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Assessment of Heavy Menstrual Bleeding Related to Copper IUCD Using Uterine Artery Doppler Indices: Pulsatility Index and Resistance Index

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ABSTRACT

Background: The copper intrauterine contraceptive device (IUCD) is a widely used long-acting reversible contraceptive method. However, one of its major drawbacks is the induction of heavy menstrual bleeding (HMB), which may lead to iron deficiency anemia (IDA) and result in early device removal. Uterine artery Doppler parameters, such as the resistance index (RI) and pulsatility index (PI), have been investigated as potential predictors of HMB in IUCD users.

Objective: This study aimed to assess HMB related to the insertion of a copper IUCD through uterine artery Doppler indices, focusing on PI and RI, both at baseline and after 3 months of use.

Patients and methods: This prospective observational study was conducted on 30 women who underwent copper IUCD insertion. Uterine artery Doppler indices—RI and PI—were measured via transvaginal ultrasound both before IUCD insertion and three months afterward. Participants were monitored clinically for signs of HMB using standardized bleeding scores and questionnaires.

Results: The study observed a significant reduction in uterine artery RI and PI in patients who developed HMB three months after IUCD insertion. A strong inverse correlation was found between Doppler indices and the severity of menstrual bleeding. Baseline Doppler indices were also predictive of HMB, with ROC analysis demonstrating satisfactory diagnostic performance.

Conclusions: It could be concluded that uterine artery Doppler indices, particularly PI and RI, serve as useful non-invasive predictors for the development of HMB following copper IUCD insertion. Early identification of at-risk patients may facilitate individualized contraceptive counseling and management.

Keywords: Copper IUCD, HMB, Pulsatility Index, Resistance Index, Uterine Artery Doppler, Transvaginal Ultrasound

INTRODUCTION

The IUCD, particularly the copper-based variant (Cu-IUCD), remains one of the most effective, safe, and widely used long-acting reversible contraceptive methods globally. Its advantages include minimal systemic effects, long duration of action, and cost-effectiveness [(1)]. Among the various types of copper IUCDs, the Cu-T380A is the most inserted due to its superior contraceptive efficacy and extended lifespan. However, despite its benefits, a significant drawback associated with copper IUCD use is the increased risk of HMB, reported in up to 30–50% of users. This adverse effect frequently results in discomfort, IDA, and, consequently, early discontinuation of the device [(2)].

The mechanisms underlying IUCD-related HMB are multifactorial. Hypotheses suggest enhanced local production of prostaglandins, increased endometrial vascular permeability, and altered fibrinolytic activity as contributing factors. Recently, attention has turned to evaluating uterine hemodynamics as a possible predictor of this complication. In this context, uterine artery Doppler ultrasound offers a non-invasive and reproducible method to assess uterine blood flow through indices such as the PI and RI. Although some studies have explored the role of Doppler parameters in various gynecological conditions, data specifically linking pre-insertion Doppler findings to the risk of developing HMB post-IUCD insertion remain limited and inconclusive [(3, 4)].

The gap in the current literature lies in the lack of prospective data evaluating whether baseline uterine artery Doppler indices can predict HMB in women receiving a copper IUCD. Existing research tends to focus on symptomatic women after HMB has developed, rather than on early identification of at-risk individuals. Furthermore, there is a paucity of data from the Middle Eastern and North African (MENA) region, particularly from Egypt, where IUCD usage remains a mainstay of family planning programs. Understanding region-specific uterine blood flow characteristics may provide culturally and physiologically relevant insights [(5)].

This study presents a novel approach by prospectively evaluating baseline uterine artery Doppler indices in women before and after copper IUCD insertion and investigating their correlation with subsequent development of HMB. To our knowledge, few studies have quantitatively assessed this predictive relationship in a structured clinical setting using PI and RI as screening tools.

We conducted this study to address the need for predictive strategies that could guide clinicians in contraceptive counseling. Identifying women at high risk of HMB prior to IUCD insertion may allow for personalized contraceptive planning and early intervention, potentially improving user satisfaction, adherence, and overall reproductive health outcomes.

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PATIENTS AND METHODS

This prospective observational clinical study included a total of 30 women seeking long-acting contraception with IUCDs at Tertiary Care Hospital at the Department of Obstetrics and Gynecology, Ain Shams University Maternity Hospital, Cairo, Egypt during the period from February 2024 to November 2024.

Inclusion Criteria: Participants were selected based on strict inclusion and exclusion criteria. Eligible women were aged 20–40 years, had regular menstrual cycles (21–35 days), and had no history of hormonal contraception or IUCD use within the previous three months.

Exclusion Criteria: included known bleeding disorders, current anticoagulant therapy, congenital uterine anomalies, active pelvic infection, uterine fibroids distorting the uterine cavity, systemic illnesses (e.g., thyroid disorders), or current pregnancy. These criteria were applied to ensure a homogeneous study population and to minimize potential confounding factors.

Study Procedures:

All participants were submitted to the following:

- **History Taking and Clinical Examination:** including:

A thorough clinical evaluation beginning with a detailed personal, obstetric, and gynecological history. Emphasis was placed on menstrual patterns, previous contraceptive use, and any history suggestive of bleeding tendency. General examination included measurement of body mass index (BMI) and vital signs. A bimanual pelvic examination was performed to assess uterine size, position, and rule out adnexal or pelvic pathology that might affect IUCD insertion or uterine blood flow.

