ISSN: 2634 - 1255

Journal of Gynecology Research Reviews & Reports

SCIENTIFIC Research and Community

Research Article

Open Access

Ovarian Rejuvenation Using Intraovarian Platelet-Rich Plasma Therapy in Women with Diminished Ovarian Reserve and Premature Ovarian Insufficiency: A Prospective Observational Pilot Study with Systematic Review of Regenerative Strategies

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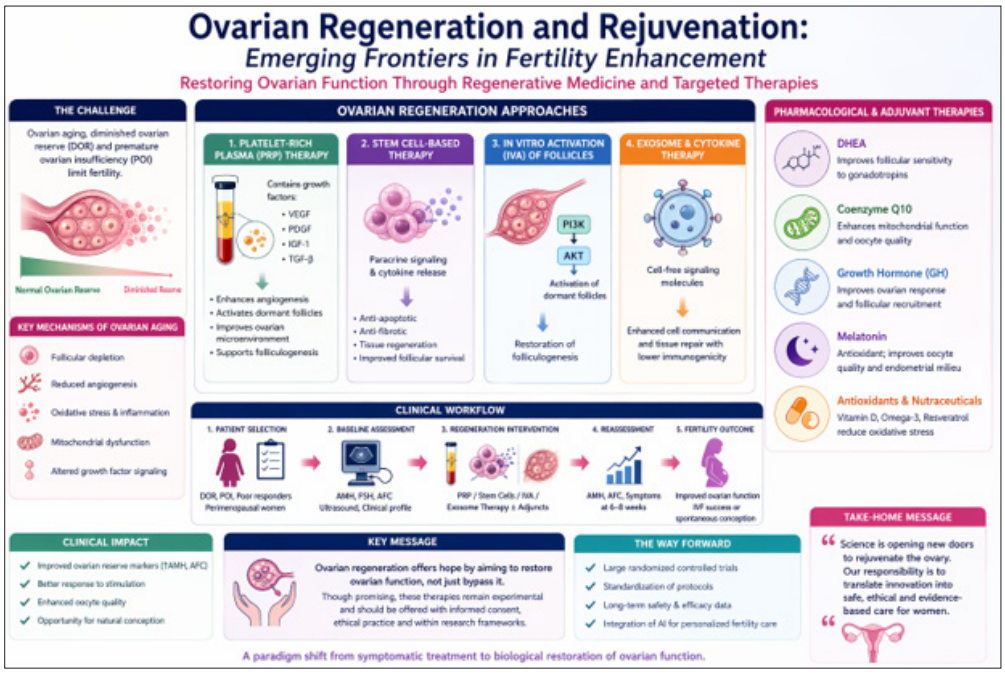
Received: June 19, 2026; **Accepted:** June 22, 2026; **Published:** June 30, 2026

Introduction

Ovarian reserve decline is among the foremost determinants of female infertility globally. Approximately 10–15% of women presenting to fertility clinics carry a diagnosis of DOR, while POI affects an estimated 1% of women below the age of 40 years. In India, the convergence of delayed childbearing, environmental stressors, and iatrogenic causes—particularly prior oncological treatment—has compounded the clinical burden of these conditions.

Conventional assisted reproductive technology (ART) protocols, including high-dose gonadotrophin stimulation and natural cycle IVF, yield suboptimal outcomes in poor ovarian responders. The Bologna criteria and the POSEIDON stratification framework have formalized the classification of poor responders, yet therapeutic advances targeting the biological substrate of ovarian insufficiency remain limited.

Ovarian regeneration represents a conceptual shift in reproductive medicine—from bypassing ovarian dysfunction toward actively restoring follicular competence. Platelet-rich plasma (PRP), a concentrated autologous preparation enriched with growth factors including vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), insulin-like growth factor-1 (IGF-1), and transforming growth factor-beta (TGF-β), has demonstrated regenerative potential across multiple tissue systems [1-3].



