Original Article

Central Asian Journal of Medical Sciences
CAJMS

Cent Asian J Med Sci. 2024 June;10(2): 57-66 https://doi.org/10.24079/CAJMS.2024.02.003

Identifying Endometrial Delay Improves Treatment Outcome in Women with Thin Endometrium and Infertility

Narangerel Namshir[1], Yanjinsuren Darmaa[1], Munkhtsetseg Davaatseren[1], Bum Chae Choi[2]

[1]Department of Obstetrics and Gynecology, School of Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia;
[2]Creation and Love Women's Hospital, Ulaanbaatar, Mongolia.

Submitted date: January 19, 2024
Accepted date: April 23, 2024

Corresponding Author:
Narangerel Namshir (M.D.,M.Sc.)
Department of gynecology and obstetrics, School of Medicine, Mongolian National University of Medical Sciences, S. Zorig street, Ulaanbaatar-14210, Mongolia
Email: narangerel99112000@gmail.com
ORCID: https://orcid.org/0000-0003-1979-6793

Running title: Correlation between endometrial delay and assisted reproductive technologies outcome

Objective: To determine the impact of endometrial delay on reproductive outcomes.
Method: We enrolled 62 infertility women with thin endometrium pre- and post-study in 2020-2023. Infertile women with an endometrial thickness of <7 mm were included and followed in the study. All participants had endometrial delay determined and adjusted before initial Assisted reproductive technologies (ART). After, infertility treatment was started. ART outcomes were evaluated by endometrial thickness and implantation rate. Endometrial thickness was compared to pre-hormone replacement treatment at 48 and 72 hours post-hormone therapy. **Results:** The study included 62 women aged 26-45 who were diagnosed with infertility and thin endometrium. Endometrial thickness was sufficiently increased before and after treatment for all participants. Histological analysis diagnosed endometrial delay (not appropriate WOI) in 73.6% of all women. After adjusting the WOI in study participants, there was a statistically significant increase in endometrial thickness post-hormone replacement therapy. The study participants were women who had failed at least one implantation, and the implantation rate after WOI adjustment was 58.5%. **Conclusions:** In 70% of infertility women, endometrial is delayed. In women with thin endometrium, the precise determination of WOI increases ART treatment outcomes.

Keywords: Endometrium, Delay, Maturation, Receptivity, Reproductive Outcome, Pregnancy

Introduction

The current reproductive failure is a priority issue in fertility that includes recurrent implantation failure and recurrent pregnancy loss. In defining these terms, recurrent implantation failure (RIF) refers to the inability to clinical pregnancy of women under the age of 40 following the transfer of at least four healthy embryos in a minimum of three fresh or frozen cycles.[1] The spontaneous loss of two or more pregnancies defines the reproductive problem known as recurrent pregnancy loss (RPL), affecting 5% of couples worldwide.[2-4] Andrea Busnelli, et al.

reported that the prevalence of RIF is 15% of the total accepted in vitro fertilization. Multiple implantation failures can have a significant psychological impact on couples faced with burdens related to their reproductive health. Hence, medical professionals are concentrating on improving care and reducing the time needed for a healthy pregnancy.[4-5]

Recent studies concluded that an aberrant endometrium is associated with RIF and RPL, and endometrium receptivity predicts successful implantation during the window of implantation (WOI), meaning the endometrial environment is receptive to a blastocyst [6-7]. An endometrium that is prepared to receive the embryo and a competent embryo are both necessary for a successful embryonic implantation.

During implantation and pregnancy, hormone-modulating receptors, including estrogen-receptor beta (ERβ) and progesterone receptor (PR), are significant controllers of endometrial decidualization [8-9]. Also, ERβ and PR are critical in endothelium angiogenesis and uterine contractions, both necessary for implantation and pregnancy continuation.[8,10,11] In the findings of previous studies, Erβ and PR expression were decreased in poor endometrial receptivity diagnosed with the infertility group.[12-14] Recently, studies reported that precise determination of the WOI can significantly improve ART outcomes. We aimed to evaluate the impact of WPI adjustment on endometrial thickness and implantation rate in the with PRP and without PRP treatment groups.

