



## Role of intra ovarian infusion of platelet rich plasma in women with poor ovarian reserve or ovarian insufficiency (poor responders)

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**Abstract: Introduction:** In order to restore injured organs or tissues, platelet rich plasma (PRP) has been employed as a treatment approach. Both endometrial and follicular growth was improved by platelet-rich plasma (PRP). According to studies, ovarian reserve was enhanced by infusing the ovary with platelet-rich plasma (PRP). **Aim of study:** To assess the impact of intraovarian infusion of platelet-rich plasma (PRP) in women with diminished ovarian reserve or premature ovarian insufficiency. **Patients and methods:** This prospective observational study was done at gala teaching hospital in the period between September 2024 and December 2025 where 20 women were diagnosed as poor responders and underwent intra ovarian PRP infusion. **Results:** The results of the study demonstrated statistically insignificant difference before and after PRP infusion in all ovarian reserve parameters regarding the mean AFC ( $2.75 \pm 0.85$  before &  $3.15 \pm 0.74$  after), mean serum AMH ( $0.36 \pm 0.19$  ng/ml before &  $0.4 \pm 0.23$  ng/ml), mean serum FSH ( $11.9 \pm 1.29$  mIU/ml before &  $11.39 \pm 1.09$  mIU/ml after) and mean number of oocytes ( $1.5 \pm 1$  before &  $1.95 \pm 1.27$  after). **Conclusion:** Intra ovarian PRP infusion in poor responders didn't significantly improve ovarian reserve parameters (AFC, serum AMH, serum FSH,) or the number of oocytes.

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**Keywords:** Role; ovarian; infusion; platelet rich plasma; women; poor ovarian reserve; ovarian insufficiency; poor responder

### 1. Introduction:

Poor responders were classified by ESHRE 2011 using the Bologna criteria, defined as females exhibiting at least two of the following conditions: advanced maternal age ( $\geq 40$  years) or other risk factors for poor ovarian response (POR), previously encountered poor response of  $\leq 3$  retrieved oocytes following conventional stimulation, or an abnormal ovarian reserve test (Antral follicular count  $< 7$  or Anti-Müllerian hormone  $< 1.1$  ng/mL).<sup>(1)</sup>

Premature ovarian insufficiency (POI), also known as diminished ovarian reserve (DOR), is a serious reproductive issue where a lower follicular count impairs ovulation. The number and quality of oocyte reserves decline with ovarian aging, which also lowers the likelihood of ART success and spontaneous pregnancy. Regardless of the reason behind ovarian failure, the main contributor is a lack of primitive follicles.<sup>(2)</sup>

Reduced granulosa cell proliferation and differentiation is likely the cause of the ovarian

dysfunction. Additionally, research indicated that a reduction in the ovarian blood flow is associated with aging and premature ovarian insufficiency.<sup>(2)</sup>

Various therapeutic modalities have been used, although with limited success, to improve the ovarian response in females with reduced ovarian reserve. A treatment line called platelet rich plasma (PRP) is being used to restore injured tissues or organs.<sup>(3)</sup>

Platelet rich plasma (PRP) infusion into the ovary has been found to improve ovarian reserve with menstrual cycle recovery, increase number and quality of oocytes, improve fertilization during ICSI, decrease FSH, improve Antral follicular count (AFC), and elevate Anti Mullerian hormone (AMH). Platelet-rich plasma (PRP) enhances endometrial development and receptivity increases the rate of pregnancy.<sup>(4, 5)</sup>

Although Platelet-rich plasma (PRP) has recently been shown to increase rate of follicular and endometrial development, the exact mechanism is unknown.<sup>(6)</sup> Platelet-rich plasma (PRP) has been

shown to enhance the ovary's response to gonadotrophins and other ovulatory stimulants.<sup>(7)</sup> Due to its antioxidant properties, platelet-rich plasma PRP plays an essential role in protecting against cyclophosphamide and other chemotherapeutic medications.<sup>(8)</sup>

It has been proposed that platelet-rich plasma PRP enhances the ovarian response to gonadotrophins by promoting follicular proliferation and growing angiogenesis. PRP also inhibits apoptosis, modulates inflammation, and influences cell migration. Growth factors like VEGF, PDGF AB, and TGF-B are discharged in response to PRP effect.<sup>(9)</sup>