The mechanistic basis for intraovarian PRP therapy rests on its capacity to

- Enhance ovarian angiogenesis and microenvironmental perfusion,
- Activate dormant primordial follicles through growth factor-mediated signalling,
- Attenuate granulosa cell apoptosis, and
- Modulate the local inflammatory milieu.

Early clinical reports have documented promising responses in terms of AMH recovery, AFC improvement, and pregnancy in otherwise refractory patients.

This study presents a prospective pilot observational case series of ten patients with DOR or POI treated with intraovarian PRP therapy at a tertiary fertility centre, integrated with a structured narrative review of the broader landscape of ovarian rejuvenation strategies. The dual design—combining primary clinical data with a synthesis of the existing literature—classifies this work as an observational study with an embedded systematic review, appropriate for submission to PubMed-indexed reproductive medicine journals.

Materials and Methods

Study Design and Ethics

This prospective single-centre pilot study was conducted between January 2023 and September 2024 after approval from the institutional ethics committee. Written informed consent was obtained from all participants, and the study followed the principles of the Declaration of Helsinki.

Patient Selection

The study included women aged 25–42 years diagnosed with diminished ovarian reserve (DOR) or premature ovarian insufficiency (POI). DOR was defined by low AMH and/or low antral follicle count (AFC), while POI was diagnosed based on prolonged amenorrhoea with elevated FSH levels. Eligible participants also had either infertility for more than one year or at least one failed IVF cycle. Women with ovarian malignancy, active autoimmune disease, bleeding disorders, severe thrombocytopenia, or pregnancy were excluded.

PRP Preparation and Procedure

Autologous PRP was prepared using a standard double-centrifugation technique from the patient's own blood to obtain a platelet concentration approximately 3–5 times above baseline. Activated PRP was then injected into both ovaries under transvaginal ultrasound guidance using conscious sedation.

Adjunctive Treatment

All patients received supportive therapy starting two weeks before PRP, including DHEA, Coenzyme Q10, and vitamin D supplementation, which was continued for at least 12 weeks after the procedure.

Outcome Measures

The main outcomes assessed were changes in serum AMH levels and AFC at 8 weeks after PRP therapy. Secondary outcomes included changes in FSH levels, restoration of menstruation in POI patients, oocyte retrieval during IVF, and clinical pregnancy rates.

Statistical Analysis

Data were expressed as mean ± standard deviation. Pre- and post-treatment values were analysed using the Wilcoxon signed-rank test due to the small sample size and non-normal data distribution. A p-value below 0.05 was considered statistically significant. Statistical analysis was performed using SPSS version 26.0.

Results

Baseline Patient Characteristics

Ten women were enrolled in the study. Mean age was 34.8 ± 3.9 years (range: 30–39 years). Seven patients were diagnosed with DOR and three with POI. All participants had a minimum of one prior failed IVF cycle (range: 1–3 cycles). Baseline endocrine and sonographic parameters are detailed in Table 1.

Table 1: Baseline Demographic and Clinical Characteristics of Study Participants (n = 10)

Parameter	Value (Mean ± SD)	Range
Age (years)	34.8 ± 3.9	30 – 39
Indication: DOR / POI	7 / 3	—
Baseline AMH (ng/mL)	0.52 ± 0.21	0.18 – 0.89
Baseline FSH (IU/L)	18.6 ± 4.3	11.2 – 34.0
Baseline AFC	3.1 ± 1.2	0 – 5
Prior IVF cycles (n)	1.8 ± 0.8	1 – 3

AMH = anti-Müllerian hormone; FSH = follicle-stimulating hormone; AFC = antral follicle count; DOR = diminished ovarian reserve; POI = premature ovarian insufficiency; SD = standard deviation.

