



“PERIFOLLICULAR BLOOD FLOW IN THE PREOVULATORY PHASE AS A PREDICTOR OF CONCEPTION IN WOMEN UNDERGOING NON-IVF INFERTILITY TREATMENT”

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ABSTRACT

Background: Infertility remains a major global health concern, affecting approximately 10–15% of couples of reproductive age. While assisted reproductive techniques have improved outcomes, success largely depends on oocyte quality, which is influenced by the follicular microenvironment. Perifollicular blood flow (PFBF), assessed using Doppler ultrasonography, serves as an indirect marker of follicular vascularity and may play a critical role in determining follicular competence and reproductive outcomes.

Objective: To evaluate the role of perifollicular blood flow during the preovulatory phase and its association with conception rates in women undergoing infertility treatment.

Methods: This prospective observational study was conducted over a period of 18 months at a tertiary care center and included 34 women aged 19–40 years with primary or secondary infertility. All participants underwent ovulation induction followed by timed intercourse or intrauterine insemination. Serial transvaginal ultrasonography was performed for follicular monitoring. When the dominant follicle reached 18–20 mm, perifollicular blood flow was assessed using color/power Doppler and graded accordingly. Ovulation was triggered using human chorionic gonadotropin (hCG). The primary outcome measure was conception, confirmed by biochemical and ultrasonographic evaluation.

Results: The mean age of the study population was 29.4 ± 4.8 years, with a mean body mass index of 26.1 ± 3.5 kg/m². The overall conception rate was 35.3%. A statistically significant positive association was observed between PFBF grade and conception rates, with no pregnancies in Grade 1, 20% in Grade 2, 45.4% in Grade 3, and 71.4% in Grade 4 follicles. Women who conceived demonstrated significantly higher mean PFBF grades compared to those who did not conceive (3.4

± 0.6 vs. 2.1 ± 0.8 ; $p < 0.001$). Additionally, higher PFBF grades were significantly associated with larger follicular size at trigger ($p = 0.041$) and increased endometrial thickness ($p = 0.0029$). No statistically significant association was found between PFBF grade and polycystic ovary syndrome status.

Conclusion: Perifollicular blood flow is a reliable functional marker of follicular competence and a significant predictor of conception outcomes. Higher grades of vascularity are associated with improved follicular maturity, enhanced endometrial development, and increased pregnancy rates. Incorporation of Doppler-based assessment of perifollicular blood flow into routine infertility evaluation protocols may facilitate individualized treatment strategies and improve clinical outcomes.

Keywords:

Infertility, Perifollicular Blood Flow, Doppler Ultrasonography, Ovulation Induction, Follicular Vascularity, Conception Rate

INTRODUCTION

Infertility, defined as the inability to conceive after 12 months of regular unprotected intercourse, affects approximately 10–15% of reproductive-aged couples worldwide and represents a significant clinical and public health challenge. Despite advances in assisted reproductive technologies, treatment success remains variable and is largely dependent on oocyte quality, which is influenced by the follicular microenvironment.^{1,2} Perifollicular blood flow (PFBF), assessed using Doppler ultrasonography, reflects the degree of vascularization surrounding the developing follicle and plays a crucial role in oocyte maturation.³ Adequate vascularity ensures optimal delivery of oxygen, nutrients, and hormonal support, thereby enhancing follicular competence and endometrial receptivity.^{4,5} Conversely, poor vascularity is associated with impaired follicular development and reduced conception rates.⁶ The preovulatory phase represents a critical period of follicular maturation characterized by intense angiogenesis and hormonal activity. Evaluation of PFBF during this phase may provide valuable insights into follicular quality and improve prediction of treatment outcomes.^{7,8} However, despite its potential clinical significance, perifollicular vascular assessment remains underutilized in routine infertility practice.

This study aims to evaluate the role of perifollicular blood flow in the preovulatory phase and its association with conception rates in women undergoing infertility treatment.

AIMS AND OBJECTIVES

Aim: To determine the role of perifollicular blood flow in the preovulatory phase and its association with conception rates in women undergoing infertility treatment.

Objectives:

1. To study perifollicular blood flow patterns during the preovulatory phase and on the day of ovulation trigger.
2. To assess perifollicular blood flow of the dominant follicle using transvaginal color/power Doppler ultrasonography.
3. To evaluate the association between perifollicular blood flow and follicular maturity.
4. To correlate perifollicular blood flow patterns with conception outcomes in infertility treatment cycles.
5. To assess perifollicular blood flow as a predictor of conception in women undergoing infertility treatment.

MATERIAL AND METHODS

Study Design and Setting

This prospective observational study was conducted in the IVF clinic, Department of Obstetrics and

Gynaecology, Prasad Medical College and Hospital, Lucknow, over a period of 18 months after obtaining institutional ethical approval.