Materials and Methods

Study design

This study is based on a pre-post-study design conducted from November 2020 to February 2023 at the CLWH Mongolia fertility clinic (Figure 1). We assessed the endometrial receptivity of all participants and performed interventions to adjust the implantation windows. Endometrial receptivity was determined before hormone therapy in all women, and the appropriate time to start treatment was adjusted and started. Hormone replacement therapy and ART therapy were performed according to Kaufmann guidelines.[13] Endometrial thickness was compared before and after treatment. Endometrial thickness was measured at 24 and 48 hours after treatment. The participants informed written consent. Endometrial biopsies were collected from 72 women: 40 participants were in regular menstrual cycles, and 32 were in irregular menstrual cycles. Seventy-two women were registered and included in the study, but women whose endometrial receptivity was not determined in tissue samples were excluded.

Participants

The study recruited women with infertility visiting CLWH Mongolia. The inclusion criteria included women aged 26 to 45 diagnosed with infertility or endometrial thinning. The study did not include women who used hormonal drugs and were diagnosed with endocrine diseases. The study participants were recruited by purposive sampling and randomly assigned to 2 groups according to the order recorded in the survey.

Endometrial receptivity tests

From 2021 to 2023, this study conducted 72 cases of in vitro fertilization (IVF) procedures due to endometrial thinning at the CL Mongolia fertility clinic. Paraffin blocks stored in the archives of the National Centre for Pathology Reference Laboratory were analysed. The 2016 WHO classification was used to determine the grade of endometrial thickening. According to the process of preparing 72 holes/slides for tissue microarray, the microarray pen was filled with a 0.5 cm diameter piece of tissue taken from the paraffin blocks.

On performing immunohistochemistry, used xylene to paraffin removal from a range of formalin-fixed paraffin-embedded tissue slices, reducing alcohol concentration, immersion, and then blocks were rinsed with phosphate buffer solution. Endogenous peroxidase was inhibited by treating antigen presentation with 0.3% hydrogen peroxide for 10 min in a humid setting, followed by 20 min of microwave exposure in citrate buffer solution. Tissue sections were painted with ERβ (1:200, Santa Cruz Biotechnology, Santa Cruz, CA), PR (1:100, DIANOVA, Hamburg, Germany), and Ki67 (1:50, Dako, Camarillo, CA, USA) markers from Ventana Medical, by automatic painting machine with DAB kit of System, Inc., USA. The Noyes protocol analyzed the endometrial biopsies. After, we compared the windows of implantation determined by the menstrual cycle and histological analysis (Table 1).

Interventions

Histological analysis accurately determined the windows of implantation and re-evaluated the ART plan. All participants in the study received hormone replacement therapy to increase the endometrium thickness. The Kaufmann protocol is a medical regimen used in the treatment of infertility, specifically address-