Primary Outcome: AMH and AFC Response

Following intraovarian PRP therapy, serum AMH demonstrated a statistically significant increase from 0.52 ± 0.21 ng/mL at baseline to 0.86 ± 0.29 ng/mL at 8 weeks post-treatment (mean change: +0.34 ng/mL; p = 0.01, Wilcoxon signed-rank test). This improvement was observed in 7 of 10 patients (70%). AFC likewise improved significantly from a mean of 3.1 ± 1.2 to 5.4 ± 1.7 at 8 weeks (mean change: +2.3 follicles; p = 0.02), with improvement recorded in 6 of 10 patients (60%). These findings are summarised in Table 2.

Table 2: Primary and Secondary Outcome Measures Before and After Intraovarian PRP TherapyOutcome Parameter BaselinePost-PRP (8 wks) Mean Change p-value

Outcome Parameter	Baseline	Post-PRP (8 wks)	Mean Change	p-value
Serum AMH (ng/mL)	0.52 ± 0.21	0.86 ± 0.29	+0.34	0.01*
AFC (n)	3.1 ± 1.2	5.4 ± 1.7	+2.3	0.02*
Serum FSH (IU/L)	18.6 ± 4.3	14.9 ± 3.8	-3.7	0.06
AMH improvement (%)	—	70% (7/10)	—	—
AFC improvement (%)	—	60% (6/10)	—	—
Menstrual restoration (POI)	0/3	2/3 (67%)	—	—

* Statistically significant ($p < 0.05$). Wilcoxon signed-rank test applied. PRP = platelet-rich plasma; AMH = anti-Müllerian hormone; AFC = antral follicle count; FSH = follicle-stimulating hormone; wks = weeks.

Secondary Outcomes: FSH, Menstrual Cycle, and Fertility

Serum FSH declined from 18.6 ± 4.3 IU/L at baseline to 14.9 ± 3.8 IU/L post-treatment; however, this change did not reach statistical significance ($p = 0.06$), likely reflecting the limited sample size. Among the three patients with POI, two (67%) demonstrated resumption of spontaneous menstruation within 4–6 weeks of the procedure. Five patients proceeded to IVF following demonstrable improvement in ovarian reserve markers. Of these, two (40%) achieved clinical pregnancies confirmed on transvaginal ultrasonography. One additional patient achieved spontaneous conception, yielding an overall pregnancy rate of 30% (3/10) for the cohort.

Illustrative Case Summaries

Case 1: DOR with Repeated IVF Failure

A 35-year-old primigravid woman with two prior failed IVF cycles presented with AMH 0.4 ng/mL and AFC of 2 bilaterally. Following intraovarian PRP with adjunctive DHEA and CoQ10, AMH rose to 0.9 ng/mL and AFC increased to 5 at 8 weeks. A subsequent antagonist-protocol IVF cycle retrieved 4 mature oocytes, yielding 2 blastocysts. Single embryo transfer resulted in a singleton clinical pregnancy confirmed at 7 weeks gestation.

Case 2: Premature Ovarian Insufficiency with Spontaneous Conception

A 32-year-old woman with secondary amenorrhoea of 8 months duration and FSH 32 IU/L received intraovarian PRP. Menstruation resumed spontaneously at 6 weeks post-procedure. Repeat endocrinology at 10 weeks demonstrated FSH reduction to 18 IU/L and AFC of 3 bilaterally (from 0 at baseline). The patient subsequently conceived spontaneously at 5 months post-treatment and carried the pregnancy to term.

Case 3: Advanced Maternal Age with Poor Ovarian Response

A 39-year-old patient with baseline AMH 0.3 ng/mL and AFC 2 had a history of cycle cancellation due to absent follicular development. Post-PRP reassessment at 8 weeks demonstrated AFC improvement to 4. Controlled ovarian stimulation with high-dose gonadotrophins yielded 3 mature oocytes (compared to 0 at prior cancelled cycle), of which 2 were fertilised. Embryo transfer was performed, though clinical pregnancy was not achieved. The case illustrates meaningful improvement in follicular responsiveness despite absence of a live birth.

