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Original Article

Impact of Doppler Indices in Uterine Hemodynamics on Primary Infertility and Secondary Infertility

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ABSTRACT

Background: Uterine perfusion is an important component of endometrial receptivity and may influence reproductive potential in women with infertility. Doppler ultrasonography provides a non-invasive method for assessing uterine artery blood-flow resistance through pulsatility index, resistive index, and systolic-to-diastolic ratio. Objective: This study aimed to compare uterine artery Doppler indices between women with primary and secondary infertility and to assess their relationship with associated gynecological conditions. Methods: An observational comparative cross-sectional study was conducted among 56 infertile women, including 33 with primary infertility and 23 with secondary infertility. Transvaginal color Doppler ultrasonography was used to assess uterine artery pulsatility index, resistive index, and systolic-to-diastolic ratio. Associated conditions, including polycystic ovary syndrome, endometrial polyps, and fibroids, were recorded. Group comparisons were performed using parametric and non-parametric tests, and categorical associations were assessed using chi-square or Fisher's exact testing. Results: Women with primary infertility had higher pulsatility index, resistive index, and systolic-to-diastolic ratio than women with secondary infertility: 2.97 ± 0.44 versus 2.34 ± 0.31, 0.88 ± 0.05 versus 0.77 ± 0.06, and 6.73 ± 0.89 versus 5.17 ± 0.90, respectively. All Doppler differences were statistically significant, with large effect sizes. PCOS, endometrial polyps, and fibroids were not significantly associated with infertility type. Conclusion: Uterine artery Doppler indices were significantly higher in women with primary infertility, suggesting greater uterine vascular resistance. Doppler assessment may serve as an adjunctive tool in infertility evaluation, although larger prospective studies are needed.
Keywords: Uterine artery Doppler, Uterine hemodynamics, Pulsatility index, Resistive index, Primary infertility, Secondary infertility, Endometrial receptivity, Transvaginal ultrasonography

INTRODUCTION

Infertility remains a major reproductive health concern with substantial clinical, psychological, and social consequences for affected couples. It is commonly defined as the inability to achieve pregnancy after 12 months of regular unprotected sexual intercourse and may present as primary infertility, in which conception has never occurred, or secondary infertility, in which pregnancy has occurred previously but subsequent conception is unsuccessful. The burden of infertility has increased over recent decades, and although assisted reproductive technologies have improved treatment possibilities, a considerable proportion of couples continue to experience delayed conception, implantation failure, or unexplained reproductive difficulty despite apparently adequate clinical evaluation (1,2). This persistent gap highlights the need to investigate physiological markers that may influence endometrial receptivity and reproductive potential beyond conventional structural and hormonal assessment.

Successful conception depends on the coordinated interaction of ovulatory function, endocrine regulation, embryo quality, endometrial maturation, and adequate uterine perfusion. The endometrium becomes receptive during a restricted period of the menstrual cycle, often referred to as the implantation window, during which vascular remodeling and low-resistance uterine blood flow are considered essential for embryo implantation and early placental development (3). Inadequate uterine perfusion may compromise endometrial receptivity, reduce implantation potential, and contribute to reproductive failure even in the absence of gross pelvic pathology. Because these vascular changes are dynamic and not fully captured by routine pelvic ultrasound, functional assessment of uterine blood flow may provide additional clinically relevant information in women presenting with infertility.

Doppler ultrasonography offers a non-invasive method for evaluating uterine hemodynamics by quantifying blood-flow resistance within the uterine arteries. The most commonly used Doppler parameters include the pulsatility index, resistive index, and systolic-to-diastolic ratio, each of which reflects downstream vascular resistance and perfusion characteristics. Higher values of these indices generally indicate increased vascular resistance and reduced diastolic flow, whereas lower-resistance flow patterns are considered more favorable for endometrial perfusion and implantation (4,5). Previous studies have reported altered uterine artery Doppler indices among infertile women, particularly those with unexplained infertility, suggesting that increased uterine vascular resistance may be associated with impaired reproductive capacity (6,7).

