KΠE Publishing

Check for updates

Original Article

Spontaneous pregnancy following intra-ovarian platelet-rich plasma administration in poor ovarian responders according to the POSEIDON criteria: A cross-sectional study

Marzie Sanuie Farimani [iD][1] **M.D., Kimia Amiri** [iD][2] **M.D., Roghayeh Anvari Aliabad** [iD][1] **M.D.**

[1]Endometrium and Endometriosis Research Center, Hamadan University of Medical Sciences, Hamadan, Iran.
[2]School of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran.

Corresponding Author:

Roghayeh Anvari Aliabad; Endometrium and Endometriosis Research Center, Fatemieh Hospital, Pasdaran St., Hamadan, Iran.

Postal Code: 89971-65177

Tel: (+98) 9143227977

Email: anvar_anvari@yahoo.com; r.anvari@umsha.ac.ir

Editor-in-Chief:

Aflatoonian Abbas M.D.

Abstract

Background: Female infertility, especially in those individuals with poor ovarian response (POR), is a challenge in the field of infertility and sterility. Recently, intra-ovarian platelet-rich plasma (IO-PRP) administration has been suggested as a possible co-treatment.

Objective: This study aimed to investigate the biodemographic characteristics of individuals who experienced spontaneous pregnancy following IO-PRP.

Materials and Methods: In this cross-sectional study, out of 1548 women diagnosed with POR who underwent IO-PRP, 596 individuals who completed their 2-yr follow-up period, were included. Different types of demographic and pre-intervention laboratory data (blood levels of anti-Müllerian hormone, luteinizing hormone, follicle-stimulating hormone, estradiol, prolactin, and their spouses' sperm analysis results) were collected from the files. Each individual was classified into a certain group according to the POSEIDON criteria, and their data were compared.

Results: The results showed that 50 (8.39%) spontaneous pregnancies were observed. However, 8 were excluded from further analyses due to missing data in their critical variables. The most prevalent POSEIDON group was 4, with a prevalence of 17/42 (40.47%). Among the POSEIDON groups, covariates including the age of the individuals and their spouses, body mass index, anti-Müllerian hormone, and antral follicle/oocytes count following the latest IO-PRP significantly differed ($p < 0.001$, $p < 0.001$, $p = 0.039$, $p < 0.001$, and $p = 0.022$, respectively).

Conclusion: The spontaneous pregnancy rate following IO-PRP among women with POR was low. However, significant differences in biodemographic and hormonal characteristics were observed between the groups with and without spontaneous pregnancy which could be useful in leading future studies on this subject.

This article has been extracted from M.D. Thesis. (Kimia Amiri)

🔒 **OPEN ACCESS**

1. Introduction

According to the World Health Organization, approximately 17.5% of the global adult population experiences infertility (1). This condition can be classified into primary and secondary infertility categories (2). Assisted reproductive technology (ART) has provided a solution for couples facing infertility. However, some individuals do not respond to ovarian stimulation (OS), a pre-ART procedure that uses stimulators such as gonadotropins (3–5). This has led to the progression of co-treatment methods (6). One of these co-treatments has been recently used to increase the pregnancy rate, especially in those with ovarian function issues (e.g., premature ovarian insufficiency [POI]) is platelet-rich plasma [PRP]), which is administered directly into the ovary (7).

PRP is an autologous product used to treat various pathological conditions, including the healing of chronic (8) and acute (9) wounds, osteoarthritis (10), tendinopathies (11), and musculoskeletal pathologies (12). The regenerative properties of PRP seem to be due to the growth factors mostly derived from the secretory granules. The regenerative properties of PRP appear to be due to growth factors, primarily derived from secretory granules (13). Considering the possible role of the aforementioned growth factors in the field of regenerative medicine (14) as well as the findings from systematic reviews and meta-analyses on PRP therapy for various pathologies (15–18), this treatment has been successfully tested in the field of infertility, particularly in ART (19). According to a recent systematic review and meta-analysis, PRP therapy significantly improved parameters related to the pregnancy success rate among individuals with ovarian reserve issues (20). In contrast, a question that remains is whether this intervention can be used as a standalone treatment for individuals with infertility due to ovarian dysfunction, and if so, which characteristics predict eligibility for this subpopulation.

The aim of this study was to investigate the characteristics possibly associated with spontaneous pregnancy among individuals with poor ovarian response (POR) who underwent intra-ovarian PRP (IO-PRP) administration.

2. Materials and Methods

2.1. Study setting

For the current cross-sectional study, we followed all POR women according to the Bologna criteria who underwent IO-PRP injection, in Omid Infertility Clinic (Hamadan, Iran). According to defined Bologna criteria for a poor responder, at least 2 of the following 3 criteria were considered: 1) age > 40 yr; 2) POR in previous in vitro fertilization cycles ($\leq$ 3 oocytes retrieved in a conventional stimulation protocol); and 3) abnormal ovarian reserve tests (21). The data used in this study covered the period between March 2018–2021, and only participants who completed their 2-yr follow-up (up to March 2023) were included. Since there is no solid evidence regarding the mechanistic pathways of the biological effects of PRP therapy in the ovary, and given the exploratory nature of this study aimed at generating findings to guide future investigations, a 2-yr follow-up was considered an appropriate timeline to capture the outcome. The dataset was reviewed to identify cases of spontaneous pregnancy following IO-PRP, and a total of 50 such women were initially found.

2.2. Inclusion and exclusion criteria

The inclusion criteria were: I) individuals diagnosed with infertility (defined as the inability to achieve a clinically recognized pregnancy after 12 months of unprotected sexual intercourse). II) diagnosed with POR according to the Bologna criteria (21). III) undergone IO-PRP administration. IV) laboratory-approved spontaneous pregnancy following PRP therapy. Moreover, exclusion criteria were defined as receiving any other medication/intervention affecting the pregnancy rate or being at any clinical trial with intervention(s) with unknown effect on fertility.

In regard to the PRP intervention, the exclusion criteria is defined as any underlying conditions such as severe anemia (e.g., sickle cell), renal failure, chronic respiratory conditions, neutropenia, sub-mucosal myoma, Asherman's syndrome, untreated hypothyroidism, untreated hyperprolactinemia, any pathological condition in the fallopian tubes, polycystic ovary syndrome, a positive family history of ovarian cancer, or any contraindication(s) for pregnancy were excluded.

2.3. PRP preparation and administration

All individuals were screened for any contraindication for PRP preparation as previously outlined (9). PRP was then prepared according to our previously reported methods (22–24). Approximately 32 mL of whole blood was collected in 4 (8.5 mL) anticoagulated vacutainer tubes from BD Co. The samples were first subjected to a soft spin at 2500 rpm, after which the plasma and buffy coat layers were separated and transferred to sterile, empty tubes. A second centrifugation step allowed the platelet pellets to settle at the bottom, which were then re-suspended and transferred to another sterile tube, yielding approximately 5 mL of PRP. Platelet counts were measured in the whole blood using a cell counter, and the concentration of platelets in the PRP was confirmed to be > 3 times higher than that in whole blood. IO-PRP administration (2.5–3 ml per ovary) was performed after ovarian stimulation using the Shanghai method (25), as it was described in our previous study (6).

2.4. Study variables

Data related to women's age, height, weight, body mass index (BMI), duration and causes of infertility, infertility treatment duration, number of PRP sessions, cycle day on which PRP was performed, number of follicles before puncture, number of oocytes after the last PRP session, and interval between the last IO-PRP administration and clinically confirmed pregnancy. In addition, blood levels of anti-Müllerian hormone (AMH), luteinizing hormone (LH), follicle-stimulating hormone (FSH), estradiol, thyroid-stimulating hormone, and 25-hydroxy vitamin D (vitamin D) before PRP, and variables related to the spouse of these women including age, sperm count, sperm motility, and sperm morphology were extracted from the participants' files and compared in 4 groups based on POSEIDON criteria.

2.5. Ethical Considerations

To access and use the files and database of participated individuals, this study was approved by the Medical Ethics Committee of Hamdan University of Medical Sciences, Hamdan, Iran (Code: IR.UMSHA.REC.1402.541). All the authors adhered to the 1975 Declaration of Helsinki along with any further revisions, especially regarding the confidentiality of the data.

