International Journal of Medical and Pharmaceutical Research

Online ISSN-2958-3683 | Print ISSN-2958-3675
Frequency: Bi-Monthly
Available online on: https://ijmpr.in/

Original Article

A Prospective Study on Instillation of Intrauterine Platelet Rich Plasma Before Intra Uterine Insemination

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OPEN ACCESS

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Received: 09-06-2026
Accepted: 29-06-2026
Available online: 15-07-2026

ABSTRACT

Background: Adequate endometrial receptivity is essential for successful implantation and pregnancy following intrauterine insemination (IUI). Platelet-rich plasma (PRP), an autologous concentration of platelets enriched with growth factors, has emerged as a potential therapy for improving endometrial thickness and implantation outcomes.
Aim: To evaluate the effect of intrauterine instillation of autologous PRP before IUI on endometrial thickness and clinical pregnancy outcomes in infertile women.
Materials and Methods: This prospective interventional study was conducted in the Department of Obstetrics and Gynaecology, ESIC Medical College and Hospital, Kalaburagi, from March 2022 to September 2023. Thirty infertile women planned for IUI and fulfilling the inclusion criteria were enrolled. Following controlled ovarian stimulation and follicular monitoring, autologous PRP was prepared using a double-spin centrifugation technique. Approximately 0.5–1.0 mL of PRP was instilled into the uterine cavity 24–48 hours before IUI. Endometrial thickness before and after PRP instillation and pregnancy outcomes were recorded and analysed.
Results: The mean age of participants was 28.4 ± 3.7 years. Primary infertility was present in 63.3% of women, and unexplained infertility was the most common indication for treatment (36.7%). Mean endometrial thickness increased significantly from 6.9 ± 0.8 mm before PRP instillation to 8.4 ± 0.9 mm after PRP instillation ($p < 0.001$). The clinical pregnancy rate was 36.7% (11/30), while β-hCG positivity was observed in 40.0% of women. Only minor self-limiting complications such as mild spotting and lower abdominal discomfort were noted, with no major adverse events.
Conclusion: Intrauterine instillation of autologous PRP before IUI significantly improved endometrial thickness and was associated with favorable clinical pregnancy rates. PRP appears to be a safe, minimally invasive, and promising adjunct for enhancing endometrial receptivity and improving IUI outcomes. Larger randomized controlled trials are recommended to confirm these findings.

Keywords: *Platelet-rich plasma, intrauterine insemination, infertility, endometrial thickness, pregnancy outcome, endometrial receptivity.*

INTRODUCTION

Infertility is a major reproductive health problem affecting approximately 10–15% of couples worldwide and is defined as the inability to achieve pregnancy after 12 months of regular unprotected sexual intercourse.[1] It has profound psychological, social, and economic consequences, particularly in developing countries where childbearing is often closely linked to social status and family well-being. Female factors, male factors, combined causes, and unexplained infertility contribute to the overall burden of infertility, with unexplained infertility accounting for nearly 15–30% of cases.[2]

Intrauterine insemination (IUI) is one of the most commonly employed first-line assisted reproductive techniques for the treatment of unexplained infertility, mild male factor infertility, cervical factor infertility, and ovulatory disorders.[3] The procedure is relatively simple, minimally invasive, and cost-effective compared with in vitro fertilization (IVF). However, the success rate of IUI remains modest, with pregnancy rates ranging between 10% and 20% per treatment cycle depending on maternal age, ovarian reserve, semen quality, and endometrial receptivity.[4]

Successful embryo implantation depends on three major factors: embryo quality, endometrial receptivity, and synchronized embryo-endometrial interaction.[5] Among these, adequate endometrial thickness is considered one of the most important predictors of implantation and pregnancy. Thin endometrium, generally defined as an endometrial thickness of less than 7 mm during the peri-ovulatory period, has been associated with reduced implantation rates and poor pregnancy outcomes.[6] Despite various treatment strategies including estrogen therapy, low-dose aspirin, sildenafil, granulocyte colony-stimulating factor (G-CSF), and stem cell therapy, management of thin endometrium remains challenging.[7]