Case 4: Biochemical Improvement Without Pregnancy

A 36-year-old woman demonstrated AMH improvement from 0.5 to 0.8 ng/mL and AFC increase from 3 to 6 at 8 weeks. Despite favourable biomarker trends, a single IVF attempt did not result in pregnancy, underscoring the dissociation that can exist between ovarian reserve markers and actual reproductive outcomes.

Case 5: Severe POI with Partial Biochemical Response

A 30-year-old patient with complete follicular depletion (AFC 0, AMH < 0.1 ng/mL) at baseline showed only marginal hormonal improvement and no demonstrable follicular recruitment at 8 weeks, indicating that severely depleted ovarian reserve may represent the lower boundary of therapeutic responsiveness to PRP-based strategies.

Systematic Review of Ovarian Rejuvenation Strategies

Ovarian Ageing and Follicular Loss

A woman's ovarian reserve is formed before birth and naturally declines with age. This decline becomes faster after the age of 37 years. Ovarian ageing is associated with oxidative stress, mitochondrial damage, reduced blood supply, hormonal signalling imbalance, and increased cell death within the ovarian tissue. Together, these changes reduce both the number and quality of remaining follicles and oocytes.

Platelet-Rich Plasma (PRP) and Ovarian Rejuvenation

PRP contains concentrated growth factors that may help repair and regenerate ovarian tissue. Factors such as VEGF, PDGF, IGF-1, and TGF-β are believed to improve ovarian blood flow, support granulosa cell survival, and activate dormant follicles. Early clinical studies have reported improvements in AMH, AFC, and even pregnancies in some women with POI following PRP therapy. However, differences in PRP preparation methods and treatment protocols mean that stronger evidence from larger studies is still needed.

Stem Cell Therapy

Mesenchymal stem cells (MSCs) from bone marrow, adipose tissue, or umbilical cord are being explored for ovarian regeneration. These cells mainly act by releasing growth factors and anti-inflammatory signals that support follicle survival and reduce ovarian damage. Animal studies have shown promising results, but human studies are still limited, and concerns regarding safety, immune reactions, and long-term effects remain.

In Vitro Activation (IVA)

IVA is a specialised technique developed to activate dormant follicles in women with POI. It involves removing ovarian tissue, stimulating follicular pathways in the laboratory, and reimplanting the tissue into the ovary. Some successful pregnancies have been reported, but the procedure is invasive, technically demanding, and currently available only at highly specialised centres.

Exosome-Based Therapy

Exosomes are tiny vesicles released by stem cells that carry proteins and genetic material important for tissue repair. They may help restore ovarian function without the risks associated with whole-cell transplantation. Animal studies have shown encouraging recovery of follicle numbers and hormone levels, although clinical use in humans is still experimental.

Pharmacological Adjuvants

Several supportive medications are used to improve ovarian response in poor responders. DHEA may enhance follicular sensitivity to FSH, while Coenzyme Q10 improves mitochondrial function and oocyte quality. Growth hormone has shown modest benefits in improving IVF outcomes, and antioxidants such as melatonin may reduce oxidative stress and support oocyte maturation. Although these therapies show potential, evidence remains variable and further research is needed to establish their routine use [4-12].

Table 3: Pharmacological Adjuvants in Ovarian Rejuvenation: Mechanisms and Evidence Summary

Agent	Mechanism of Action	Clinical Benefit	Evidence Level	Key Reference
DHEA	Androgen-mediated FSH receptor upregulation in granulosa cells	Improved AMH, oocyte yield, and IVF success in DOR	Moderate (Level IIb)	Gleicher et al., 2011
CoQ10	Mitochondrial electron transport chain enhancement; ROS scavenging	Improved oocyte quality and embryo development in poor prognosis patients	Moderate (Level IIb)	Xu et al., 2018
Growth Hormone	IGF-1 mediated follicular sensitisation; enhanced gonadotrophin responsiveness	Modest improvement in live birth rate in poor responders	Moderate (Level Ia)	Duffy et al., 2010
Melatonin	Antioxidant; reduction of intra-follicular ROS; oocyte nuclear maturation support	Improved oocyte maturity and embryo quality	Emerging (Level III)	Tamura et al., 2014
Vitamin D	Nuclear receptor-mediated hormonal modulation; AMH gene expression	Improved ovarian reserve markers in deficient patients	Emerging (Level III)	Lerchbaum et al., 2012

