–Lemeshow goodness-of-fit test was not significant (χ^2 = 7.71, df = 8, p = 0.46). No evidence of multicollinearity was detected, with all adjusted GVIF values close to 1 (1.01–1.09), indicating independence among predictors. The model demonstrated acceptable discrimination, with an area under the ROC curve (AUC) of 71.5% (95% CI: 62.3–80.7), reflecting fair predictive ability as shown in figure 2.

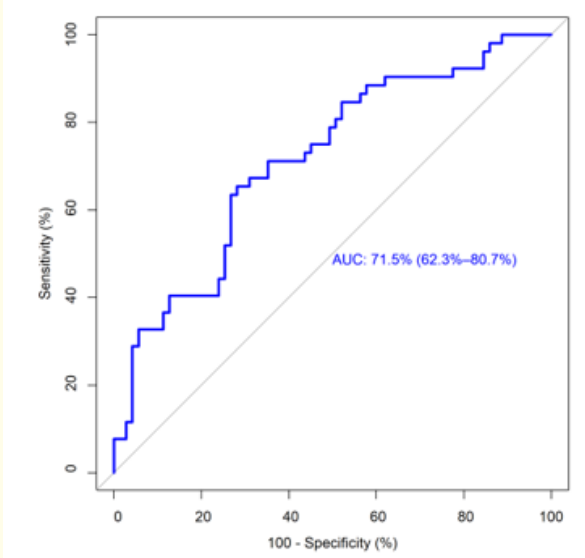

Figure 2: Model performance and diagnostics.

Secondary outcomes were presented in table 5. In the adjusted linear regression model, BMI remained the only significant predictor of endometrial thickness (β = -0.10, 95% CI: -0.19 to -0.01, p = 0.03). Estradiol dose (Dose E2) was not significantly associated with endometrial thickness (β = 0.01, 95% CI: -0.18 to 0.20, p = 0.935), nor were PRP route, age, duration of infertility, or number of embryos transferred. Higher BMI is associated with slightly thinner endometrium, and this effect remains significant after adjusting for other variable.

Variable	β Coefficient	95% CI	p-value
PRP route: Intrauterine vs. Hysteroscopic	-0.06	-0.54 – 0.43	0.82
Age (years)	0.01	-0.06 – 0.08	0.82
BMI (kg/m^2)	-0.10	-0.19 – -0.01	0.03
Duration of infertility (years)	-0.01	-0.06 – 0.04	0.67
Embryos transferred (n)	0.01	-0.18 – 0.20	0.92
Estradiol dose (Dose E2)	0.01	-0.18 – 0.20	0.935

Table 5: Secondary outcomes analysis.

In the adjusted linear regression model, BMI remained the only significant predictor of endometrial thickness (β = -0.10, 95% CI: -0.19 to -0.01, p = 0.03). Estradiol dose (Dose E2) was not significantly associated with endometrial thickness (β = 0.01, 95% CI: -0.18 to 0.20, p = 0.935), nor were PRP route, age, duration of infertility, or number of embryos transferred. Higher BMI is associated with slightly thinner endometrium, and this effect remains significant after adjusting for other variable) as shown in figure 3.

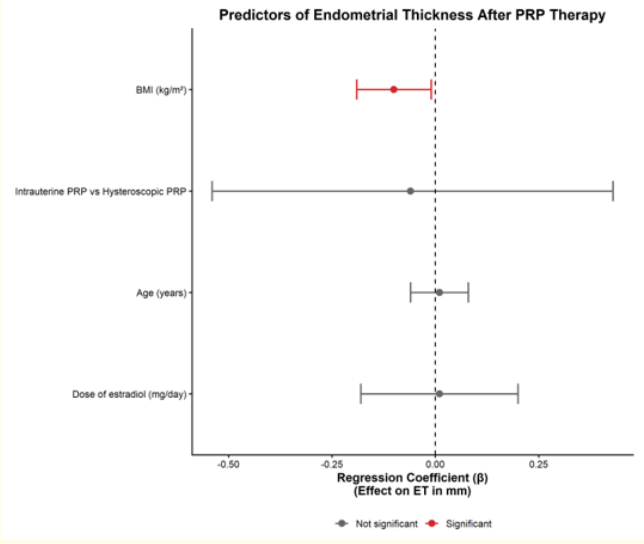

Figure 3: Model predictors of endometrial thickness.