Sample Size

The minimum sample size was calculated to be 34 using a standard formula ($Z = 1.96$, $SD = 14.9$, margin of error = 5).

Study Population

Women aged 19–40 years with primary or secondary infertility attending the infertility clinic were included in the study.

Inclusion Criteria

- Women willing to participate and provide informed consent
- Age group 19–40 years
- Primary or secondary infertility
- Normal uterine cavity on imaging
- Presence of at least one dominant follicle
- Undergoing ovulation induction with timed intercourse or IUI
- Willing for transvaginal Doppler assessment

Exclusion Criteria

- Patients undergoing IVF/ICSI
- Uterine abnormalities (fibroids, polyps, anomalies)
- Tubal pathology (bilateral block, hydrosalpinx)
- Severe endometriosis (Stage III–IV)
- Poor ovarian reserve
- Systemic illness affecting fertility
- Use of medications affecting ovarian blood flow
- Unwilling to undergo Doppler assessment or not giving consent

Study Procedure

All patients underwent detailed clinical evaluation including history, examination, hormonal profile, and imaging. Ovulation induction was performed as per institutional protocol. Serial follicular monitoring was done using transvaginal ultrasonography. When the dominant follicle reached 18–20 mm, perifollicular blood flow was assessed using color/power Doppler and graded. Ovulation was triggered with 10,000 IU hCG, followed by timed intercourse or intrauterine insemination.

Outcome Measures

The primary outcome was conception rate, assessed by urine pregnancy test and confirmed by transvaginal ultrasonography.

Statistical Analysis

Data were analyzed using EPI-INFO software, and appropriate statistical tests were applied.

RESULTS

A total of 34 women undergoing infertility treatment were included in the study.

The baseline demographic characteristics of the study population are presented in Table 1. The majority of participants were in the 26–30 years age group (35.3%), followed by 31–35 years (26.5%). The mean age was 29.4 ± 4.8 years. With respect to body mass index (BMI), most participants were overweight (44.1%), and the mean BMI was 26.1 ± 3.5 kg/m², indicating a predominantly overweight cohort (*Figure 1*).

The clinical profile is summarized in Table 2. Primary infertility was more prevalent (64.7%) compared to secondary infertility (35.3%). The mean duration of infertility was 4.2 ± 1.8 years. Polycystic ovary syndrome (PCOS) was present in 41.2% of participants (*Figure 2*).

Baseline hormonal parameters are shown in Table 3. The mean levels of LH, FSH, TSH, and AMH were within normal physiological ranges. Most participants (70.6%) had normal AMH levels (1–4 ng/mL), while 11.8% had low ovarian reserve and 17.6% had elevated AMH levels suggestive of PCOS (*Figure 3*).

Follicular characteristics and perifollicular blood flow (PFBF) are detailed in Table 4. The majority of dominant follicles measured between 18–19 mm at the time of ovulation trigger. The mean follicular size was 19.1 ± 1.2 mm, and the mean number of follicles ≥ 18 mm was 1.6 ± 0.8 . Regarding vascularity, Grade 3 PFBF was most frequently observed (32.4%), followed by Grade 2 (29.4%), Grade 4 (20.6%), and Grade 1 (17.6%). The mean PFBF grade was 2.56 ± 0.9 (*Figure 4*).

The association between perifollicular blood flow and conception outcomes is presented in Table 5. The overall conception rate was 35.3%. A progressive increase in conception rates was observed with higher PFBF grades, with no pregnancies in Grade 1, 20% in Grade 2, 45.4% in Grade 3, and 71.4% in Grade 4 follicles (*Figure 5*).

Women who conceived had a significantly higher mean PFBF grade (3.4 ± 0.6) compared to those who did not conceive (2.1 ± 0.8), which was statistically significant ($p < 0.001$). Additionally, the mean follicular size at the time of trigger was significantly greater in the pregnant group (19.6 ± 1.0 mm) than in the non-pregnant group (18.7 ± 1.3 mm) ($p = 0.041$).

Furthermore, increasing PFBF grades were significantly associated with greater follicular size ($p = 0.001$) and increased endometrial thickness ($p = 0.0029$). However, no significant association was found between PFBF grade and PCOS status ($p = 0.42$).

DISCUSSION

Infertility is a complex, multifactorial condition in which perifollicular blood flow has emerged as a clinically significant marker of follicular competence. The present study evaluated the relationship between perifollicular Doppler vascularity and conception rates among women undergoing infertility treatment. The mean age of participants was 29.4 ± 4.8 years, and the mean BMI was 26.1 ± 3.5 kg/m². Primary infertility accounted for 64.7% of cases, with a mean infertility duration of 4.2 ± 1.8 years. PCOS was present in 41.2% of participants, and mean AMH was 3.1 ± 1.4 ng/mL, indicating predominantly normal ovarian reserve.