DHEA = dehydroepiandrosterone; CoQ10 = Coenzyme Q10; IGF-1 = insulin-like growth factor-1; ROS = reactive oxygen species; DOR = diminished ovarian reserve; AMH = anti-Müllerian hormone; IVF = in vitro fertilisation.

Table 4: Comparative Analysis of Emerging Ovarian Regeneration Techniques

Technique	Mechanism	Evidence Level	Advantages	Limitations
PRP Therapy	Growth factor-mediated angiogenesis and follicular activation	Moderate (clinical studies)	Autologous, minimally invasive, cost-accessible	Protocol heterogeneity; lack of RCT data
Stem Cell Therapy	Paracrine signalling, anti-apoptotic, cellular differentiation	Low–Moderate (mainly preclinical)	Potential for true biological restoration	Safety, tumorigenicity, ethical and regulatory barriers
In Vitro Activation	PI3K-AKT pathway stimulation of dormant primordial follicles	Moderate (limited clinical)	Documented pregnancies in POI; targeted approach	Surgical intervention required; centres of excellence only
Exosome Therapy	Cell-free miRNA and protein signalling for ovarian repair	Emerging (preclinical)	Lower immunogenicity; scalable production	No published human trials; optimisation of dosing required

RCT = randomised controlled trial; POI = premature ovarian insufficiency; PRP = platelet-rich plasma.

Discussion

This prospective pilot study is among the few Indian centre-based studies exploring the role of intraovarian PRP therapy in women with diminished ovarian reserve (DOR) and premature ovarian insufficiency (POI). The findings showed significant improvement in both AMH and antral follicle count (AFC) within 8 weeks after treatment, supporting growing international evidence that PRP may help improve ovarian function [13-16].

AMH levels increased from 0.52 to 0.86 ng/mL, while AFC also showed a meaningful rise despite the very low baseline ovarian reserve of these patients. Even a small increase in follicle number can be clinically important in poor ovarian responders, where a single mature oocyte may determine treatment success. Interestingly, two of the three POI patients resumed spontaneous menstruation after PRP therapy. Both had some residual follicular activity at baseline, suggesting that patients with a remaining follicular pool may respond better to regenerative treatments, whereas patients with complete follicular depletion may have limited benefit.

The exact mechanism of PRP is still being studied, but it is believed to improve ovarian blood supply, reduce cellular damage, and create a healthier environment for dormant follicles through growth factors such as VEGF, PDGF, and TGF-β. The additional use of DHEA and CoQ10 may also have supported ovarian recovery by improving hormonal responsiveness and mitochondrial function.

The overall pregnancy rate of 30% in this study is encouraging considering the poor prognosis of women with very low AMH and AFC. Two pregnancies occurred following IVF, while one was spontaneous. Although the contribution of PRP alone cannot be clearly separated from supportive supplements, these outcomes suggest possible therapeutic benefit.

In the Indian setting, PRP may offer practical advantages because it is less expensive and more accessible than donor oocyte programs, while also allowing women the possibility of achieving a genetically related pregnancy. However, the study has important limitations, including the small sample size, lack of a control group, short follow-up period, and use of additional therapies in all patients. Larger, well-designed randomised trials are needed to confirm these findings, identify which patients benefit most, and determine the long-term effectiveness of ovarian regenerative therapies.