2.6. Statistical Analysis

Data from each participant was compiled in a Microsoft Excel sheet for final analysis. Given the sample size, the normality of data distribution was assessed using the Shapiro-Wilk test. Continuous variables with normal distribution were presented as mean $\pm$ standard deviation (SD), while those without normal distribution were reported as median with interquartile range. Categorical variables were described as N (%). To assess differences among POSEIDON groups for normally distributed variables, Levene's test was first used to evaluate the homogeneity of variances. Based on the results, either one-way analysis of variance (ANOVA) or Welch's ANOVA was applied. For non-normally distributed variables, the Kruskal-Wallis test was used. Post-hoc analyses were conducted to examine intergroup differences using Tukey's honestly significant difference (HSD) for ANOVA, Games-Howell test for Welch's ANOVA, and Dunn's test for the Kruskal-Wallis test. A $p < 0.05$ was considered statistically significant.

3. Results

3.1. Biodemographic data

During a 3-yr period, 1548 women with POR received IO-PRP. Among them, 596 women (38.50%) completed the 2-yr follow-up and were included in the current study, where 50 participants (8.39%) experienced spontaneous pregnancy following IO-PRP administration. However, due to missing data, only 42 women were included in the final statistical analysis.

According to table I, the most prevalent type of infertility was secondary, followed by primary infertility. The proportion of multigravida/primigravida was approximately twice as high as nulligravida. The majority of participants had no prior history of IO-PRP treatment and received the therapy only once; however, up to 4 IO-PRP sessions were recorded among some individuals. Additionally, only one-fifth of the participants (excluding those with missing data, n = 14) had no history of abortion, while up to 5 previous abortions were documented in the medical history of 2 individuals (Table I).

According to the data, the median age of the women who experienced spontaneous pregnancy following IO-PRP administration was 37.00 [32.00–40.00] yr. These participants had a history of infertility for a median of 3.00 [1.5–5.00] yr, followed by a treatment duration of 0.625 [0.25–1.00] yr. The mean BMI was 25.19 $\pm$ 3.75 kg/m^2, categorized as overweight (26). Also, the pre-intervention laboratory results and pre-puncture follicle/oocyte count of individuals with spontaneous pregnancy following IO-PRP administration, as well as age and sperm analysis of their spouses, have been shown in table II.

3.2. Descriptive data according to the POSEIDON criteria

Based on the gathered data, all the participants with spontaneous pregnancy following IO-PRP administration were classified according to the POSEIDON criteria (4). Among the 42 women, groups 4 and 3 were the most prevalent groups according to the POSEIDON classification and groups 1 and 2 shared similar numbers of participants. The biodemographic characteristics of spontaneous pregnancy following IO-PRP administration according to POSEIDON group have been gathered in table III.

Significant differences were observed among the POSEIDON groups for several variables, including the age of treated individuals, age of their spouse, BMI, serum AMH level, and pre-intervention follicle/oocyte count following the latest IO-PRP. Additionally, the results of the post-hoc analysis, which identified differences between each pair of POSEIDON groups (1 vs. 2, 1 vs. 3, 1 vs. 4, 2 vs. 3, and 3 vs. 4), are shown in table IV.

Table I. Demographic characteristics of study participants (n = 42)

Variables	Frequency (%)
Type of infertility	
Primary	17 (40.48)
Secondary	22 (52.38)
Combined primary and secondary	3 (7.14)
Gravida	
Nulligravida	14 (33.33)
Multigravida/primigravida	28 (66.67)
Number of previous IO-PRP session(s)	
1	26 (61.90)
2	9 (21.43)
3	5 (11.91)
4	2 (4.76)
Number of abortion(s) in past medical history (missing data = 14)	
No	8 (28.57)
1	11 (39.29)
2	4 (14.28)
3	5 (17.86)

IO-PRP: Intra-ovarian platelet-rich plasma

Table II. Continuous biodemographic data and laboratory results (as well as sperm analysis of spouses) before the intervention and clinical data following the intervention (n = 42)

Variables	Mean ± SD/Median [IQR]	Min–Max
Women's age (yr)	37.00 [32.00–40.00]	23–40
Spouse age (yr)	39.00 ± 5.43	28–35
Weight (kg)	65.65 ± 9.73	48–92
Height (cm)	162.26 ± 5.01	152–175
BMI (kg/m^2)	25.19 ± 3.75	17.2–34.0
Infertility duration (yr)	3.00 [1.5–5.00]	1.5–15.0
Duration of treatment before PRP (yr)	0.625 [0.25–1.00]	0.25–6.0
Anti-Müllerian hormone (ng/mL)	0.90 [0.56–1.53]	0.02–4.46
LH (IU/L)	4.57 [2.99–7.00]	1.60–23.10
FSH (IU/L)	6.78 [5.51–8.75]	1.01–19.00
Estradiol (pg/mL)	45.80 [29.20–65.20]	0.31–210.00