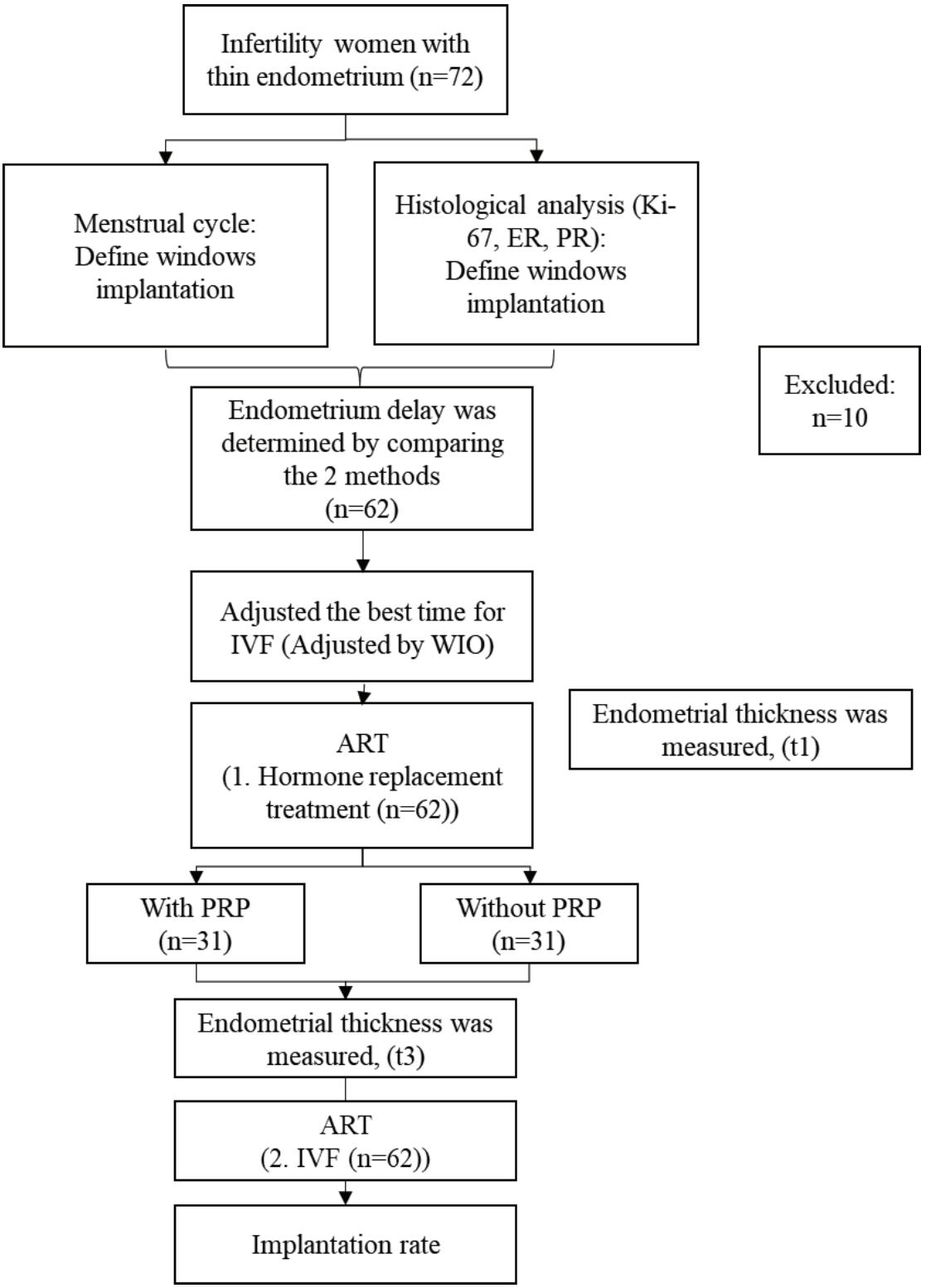

Figure 1. The study design follows the chart

ing issues related to thin endometrium. It typically involves a combination of hormonal medications and procedures designed to promote endometrial thickening and improve receptivity for successful implantation of an embryo during assisted reproductive techniques such as in vitro fertilization (IVF) or intrauterine insemination (IUI).

We evaluated endometrium thickness, and if there was a sufficient increase, IVF was performed according to guidelines. Overall, 43%(n=31) of women in the study received standard PRP treatment.

Outcome measures

We measured adjusted implantation windows in (1) increase of endometrium thickness and (2) implantation rate in participants. Pre- and post-hormone replacement treatment measurements are essential for study participants to review changes in endometrium thickness. Endometrial thickness was compared to pre-hormone replacement treatment at 48 and 72 hours post-hormone therapy. Endometrial thickness was assessed by ultrasonography. The endometrium thickness does not increase for thin endometrium women when the implantation windows are not well-defined.

Statistical Analysis

According to descriptive statistics, continuous variables are expressed as mean and standard deviation because all variables are normal distributions. Categorical variables are expressed as numbers and percentages. Differences in mean endometrial thickness measured before and after hormone replacement therapy were compared by mixed effect two-way ANOVA (tables 2 and 3). Differences in implantation rate between PRP and non-PRP groups were evaluated using the chi-square test. A mixed-effect two-way ANOVA calculated endometrial thickness. Test with the greenhouse-geyser method. Multiple comparisons were not performed because mixed effect two-way ANOVA group effects had two groups (PRP and without PRP). However, there was no significant difference in endometrium thickness changes in the two groups (Subjects between). We used IBM SPSS 26.0 for statistical analysis.

Ethical Statement

This study received ethics approval from the Mongolian National University of Medical Sciences in Ulaanbaatar, Mongolia (2021/03-04). Before our prospective interventional study, a couple confirmed their interest and signed an informed consent form.