Conclusion

This prospective pilot series demonstrates that intraovarian PRP therapy, administered within a structured adjunctive pharmacotherapy protocol, produces statistically significant improvements in serum AMH and AFC in women with diminished ovarian reserve and premature ovarian insufficiency. Clinical benefit—including menstrual cycle restoration, enhanced oocyte yield, and pregnancy—was observed in a meaningful proportion of patients, with greatest responsiveness in those retaining at least minimal residual follicular activity. These findings, integrated with a structured review of the emerging landscape of ovarian regenerative strategies, support the classification of intraovarian PRP as a promising adjunctive investigational intervention warranting evaluation in larger randomised trials. Standardisation of protocols, development of robust response-prediction biomarkers, and FOGSI-led multicentre collaboration are essential next steps toward establishing evidence-based clinical guidelines for ovarian rejuvenation in India and globally.

References

1. Sills ES, Wood SH (2019) Autologous platelet-rich plasma injection into adult human ovary tissue: molecular mechanism, analysis, and discussion of reproductive response. Biosci Rep 39: BSR20190805.
2. Cakiroglu Y, Saltik A, Yuceturk A, Karaosmanoglu O, Kopuk SY, et al. (2020) Effects of intraovarian injection of autologous platelet rich plasma on ovarian reserve and IVF outcome parameters in women with primary ovarian insufficiency. Aging (Albany NY) 12: 10211-10222.
3. Sfakianoudis K, Simopoulou M, Nitsos N, Rapani A, Pantou A, et al. (2019) Autologous platelet-rich plasma treatment enables pregnancy for a woman in premature menopause. J Clin Med 8: 1.
4. Herraiz S, Pellicer A (2020) Activation of primordial follicles to rescue fertility in patients with premature ovarian insufficiency. Fertil Steril 113: 731-732.
5. Kawamura K, Cheng Y, Suzuki N, Deguchi M, Sato Y, et al. (2013) Hippo signaling disruption and Akt stimulation of ovarian follicles for infertility treatment. Proc Natl Acad Sci USA 110: 17474-17479.
6. Ding C, Zou Q, Wang F, Wu H, Chen R, et al. (2018) Stem cell therapy for ovarian failure: current status and future perspective. Cell Physiol Biochem 45: 2338-2355.
7. Mohamed SA, Shalaby SM, Abdelaziz M, Brakta S, Hill WD, et al. (2018) Human mesenchymal stem cells partially reverse infertility in chemotherapy-induced ovarian failure. Reprod Sci 25: 51-63.
8. Xu L, Zhang Y, Wang L (2022) Exosomes derived from stem cells: a promising therapeutic strategy for ovarian dysfunction. Stem Cell Res Ther 13: 1-12.
9. Gleicher N, Barad DH (2011) Dehydroepiandrosterone (DHEA) supplementation in diminished ovarian reserve. Reprod Biol Endocrinol 9: 67.
10. Xu Y, Nisenblat V, Lu C, Li R, Qiao J, et al. (2018) Pretreatment with coenzyme Q10 improves ovarian response and embryo quality in low-prognosis young women. Reprod Biol Endocrinol 16: 29.
11. Duffy JM, Ahmad G, Mohiyiddeen L, Nardo LG, Watson A (2010) Growth hormone for in vitro fertilization. Cochrane Database Syst Rev 1: CD000099.
12. Tamura H, Takasaki A, Taketani T, Tanabe M, Kizuka F, et al. (2014) Melatonin and female reproduction. J Obstet Gynaecol Res 40: 1-11.
13. Tatone C, Amicarelli F (2013) The aging ovary—the poor granulosa cells. Fertil Steril. 99: 12-7.
14. Practice Committee of the American Society for Reproductive Medicine (2018) Management of poor ovarian response. Fertil Steril 109: 993-1003.
15. Poseidon Group (2016) A poor ovarian response to ovarian stimulation: towards a smart classification. Hum Reprod 31: 2373-2378.
16. Lerchbaum E, Obermayer-Pietsch B (2012) Vitamin D and fertility: a systematic review. Eur J Endocrinol 166: 765-778.