Model performance and diagnostics

No multicollinearity was observed (VIF = 1.02–1.21), and residuals were normally distributed (Shapiro–Wilk p = 0.174) as shown in figure 4.

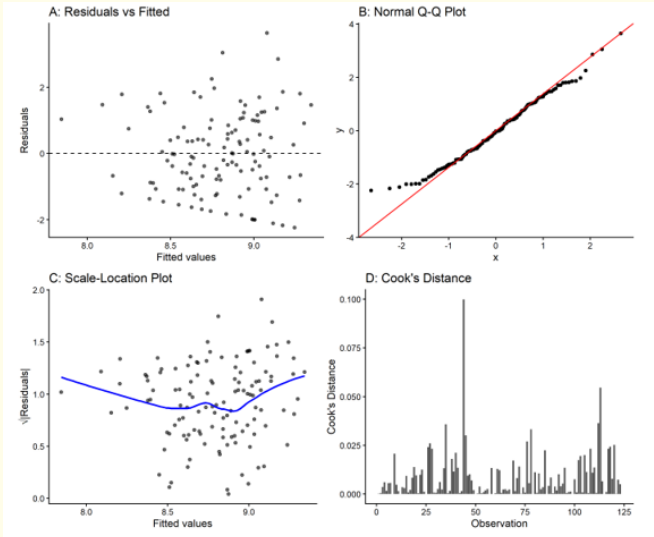

Figure 4: Analysis of performance model and diagnostics.

Discussion

This cohort study compared hysteroscopic subendometrial PRP injection with intrauterine PRP infusion in women with thin

endometrium undergoing FET cycles, all of whom had a history of repeated IVF failure. The hysteroscopic group achieved a clinical pregnancy rate of 60.0%, compared with 30.1% in the intrauterine infusion group; a difference that held after adjustment for age, BMI, duration of infertility, endometrial thickness, estradiol dose, and number of embryos transferred (adjusted OR 0.33, 95% CI 0.15–0.74, $p < 0.01$). In the secondary analysis, PRP route did not independently predict post-treatment endometrial thickness ($\beta = -0.06$, $p = 0.82$), whereas BMI was the only significant predictor ($\beta = -0.10$, $p = 0.03$). Hysteroscopic delivery therefore appears to act primarily on endometrial receptivity, not on measurable thickness.

The observed difference in clinical pregnancy rate between the two PRP delivery routes warrants careful mechanistic consideration. PRP is an autologous platelet concentrate enriched with several growth factors including PDGF, TGF-β, VEGF, and EGF that are implicated in sub-endometrial angiogenesis, stromal proliferation, and endometrial regeneration [1,2]. PDGF initiates connective tissue healing through collagen synthesis, TGF-β regulates smooth muscle and endothelial cell growth, and VEGF drives new vessel formation [3]. These biological effects collectively improve endometrial receptivity and are proposed to explain the pregnancy rate gains seen with PRP in our results [4,5].

The superior reproductive outcomes in the hysteroscopic group are biologically plausible. Intrauterine infusion deposits PRP as a fluid layer within the uterine cavity, relying on passive diffusion of growth factors across the endometrial epithelium. Subendometrial injection, by contrast, places PRP directly into the basal endometrial layer adjacent to the endomyometrial junction; the regenerative compartment responsible for cyclical endometrial renewal [6]. This targeted delivery is hypothesized to produce higher local growth factor concentrations, more direct stromal activation, and a longer tissue retention time compared with intracavitary instillation [7,8]. Consistent with this, endometrial thickness did not differ significantly between groups in our adjusted model, suggesting that both routes comparably stimulate superficial proliferation, but that hysteroscopic injection may confer an additional advantage in deeper stromal and vascular remodeling that determines implantation potential.

The finding that BMI negatively predicted endometrial thickness ($\beta = -0.10$, $p = 0.03$) is consistent with prior evidence linking adiposity-related estrogen dysregulation and uterine perfusion changes to impaired endometrial growth, though this relationship lies outside the primary scope of the present comparison [9,10].