Results

In the study, 62 women aged 26-45 who were diagnosed with infertility and thin endometrium women were included. Of all infertile women, 79.0% had higher education, and 87.1% were married. Endometrial thickness was sufficiently increased before and after treatment for all participants (see Table 2).

Table 1. The study design follows the chart

Endometrial dating methods	Windows of implantation	
	No	Yes
Menstrual cycle	-	+
Histological analysis (ER, PR and Ki67)	+	+
Compared outcome (Menstrual cycle and Histological analysis)	Endometrial Delayed	Endometrial not delayed

Table 2. General characteristics include participants, pre- and post-HRT.

Variables	N (%)	Endometrium thickness			P-value
		Pre	Post (48h)	Post (72h)	
		Mean ± SD	Mean ± SD	Mean ± SD	
Education level					
Medium	13 (21)	6.14 ± 0.74	7.6 ± 0.83	7.8 ± 0.62	0.000
University	49 (79)	6.19 ± 0.94	8.53 ± 11.15	8.94 ± 11.15	0.000
Marital status					
Married	54 (87.1)	6.21 ± 0.92	8.86 ± 10.62	9.91 ± 10.71	0.000
Partner	8 (12.9)	5.98 ± 0.72	7.28 ± 0.73	8.19 ± 0.71	0.000
Work conditions					
Office worker	49 (79.1)	6.5 ± 0.96	7.21 ± 1.15	8.26 ± 0.95	0.000
Hard workers	8 (12.9)	6.06 ± 0.78	7.79 ± 0.58	8.57 ± 0.61	0.000
Unemployment	5 (8.1)	5.98 ± 0.59	8.4 ± 0.84	9.6 ± 0.64	0.000
ABO types					
O	29 (46.8)	5.58 ± 0.92	9.11 ± 0.97	10.51 ± 0.87	0.000
A	12 (19.4)	6.15 ± 0.67	8.48 ± 1.09	9.54 ± 1.91	0.000
B	16 (25.8)	6.21 ± 1.03	7.21 ± 0.96	8.34 ± 0.69	0.000
AB	5 (8.1)	6.46 ± 1.07	7.6 ± 0.55	8.47 ± 0.34	0.000
Smoke					
Yes	25 (40.3)	5.9 ± 0.75	7.8 ± 0.61	8.52 ± 0.62	0.000
No	37 (59.7)	6.4 ± 0.85	8.3 ± 1.06	8.71 ± 0.96	0.000
Alcoholic					
Yes	25 (40.3)	5.9 ± 0.75	7.8 ± 0.61	8.52 ± 0.62	0.000
No	37 (59.7)	6.4 ± 0.85	8.3 ± 1.06	8.71 ± 0.96	0.000

Descriptive statistics, mixed effect two-way ANOVA Differences in mean endometrial thickness measured before and after hormone replacement therapy

Histological analysis diagnosed endometrial delay (not appropriate WOI) in 73.6% of all women (Figure 2). After adjusting the WOI in study participants, there was a statistically significant increase in endometrial thickness post-hormone replacement therapy (P=0.0001).

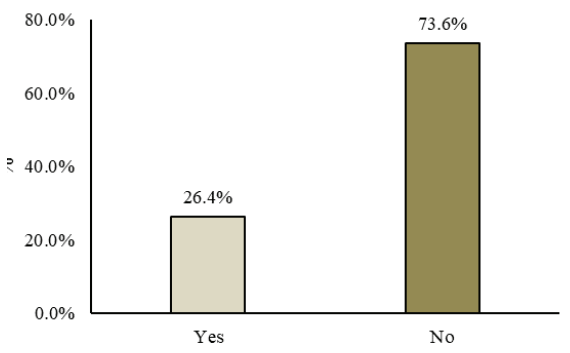

Figure 2. WIO determined by histological analysis

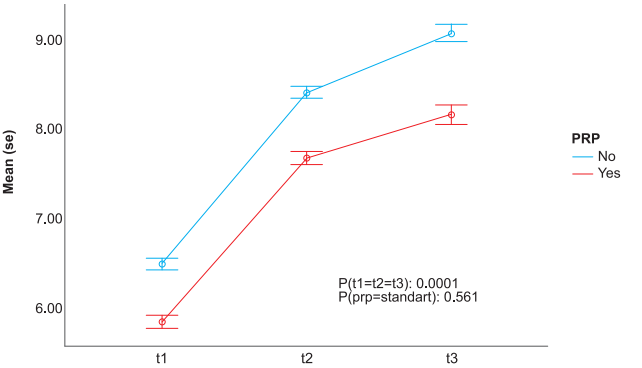

Figure 3. After adjusting for WIO based on histological analysis

Of the participants, 61.3% had secondary infertility, 12.9% were diagnosed with mycoplasma infection, and all women had recurrent implantation failure (Table 3).

Table 3. Factors influencing endometrial thickness.

Variables	N (%)	Endometrium thickness			P-value
		Pre	Post (48h)	Post (72h)	
		Mean ± SD	Mean ± SD	Mean ± SD	
Hormone replacement treatment history					
Yes	27(43.5)	6.04±0.61	8.46±0.91	10.52±0.95	0.000
No	35(56.5)	6.37±1	7.78±0.99	8.32±0.94	0.000
Mycoplasma infection					
Yes	54(87.1)	6.11±0.81	8.49±0.63	9.42±0.63	0.000
No	8(12.9)	6.35±1.34	7.69±0.8	8.10±0.8	0.000
Urea plasma infection					
Yes	58(93.5)	6.09±0.82	8.71±0.25	9.12±0.35	0.000
No	4(6.5)	6.43±1.23	7.15±0.5	8.23±0.25	0.000
Infertility causes					
Primary	24(38.7)	6.38±0.8	8.19±0.85	8.40±1.50	
Secondary	38(61.3)	5.91±0.96	7.58±0.79	8.91±1.01	0.000
Infertility times					
1-4 years	12(19.3)	6.44±0.67	7.81±0.83	8.14±0.84	0.000
5-9 years	36(58.1)	6.25±0.87	7.41±0.9	8.01±0.91	0.000
10< years	14(22.6)	5.86±1.07	9.63±0.74	9.71±0.85	0.000
Infertility types (or causes)					
Tubal	42(67.7)	6.28±0.88	8.1±0.08	8.7±0.58	0.000
Endometriosis	14(22.6)	6.26±0.94	8.2±0.74	8.3±0.14	0.000
Ovarian	22(35.5)	5.93±0.97	8.52±0.45	8.61±0.46	0.000
Uterine	13(21)	6.43±0.91	7.5±0.66	8.31±0.96	0.000
Aged	9(14.5)	6.0±0.7	7.6±1.0	7.8±0.91	0.000
Unexplained	2(3.2)	6.4±0	8.2±0.7	7.9±0.81	0.000
ART cancellation caused by a thin endometrium					
Yes	35(56.5)	6.1±1	7.4±1	8.21±1.03	0.000
No	26(41.9)	6.2±0.7	8.5±0.82	10.8±0.97	0.000
Recurrent implantation failure					
1-2 times	32(51.6)	6.3±0.7	8.6±1.2	8.8±1.2	0.000
3-4 times	22(35.5)	6.0±0.8	8.2±0.67	9.8±0.61	0.000
5< times	8(12.9)	5.8±1.8	7.7±0.74	8.0±0.81	0.000

Descriptive statistics, mixed effect two-way ANOVA Differences in mean endometrial thickness measured before and after hormone replacement therapy

Yes Histological analysis and menstrual cycle dating matched; No Histological analysis and menstrual cycle dating did not match, so the date of the ART plan was reset for this group.

Moreover, this increase was similar in the with PRP and without PRP treatment groups(p=0.561) (Figure 3). In participants, the thickness of the endometrium increased by 6.2±0.8 mm before HRT and 8.59±0.96 after HRT (P=0.0001). Women with very low endometrial thickness (mean 5.6 mm) in PRP treatment increased to 8 mm after treatment (P=0.0001) (Figure 3).

Mean endometrial thickness was significantly increased during ART compared to base assessment, t1 - Pre HR-Treatment, with mixed effect two-way ANOVA with subject between effect (two groups).

Table 4 shows the multiple comparisons. Endometrial thickness changes depend on recurrent implantation failure times (P=0.047).

The study participants were women who had failed at least one implantation, and the fertility rate after WOI adjustment was 58.5%. Also, the implantation rate in the PRP group was 69% (P=0.036) (Figure 4).

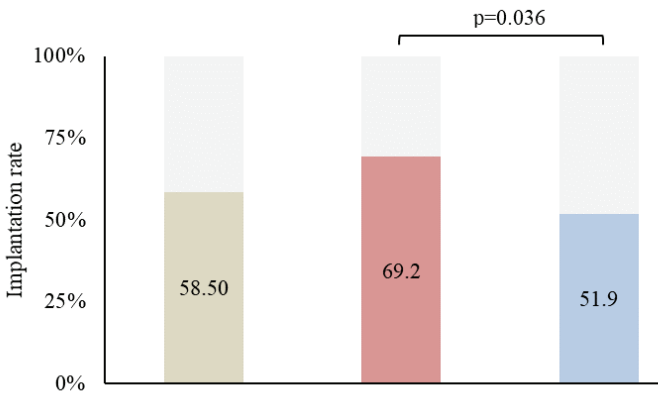

Figure 4. Implantation rates were compared between groups that underwent PRP and standard HRT

Discussion

Our study showed that the analysis of ERβ and PR is a valuable tool for accurately identifying the WOI. Precisely determining WOI improves ART outcomes. M Enciso, et al. (2021) reported that precise determination of the WOI can significantly improve clinical outcomes.[14]

Endometrial thinning is a negative influencing factor in infertility treatment outcomes. ART outcomes are inadequate in thin endometrial women. Recent studies have reported a 24-34% pregnancy rate when the endometrium thickness is 4-7 mm.[15-16] Therefore, if the endometrium thickness is less than 7 mm, it is defined that the endometrium is thin, hormone replacement therapy is ineffective, and the probability of fertilization rate is low.[17] Our study participants had endometrial thicknesses of less than 7 mm in pre-HRT. However, the implantation rate was 59% when adjusted for WOI, which is higher than that of other studies with undetermined WOI.

Recent studies suggest that the pregnancy rate may increase with growing endometrial thickness within a specific range.[18-19] It has been suggested that the minimal endometrial thickness required for embryo transfer is 7 mm at the end of the follicular phase.[20] It has been confirmed that the thickness of the endometrium influences implantation rates. While there isn't an accepted cut-off point for appropriate endometrial thickness, it's generally accepted that 8 mm is the minimum at which ART is still typically compelling. The probability of becoming pregnant rises from 53 to 77% for 9 and 16 mm thicknesses, indicating a discernible variation in implantation rates. It has been established that the thickness of the endometrium influences implantation rates. In the study participants, endometrium thickness was 6.2±0.8 mm before Hormone replacement therapy and 9.59±0.96 after treatment, confirming the above studies' outcome. According to the results of our research, PRP therapy increases the thickness of the endometrium in women with endometrial thinning and creates conditions for fertilization. Women with very low endometrial thickness (mean 5.6 mm) in PRP treatment increased to 8 mm after treatment (P=0.0001). The PRP treatment group's implantation rate was significantly higher (P=0.036). This result supports the hypothesis of other studies. Centrifuging the patient's peripheral blood yields a volume of plasma with a platelet count above baseline, known as platelet-rich plasma (PRP).[21,22] Platelets are pieces of non-nucleated cells originating from megakaryocytes generated from bone marrow. The granules' accumulated chromo-mere and the agranular hyalomere, rich in cytoskeletal proteins, comprise the two components of platelets' cytoplasm. Multiple proteins are contained in platelet granules. When injuries occur, these proteins are secreted, activating platelets and directing them to the site of injury or deficiency.[22,23] This enables PRP to participate in inflammatory processes24, chemotaxis, immune responses, cell proliferation, migration, tissue growth and

Table 4. Multiple comparison tests in two-way mixed ANOVA

Variable		Mean Difference	Std. Error	P-value	95% Confidence Interval		P-value
					Lower Bound	Upper Bound	
Work conditions							
Office worker	Hard workers	0.3608	0.261	0.173	-0.163	0.885	0.891
	Unemployment	-0.1654	0.278	0.556	-0.725	0.394	
Hard workers	Office worker	-0.3608	0.261	0.173	-0.885	0.163	0.114
	Unemployment	-1.5262	0.353	0.043	-1.236	0.184	
Unemployment	Office worker	0.1654	0.278	0.556	-0.394	0.725	0.451
	Hard workers	1.5262	0.353	0.043	-0.184	1.236	
Recurrent implantation failure							
1-2 times	3 - 4 times	.3220*	0.137	0.047	0.005	0.639	0.614
	4< times	0.2675	0.220	0.261	-0.242	0.777	
3-4 times	1 - 2 times	-.3220*	0.137	0.047	-0.639	-0.005	
	4< times	-0.0545	0.234	0.822	-0.594	0.485	
4< times	1 - 2 times	-0.2675	0.220	0.261	-0.777	0.242	
	3 - 4 times	0.0545	0.234	0.822	-0.485	0.594	
Infertility times							
1-4 years	5 - 9 years	0.1857	0.172	0.313	-0.212	0.583	0.914
	15< years	0.4009	0.203	0.084	-0.067	0.869	
5-9 years	1 - 4 years	-0.1857	0.172	0.313	-0.583	0.212	
	15< years	0.2152	0.154	0.201	-0.141	0.571	
15< years	1 - 4 years	-0.4009	0.203	0.084	-0.869	0.067	
	5 - 9 years	-0.2152	0.154	0.201	-0.571	0.141	

Two-way mixed ANOVA test and various comparisons: a RIF vs. Control, P-value 0.047

healing, and neo angiogenesis.

This study has several strengths: it included women with endometrial thinning, defined WOI precisely by histological analysis, and evaluated adjusted outcomes. Also, the results of the PRP treatment were compared with those of the control group. A limitation of the study is the small sample size. In the future, IVF centers must identify WOI precisely and plan ART treatment to study clinical outcomes. Also, for RIF women, PRP therapy may be an effective method. PRP is still a new application in Gynaecology and reproductive medicine for treating thin endometrium. After publishing the guideline, some RCT studies have been conducted to prove its effectiveness. So, a systematic review of the efficacy and safety of PRP for treating thin endometrium is necessary.

Conclusion

In infertility women, 73% had a menstrual cycle-defined WOI delay. Precisely identifying WOI and planning treatment for women who have recurrent failed implantation and thin endometrium can effectively increase the thickness of the endometrium and improve the implantation rate. PRP significantly improved implantation rates in women with thin endometrium.

Conflict of Interest

The authors state no conflict of interest.

Acknowledgements

The authors acknowledge all the participants and their families for the time and great efforts they made to attend our study.

References

1. Günther V, Otte SV, Freytag D, et al. Recurrent implantation failure - an overview of current research. *Gynaecol Endocrinol.* 2021;37(7):584–590. https://doi.org/10.1080/.2021.1878136
2. Practice Committee of the American Society for Reproductive Medicine. Definitions of infertility and recurrent pregnancy loss: a committee opinion. *Fertil Steril.* 2013;99(1):63. https://doi.org/10.1016/j.fertnstert.2012.09.023
3. Hong LiY, Marren A. Recurrent pregnancy loss: A summary of international evidence-based guidelines and practice. *Aust J Gen Prac*. 2018;47(7):432–436. https://doi.org/10.31128/AJGP-01-18-4459
4. El Hachem H, Carpeaux V, May-Panloup P, et al. Recurrent pregnancy loss: current perspectives. *Int J Womens Health*. 2017;9:331–345. https://doi.org/10.2147/IJWH.S100817
5. Voss P, Schick M, Langer L, et al. Recurrent pregnancy loss: a shared stressor---couple-orientated psychological research finding. *Fertil Steril*. 2020;114(6):1288–1296. https://doi.org/10.1016/j.fertnstert.2020.08.1421
6. Al-Lamee H, Hill CJ, Turner F, et al. The Role of Endometrial Stem/Progenitor Cells in Recurrent Reproductive Failure. *J Pers Med*. 2022;12(5):775. https://doi.org/10.3390/jpm12050775
7. Panagiotopoulou N, Karavolos S, Choudhary M. Endometrial injury before assisted reproductive techniques for recurrent implantation failure: a systematic literature review. *Eur J Obstet Gynecol Reprod Biol*. 2015;193:27–33. https://doi.org/10.1016/j.ejogrb.2015.06.026
8. Rumi MAK, Singh P, Roby KF, et al. Defining the Role of Estrogen Receptor β in the Regulation of Female Fertility. *Endocr.* 2017;158(7):2330–2343. https://doi.org/10.1210/en.2016-1916
9. Hapangama DK, Kamal AM, Bulmer JN. Estrogen receptor β: the guardian of the endometrium. *Hum Reprod Update.* 2015;21(2):174–193. https://doi.org/10.1093/humupd/dmu053
10. Alfer J, Happel L, Dittrich R, et al. Insufficient Angiogenesis: Cause of Abnormally Thin Endometrium in Subfertile Patients? *Geb Fra*. 2017;77(7):756–764. https://doi.org/10.1055/s-0043-111899
11. Haas DM, Hathaway TJ, Ramsey PS. Progestogen for preventing miscarriage in women with recurrent miscarriage of unclear etiology. *Cochrane Database Syst Rev.* 2019;(11):CD003511. https://doi.org/10.1002/14651858.CD003511.pub5
12. Wang A, Ji L, Shang W, et al. Expression of GPR30, Erα, and ERβ in the endometrium during the window of implantation in patients with polycystic ovary syndrome: a pilot study. *J Gynaecol Endocrinol*. 2011;27(4):251–255. https://doi.org/10.3109/09513590.2010.487584
13. Makker A, Tandon I, Goel MM, et al. Effect of ormeloxifene, a selective estrogen receptor modulator, on biomarkers of endometrial receptivity and propose the development and its relation to fertility and infertility in Indian subjects. *Fertil Steril*. 2009;91(6):2298–2307. https://doi.org/10.1016/j.fertnstert.2008.04.018
14. Al-Lamee H, Ellison A, Drury J, et al. Altered endometrial oestrogen-responsiveness and recurrent reproductive failure. *Reprod Fertil.* 2022;3(1):30–38. https://doi.org/10.1530/RAF-21-0093
15. Enciso M, Aizpurua J, Rodríguez-Estrada B, et al. The precise determination of the window of implantation significantly improves ART outcomes. *Sci Rep*. 2021;11(1):13420. https://doi.org/10.1038/s41598-021-92955-w
16. Eftekhar M, Mehrjardi SZ, Molaei B. et al. The correlation between endometrial thickness and pregnancy outcomes in fresh ART cycles with different age groups: a retrospective study. *Middle East Fertil Soc J*. 2020;24:10. https://doi.org/10.1186/s43043-019-0013-y
17. Mahajan N, Sharma S. The endometrium in assisted reproductive technology: How thin is thin? *J Hum Reprod Sci*. 2016;9(1):3–8. https://doi.org/10.4103/0974-1208.178632
18. Abdalla HI, Brooks AA, Johnson MR, et al. Endometrial thickness: a predictor of implantation in ovum recipients? *Hum Reprod.* 1994;9(2):363–365. https://doi.org/10.1093/

oxfordjournals.humrep.a138509
19. El-Toukhy T, Coomarasamy A, Khairy M, et al. The relationship between endometrial thickness and outcome of medicated frozen embryo replacement cycles. *Fertil Steril*. 2008;89(4):832–839. https://doi.org/10.1016/j.fertnstert.2007.04.031
20. Tomic V, Kasum M, Vucic K. Impact of embryo quality and endometrial thickness on implantation in natural cycle IVF. *Arch Gynaecol Obstet*. 2020;301(5):1325–1330. https://doi.org/10.1007/s00404-020-05507-4
21. Bos-Mikich A, de Oliveira R, Frantz N. Platelet-rich plasma therapy and reproductive medicine. J *Assist Reprod Genet*. 2018;35(5):753–756. https://doi.org/10.1007/s10815-018-1159-8
22. Bos-Mikich A, Ferreira MO, de Oliveira R, et al. Platelet-rich plasma or blood-derived products to improve endometrial receptivity? *J Assist Reprod Genet*. 2019;36(4):613–620. https://doi.org/10.1007/s10815-018-1386-z
23. Urman B, Boza A, Balaban B. Platelet-rich plasma another add-on treatment getting out of hand? How can clinicians preserve the best interests of their patients? *Hum Reprod.* 2019;34(11):2099–2103. https://doi.org/10.1093/humrep/dez190
24. Bendinelli P, Matteucci E, Dogliotti G, et al. Molecular basis of anti-inflammatory action of platelet-rich plasma on human chondrocytes: mechanisms of NF-κB inhibition via HGF. *J Cell Physiol*. 2010;225(3):757–766. https://doi.org/10.1002/jcp.22274