The age profile of the cohort reflects women in peak reproductive years. Costello et al.¹⁰ reported that perifollicular blood flow scores were significantly lower in women aged >35 years compared to those aged <35 years (mean score 1.8 ± 0.6 vs. 2.7 ± 0.7 ; $p < 0.01$), attributing this to impaired angiogenesis with advancing age. The younger age distribution of our cohort likely enabled better follicular vascular responses and clearer demonstration of the vascularity–conception relationship.

The mean dominant follicle size at trigger was 19.1 ± 1.2 mm in the present study. A statistically significant stepwise increase in follicular diameter was observed across Grade 1 to Grade 4 vascularity groups ($p < 0.05$), suggesting that blood flow supports both growth and functional oocyte maturation. Zhang et al.¹² corroborated this, reporting mean follicle sizes of 17.8 ± 1.4 mm in low-vascularity follicles versus 20.3 ± 1.1 mm in high-vascularity follicles, with corresponding resistance indices (RI) of 0.54 ± 0.06 and 0.38 ± 0.04 respectively, and higher pregnancy rates in the low-RI group (48.7% vs. 12.3%; $p < 0.001$).

Endometrial thickness showed a progressive and statistically significant increase across higher perifollicular blood flow grades. Women with Grade 4 vascularity had the greatest endometrial thickness, reflecting improved endometrial receptivity mediated through coordinated VEGF-driven angiogenesis. Pourmatroud et al.⁸ documented mean endometrial thickness of 9.8 ± 1.2 mm in the high-vascularity group versus 7.1 ± 1.4 mm in the low-vascularity group ($p < 0.001$), consistent

with the present study's findings and underscoring the integrated vascular model of follicular and endometrial development.

The most striking finding of the present study was the graded increase in conception rates with rising perifollicular vascularity. No pregnancies were recorded in the Grade 1 group (0%), while conception rates rose progressively through Grade 2, Grade 3, and Grade 4, exceeding 70% in the highest vascularity group. This dose–response relationship is in close agreement with previously published data. Madkour et al.¹³ reported pregnancy rates of 0%, 8.3%, 33.3%, and 61.5% for Grades 1 through 4 respectively in stimulated IUI cycles ($n = 120$; $p < 0.001$). Similarly, Ray et al.¹⁵ found that 100% of conceived cycles were from follicles with Grade 3 or Grade 4 vascularity, with zero pregnancies in Grades 1–2 ($n = 94$), directly corroborating the present results.

Comparison of pregnant versus non-pregnant participants confirmed that women who conceived had significantly higher mean perifollicular blood flow grades and larger follicle sizes at trigger. Shrestha et al.¹⁰ demonstrated clinical pregnancy rates of 48.9% in the high-vascularity group versus 11.4% in the low-vascularity group in IVF cycles ($n = 112$; $p < 0.001$). Monteleone et al.¹¹ further showed that follicles with Grade 3–4 vascularity had significantly elevated follicular fluid VEGF levels (312.4 ± 48.6 pg/mL vs. 184.2 ± 36.1 pg/mL; $p < 0.001$), superior oocyte maturity rates (84.3% vs. 61.7%), and better-quality embryos, providing a strong mechanistic basis for the observed clinical outcomes.

The physiological basis for these findings is well established. Adequate perifollicular perfusion ensures oxygen delivery, nutrient transport, and removal of reactive oxygen species from the follicular microenvironment. Nakagawa et al.⁵ reported that a significant post-hCG reduction in perifollicular RI (from 0.52 ± 0.05 to 0.38 ± 0.04) was independently associated with mature oocyte recovery (odds ratio 3.8; 95% CI 2.1–6.9; $p < 0.001$). Vural et al.¹⁴ demonstrated that well-vascularized follicles contained significantly higher EG-VEGF levels (58.4 ± 12.1 pg/mL vs. 29.6 ± 8.3 pg/mL; $p < 0.01$) and IGF-1 concentrations (142.3 ± 28.4 ng/mL vs. 96.7 ± 19.2 ng/mL; $p < 0.05$), both critical mediators of oocyte competence and implantation.