The benefit of intrauterine PRP infusion for thin endometrium and recurrent implantation failure has been documented across multiple study designs. Chang., *et al*. reported significantly greater endometrial thickness and a clinical pregnancy rate of 44.12% versus 20.0% in controls among women receiving PRP infusion in FET cycles [1]. In a prospective cohort observational study, carried out at Akanksha IVF Centre, the clinical pregnancy rate reached 35.71% in the PRP group compared with 10% in women not receiving PRP ($p = 0.025$) [11]. A retrospective study from Seoul restricted to euploid FET cycles similarly showed higher clinical pregnancy rates (51.1% vs. 30.2%, $p = 0.024$) and ongoing pregnancy rates (44.3% vs. 16.3%, $p = 0.002$) with PRP infusion [12]. These figures align with the 30.1% clinical pregnancy rate observed in our own intrauterine infusion group, which enrolled a population with a substantial prior failure burden (median of 5–6 failed IVF cycles).

Direct comparisons between intrauterine infusion and hysteroscopic injection are fewer, but consistently favour the injectable route for pregnancy outcomes. Yu., *et al*. published the most methodologically comparable study to ours: a prospective case-control trial enrolling 116 women with persistent thin endometrium undergoing euploid FET. Both intrauterine infusion (n = 55) and hysteroscopic injection (n = 38) increased the proportion of patients achieving an endometrial thickness exceeding 7 mm (78.2% and 55.3%, respectively), but hysteroscopic injection was associated with a higher implantation rate (52% vs. group comparator), a trend toward higher clinical pregnancy rate (52%), and a higher live birth rate (38%), leading the authors to conclude that both methods can expand the endometrium but that hysteroscopic injection provides more consistent support for implantation and live birth [13]. The clinical pregnancy advantage we observed for hysteroscopic delivery (60.0% vs. 30.1%) is of a larger magnitude, which may reflect differences in patient selection; since our cohort was explicitly restricted to women with repeated prior IVF failure, a group with deeper endometrial pathology in whom targeted tissue delivery may confer a proportionally greater benefit.

A 2025 systematic review and meta-analysis by Kumar., *et al*. formally addressed this question by pooling evidence

on subendometrial PRP injection (whether hysteroscopic or ultrasound-guided) versus placebo or intracavitary infusion in women with recurrent implantation failure or refractory thin endometrium [14]. The review reported significant increases in clinical pregnancy rate (OR 5.14, $p < 0.001$) and live birth rate (OR 4.60, $p < 0.001$) for subendometrial injection versus controls, with a reduction in miscarriage rate (OR 0.60, $p = 0.036$). In the subgroup restricted to women with a resistant thin endometrium, the benefit of injection over infusion was statistically significant ($p = 0.03$), a finding that directly supports our results [14]. Separately, a 2020 prospective pilot study on subendometrial injection using ultrasound guidance documented improvements in both endometrial thickness and implantation potential, with a clinical pregnancy rate of 41.66% following hysteroscopic PRP at the endomyometrial junction; consistent with the range observed in our hysteroscopic group [6].

Taken together, the literature suggests that intrauterine infusion is an effective first-line approach for many patients, but that hysteroscopic subendometrial injection may offer a clinically meaningful advantage; particularly in those with a refractory, treatment-resistant thin endometrium [7,8,14]. Whether this benefit justifies the additional procedural complexity of hysteroscopy for all patients, or only for those who have not responded to prior infusion cycles, remains an open question that the existing evidence does not yet resolve [14].

Clinical implications

Thin endometrium affects approximately 15–25% of infertile women and up to 30% of those with repeated implantation failure, with an estimated incidence of 15% among embryo transfer cycles in large IVF registries [15-17]. Despite its clinical impact, therapeutic options remain limited: estrogen dose escalation, vasodilators such as sildenafil, granulocyte colony-stimulating factor, and hysteroscopic adhesiolysis each address only a subset of aetiologies and lack consistent evidence across trials [18-21]. PRP offers a distinct mechanism, autologous, biocompatible, and platelet-derived, that acts on angiogenesis, stromal proliferation, and immune modulation simultaneously [1,4,5].

The present findings carry practical implications for the sequencing of PRP interventions. Our data, consistent with existing comparative evidence [13,14], suggest that intrauterine infusion and hysteroscopic injection are not equivalent approaches for patients with a high prior failure burden. If confirmed, hysteroscopic subendometrial injection may be the preferred initial strategy in this subgroup, rather than reserving it for cases that have already failed intracavitary infusion. For patients at earlier stages of IVF treatment or with a thinner failure history, intrauterine infusion remains a reasonable and substantially less invasive option, given its comparable safety profile and the technical accessibility of transcervical catheter delivery [8,13].

Strengths and limitations

We believe that our study has several features that strengthen the validity of our findings. Most directly, it provides a head-to-head comparison of two PRP delivery techniques in a clearly defined failure population, which is rarely the primary focus of individual studies and has been formally addressed in only one prior prospective case-control study [13] and one systematic review [14]. Baseline characteristics, including age, BMI, infertility duration, estradiol dose, endometrial thickness, and prior failed cycle distribution, were well matched across groups, reducing the likelihood that demographic differences account for the observed pregnancy rate discrepancy. The adjusted logistic regression model confirmed that PRP route remained an independent predictor of clinical pregnancy after controlling for these potential confounders, and the model showed adequate calibration (Hosmer–Lemeshow $p = 0.46$) and acceptable discrimination (AUC 71.5%). Endometrial thickness was measured by a standardized ultrasound protocol, avoiding inter-operator variability in the primary secondary outcome.

However, this study still has several limitations that qualify the strength of the conclusions. Most fundamentally, the non-randomized design means that treatment allocation was not governed by chance, introducing the possibility of selection bias: unmeasured differences between patients who received hysteroscopic injection versus intrauterine infusion, such as uterine cavity abnormalities identified at hysteroscopy, clinician preference, or patient willingness to undergo a more invasive procedure, could confound the outcome association in directions that the adjusted model did not fully capture. The study setting limits generalizability to settings with different PRP preparation protocols, laboratory practices, or patient demographics. Sample size, while adequate for the primary logistic regression, was modest

(n = 123 overall; 50 and 73 per group), constraining statistical power for subgroup analyses and precision of effect estimates. No live birth data were available, which is the clinically most meaningful endpoint in this patient population; clinical pregnancy rate, while a standard surrogate, may not translate proportionally to live birth differences across the two groups. PRP preparation was not reported to an internationally standardized protocol, and variation in platelet concentration, activation method, and volume may influence the magnitude of effect independently of delivery route. Finally, absence of blinding to treatment assignment, inherent in a surgical versus non-surgical comparison, may have introduced differential unmeasured co-interventions.

Future Directions

The evidence base for PRP in thin endometrium continues to grow, but several gaps restrict the translation of current findings into confident practice guidelines. Large, multi-centre randomized controlled trials with live birth as the primary endpoint are needed to confirm whether hysteroscopic subendometrial injection is superior to intrauterine infusion in patients with refractory thin endometrium and repeated implantation failure, and to identify whether any patient subgroup, defined by prior failure number, etiology of thin endometrium, or PRP response in a prior cycle, derives differential benefit. Standardization of PRP protocols, including target platelet concentration, activation status, infusion volume, and timing relative to the FET cycle, remains a prerequisite for robust cross-trial comparisons. Long-term neonatal safety data for PRP-conceived pregnancies are also lacking and should be reported in future prospective registries. Whether subendometrial injections should be offered as a first-line intervention or reserved for patients who have not responded to intrauterine infusion is a clinically actionable question that a well-designed sequential or comparative RCT could address.

Conclusions

Both routes thickened the endometrium similarly, but hysteroscopic subendometrial injection achieved clinical pregnancy at roughly twice the rate of intrauterine infusion, and the difference held after adjustment. That thickness rose comparably while pregnancy did not suggests the injectable route works through the deeper stromal and vascular changes that govern receptivity, not the lining growth an ultrasound can measure. For patients who have already failed several transfers, this argues for offering subendometrial injection sooner rather than holding it in reserve. Given the retrospective design and absence of live birth data, a randomized trial powered for live birth is needed before this route can be recommended as standard.

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