### **Anatomical Basis for Intra-Ovarian PRP Therapy in Poor Ovarian Responders**

The ovaries, the primary female gonads, are paired intraperitoneal organs located in the ovarian fossae on the lateral pelvic wall. Each ovary is approximately 3 cm in length, 1.5 cm in width, and 1 cm in thickness during reproductive years, with size diminishing post-menopause.<sup>(10-12)</sup>

Structurally, the ovary is divided into: 1) Cortex: The outer region containing ovarian follicles at various stages of development, embedded within a dense stroma. 2) Medulla: the center area made up of loose connective tissue that is abundant in lymphatics, blood arteries, and autonomic nerves. 3) Tunica albuginea: A dense connective tissue capsule beneath the surface epithelium.<sup>(10)</sup>

The vascular supply is primarily via the ovarian artery and the uterine artery, forming a rich anastomotic network. Venous drainage occurs through the ovarian veins.<sup>(12)</sup> Ovarian reserve reflects the quantity and quality of primordial follicles within the ovarian cortex. In poor ovarian responders or women with premature ovarian insufficiency, the cortical stroma often exhibits fibrosis, reduced vascularity, and diminished follicular density.<sup>(13-15)</sup>

An autologous concentrate of platelets that is high in growth factors including PDGF, VEGF, TGF- $\beta$ , and EGF is called platelet-rich plasma (PRP). These promote angiogenesis, cell proliferation, and tissue remodeling.<sup>(16-18)</sup> The anatomical rationale for intra-ovarian PRP infusion lies in targeting the ovarian cortex, enhancing stromal vascularization, stimulating granulosa and theca cell proliferation, and modulating the ovarian microenvironment<sup>(19-21)</sup>.

Understanding the anatomical localization of ovarian follicles and vascular networks is essential for optimizing PRP delivery. Ultrasound-guided transvaginal injection techniques aim to deposit PRP into the subcortical region, maximizing exposure of residual follicles to trophic factors.<sup>(21, 22)</sup>

### **Aim of study:**

To assess the impact of intraovarian infusion of platelet-rich plasma (PRP) in women with

diminished ovarian reserve or premature ovarian insufficiency.

### **2. Patients and methods:**

This is a prospective observational study. It was done at El Galaa Assisted Reproductive Center in El Gala teaching Hospital from December 2024 till September 2025. Where 20 patients were diagnosed as poor responders and underwent intraovarian PRP infusion.

### **Inclusion criteria:**

Poor responders were diagnosed according to ESHRE 2011 by the Bologna criteria as female who at least has two of the following conditions: advanced maternal age ( $\geq 40$  years) or other risk factors for poor ovarian response (POR), previously encountered poor response of  $\leq 3$  retrieved oocytes following conventional stimulation, or an abnormal ovarian reserve test (Antral follicular count  $< 7$  or Anti-Müllerian hormone  $< 1.1$  ng/mL).<sup>(1)</sup>

### **Exclusion criteria:**

- A female who does not meet the Bologna criteria for poor responders.
- Gonadal dysgenesis
- Chromosomal abnormalities
- History of cancer.
- Current infection
- Medical disorders

### **Preparation of PRP:**

20 ml of venous blood was withdrawn from the female and then we put the blood in specific PRP collection tube, then we put the PRP tube in the centrifuge at 1200 RPM for 12 minutes. After centrifugation, the blood separated into 3 layers, upper layer consisted of platelets and WBCs, Intermediate cell layer was buffy coat rich in WBCs, bottom layer consisted of RBCs, then we separated the upper plasma part separating it from condensed RBCs, then we put this plasma in another PRP tube and put this tube in centrifuge again at 3300 RPM for another 7 minutes, for separating platelet from WBCs, Where platelets were be the upper layer and WBCs were be the lower layer, then took the upper layer where its upper two third was PPP platelet poor plasma and lower one third was PRP platelet rich plasma.<sup>(1)</sup>

2ml of PRP sample was injected in each ovary by transvaginal ultrasound guided injection using a 17 gauge single lumen needle. This was done under anesthesia, in early proliferative phase of cycle (day 6 or 7) and under good antibiotic cover. After procedure completed, U/S was done to assess the vascular integrity and amount of blood in pelvic region. ICSI cycle was started in menstrual cycle following PRP injection.