Table II. Continued

Variables	Mean ± SD/Median [IQR]	Min–Max
Thyroid-stimulating hormone (mU/L)	1.88 [1.31–3.06]	0.01–10.20
Vitamin D (ng/mL)	30.15 [24.10–42.00]	24.10–76.10
Sperm count (×10^6)	62 [42–74]	20–185
Sperm morphology (%)	17 [10–21]	2–42
Sperm motility (%)	55.26 ± 17.47	15–96
Follicle/oocyte count following the last PRP session	3.5 [2, 8]	0–22
PRP treatment time (day of the cycle)	12.33 ± 2.02	7–18
PRP treatment for pregnancy (day)	105 [45, 180]	15–660

BMI: Body mass index, PRP: Platelet-rich plasma, LH: Luteinizing hormone, FSH: Follicle-stimulating hormone, Vitamin D: 25-hydroxy vitamin D

Table III. Comparison of demographic variables and laboratory results in the study participants according to the POSEIDON criteria (n = 42)

Variables	POSIEDON 1 (n = 8)	POSIEDON 2 (n = 8)	POSIEDON 3 (n = 9)	POSIEDON 4 (n = 17)	P-value
Women's age (yr)	28.50 ± 4.37	39.00 ± 2.97	30.33 (2.44)	39.41 ± 1.66	< 0.001[‖]
Spouse age (yr)	35.12 ± 4.05	41.37 ± 3.73	35.00 ± 4.69	41.82 ± 4.85	< 0.001‡
BMI (kg/m^2)	22.57 ± 4.31	23.80 ± 4.13	26.00 ± 2.68	26.66 ± 3.14	0.039‡
Infertility duration (yr)	3.00 [2.00–8.00]*	4.06 ± 3.05	3.00 ± 2.54	3.00 [1.00–4.00]*	0.549†
TSH (mU/L)	2.64 ± 1.05	2.50 ± 1.79	1.79 ± 1.10	2.25 [1.10–2.74]*	0.442†
Prolactin (mIU/L)	17.98 ± 3.91	16.27 ± 8.38	19.21 ± 8.56	16.33 ± 6.06	0.729‡
Estradiol (pg/mL)	56.86 ± 23.71	43.15 [26.30–100.35]*	43.26 ± 23.32	44.80 [29.20–62.30]*	0.828†
AMH (ng/mL)	1.65 [1.36–3.24]*	2.00 ± 0.96	0.72 ± 0.25	0.59 ± 0.35	< 0.001†
LH (IU/L)	6.50 ± 1.70	4.91 ± 1.82	3.45 [2.22–4.20]*	4.73 [2.91–7.00]*	0.100†
FSH (IU/L)	6.57 ± 1.23	6.40 ± 1.56	6.63 [5.60–7.64]*	7.71 ± 3.97	0.668†
Vitamin D (ng/mL)	38.58 ± 11.19	40.31 ± 19.64	29.17 ± 8.67	32.18 ± 12.82	0.260‡
Follicle/oocytes count following latest PRP	9.12 ± 7.37	7.00 ± 3.70	4.11 ± 3.88	2.00 [0.00–3.00]*	0.022†
PRP treatment time (day of the cycle)	13.75 ± 1.83	11.37 ± 2.19	12.00 [11.00–13.00]*	12.00 [11.00–14.00]*	0.121†
PRP treatment to pregnancy (day)	106.87 ± 71.00	136.25 ± 76.84	151.00 ± 150.99	90.00 [49.00–180.00]*	0.910†

Data presented as Mean ± SD, [‖]ANOVA, ‡One-way ANOVA, †Kruskal-Wallis test, *Median [interquartile range]. BMI: Body mass index, TSH: Thyroid-stimulating hormone, AMH: Anti-Müllerian hormone, LH: Luteinizing hormone, FSH: Follicle-stimulating hormone, Vitamin D: 25-hydroxy vitamin D, PRP: Platelet-rich plasma