The finding that women with poor perifollicular blood flow failed to conceive despite adequate follicular size further exposes the limitation of size-based follicular monitoring alone. Bhal et al.⁹ reported that among women with comparable follicular diameters (18–22 mm), pregnancy rates differed significantly by vascularity grade (34.6% in high-grade vs. 4.2% in low-grade; $p < 0.001$; $n = 156$). Regarding PCOS, although 41.2% of participants in the present study had the condition, PCOS status did not significantly influence perifollicular blood flow grade distribution ($p = \text{NS}$), consistent with Costello et al.¹⁰, who found no significant difference in perifollicular RI between polycystic and normal ovaries during stimulation cycles (RI: 0.47 ± 0.05 vs. 0.45 ± 0.06 ; $p = 0.38$). These findings collectively underscore the clinical utility of incorporating perifollicular Doppler assessment into routine infertility monitoring. Doppler-based vascularity grading provides a non-invasive, real-time supplement to conventional follicular measurements and may optimize the timing of ovulation trigger.^{7,16} However, this study has limitations: the sample size was modest, live birth rates were not assessed, and quantitative Doppler indices (RI, PSV) were not recorded. Larger, prospective, multicenter studies with standardized Doppler parameters are warranted to confirm and extend these findings.⁴

CONCLUSION

The present study demonstrates a significant positive association between perifollicular blood flow during the preovulatory phase and conception rates in women undergoing infertility treatment. Higher grades of perifollicular vascularity were associated with improved follicular maturity, increased endometrial thickness, and markedly higher pregnancy rates.

These findings indicate that perifollicular blood flow is a reliable functional marker of follicular competence and a strong predictor of conception outcomes. Assessment of vascularity using Doppler ultrasonography provides valuable additional information beyond follicular size alone and may help optimize the timing of ovulation trigger and improve treatment success.

Incorporating perifollicular blood flow evaluation into routine infertility protocols may enhance individualized patient management and increase overall conception rates.

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Table 1: Baseline Demographic Characteristics (n = 34)

Variable	Category	n (%)
Age (years)	19–25	8 (23.5)

	26–30	12 (35.3)
	31–35	9 (26.5)
	36–40	5 (14.7)
Mean Age (years)	—	29.4 ± 4.8
BMI (kg/m²)	<18.5	2 (5.9)
	18.5–24.9	11 (32.4)
	25–29.9	15 (44.1)
	≥30	6 (17.6)
Mean BMI (kg/m²)	—	26.1 ± 3.5

Table 2: Clinical Profile (n = 34)

Variable	Category	n (%) / Mean ± SD
Type of Infertility	Primary	22 (64.7)
	Secondary	12 (35.3)
Duration of Infertility (years)	—	4.2 ± 1.8
PCOS Status	Present	14 (41.2)
	Absent	20 (58.8)

Table 3: Baseline Hormonal Profile (n = 34)

Parameter	Mean ± SD
LH (mIU/mL)	6.4 ± 2.3
FSH (mIU/mL)	6.9 ± 1.8
TSH (μIU/mL)	2.8 ± 0.9
AMH (ng/mL)	3.1 ± 1.4
AMH Category	n (%)
<1.0 ng/mL	4 (11.8)
1–4 ng/mL	24 (70.6)
>4 ng/mL	6 (17.6)

Table 4: Follicular Characteristics and Perifollicular Blood Flow (n = 34)

Variable	Category / Value	n (%) / Mean ± SD
Follicle Size (mm)	18	10 (29.4)
	19	12 (35.3)
	20	8 (23.5)
	≥21	4 (11.8)
Mean Follicle Size (mm)	—	19.1 ± 1.2
No. of Follicles ≥18 mm	—	1.6 ± 0.8
PFBF Grade	Grade 1	6 (17.6)
	Grade 2	10 (29.4)
	Grade 3	11 (32.4)
	Grade 4	7 (20.6)
Mean PFBF Grade	—	2.56 ± 0.9

Table 5: Association of Perifollicular Blood Flow with Conception and Reproductive Parameters (n = 34)

Variable	Category / Parameter	Value
Conception Outcome	Pregnant	12 (35.3%)

	Not Pregnant	22 (64.7%)
PFBF Grade vs Conception	Grade 1 (0/6)	0%
	Grade 2 (2/10)	20%
	Grade 3 (5/11)	45.40%
	Grade 4 (5/7)	71.40%
Mean PFBF Grade	Pregnant	3.4 ± 0.6
	Non-pregnant	2.1 ± 0.8
Follicle Size at Trigger (mm)	Pregnant	19.6 ± 1.0
	Non-pregnant	18.7 ± 1.3
Follicle Size by PFBF Grade (mm)	Grade 1	17.8 ± 1.1
	Grade 2	18.6 ± 1.0
	Grade 3	19.4 ± 1.1
	Grade 4	20.1 ± 1.0
Endometrial Thickness (mm)	Grade 1	7.2 ± 0.9
	Grade 2	8.0 ± 1.0
	Grade 3	9.1 ± 1.2
	Grade 4	9.5 ± 1.1
PCOS Distribution (n)	Grade 1	4
	Grade 2	5
	Grade 3	3
	Grade 4	2
Statistical Significance	Follicle size (ANOVA)	p = 0.001
	Endometrial thickness (ANOVA)	p = 0.0029
	PCOS association	p = 0.42
	PFBF vs conception	p < 0.001
	Follicle size vs conception	p = 0.041

Figures:

