The Role of Platelet-Rich Plasma (PRP) in Enhancing IVF Success in Women With Ovarian Insufficiency: A Cohort Study

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Received: 11 Feb. 2024; Accepted: 28 Aug. 2024

Abstract- Ovarian insufficiency is a significant cause of infertility in women, with limited effective treatment options. Platelet-Rich Plasma (PRP), rich in concentrated growth factors, has shown regenerative potential in various medical fields. However, its efficacy as an adjunct in infertility treatment, particularly in women with ovarian insufficiency, remains unclear. This study investigates whether PRP administration improves the success of IVF cycles in this specific population. This cohort study followed women with ovarian insufficiency undergoing IVF at a fertility center. Participants were divided into two groups: the intervention group, which received PRP alongside the standard IVF protocol, and the control group, which received only the standard protocol. Data collected included patient demographics, hormonal levels, number and quality of retrieved oocytes, fertilization rates, embryo quality, and pregnancy outcomes. The primary outcome was IVF success, defined by clinical pregnancy rates. Secondary outcomes included hormonal changes, oocyte quality, and embryo development. Statistical analysis utilized descriptive statistics, chi-square tests, and t-tests to compare outcomes between groups. PRP administration led to significant reductions in FSH levels (P<0.001) and marked increases in AMH levels and antral follicle count (AFC) (P=0.001 and P<0.001, respectively). The number of oocytes, mature MII oocytes, and Grade A embryos also improved significantly (P ranging from 0.004 to 0.017). Although the increase in Grade B embryos was not statistically significant, it was higher post-PRP. Chemical pregnancies occurred in 25% of participants, with 20.83% resulting in clinical pregnancies, including 2.1% spontaneous pregnancies. PRP significantly enhanced ovarian reserve markers (FSH, AMH, AFC), oocyte quality, and embryo development, translating into improved fertility outcomes. The findings suggest that with longer follow-up and larger sample sizes, PRP could be validated as a promising adjunctive therapy for women with ovarian insufficiency undergoing IVF. These results align with prior research and highlight PRP's potential to advance reproductive outcomes in this challenging patient population.

Acta Med Iran 2024;62(September-October):264-272.

Keywords: Infertility; Ovarian insufficiency; Platelet-rich plasma (PRP); In vitro fertilization (IVF); Oocyte quality; Embryo quality; Clinical pregnancy

Introduction

Platelet-Rich Plasma (PRP) is an autologous product derived from a patient's whole blood, which is centrifuged to remove red blood cells. The remaining plasma is enriched with growth factors at concentrations 5 to 10 times higher than those in whole blood. These growth factors have been shown to enhance natural healing processes, as evidenced by research in fields such as dentistry, dermatology, urology, and gynecology (1,2).

PRP is also widely used in orthopedics and sports

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medicine to alleviate pain and promote the natural healing of musculoskeletal conditions, including tendonitis, arthritis, ligament sprains, and tears (3). The underlying mechanism of PRP therapy mimics the body's natural healing response, where platelets are delivered to the site of tissue injury. These platelets not only initiate healing but also attract stem cells to the injured area. As PRP has transitioned from bench to bedside, its application in treating ligaments, tendons, and joints has demonstrated remarkable regenerative outcomes (4).

In the field of female infertility, PRP has emerged as a novel therapeutic option for conditions resistant to conventional treatments (5-7). A comprehensive evaluation by Dawood (2018) explored the theoretical and practical applications of PRP in gynecology. Literature searches conducted using PubMed, Google Scholar, Clinical Key, and Medline, spanning January 2000 to December 2017, identified studies investigating PRP applications in women. Search terms included "Platelet-Rich Plasma," "procedures," "applications," "endometrium," "infertility," and "women." The retrieved studies primarily consisted of case series, case reports, correspondence, and small-scale pilot studies. Notably, no randomized clinical trials with sufficient sample sizes were found (5).

As highlighted in Dawood's review, there remains a significant gap in the literature on the use of PRP in reproductive medicine. Addressing this gap, the present study evaluates the effects of intrauterine and ovarian PRP injections in patients with infertility resistant to standard IVF protocols. This research aims to contribute valuable insights into the potential of PRP as a regenerative therapy in improving fertility outcomes

Materials and Methods

Study population and sampling

This study targeted women diagnosed with ovarian insufficiency who were candidates for IVF cycles at the Sayad Shirazi Hospital Infertility Center during 2022-2023. Participants underwent Platelet-Rich Plasma (PRP) injection during the luteal phase of their cycle. Sampling was conducted using a census method based on available cases.

Inclusion criteria

- Women aged 20-39 years.
- Diagnosed with ovarian insufficiency based on ESHRE criteria.
- Candidates for IVF.
- PRP injection during the luteal phase.

Exclusion criteria

- Incomplete patient records.
- Body mass index (BMI) outside the range of 18–30 kg/m².
- Additional endocrine disorders, including thyroid dysfunction, hyperprolactinemia, diabetes, Addison's disease, congenital adrenal hyperplasia, or Cushing's syndrome.
- Structural uterine abnormalities (corrected or uncorrected).
- Infertility due to azoospermia.

This retrospective cohort study utilized medical records from eligible women undergoing IVF. Patient data included age, clinical pregnancy outcomes, fertilization rates, the number of MII oocytes, three-day embryos, Grade 1 and 2 embryos, total retrieved oocytes, and live birth rates. Eligibility was determined based on ESHRE criteria for diagnosing primary ovarian insufficiency (POI) and Bologna criteria for defining poor ovarian responders.

Preparation and application of PRP

Standardized protocols were used for PRP preparation and administration.

1. Blood Collection and PRP Preparation:
- Twenty milliliters of blood were drawn into two tubes.
- Tubes were centrifuged at 1500g for 8 minutes to separate plasma from red blood cells.
- Approximately 2 mL of plasma from each tube was collected into a syringe using a 16-gauge needle.
- The plasma was transferred to a suspension tube, gently mixed for 30-60 seconds, and prepared for use.

2. PRP Injection Procedure:
- A total of 4 mL of PRP was divided into two equal portions for injection into each ovary.
- Injections were performed under sedation using a 17-gauge, 35-cm needle guided by transvaginal ultrasound.
- Two milliliters of PRP were injected into the stromal region of each ovary within two hours of preparation.

Post-PRP monitoring

Patients were monitored monthly for menstrual regularity, antral follicle count (AFC), and serum hormone levels for at least six months post-PRP. Ovarian stimulation was initiated during the first five days of the menstrual cycle for eligible patients. Follicular growth was tracked using serial transvaginal ultrasounds and

serum hormone levels.

When the leading follicle reached 12-14 mm, 0.25 mg of a GnRH antagonist was administered to suppress premature luteinizing hormone (LH) surges. Oocyte maturation was induced using a dual-trigger approach (0.2 mg GnRH agonist and 250 µg human chorionic gonadotropin). Oocytes were retrieved 35-36 hours later under ultrasound guidance.

Fertilization was performed via intracytoplasmic sperm injection (ICSI), and embryos (day 3 or day 5) were transferred using an abdominal ultrasound-guided catheter. Up to two embryos were transferred per attempt. Luteal-phase support with 200 mg vaginal progesterone (twice daily) was provided until the 8th-10th week of pregnancy.

Data analysis

Statistical analyses were performed using IBM SPSS (version 26). Descriptive statistics were expressed as mean±standard deviation (for normally distributed data) or median (minimum–maximum) for skewed data. Categorical variables were presented as numbers and percentages. Group differences in means and medians were assessed using t-tests and ANOVA. A P<0.05 was considered statistically significant.

Definitions

Poor ovarian response in IVF was defined per the Bologna criteria, requiring at least two of the following:

1. Advanced maternal age or other risk factors for poor ovarian response.
2. Previous poor ovarian response.
3. Abnormal ovarian reserve tests.

A poor ovarian response in the absence of advanced maternal age or abnormal ovarian reserve required at least two poor responses after maximal ovarian stimulation (8).

Results

Before the intervention

A total of 48 eligible participants were identified for this study. The mean age of participants was 36.73±4.95 years, and the mean duration of marriage was 6.47±4.25 years. Baseline hormonal levels included a mean FSH of 10.83±6.46 IU/L, AMH of 0.57±0.25 ng/mL, and AFC of 3.31±1.11. Among the participants, 18.8% had one living child, 16.7% had a history of cesarean section, and 58.3% had no underlying medical conditions. Additionally, 12.5% had undergone previous IVF cycles, 6.3% had a history of hypothyroidism, 4.2% had undergone laparoscopic surgery for ovarian cysts, and 6.3% had a history of endometrioma (Table 1).

Out of all participants, 58.3% had no oocytes retrieved before the intervention, and 77.1% had two or fewer oocytes. Furthermore, 70.8% had no mature (MII) oocytes, no embryos, or Grade A embryos (Table 2).

Table 1. Participant characteristics before intervention

		Minimum	Maximum	Mean	Standard deviation
Age		23	45	36.73	4.958
Years of marriage		1.0	18.0	6.479	4.2589
FSH		2.37	29.41	10.8317	6.46427
AMH		.060	1.200	.57438	.256671
AFC		2	6	3.31	1.114
Number of oocytes		0	12	1.44	2.378
Number of M II type oocytes		0	9	.75	1.618
Number of embryos		0	9	.77	1.666
Number of type A embryos		0	6	.48	1.148
Number of type B embryos		0	2	.17	.476
		Frequency		**Percent**	
Number of living children	**0**	39		81.3	
	1	9		18.8	
History of cesarean section	**0**	40		83.3	
	1	8		16.7	

Cont. table 1

Past medical history	**Without disease**	28	58.3
	Pulpectomy	1	2.1
	Previous IVF	6	12.5
	DVT	1	2.1
	IUI	1	2.1
	Hypothyroidism	3	6.25
	Hysteroscopy	1	2.1
	Rheumatoid arthritis	2	4.2
	Laparoscopy (ovarian cyst)	2	4.2
	Endometrioma	3	6.25

Table 2. Participants' oocytes and embryos before intervention

		Frequency	Percent	Cumulative percentage
Number of oocytes	**0**	28	58.3	58.3
	1	5	10.4	68.8
	2	4	8.3	77.1
	3	1	2.1	79.2
	4	5	10.4	89.6
	5	3	6.3	95.8
	6	1	2.1	97.9
	12	1	2.1	100.0
Number of M II oocytes	**0**	34	70.8	70.8
	1	4	8.3	79.2
	2	6	12.5	91.7
	3	1	2.1	93.8
	4	2	4.2	97.9
	9	1	2.1	100.0
Number of embryos	**0**	34	70.8	70.8
	1	5	10.4	81.3
	2	4	8.3	89.6
	3	1	2.1	91.7
	4	3	6.3	97.9
	9	1	2.1	100.0
Number of type A embryos	**0**	37	77.1	77.1
	1	5	10.4	87.5
	2	4	8.3	95.8
	4	1	2.1	97.9
	6	1	2.1	100.0
Number of type B embryos	**0**	42	87.5	87.5
	1	4	8.3	95.8
	2	2	4.2	100.0

After the intervention

Following the PRP intervention, significant improvements were observed in ovarian reserve markers and reproductive outcomes. The mean FSH decreased to 9.63±6.96 IU/L (P<0.001), AMH increased to 1.06±0.58 ng/mL (P=0.001), and AFC increased to 6.23±2.43 (P<0.001). The number of retrieved oocytes increased from 1.44±2.38 to 4.15±3.61 (P=0.017), and the number of MII oocytes rose from 0.75±1.61 to 2.52±2.75 (P=0.013). Similarly, the number of embryos increased from 0.77±1.66 to 2.42±2.42 (P=0.004), and the number of Grade A embryos improved from 0.48±1.15 to 1.77±2.23 (P=0.004). Although the number of Grade B embryos increased from 0.17±0.48 to 0.48±0.77, the change was not statistically significant (P=0.396) (Table 3).

Among the participants, 25% achieved pregnancy, with 2.1% being spontaneous pregnancies and 4.2% experiencing chemical pregnancies that did not progress to clinical pregnancies. Ultimately, 6.3% underwent cesarean delivery, 8.3% were still pregnant at the study's conclusion, and 4.2% experienced chemical pregnancies that did not develop further (Table 4).

Comparison of pre- and post-intervention outcomes

Post-intervention analysis revealed significant improvements in FSH, AMH, AFC, oocyte counts, and embryo quality. The number of participants with more than three oocytes increased from 0% to 47.9%. Additionally, 25% of participants had no MII oocytes after the intervention, compared to 70.8% before the intervention. In terms of embryos, 27.1% had no embryos post-intervention compared to 70.8% pre-intervention. Similarly, the number of participants with no Grade A embryos decreased from 77.1% to 43.8%, with 18.8% having 4-9 Grade A embryos (Table 5).

Despite significant improvements in FSH, AMH, and AFC post-intervention, these changes were not influenced by participant age, duration of marriage, number of living children, cesarean history, underlying medical conditions, or pregnancy outcomes (P>0.05 for all) (Table 6).

Table 3. Participant characteristics after intervention

		Minimum	Maximum	Mean	Standard deviation
FSH		1.52	32.20	9.6340	6.96370
AMH		.200	2.700	1.06192	.584767
AFC		2	12	6.23	2.434
Number of oocytes		0	18	4.15	3.608
Number of M II type oocytes		0	13	2.52	2.752
Number of embryos		0	10	2.42	2.422
Number of type A embryos		0	9	1.77	2.234
Number of type B embryos		0	4	.48	.772
		Frequency		Percent	
Pregnancy	**Spontaneous pregnancy**	1		2.1	
	Pregnancy in the cycle	9		18.75	
	Non-pregnant	36		75.0	
	Chemical pregnancy	2		4.2	
Delivery	**None**	36		54.0	
	Cesarean section	3		6.3	
	Pregnant	4		8.3	
	Abortion	5		10.41	

Table 4. Oocytes and embryos after intervention

		Frequency	Percent	Cumulative percentage
Number of oocytes	**0**	5	10.4	10.4
	1-3	20	41.66	52.1
	4-6	14	29.16	81.3
	6-10	7	14.58	93.8
	>10	3	6.3	100.0

Cont. table 4

Number of M II type oocytes	**0**	12	25.0	25.0
	1-3	22	45.83	70.8
	4-6	10	14.6	91.7
	8≤	4	8.3	100.0
Number of embryos	**0**	13	27.1	27.1
	1-3	21	43.75	70.8
	4-6	11	22.91	93.8
	7-10	3	6.3	100.0
Number of type A embryos	**0**	21	43.8	43.8
	1-3	18	37.5	81.3
	4-9	9	18.75	100.0
Number of type B embryos	**0**	30	62.5	62.5
	1	15	31.3	93.8
	2-4	3	6.3	100.0

Table 5. Comparison of FSH, AMH, AFC, and oocytes and embryos before and after intervention

		Mean	Standard deviation	Standard error	*P**
FSH	**Before**	10.8317	6.46427	.93304	
	After	9.6340	6.96370	1.00512	.000
	After-Before	-1.1977	6.21283		
AMH	**Before**	.57438	.256671	.037047	
	After	1.06192	.584767	.084404	.001
	After-Before	.4875	.51932		
AFC	**Before**	3.31	1.114	.161	
	After	6.23	2.434	.351	.000
	After-Before	2.9167	2.08167		
Number of oocytes	**Before**	1.44	2.378	.343	
	After	4.15	3.608	.521	.017
	After-Before	2.7083	3.57865		
Number of M II oocytes	**Before**	.75	1.618	.233	
	After	2.52	2.752	.397	.013
	After-Before	1.7708	2.65169		
Number of embryos	**Before**	.77	1.666	.240	
	After	2.42	2.422	.350	.004
	After-Before	1.6458	2.31084		
Number of type A embryos	**Before**	.48	1.148	.166	
	After	1.77	2.234	.322	.004
	After-Before	1.2917	2.05207		
Number of type B embryos	**Before**	.17	.476	.069	
	After	.48	.772	.111	.396
	After-Before	.3125	.85443		

* Based on paired T-test

Table 6. Study of the effect of variables on FSH, AMH, and AFC levels before and after PRP

Variables		*P**
FSH	Age	.376
	Years of marriage	.597
	Number of living children	.778
	History of cesarean section	.549
	Past medical history	.169
	Pregnancy	.808
AMH	Age	.422
	Years of marriage	.951
	Number of living children	.389
	History of cesarean section	.414
	Past medical history	.131
	Pregnancy	.806
AFC	Age	.771
	Years of marriage	.937
	Number of living children	.829
	History of cesarean section	.872
	Past medical history	.754
	Pregnancy	.538