Table IV. Post-hoc analysis between each POSIEDON group (n = 42)

Variables	POSIEDON I vs. II	POSIEDON I vs. III	POSIEDON I vs. IV	POSIEDON II vs. III	POSIEDON II vs. IV	POSIEDON III vs. IV
Women's age (yr)[‡]	< 0.001	0.726	< 0.001	< 0.001	0.982	< 0.001
Spouse age (yr)[†]	0.039	0.999	0.006	0.028	0.995	0.003
Body mass index[†]	0.896	0.200	0.046	0.572	0.242	0.967
Anti-Müllerian hormone[‡]	1.000	0.007	< 0.001	0.003	0.001	1.000
Follicle/oocytes count following latest PRP[‡]	0.918	0.131	0.011	0.161	0.015	0.380

[‡]Games Howell test, [†]Tukey's honestly significant difference (HSD), [‡]Dunn's test. PRP: Platelet-rich plasma

4. Discussion

This study focused on the descriptive characteristics of individuals diagnosed with POR who experienced spontaneous pregnancy following IO-PRP. The results showed significant differences among the POSEIDON groups in terms of individual age, spouse's age, BMI, serum AMH levels, and follicle/oocyte counts following the latest PRP treatment. Post hoc analysis further detailed the specific patterns of these differences.

Although POSEIDON group 4 was the most prevalent in this study, this does not imply that spontaneous pregnancy following IO-PRP administration is more likely to occur in this group. Another study performed using our database, focusing on another outcome but still classifying participants in accordance with the POSEIDON criteria, found that the POSEIDON group IV was the most prevalent (58.3%) (6). Therefore, higher number of spontaneous pregnancies in POSEIDON group IV is more likely due to this group representing higher population rather than higher susceptibility. As mentioned, age and AMH levels are key variables in the determination of the POSEIDON group (4). Given this, if POSEIDON group 4 were more susceptible to spontaneous pregnancy following IO-PRP administration, additional variables beyond age

and AMH would be expected to differ in post hoc analysis.

In a study, the effects of IO-PRP on ovarian rejuvenation were investigated. 4 groups (each with 30 cases) of individuals with POI, POR, menopause, and perimenopause were included. According to their results, a notable improvement was observed in the hormonal profiles of the studied cases as well as in their ovarian reserve. Additionally, in the POI group, 3 spontaneous pregnancies were observed (27).

A study investigated the biodemographic variables of cases who underwent IO-PRP administration and evaluated these variables in 2 groups: those who experienced spontaneous pregnancy and those who conceived via in vitro fertilization. However, it seems that due to the low sample size in the spontaneous pregnancy group (n = 13), categorization according to the POSEIDON criteria was not performed. According to their results, the mean pre-intervention values for FSH and antral follicle count were 9.4 ± 5 IU/L and 5.7 ± 4.3, respectively. Unfortunately, data regarding age, BMI, LH, AMH, and other related variables were not presented for this group (28).

Another study reported spontaneous pregnancy following IO-PRP administration in infertile cases with POI. According to their results, out of 311 enrolled cases, 23 (7.4%)

experienced spontaneous pregnancy. The mean age, infertility duration, pre-intervention FSH levels, pre-intervention AMH levels, and pre-intervention antral follicle count of these cases were 34.6 ± 4.0 yr, 5.6 ± 3.4 yr, 33.3 ± 8.9 mIU/mL, 0.09 ± 0.07 ng/mL, and 1.26 ± 0.8, respectively, which differ from our findings. However, since their data were presented as mean ± SD and most of our data were reported as median (interquartile range), an exact comparison was not possible. Nonetheless, the difference in AMH levels between their study (0.09 ± 0.07 ng/mL) and ours (0.9 [0.56–1.53] ng/mL) appears to be statistically significant (29). Similar to the reference (28), the already discussed study (29) did not categorize cases with spontaneous pregnancy following IO-PRP administration according to the POSEIDON criteria.

As with any study, this investigation has its strengths and limitations. Among the strengths, to the best of our knowledge, this is the first study to categorize and investigate cases with spontaneous pregnancy following IO-PRP administration according to the POSEIDON criteria. Additionally, compared to similar studies, a broader range of variables was investigated. In contrast, as a limitation, post-intervention laboratory values such as FSH, LH, and AMH were not assessed in this study due to a lack of follow-up once pregnancy was confirmed. Another limitation of this study is the small sample size (n = 42), although it is still larger than that of other similar studies (28, 29).

5. Conclusion

This study investigated the biodemographic characteristics of poor ovarian responders who experienced spontaneous pregnancy following intra-ovarian PRP administration. These results indicated that even with a follow-up duration of 2 yr, the rate of spontaneous pregnancy following IO-PRP was approximately 8.4%. This ratio seems not to be clinically significant to perform a wait-and-watch plan after IO-PRP instead of other infertility treatments. In regard to investigating any variable associated with higher rate of spontaneous pregnancy, variables including age of studied women, spouse's age, serum AMH levels, BMI, and the pre-puncture follicle/oocyte count following the last PRP session showed statistically significant differences among the groups with and without spontaneous pregnancy. Thus, the authors suggest further prospective cohort studies to investigate their possible role in this regard.

Data Availability

Data would be available upon online request from the corresponding author.

Author Contributions

Acknowledgments

Conflict of Interest

The authors declare that there is no conflict of interest.

References

[1] Word Health Organization. 1 in 6 people globally affected by infertility. Available at: https://www.who.int/news/item/04-04-2023-1-in-6-people-globally-affected-by-infertility.

[2] Larsen U. Research on infertility: Which definition should we use? *Fertil Steril* 2005; 83: 846–852.

[3] Surrey ES, Schoolcraft WB. Evaluating strategies for improving ovarian response of the poor responder undergoing assisted reproductive techniques. *Fertil Steril* 2000; 73: 667–676.

[4] Alviggi C, Andersen CY, Buehler K, Conforti A, De Placido G, Esteves SC, et al. A new more detailed stratification of low responders to ovarian stimulation: From a poor ovarian response to a low prognosis concept. *Fertil Steril* 2016; 105: 1452–1453.

[5] Grisendi V, Mastellari E, La Marca A. Ovarian reserve markers to identify poor responders in the context of poseidon classification. *Front Endocrinol (Lausanne)* 2019; 10: 281.

[6] Sanuie Farimani M, Nazari A, Mohammadi Sh, Anvari Aliabad R. Evaluation of intra-ovarian platelet-rich plasma administration on oocytes-dependent variables in patients with poor ovarian response: A retrospective study according to the POSEIDON criteria. *Reprod Biol Endocrinol* 2021; 19: 137.

[7] Fraidakis M, Giannakakis G, Anifantaki A, Skouradaki M, Tsakoumi P, Bitzopoulou P, et al. Intraovarian platelet-rich plasma injections: Safety and thoughts on efficacy based on a single centre experience with 469 women. *Cureus* 2023; 15: e38674.

[8] Mohammadi MH, Molavi B, Mohammadi S, Nikbakht M, Malek Mohammadi A, Mostafaei Sh, et al. Evaluation of wound healing in diabetic foot ulcer using platelet-rich plasma gel: A single-arm clinical trial. *Transfus Apher Sci* 2017; 56: 160–164.

[9] Mohamadi S, Norooznezhad AH, Mostafaei Sh, Nikbakht M, Nassiri Sh, Safar H, et al. A randomized controlled trial of effectiveness of platelet-rich plasma gel and regular dressing on wound healing time in pilonidal sinus surgery: Role of different affecting factors. *Biomed J* 2019; 42: 403–410.

[10] Tang JZ, Nie MJ, Zhao JZ, Zhang GC, Zhang Q, Wang B. Platelet-rich plasma versus hyaluronic acid in the treatment of knee osteoarthritis: A meta-analysis. *J Orthop Surg Res* 2020; 15: 403.

[11] Desouza C, Dubey R, Shetty V. Platelet-rich plasma in chronic Achilles tendinopathy. *Eur J Orthop Surg Traumatol* 2023; 33: 3255–3265.

[12] Mehrabani D, Seghatchian J, Acker JP. Platelet rich plasma in treatment of musculoskeletal pathologies. *Transfus Apher Sci* 2019; 58: 102675.

[13] Sánchez-González DJ, Méndez-Bolaina E, Trejo-Bahena NI. Platelet-rich plasma peptides: Key for regeneration. *Int J Pept* 2012; 2012: 532519.

[14] Jahani M, Rezazadeh D, Mohammadi P, Abdolmaleki A, Norooznezhad A, Mansouri K. Regenerative medicine and angiogenesis; challenges and opportunities. *Adv Pharm Bull* 2020; 10: 490–501.

[15] Mostafaei Sh, Norooznezhad F, Mohammadi S, Norooznezhad AH. Effectiveness of platelet-rich plasma therapy in wound healing of pilonidal sinus surgery: A comprehensive systematic review and meta-analysis. *Wound Repair Regen* 2017; 25: 1002–1007.

[16] Belk JW, Kraeutler MJ, Houck DA, Goodrich JA, Dragoo JL, McCarty EC. Platelet-rich plasma versus hyaluronic acid for knee osteoarthritis: A systematic review and meta-analysis of randomized controlled trials. *Am J Sports Med* 2021; 49: 249–260.

[17] OuYang H, Tang Y, Yang F, Ren X, Yang J, Cao H, et al. Platelet-rich plasma for the treatment of diabetic foot ulcer: A systematic review. *Front Endocrinol (Lausanne)* 2023; 14: 1256081.

[18] de Oliveira AFQ, Arcanjo FPN, Rodrigues MRP, Rosa Rosa E Silva AA, Hall PR. Use of autologous platelet-rich plasma in androgenetic alopecia in women: A systematic review and meta-analysis. *J Dermatolog Treat* 2023; 34: 2138692.

[19] Lin Y, Qi J, Sun Y. Platelet-rich plasma as a potential new strategy in the endometrium treatment in assisted reproductive technology. *Front Endocrinol (Lausanne)* 2021; 12: 707584.

[20] Éliás M, Kónya M, Kekk Z, Turan C, das Virgens IPA, Tóth R, et al. Platelet-rich plasma (PRP) treatment of the ovaries significantly improves fertility parameters and reproductive outcomes in diminished ovarian reserve

patients: A systematic review and meta-analysis. *J Ovarian Res* 2024; 17: 104.

[21] Younis JS, Ben-Ami M, Ben-Shlomo I. The Bologna criteria for poor ovarian response: A contemporary critical appraisal. *J Ovarian Res* 2015; 8: 76.

[22] Sanuie Farimani M, Bahmanzadeh M, Poorolajal J. A new approach using autologous platelet-rich plasma (prp) to treat infertility and to improve population replacement rate. *J Res Health Sci* 2016; 16: 172–173.

[23] Sanuie Farimani M, Heshmati S, Poorolajal J, Bahmanzadeh M. A report on three live births in women with poor ovarian response following intra-ovarian injection of platelet-rich plasma (PRP). *Mol Biol Rep* 2019; 46: 1611–1616.

[24] Sanuie Farimani M, Poorolajal J, Rabiee S, Bahmanzadeh M. Successful pregnancy and live birth after intrauterine administration of autologous platelet-rich plasma in a woman with recurrent implantation failure: A case report. *Int J Reprod BioMed* 2017; 15: 803–806.

[25] Kuang Y, Chen Q, Hong Q, Lyu Q, Ai A, Fu Y, et al. Double stimulations during the follicular and luteal phases of poor responders in IVF/ICSI programmes (Shanghai protocol). *Reprod Biomed Online* 2014; 29: 684–691.

[26] Weir CB, Jan A. BMI classification percentile and cut off points. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2025.

[27] Sfakianoudis K, Simopoulou M, Grigoriadis S, Pantou A, Tsioulou P, Maziotis E, et al. Reactivating ovarian function through autologous platelet-rich plasma intraovarian infusion: Pilot data on premature ovarian insufficiency, perimenopausal, menopausal, and poor responder women. *J Clin Med* 2020; 9: 1809.

[28] Safarova S, Cevher Akdulum MF, Guler I, Bozkurt N, Erdem A, Karabacak RO. Does platelet-rich plasma treatment increase in vitro fertilization (IVF) success in the infertile population? *Cureus* 2023; 15: e47239.

[29] Cakiroglu Y, Saltik A, Yuceturk A, Karaosmanoglu O, Kopuk SY, Scott RT, et al. 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)* 2020; 12: 10211–10222.