Evidence from comparative Doppler studies has shown that women with infertility may demonstrate higher uterine artery pulsatility and resistive indices than fertile women, along with reduced endometrial or subendometrial blood flow in some populations (6,8). In assisted reproductive settings, uterine artery Doppler indices and endometrial perfusion have also been explored as potential predictors of implantation and pregnancy outcomes, with lower uterine artery resistance and better endometrial vascularity generally associated with improved reproductive success (9–11). However, published findings remain heterogeneous because of variation in patient populations, infertility causes, menstrual-cycle timing of Doppler examination, ultrasound technique, and treatment context. As a result, the diagnostic and prognostic value of uterine artery Doppler assessment in routine infertility evaluation remains incompletely defined.

Most available evidence has focused on comparisons between infertile and fertile women, unexplained infertility cohorts, or assisted reproductive technology outcomes, while fewer studies have specifically examined whether uterine artery Doppler indices differ between women with primary and secondary infertility. This distinction is clinically important because primary infertility may reflect more persistent or fundamental reproductive dysfunction, whereas secondary infertility may occur after prior evidence of reproductive capability. If uterine vascular resistance differs between these groups, Doppler indices may help identify a hemodynamic component of infertility and guide further individualized evaluation. Therefore, this study aimed to compare uterine artery pulsatility index, resistive index, and systolic-to-diastolic ratio between women with primary and secondary infertility and to assess whether associated gynecological conditions, including polycystic ovary syndrome, endometrial polyps, and fibroids, were related to infertility type or Doppler patterns.

MATERIALS AND METHODS

This study was conducted as an observational comparative cross-sectional study to evaluate uterine artery Doppler indices among women diagnosed with primary or secondary infertility. The design was selected because the objective was to compare Doppler-derived uterine hemodynamic parameters between two naturally occurring infertility groups at a single point of assessment without assigning any intervention. The study was carried out in a private diagnostic ultrasound center over a 90-day period after approval of the research synopsis.

Women of reproductive age who presented for infertility-related ultrasound evaluation were recruited after assessment for eligibility. Participants were included if they had infertility, defined as failure to conceive after at least 12 months of regular unprotected intercourse, and were classified as having either primary infertility when they had no previous conception or secondary infertility when they had a prior history of conception but were unable to conceive again. Women were enrolled after informed consent and willingness to participate. Participants were excluded if they were pregnant during the study period, were currently using hormonal therapy that could alter Doppler measurements, had systemic vascular or metabolic illness likely to affect uterine blood flow such as diabetes mellitus or hypertension, or had clinical conditions that prevented standardized transvaginal Doppler assessment. Associated gynecological conditions identified during evaluation, including polycystic ovary syndrome, endometrial polyps, and fibroids, were recorded as clinical variables rather than used as automatic exclusion criteria, because one objective of the analysis was to assess their association with infertility type and Doppler indices.

The minimum required sample size was calculated using the single-proportion formula $n = Z^2p(1 - p)/E^2$, where Z was 1.96 for a 95% confidence level, the expected prevalence was 0.175, and the margin of error was 0.10. Substitution of these values produced an estimated sample size of 55.46, which was rounded to 56 participants. A total of 56 women meeting the eligibility criteria were included in the final analysis, comprising 33 women with primary infertility and 23 women with secondary infertility.

Clinical and demographic information was recorded using a structured data collection approach. Variables included age, infertility type, relevant reproductive history, and the presence or absence of associated gynecological conditions, including polycystic ovary syndrome, endometrial polyp, and fibroid. The primary Doppler variables were uterine artery pulsatility index, resistive index, and systolic-to-diastolic ratio. Pulsatility index was defined as the difference between peak systolic velocity and end-diastolic velocity divided by mean flow velocity across the cardiac cycle. Resistive index was defined as the difference between peak systolic velocity and end-diastolic velocity divided by peak systolic velocity. The systolic-to-diastolic ratio was calculated as peak systolic velocity divided by end-diastolic velocity. Higher values of these indices were interpreted as reflecting increased uterine arterial resistance.

Transvaginal color Doppler ultrasonography was performed to assess uterine artery blood-flow parameters. Doppler examination was standardized as far as possible with respect to patient preparation, scanning approach, and measurement technique. Uterine artery waveforms were obtained using color Doppler guidance, and spectral Doppler measurements were recorded after obtaining stable and reproducible waveforms. Doppler indices were documented for analysis, and measurements were interpreted in relation to infertility type. To reduce measurement variability, Doppler assessment was performed under consistent scanning conditions, and the same measurement definitions were applied across all participants. Clinical variables were recorded before statistical analysis to reduce selective reporting bias.

Potential confounding was addressed by recording age and associated gynecological conditions and by examining whether polycystic ovary syndrome, endometrial polyps, and fibroids differed between primary and secondary infertility groups. Because these conditions may influence reproductive status or uterine characteristics, their distribution was assessed separately rather than assuming that Doppler differences were solely attributable to infertility type. Bias was further minimized by using predefined eligibility criteria, consistent operational definitions of infertility type and Doppler indices, and uniform statistical procedures for all participants. Data were checked for completeness, internal consistency, and coding accuracy before analysis.

Data were analyzed using descriptive and inferential statistical methods. Categorical variables were summarized as frequencies and percentages, while continuous variables were summarized using mean and standard deviation when approximately normally distributed and median with interquartile range when distributional assumptions were not satisfied. Doppler indices were compared between primary and secondary infertility groups using independent-samples t-tests when parametric assumptions were met. Normality and variance assumptions were assessed before group comparison, and Mann–Whitney U testing was used as a non-parametric confirmation when the distribution of Doppler indices did not satisfy normality assumptions. Associations between infertility type and categorical gynecological conditions were evaluated using Pearson's chi-square test or Fisher's exact test when expected cell counts were small. The effect of polycystic ovary syndrome on Doppler indices was assessed by comparing mean Doppler values between women with and without polycystic ovary syndrome. Logistic regression was used to examine the combined discriminatory performance of Doppler indices for classifying primary and secondary infertility, and classification accuracy was reported from the model output. Statistical significance was set at $p < 0.05$.

Ethical approval was obtained before data collection. All participants provided informed consent before inclusion in the study. Confidentiality was maintained throughout data collection, coding, analysis, and reporting. Participant data were used only for research purposes, and no personally identifiable information was included in the analysis or manuscript. Data integrity was supported through structured data recording, verification of entered values, consistent variable definitions, and preservation of the original analytic dataset for reproducibility.

RESULTS

A total of 56 women with infertility were included in the analysis. Of these, 33 participants had primary infertility and 23 had secondary infertility.

Table 1. Distribution of Infertility Type Among Study Participants

Infertility Type	n	%
Primary infertility	33	58.9
Secondary infertility	23	41.1
Total	56	100.0

Primary infertility was more frequent than secondary infertility in the study population, accounting for 33 of 56 participants. Secondary infertility was reported in 23 participants. This distribution established the two comparison groups used for subsequent Doppler and clinical analyses.

Table 2. Distribution of Associated Gynecological Conditions

Condition	Present n	Absent n	Present %
Endometrial polyp	12	44	21.4
Polycystic ovary syndrome	28	28	50.0
Fibroid	20	36	35.7

Polycystic ovary syndrome was the most frequently recorded associated gynecological condition, present in 28 of 56 participants. Fibroids were identified in 20 participants, while endometrial polyps were identified in 12 participants. These conditions were analyzed as associated clinical variables rather than as exclusionary diagnoses.

Table 3. Descriptive Statistics of Uterine Artery Doppler Indices

Variable	n	Minimum	Maximum	Mean	SD	Median	IQR
Pulsatility index	56	1.94	3.72	2.71	0.50	2.62	2.43–3.02
Resistive index	56	0.65	0.95	0.83	0.08	0.83	0.79–0.91
S/D ratio	56	3.63	8.38	6.09	1.18	6.19	5.20–7.07

The uterine artery Doppler indices showed measurable variability across participants. The pulsatility index ranged from 1.94 to 3.72, with a mean of 2.71 and median of 2.62. The resistive index ranged from 0.65 to 0.95, with a mean and median of 0.83. The S/D ratio showed the widest absolute dispersion, ranging from 3.63 to 8.38, with a mean of 6.09 and median of 6.19.

All three Doppler indices were numerically higher among women with primary infertility than among women with secondary infertility. The largest absolute between-group difference was observed for the

S/D ratio, with a mean difference of 1.56. The pulsatility index differed by 0.63, while the resistive index differed by 0.12 between groups.

Table 4. Comparison of Uterine Artery Doppler Indices by Infertility Type

Variable	Primary Infertility n	Primary Mean ± SD	Secondary Infertility n	Secondary Mean ± SD	Mean Difference
Pulsatility index	33	2.97 ± 0.44	23	2.34 ± 0.31	0.63
Resistive index	33	0.88 ± 0.05	23	0.77 ± 0.06	0.12
S/D ratio	33	6.73 ± 0.89	23	5.17 ± 0.90	1.56

Table 5. Independent-Samples t-Test Comparing Doppler Indices by Infertility Type

Variable	t	df	p-value	Mean Difference	95% CI	Cohen's d
Pulsatility index	5.93	54	<0.001	0.63	0.42–0.84	1.61
Resistive index	7.67	54	<0.001	0.12	0.09–0.15	2.08
S/D ratio	6.42	54	<0.001	1.56	1.07–2.04	1.74

Independent-samples t-testing demonstrated statistically significant differences in all three Doppler indices between primary and secondary infertility groups. The pulsatility index was higher in the primary infertility group by 0.63, with a 95% confidence interval from 0.42 to 0.84. The resistive index showed a mean difference of 0.12, with a 95% confidence interval from 0.09 to 0.15. The S/D ratio showed a mean difference of 1.56, with a 95% confidence interval from 1.07 to 2.04. The reported Cohen's d values indicated large standardized between-group differences for all three Doppler measures, with the largest effect observed for the resistive index.

Table 6. Mann–Whitney U Test Comparing Doppler Indices by Infertility Type

Variable	Primary Mean Rank	Secondary Mean Rank	U	Z	p-value
Pulsatility index	37.23	15.98	91.5	-4.80	<0.001
Resistive index	38.42	14.26	52.0	-5.46	<0.001
S/D ratio	37.44	15.67	84.5	-4.91	<0.001

The non-parametric comparison confirmed the same pattern observed in the t-test analysis. Mean ranks for pulsatility index, resistive index, and S/D ratio were consistently higher in the primary infertility group than in the secondary infertility group. The Mann–Whitney U results supported statistically significant between-group differences for all three Doppler indices.

Table 7. Association Between Associated Gynecological Conditions and Infertility Type

Condition	Primary Present n	Primary Absent n	Secondary Present n	Secondary Absent n	χ^2	p-value
Endometrial polyp	6	27	6	17	0.50	0.478
Polycystic ovary syndrome	15	18	13	10	0.66	0.415
Fibroid	12	21	8	15	0.02	0.903

No statistically significant association was observed between infertility type and the recorded gynecological conditions. Endometrial polyps were present in 6 women with primary infertility and 6 women with secondary infertility. Polycystic ovary syndrome was recorded in 15 women with primary infertility and 13 women with secondary infertility. Fibroids were recorded in 12 women with primary infertility and 8 women with secondary infertility. The reported p-values for all three comparisons were greater than 0.05.

Table 8. Comparison of Doppler Indices According to Polycystic Ovary Syndrome Status

Variable	PCOS Present n	PCOS Present Mean ± SD	PCOS Absent n	PCOS Absent Mean ± SD	t	p-value
Pulsatility index	28	2.62 ± 0.46	28	2.80 ± 0.52	-1.40	0.168
Resistive index	28	0.83 ± 0.08	28	0.84 ± 0.08	-0.44	0.664
S/D ratio	28	5.97 ± 1.22	28	6.21 ± 1.14	-0.77	0.447

Doppler indices did not differ significantly between women with and without polycystic ovary syndrome. The mean pulsatility index was 2.62 among women with polycystic ovary syndrome and 2.80 among women without polycystic ovary syndrome. The mean resistive index was similar between groups, while the S/D ratio was 5.97 among women with polycystic ovary syndrome and 6.21 among women without polycystic ovary syndrome.

Table 9. Classification Accuracy of the Doppler-Based Regression Model

Observed Infertility Type	Predicted Primary n	Predicted Secondary n	Correct %
Primary infertility	32	1	97.0
Secondary infertility	2	21	91.3
Overall	34	22	94.6

The Doppler-based regression model classified 32 of 33 women with primary infertility and 21 of 23 women with secondary infertility correctly. The overall classification accuracy was 94.6%. This finding suggests strong apparent discrimination within the analyzed sample; however, model coefficients, odds ratios, confidence intervals, calibration statistics, and external validation were not available in the reported data and should be included in the final manuscript before presenting the model as a diagnostic tool.

Overall, the results demonstrate that uterine artery pulsatility index, resistive index, and S/D ratio were consistently higher among women with primary infertility than among women with secondary infertility. The magnitude of these differences was statistically significant and supported by both parametric and non-parametric analyses. In contrast, recorded gynecological conditions, including polycystic ovary syndrome, endometrial polyp, and fibroid, were not significantly associated with infertility type. Within the available analysis, polycystic ovary syndrome also did not show a significant independent association with Doppler index values.

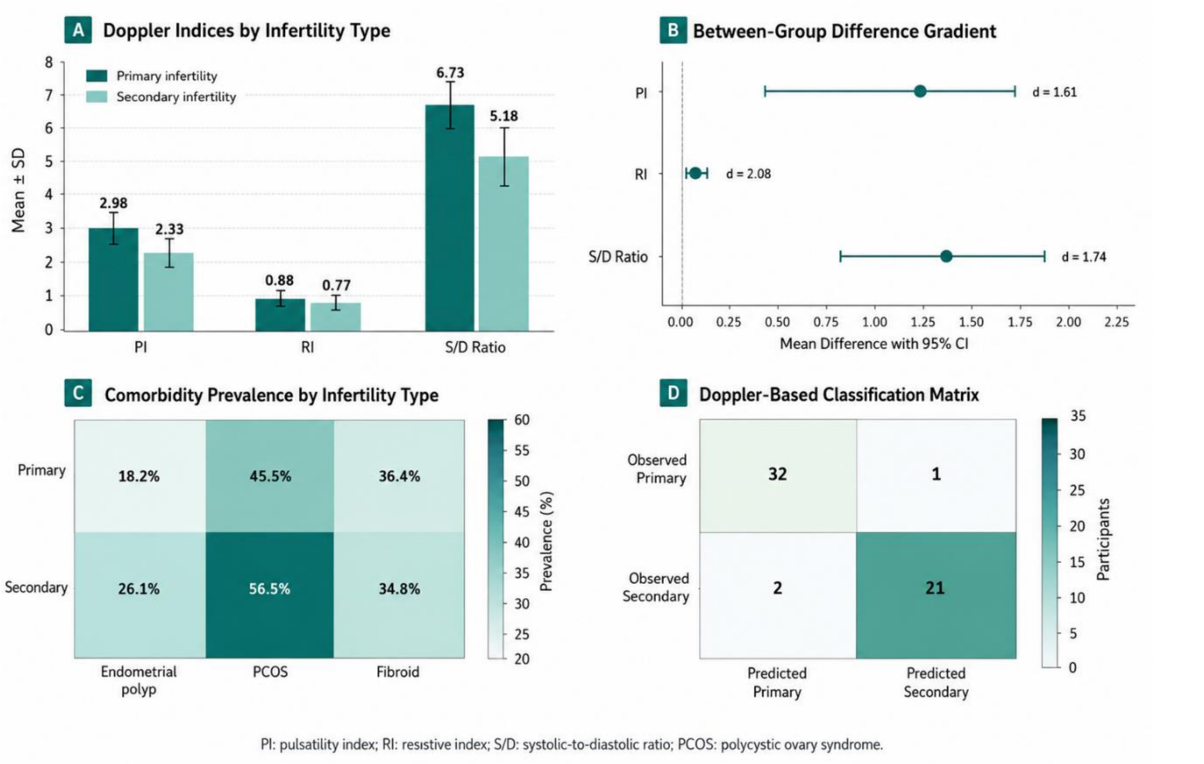

Figure 1. Uterine artery Doppler indices, clinical comorbidity profile, and model discrimination by infertility type. The panelled figure demonstrates that women with primary infertility had consistently higher uterine artery Doppler indices than women with secondary infertility, with mean PI of 2.97 ± 0.44 versus 2.34 ± 0.31, RI of 0.88 ± 0.05 versus 0.77 ± 0.06, and S/D ratio of 6.73 ± 0.89 versus 5.17 ± 0.90. The between-group difference gradient showed large standardized effects across all Doppler parameters, with Cohen's d values of 1.61 for PI, 2.08 for RI, and 1.74 for S/D ratio, indicating a marked hemodynamic separation between infertility types. In contrast, the comorbidity prevalence panel showed overlapping clinical profiles, with PCOS present in 45.5% of primary and 56.5% of secondary infertility cases, fibroids in 36.4% and 34.8%, and endometrial polyps in 18.2% and 26.1%, respectively. The classification matrix further showed that the Doppler-based model correctly classified 32 of 33 primary infertility cases and 21 of 23 secondary infertility cases, yielding an apparent overall classification accuracy of 94.6%, although this discriminatory performance requires confirmation through full regression reporting and external validation.

DISCUSSION

This observational comparative study evaluated uterine artery Doppler indices among women with primary and secondary infertility and found that all three Doppler parameters—pulsatility index, resistive index, and systolic-to-diastolic ratio—were consistently higher in the primary infertility group. Women with primary infertility had a mean PI of 2.97 ± 0.44 compared with 2.34 ± 0.31 among women with secondary infertility, a mean RI of 0.88 ± 0.05 compared with 0.77 ± 0.06, and a mean S/D ratio of 6.73 ± 0.89 compared with 5.17 ± 0.90. These differences were statistically significant and were supported by large effect sizes, indicating a marked hemodynamic separation between the two infertility groups. Because higher Doppler indices generally reflect increased downstream vascular resistance and reduced diastolic perfusion, these findings suggest that women with primary infertility in this sample had greater uterine arterial resistance than women with secondary infertility.

The observed Doppler pattern is biologically plausible because successful conception depends on adequate uterine perfusion, endometrial receptivity, and coordinated vascular remodeling during the peri-implantation period. Doppler ultrasonography allows non-invasive assessment of uterine arterial blood-flow resistance and has been used to evaluate reproductive vascular physiology in infertile women. Previous work has shown that altered uterine artery PI and RI may be associated with impaired uterine perfusion and reduced receptivity, particularly in women with unexplained infertility (3,4). Ali Zarad et al. reported that uterine artery Doppler assessment may provide clinically relevant information in unexplained infertility, while Smart et al. found differences in uterine artery Doppler parameters and endometrial characteristics between infertile and fertile women (6,8). Although those studies primarily focused on infertile versus fertile comparisons, the present study extends this concept by comparing primary and secondary infertility and suggests that hemodynamic resistance may not be uniform across infertility types.

The present findings also align with evidence from assisted reproductive technology settings, where uterine artery Doppler indices and endometrial blood-flow patterns have been investigated as markers of implantation potential. Fan et al. reported that uterine artery Doppler assessment during the implantation window may have predictive relevance in frozen embryo transfer outcomes, while Bayati et al. and Bahrami et al. further emphasized the importance of uterine artery and subendometrial blood-flow parameters in women undergoing frozen embryo transfer (9–11). These findings support the broader concept that uterine vascular resistance may influence reproductive success. However, the current study did not evaluate embryo transfer, implantation, pregnancy rate, or live birth outcomes; therefore, its results should be interpreted as evidence of hemodynamic difference between infertility groups rather than direct evidence of treatment prognosis or pregnancy prediction.

The absence of statistically significant associations between infertility type and recorded gynecological conditions is clinically relevant. PCOS was present in 50.0% of participants, fibroids in 35.7%, and endometrial polyps in 21.4%, yet none of these conditions showed a significant association with primary versus secondary infertility. Doppler indices also did not differ significantly between women with and without PCOS. These findings suggest that the observed differences in uterine artery PI, RI, and S/D ratio were not simply explained by the distribution of these recorded comorbidities in this sample. Nevertheless, this interpretation should be cautious because the study did not stratify PCOS phenotypes, fibroid size or location, endometrial polyp characteristics, hormonal profiles, ovarian reserve markers, or male-factor infertility. Hantoushzadeh et al. highlighted the importance of uterine artery Doppler indices in infertility patients with intramural fibroids before in vitro fertilization, indicating that fibroid-related interpretation requires detailed anatomical and reproductive context (12).

The findings are also consistent with studies suggesting that altered uterine hemodynamics may contribute to unexplained or difficult-to-classify infertility. El-Mazny et al. reported abnormal uterine hemodynamic findings among women with unexplained infertility, supporting the role of vascular resistance as one potential component of impaired reproductive potential (13). Pace et al. showed improvement in uterine artery Doppler indices following hysteroscopic metroplasty in women with uterine abnormalities, suggesting that uterine structural and vascular factors may interact in reproductive outcomes (14). Elswah et al. also emphasized the value of Doppler assessment of uterine and ovarian arteries in unexplained infertility (15). Taken together, these studies support the clinical relevance of uterine Doppler assessment, but they also highlight that Doppler indices should be interpreted within a broader infertility workup rather than used as standalone diagnostic markers.

The Doppler-based regression model showed high apparent classification accuracy, correctly identifying 32 of 33 women with primary infertility and 21 of 23 women with secondary infertility, with an overall accuracy of 94.6%. This suggests strong discrimination within the analyzed sample. However, the model should not be presented as a validated diagnostic tool because the manuscript does not provide complete regression coefficients, odds ratios, confidence intervals, calibration measures, assessment of multicollinearity, or internal/external validation. PI, RI, and S/D ratio are physiologically related measures of vascular resistance, so multicollinearity is likely and may affect model stability. Therefore, the classification findings should be framed as exploratory and hypothesis-generating. Future studies should report full multivariable models and validate Doppler-based classification in larger, independent cohorts.

The study has several limitations. Its modest sample size and single-center design may limit generalizability. The cross-sectional design prevents causal inference, so increased uterine artery resistance cannot be concluded to be the cause of primary infertility. Doppler measurements may vary according to menstrual-cycle timing, hormonal status, ultrasound machine settings, operator technique, and measurement protocol. Although the study recorded common gynecological conditions, it did not include detailed endocrine, ovarian reserve, tubal, male-factor, lifestyle, or pregnancy-outcome data. The absence of full regression output also limits interpretation of the reported classification model. Despite these limitations, the study provides useful preliminary evidence that uterine artery Doppler indices are significantly higher in women with primary infertility than in women with secondary infertility and supports further investigation of uterine hemodynamics as an adjunctive component of infertility evaluation.

CONCLUSION

Women with primary infertility demonstrated significantly higher uterine artery pulsatility index, resistive index, and systolic-to-diastolic ratio than women with secondary infertility, indicating greater uterine arterial resistance in the primary infertility group. Recorded gynecological conditions, including PCOS, endometrial polyps, and fibroids, were not significantly associated with infertility type, and PCOS status did not significantly influence Doppler index values in this sample. These findings suggest that uterine artery Doppler ultrasonography may provide useful adjunctive information in infertility evaluation, particularly for identifying altered uterine hemodynamic patterns among women with primary infertility. However, because this was a cross-sectional single-center study with a modest sample size, the findings should be interpreted as associative rather than causal, and the reported classification accuracy requires confirmation through complete regression reporting and validation in larger prospective studies.

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