* According to repeated measures ANOVA test

Discussion

Platelet-Rich Plasma (PRP) therapy has been explored as a complementary treatment for women with severely diminished ovarian reserve and premature ovarian insufficiency. Intracellular injection of PRP appears to have rejuvenating effects on the ovaries. Studies in both humans and animals have demonstrated promising outcomes in subsequent ICSI cycles following PRP treatment. This includes improvements in ovarian reserve indicators such as increased serum Anti-Müllerian Hormone (AMH) levels, antral follicle count (AFC), and decreased follicle-stimulating hormone (FSH) levels. Furthermore, improvements in clinical ICSI cycle parameters—such as the number of retrieved oocytes, high-quality embryos, fertilization rates, and cycle cancellation rates—have been reported (9,10).

Despite these promising findings, the lack of large-scale clinical trials remains a significant limitation in this area of research (5). Dawood *et al*., highlighted the scarcity of robust studies on the efficacy of PRP in fertility treatments, emphasizing the need for further investigation (5).

In our study, PRP therapy led to a significant reduction in FSH levels, consistent with findings from Elias *et al*., who reported a substantial decrease in FSH levels three months post-PRP treatment, with levels dropping to 7-11 IU/L (11). Similarly, studies by Fraidakis *et al*., Sfakianoudis *et al*., and Saydah *et al*., also observed significant reductions in FSH post-PRP, supporting the results of our study (12,14).

Our results also showed a significant increase in AMH levels post-PRP, corroborated by meta-analyses conducted by Elias *et al*., and Li *et al*., which demonstrated similar findings. Although Davari-Tanha *et al*., reported a 4.5% increase in AMH that did not reach statistical significance, Cakiroglu *et al*., reported significant improvements in ovarian AMH levels post-PRP (11,15-17).

AFC, a critical indicator of ovarian reserve, also showed marked improvement in our study. Elias *et al*., (2024) reported an increase of 1.6-fold in AFC post-PRP, a statistically significant finding that aligns with the outcomes of Hosseini-Sadat *et al*., who also observed a substantial rise in AFC (11,18).

Notably, 87.5% of our participants experienced improvements in both AFC and AMH, with separate improvements in 95.8% and 87.5% of participants, respectively. These rates were significantly higher than those reported by Molinaro *et al*., who observed improvement rates of 59.1% for both, 68.8% for AMH alone, and 81.7% for AFC alone (19).

Additionally, our study demonstrated improvements in oocyte and embryo numbers and their quality post-

PRP. Shrivastava *et al*., similarly reported increases in follicle counts, oocyte quality, and successful pregnancy outcomes in second IVF cycles post-PRP (20). Parvanov *et al*., also documented significant increases in mature follicles, retrieved oocytes, Grade A blastocysts, and MII oocytes post-PRP treatment (21). Farimani *et al*., reported consistent findings in an Iranian cohort, further reinforcing the therapeutic potential of PRP (22).

Overall, our study demonstrated significant reductions in FSH levels and substantial increases in AMH and AFC levels post-PRP. These changes were accompanied by notable improvements in oocyte and embryo quality and count, translating to higher fertility outcomes. With longer follow-up periods, these findings suggest even greater potential for PRP in improving fertility outcomes. The results of our study are consistent with prior research, supporting the promise of PRP as an emerging adjunctive treatment for infertility.

Ovarian insufficiency is a major cause of infertility in women, with current treatment options remaining limited. PRP, enriched with growth factors, has shown regenerative potential across various medical fields. However, its role as a complementary therapy for infertility, particularly in women with ovarian insufficiency, remains underexplored.

This study aimed to address this gap by assessing the effects of PRP on ovarian function in IVF candidates. Our findings demonstrated significant reductions in FSH levels, increases in AMH and AFC levels, and marked improvements in oocyte and embryo quality and count post-PRP. These outcomes suggest PRP as a valuable adjunct to IVF, with potential to improve reproductive success rates.

Given these results, further large-scale, systematic reviews and meta-analyses are recommended to comprehensively evaluate the efficacy of PRP as a complementary treatment for women with ovarian insufficiency.

Limitations

1. PRP administration by different practitioners may have introduced variability, potentially biasing the results.

2. The retrospective nature of the study relied on patient records, which may limit data quality and completeness.

3. The limited sample size was constrained by the study timeline, which may affect the generalizability of the findings.

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