Hormonal levels (AMH, FSH) and AFC on day 3 of the menstruating cycle were documented before and after injection. Also, the number of oocytes retrieved after ICSI cycle was documented.

### 3. Results:

In Our study, the mean age of 20 poor responder females was  $39.5 \pm 3.7$  years. The mean BMI of those females was  $26.9 \pm 2.6$ . As regarding mean of AMH before the PRP injection was  $0.36 \pm 0.19$  ng/ml and after PRP injection was  $0.4 \pm 0.23$  ng/ml. This was statistically insignificant, where P value was 0.6 (P value was  $> 5\%$ ).

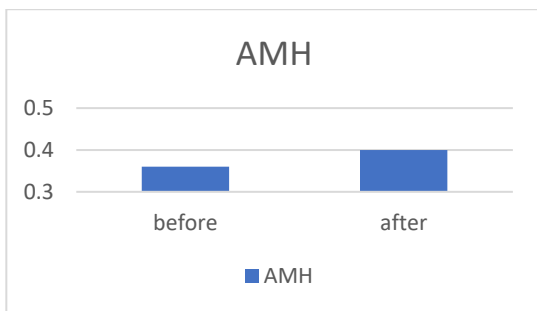


Figure 1: AMH before and after PRP

Regarding the mean FSH before and after PRP injection, showed statistically insignificant difference ( $11.99 \pm 1.29$  mIU/ml before &  $11.39 \pm 1.09$  mIU/ml after) with P value was 0.11.

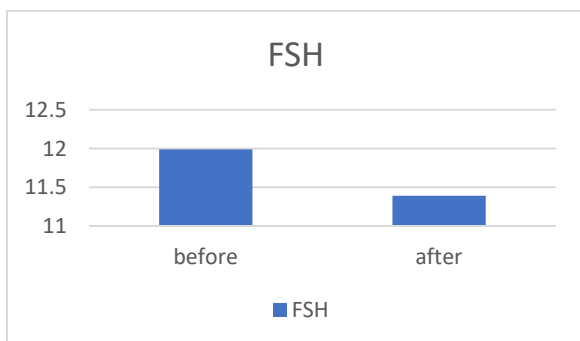


Figure 2: FSH before and after PRP

The mean AFC before and after PRP injection was statistically insignificant ( $2.75 \pm 0.85$  before &  $3.15 \pm 0.74$  after) with P value was 0.12.

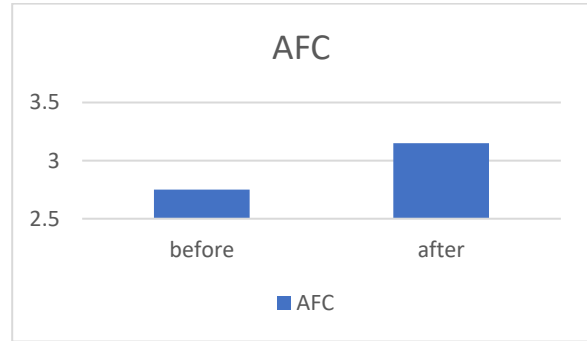


Figure 3: AFC before and after PRP

We also found a statistically insignificant difference in the mean of oocyte number before and after PRP injection ( $1.5 \pm 1$  before &  $1.95 \pm 1.27$  after) with P value 0.22.

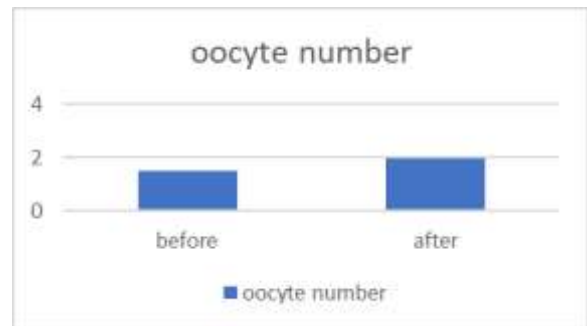


Figure 4: Oocyte number before and after PRP

### 4. Discussion:

Our current work is a prospective observational study that was done at Assisted Reproductive Center, El Galaa teaching Hospital, Cairo, Egypt. The duration extended from September 2024 to December 2025. 20 patients were diagnosed as poor responders and underwent intraovarian PRP injection. The patients' mean age was  $39.5 \pm 3.7$  years while the mean BMI was  $26.9 \pm 2.6$ .