Platelet-rich plasma (PRP) has recently emerged as a promising regenerative therapy in reproductive medicine. PRP is an autologous concentration of platelets suspended in plasma that contains platelet levels approximately three to five times higher than baseline blood concentrations.[8] Activated platelets release numerous growth factors and cytokines including platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), transforming growth factor-beta (TGF-β), epidermal growth factor (EGF), insulin-like growth factor (IGF), and fibroblast growth factor (FGF), all of which promote angiogenesis, cellular proliferation, tissue remodeling, and endometrial regeneration.[9]

Several studies have demonstrated that intrauterine PRP instillation improves endometrial thickness, enhances vascularity, and increases implantation and pregnancy rates in women with recurrent implantation failure or refractory thin endometrium undergoing assisted reproductive techniques.[10,11] Owing to its autologous origin, PRP is considered safe, inexpensive, minimally invasive, and associated with negligible risk of immunological reactions or disease transmission.[12]

Although encouraging evidence exists regarding PRP use in IVF cycles, data regarding its effectiveness before intrauterine insemination are still limited. Improving endometrial receptivity before IUI may represent an affordable strategy for enhancing pregnancy outcomes, particularly in resource-limited settings where IVF may not be readily accessible.[13]

Therefore, the present prospective study was undertaken to evaluate the effect of intrauterine instillation of autologous Platelet-Rich Plasma before intrauterine insemination on endometrial thickness and pregnancy outcomes among infertile women attending the Department of Obstetrics and Gynaecology at ESIC Medical College, Kalaburagi.

MATERIALS AND METHODS

Study Design and Setting

This prospective interventional study was conducted in the Department of Obstetrics and Gynaecology, ESIC Medical College and Hospital, Kalaburagi, Karnataka, over a period of 6 months from **March 2022 to September 2023**. The study was undertaken after obtaining approval from the Institutional Ethics Committee (IEC), and written informed consent was obtained from all participants prior to enrolment.

Study Population

A total of **30 women** with infertility who were planned for **intrauterine insemination (IUI)** were included in the study. Eligible participants underwent intrauterine instillation of autologous Platelet-Rich Plasma (PRP) before the IUI procedure to evaluate its effect on endometrial receptivity and pregnancy outcomes.

Sample Size

The study included **30 consecutive eligible patients** fulfilling the inclusion and exclusion criteria during the study period.

Inclusion Criteria

- Women aged **20–38 years**.
- Primary or secondary infertility.
- Indicated for IUI due to unexplained infertility, mild male factor infertility, ovulatory dysfunction, or cervical factor infertility.
- At least one patent fallopian tube confirmed by hysterosalpingography (HSG) or diagnostic laparoscopy.
- Endometrial thickness <8 mm during the peri-ovulatory period or patients planned for PRP to improve endometrial receptivity.
- Normal uterine cavity on ultrasonography or hysteroscopy.

- Willingness to participate and provide informed consent.

Exclusion Criteria
- Bilateral tubal block.
- Severe male factor infertility requiring IVF/ICSI.
- Congenital uterine anomalies.
- Active pelvic inflammatory disease.
- Untreated endocrine disorders such as uncontrolled thyroid disease or hyperprolactinemia.
- Coagulation disorders or thrombocytopenia.
- Active genital tract infection.
- History of malignancy.
- Refusal to participate.

Baseline Evaluation
All participants underwent detailed clinical evaluation, including:
- Detailed medical, menstrual, obstetric, and infertility history.
- General physical and systemic examination.
- Gynecological examination.
- Body Mass Index (BMI) calculation.

Baseline Investigations
- Complete Blood Count (CBC)
- Blood grouping and Rh typing
- Blood sugar profile
- Thyroid function tests (TSH)
- Serum Prolactin
- Serum Anti-Müllerian Hormone (AMH)
- Day 2/3 FSH and LH
- Viral markers (HIV, HBsAg, HCV)
- Transvaginal ultrasonography (TVS)
- Follicular monitoring
- Hysterosalpingography (HSG) where indicated
- Semen analysis of the husband according to WHO guidelines (2021)

Ovarian Stimulation Protocol
Controlled ovarian stimulation was performed using either:
- Letrozole (2.5–5 mg/day) from Day 2 to Day 6 of the menstrual cycle, or
- Clomiphene citrate (50–100 mg/day) from Day 2 to Day 6,

with or without injectable gonadotropins according to ovarian response.
Serial transvaginal ultrasonography was performed from Day 9 onwards for monitoring follicular development and endometrial thickness.

Ovulation was triggered using **10,000 IU human chorionic gonadotropin (hCG)** or recombinant hCG once at least one dominant follicle reached **18–20 mm** in diameter.

Preparation of Platelet-Rich Plasma
Approximately **20 mL of autologous venous blood** was collected under aseptic precautions into anticoagulant-containing tubes.

PRP was prepared using a standardized **double-spin centrifugation technique**:
- First centrifugation: 1500 rpm for 10 minutes.
- Plasma layer collected carefully.
- Second centrifugation: 3000 rpm for 10 minutes.
- Platelet-poor plasma discarded.
- Approximately **0.5–1.0 mL of PRP** was obtained.

The final PRP contained platelet concentrations approximately **3–5 times higher** than baseline peripheral blood platelet count.

PRP Instillation Procedure

PRP instillation was performed **24–48 hours before scheduled IUI**.

Under aseptic precautions:

- A sterile Cusco's speculum was introduced.
- Cervix cleaned using normal saline.
- A soft intrauterine insemination catheter was passed gently through the cervical canal.
- Approximately **0.5–1 mL autologous PRP** was slowly instilled into the uterine cavity.
- Patients remained in the supine position for **15–20 minutes** following the procedure.

No complications related to PRP administration were encountered.

Intrauterine Insemination Procedure

Processed semen samples were prepared using the density-gradient or swim-up technique.
IUI was performed **36 hours after ovulation trigger** using a sterile soft catheter.

Following insemination, patients remained in the dorsal position for approximately **15–20 minutes**.

Luteal phase support was provided using **micronized progesterone (200–400 mg/day)** until pregnancy testing.

Outcome Measures

Primary Outcome

- Clinical pregnancy rate confirmed by ultrasonographic visualization of an intrauterine gestational sac with fetal cardiac activity.

Secondary Outcomes

- Endometrial thickness before and after PRP instillation.
- Number of mature follicles.
- Biochemical pregnancy rate.
- Clinical pregnancy rate per cycle.
- Implantation rate.
- Miscarriage rate.
- Multiple pregnancy rate.
- Procedure-related adverse events.

Follow-up

Serum β-hCG estimation was performed **14 days after IUI**.
Women with positive β-hCG underwent transvaginal ultrasonography after **6–7 weeks of gestation** to confirm clinical pregnancy.

Patients were followed until confirmation of clinical pregnancy or menstruation in non-conceived cycles.

Data Collection

Data recorded for each participant included:

- Age
- Duration and type of infertility
- BMI
- Cause of infertility
- AMH level
- Baseline hormonal profile
- Endometrial thickness before and after PRP
- Number of mature follicles
- Semen parameters
- Pregnancy outcome
- Complications

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using Statistical Package for Social Sciences (SPSS) version 25.0. Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequency and percentage.

Comparisons of continuous variables were performed using the paired t-test or Student's t-test, as appropriate. Categorical variables were analyzed using the Chi-square test or Fisher's exact test.
A p-value <0.05 was considered statistically significant.

RESULTS AND OBSERVATIONS

A total of 30 infertile women undergoing intrauterine insemination (IUI) received autologous intrauterine Platelet-Rich Plasma (PRP) instillation 24–48 hours before IUI. All participants completed follow-up until pregnancy testing. The demographic profile, infertility characteristics, endometrial response, and pregnancy outcomes are presented below.

Table 1. Age Distribution of the Study Population

Age Group (Years)	Number (n=30)	Percentage (%)
20–24	6	20.0
25–29	14	46.7
30–34	8	26.7
≥35	2	6.6

Mean Age:28.4 ± 3.7 years

Observation: Most women (46.7%) belonged to the **25–29 years** age group.

Table 2. Type of Infertility

Type	Number	Percentage (%)
Primary infertility	19	63.3
Secondary infertility	11	36.7

Observation: Primary infertility was more common than secondary infertility.

Table 3. Duration of Infertility

Duration (Years)	Number	Percentage (%)
<2	7	23.3
2–5	16	53.3
>5	7	23.4

Mean Duration:3.8 ± 1.9 years

Observation: More than half of the patients had infertility for **2–5 years**.

Table 4. Etiology of Infertility

Cause	Number	Percentage (%)
Unexplained infertility	11	36.7
Ovulatory dysfunction	8	26.7
Mild male factor	6	20.0
Cervical factor	3	10.0
Endometriosis (minimal)	2	6.6

Observation: Unexplained infertility was the most common indication for IUI.

Table 5. Baseline Clinical Characteristics

Variable	Mean ± SD
BMI (kg/m²)	24.3 ± 2.8
AMH (ng/mL)	2.6 ± 1.1
Baseline Endometrial Thickness (mm)	6.9 ± 0.8
Dominant Follicle Size (mm)	19.1 ± 1.3

Observation: The average baseline endometrial thickness was below the optimal value for implantation.

Table 6. Endometrial Thickness Before and After PRP Instillation

Parameter	Mean ± SD	p-value
Before PRP	6.9 ± 0.8 mm	
After PRP	8.4 ± 0.9 mm	<0.001

Mean Increase:1.5 ± 0.6 mm

Observation: PRP instillation significantly improved endometrial thickness before IUI (**p <0.001**).

Table 7. Ovarian Response During IUI Cycle

Variable	Mean ± SD
Mature follicles	1.8 ± 0.7
Endometrial Thickness on IUI Day	8.6 ± 0.8 mm

Observation: Most women developed one to two mature follicles with satisfactory endometrial growth following PRP.

Table 8. Pregnancy Outcome

Outcome	Number	Percentage (%)
Clinical pregnancy	11	36.7
Not pregnant	19	63.3

Observation: The clinical pregnancy rate following PRP-assisted IUI was **36.7%**.

Table 9.β-hCG Positivity and Clinical Pregnancy

Outcome	Number	Percentage (%)
Positive β-hCG	12	40.0
Clinical pregnancy confirmed	11	36.7
Biochemical pregnancy loss	1	3.3

Observation: One patient experienced biochemical pregnancy loss, while clinical pregnancy was confirmed in 11 women.

Table 10. Procedure-Related Complications

Complication	Number	Percentage (%)
None	28	93.3
Mild spotting	1	3.3
Mild lower abdominal pain	1	3.3
Infection	0	0
Severe adverse event	0	0

Observation: Intrauterine PRP instillation was safe and well tolerated, with only minor self-limiting complications observed.

DISCUSSION

The present prospective study evaluated the role of intrauterine instillation of autologous Platelet-Rich Plasma (PRP) before intrauterine insemination in improving endometrial receptivity and pregnancy outcomes among infertile women. PRP has gained increasing attention in reproductive medicine because of its regenerative potential mediated by a high concentration of growth factors involved in angiogenesis, cellular proliferation, and tissue repair.[8,9]

The mean age of women in the present study was **28.4 ± 3.7 years**, with nearly half of the participants belonging to the 25–29-year age group. This finding is comparable to studies by Chang et al. and Eftekhar et al., where most women undergoing fertility treatment were younger than 30 years.[10,11] Younger maternal age is well recognized as an important determinant of ovarian reserve, oocyte quality, implantation potential, and overall pregnancy success.

Primary infertility constituted **63.3%** of cases, while unexplained infertility was the most common indication for treatment (36.7%). Similar observations have been reported by Coksuer et al., who found unexplained infertility to be one of the leading indications for IUI and assisted reproductive therapies.[14] Couples with unexplained infertility often have normal ovulation, patent fallopian tubes, and satisfactory semen parameters, suggesting that subtle defects in implantation or endometrial receptivity may contribute to infertility.

One of the most significant findings of the present study was the marked improvement in endometrial thickness following PRP instillation. Mean endometrial thickness increased from **6.9 ± 0.8 mm** before PRP to **8.4 ± 0.9 mm** after treatment, demonstrating a statistically significant improvement. These findings closely resemble those reported by Chang et al., who observed significant endometrial growth after PRP administration in women with thin endometrium undergoing IVF.[10] Similarly, Kim et al. demonstrated enhanced endometrial proliferation following intrauterine PRP infusion, suggesting improved endometrial receptivity.[15]

The beneficial effects of PRP are attributed to its rich content of platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), transforming growth factor-beta (TGF-β), epidermal growth factor (EGF), insulin-like growth factor (IGF), and fibroblast growth factor (FGF). These bioactive molecules stimulate angiogenesis, stromal regeneration, epithelial proliferation, extracellular matrix remodeling, and local cytokine production, thereby creating a favorable environment for embryo implantation.[8,9]

The present study demonstrated a **clinical pregnancy rate of 36.7%**, which is higher than conventional pregnancy rates reported for stimulated IUI cycles. This finding supports the hypothesis that improved endometrial receptivity following PRP administration contributes to enhanced implantation. Similar improvements in pregnancy outcomes have been reported by Nazari et al. and Tandulwadkar et al., who observed higher implantation and pregnancy rates following intrauterine PRP treatment in women with thin endometrium and recurrent implantation failure.[16,17]

The procedure was found to be safe, with only minor transient complications such as mild spotting and lower abdominal discomfort in a small proportion of patients. No infections, allergic reactions, or serious adverse events were encountered. These findings agree with previous reports demonstrating the excellent safety profile of autologous PRP because it eliminates the risks of immune reactions and disease transmission associated with allogenic biological products.[12,18]

The present study supports the growing body of evidence suggesting that PRP represents a promising adjunctive treatment for improving endometrial receptivity before assisted reproductive procedures. Compared with more expensive interventions, PRP is relatively inexpensive, easy to prepare, minimally invasive, and can be performed in an outpatient setting. These advantages make it particularly attractive in developing countries and fertility centers with limited resources.[17,18]

Nevertheless, the study has certain limitations. The relatively small sample size and absence of a control group limit the ability to draw definitive conclusions regarding treatment efficacy. Furthermore, long-term reproductive outcomes such as live birth rate and neonatal outcomes were not evaluated. Larger multicentric randomized controlled trials are required to establish standardized protocols regarding PRP preparation, platelet concentration, timing of administration, and patient selection before widespread clinical adoption.[19]

Overall, the findings of the present study indicate that intrauterine PRP instillation before IUI significantly improves endometrial thickness and may enhance clinical pregnancy rates without increasing complications, supporting its potential role as a valuable adjunct in infertility management.

CONCLUSION

Intrauterine instillation of autologous platelet-rich plasma (PRP) before intrauterine insemination (IUI) significantly improved endometrial thickness and was associated with favorable clinical pregnancy rates. The procedure was safe, minimally invasive, and well tolerated, with no major complications. PRP may serve as a promising adjunct to enhance endometrial receptivity and improve IUI outcomes; however, larger randomized controlled studies are needed to validate its routine clinical use.

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