The study did not show any significant improvement in neither ovarian reserve parameters (AFC, FSH, and AMH) nor the number of retrieved mature oocytes. AMH was insignificantly increased after PRP injection. FSH was insignificantly decreased after PRP injection. Regarding AFC, there was slight increase but no significant difference before and after PRP injection. Although, an improvement in all parameters noted, it had no clinical significance for better fertility outcomes.

Our findings were consistent with those of a previous multicenter randomized clinical trial conducted by Herlihy et al. <sup>(23)</sup>, which investigated the impact of intraovarian PRP injections on IVF outcomes in women with poor ovarian response.

When IVF cycles were initiated in the first menstrual cycle following therapy, they found no improvements in terms of AFC, AMH, oocyte yield, blastocyst, and euploid blastocyst number when compared with no intervention. Similar findings have been reported by Barad et al.<sup>(24)</sup> in 28-54-year-old women suggesting that treatment success could be age and patient dependent. In line with our study, Farimani M et al.<sup>(25)</sup> found no change in ovarian reserve markers (AFC, AMH, FSH). Also another study by Parvanov et al.<sup>(26)</sup> showed no statistically significant increase in oocyte count and embryo quality.

Similarly, Aflatoonian et al.<sup>(27)</sup> reported no significant change in FSH levels among women with POI who received PRP injections. In agreement with Molinaro et al.<sup>(28)</sup>, in their retrospective study evaluating PRP treatment in poor responders, found no improvement in AFC, AMH, or oocyte count. However, they observed a significant enhancement in oocyte maturation, fertilization, and cleavage rates. These findings may offer hope to women who struggle to produce high-quality embryos.

Although theoretic mechanism by which the PRP can improve the ovarian function is not clear. Any stage of folliculogenesis is susceptible to apoptosis and atresia. The growth factor gene that is expressed or altered during atresia or apoptosis is unclear. Growth factors can affect embryo quality and implantation and are important at every stage of folliculogenesis. PDGF-B and VEGF are among the growth factors found in PRP that promote angiogenesis, cellular proliferation, and tissue regeneration. Additionally, PRP has anti-inflammatory qualities that provide an optimum ovarian microenvironment that can promote oocyte quality and follicular development.<sup>(29)</sup>

Furthermore, PRP has been demonstrated to stimulate latent primordial follicles, expand the pool of ovarian follicles, and enhance ovarian cell proliferations. All of which are critical for the best possible ovarian function. Granulosa cells within developing follicles are the primary source of AMH secretion. PRP may help prevent follicular atresia, which could lead to a modest improvement in AMH levels. The reduction in FSH level indicates an improvement in ovarian function and the potential for enhanced follicular growth.<sup>(30)</sup> Therefore, molecular research could be useful in identifying PRP's precise mode of action in ovarian reactivation.

This is consistent with previous case series and prospective cohort studies, but it contradicts the findings of our investigation, which showed an improvement in ovarian reserve indicators.<sup>(22,31,32)</sup> The oocytes quantity and embryo yield for POR women following intraovarian PRP injection.<sup>(6,22,25,33)</sup>

In disagreement with our study, Adiga et al.<sup>(1)</sup> noted a statistically significant improvement in AFC. However, there was no sufficient data to support the claim PRP increases the number of AFC as there is no clinically relevant utility in the mean difference of just 1.78 following injection. Additional randomized controlled studies are still required to validate therapeutic efficacy, despite comprehensive reviews suggesting that autologous intraovarian injection of PRP could increase ovarian reserve markers, IVF and fertility outcomes in poor responder patients.<sup>(34)</sup>

This discrepancy in results among different studies may be attributed to many reasons such as difference in methodology, sample size, patient characteristics, PRP preparation, dosage, injection frequency, and timing. Larger, well-designed randomized controlled trials are therefore essential to assess the impact of PRP injection prior to its use in the treatment of women with poor ovarian response, and additional research should address and improve these limitations.

#### Conclusion:

In poor responders, intra-ovarian injection of autologous PRP did not significantly improve of mature oocytes, AMH, AFC and FSH.

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