- **Investigations**

Baseline investigations included a complete blood count (CBC) to evaluate anemia, a urine pregnancy test to exclude pregnancy, and transvaginal ultrasonography (TVUS) (GE Logiq P7 device with a 7,5 MHz curved transvaginal transducer) to assess uterine anatomy and exclude structural anomalies. Uterine artery Doppler ultrasound was carried out using color Doppler imaging to measure the PI and RI of both uterine arteries. These measurements were taken immediately before IUCD insertion and repeated after three months to observe any hemodynamic changes.

Surgical Procedure

IUCD insertion was performed in the post-menstrual phase under aseptic conditions. The copper T-380A device was used in all cases. The procedure involved cervical cleaning with antiseptic solution, uterine sounding, and standard IUCD placement. The proper positioning of the device was confirmed by transvaginal ultrasound immediately following insertion. For a brief time after the surgery, patients were monitored for any potential complications.

Outcome measures:

- **The primary outcome** measures of this study were the relationships between RI and PI, measured prior to IUCD insertion, and the subsequent development of heavy menstrual bleeding (HMB).
- **Secondary outcomes** included:
  1. Comparison between RI and PI of uterine artery doppler pre and post insertion of IUCD and effect on HMB.
  2. Incidence of displaced copper IUCD.
  3. Incidence of HMB associated with cupper IUCD.
  4. The relationship between demographic data and HMB associated with IUCD.

Sample Size: Examining the findings of earlier study, **Attia *et al.*** [(11)] shown that among women using copper IUDs, RI of uterine artery doppler was lower in patients reported HMB than in patients reported no HMB (0.78+/-0.05 versus 0.90+/-0.05 respectively); a sample size of at least 30 women aged 20-40 years old who desired long acting contraception achieved 100% power, at significance level 0.05,by using Power Analysis and Sample Size Software (PASS15- Version 15.0.10) for sample size calculation, setting power at 99%, with taking into consideration 10% attrition rate.

Ethical Considerations:

The Research Ethics Committee of Ain Shams University's Faculty of Medicine gave its approval to this study. After being made aware of the goals, methods, and rights of the study, each participant gave signed informed consent. Participants were allowed to leave at any moment without compromising their treatment, and confidentiality was upheld. Every procedure adhered to the Helsinki Declaration.

Statistical analysis

Using IBM SPSS version 22.0, the gathered data was coded, tabulated, and statistically examined. For quantitative data, descriptive statistics were calculated as the minimum and maximum of the range and the mean ±SD for quantitative normally distributed data, but for qualitative data, they were calculated as numbers and percentages. Using the independent t-test where there were two independent groups with normally distributed data and the Shapiro-Wilk test for normality testing, inferential analyses were performed for quantitative variables. Fisher's Exact test was used for variables with tiny, anticipated numbers, while the X^2-test was used for proportional differences in inferential analyses of qualitative data. P values < 0.050 were considered significant; otherwise, they were considered non-significant.

RESULTS

A total of 37 women were assessed for eligibility, of whom 2 declined to participate and 5 were excluded based on the inclusion criteria. Ultimately, 30 women who underwent IUCD insertion were included in the study, and their data formed the basis for the final analysis. **(Figure 1)**.

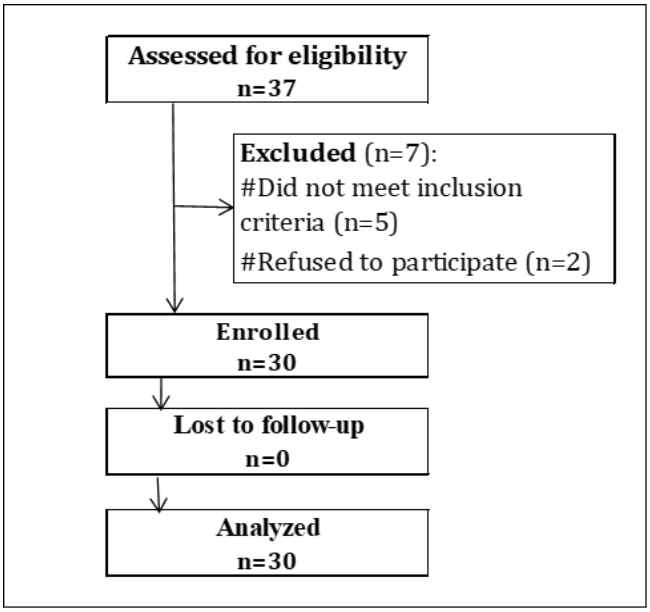

Figure (1): Flow chart of the studied cases

Table (1) presents the baseline demographic and obstetric profiles of the 30 women enrolled in the study. The average age was 27.5 years, and BMI averaged 27.9 kg/m², placing most participants in the overweight category. The time since the last delivery averaged 3.1 years. Parity had a median value of 2.0, indicating most women had two previous births. Notably, 60% of deliveries were vaginal, while 40% were cesarean.

Table (1): Demographic characteristics of the studied cases

Characteristics		Mean± SD	Range
Age (years)		27.5±4.4	20.0–36.0
BMI (kg/m²)		27.9±2.6	22.3–34.4
Time since delivery (years)		3.1±0.9	1.0–5.0
		Median (1st–3rd IQ)	**Range**
Parity		2.0 (2.0–3.0)	1.0–4.0
		n	**%**
Mode of delivery	**Vaginal**	18	60.0%
	Cesarean	12	40.0%

Total=30. IQ: Interquartiles.

Table (2) demonstrates significant reductions in both **PI** and **RI** from baseline to the 3-month follow-up after IUCD insertion. The mean PI dropped from 2.41 to 2.26, and RI declined from 0.92 to 0.88. Both reductions were statistically significant ($p < 0.001$).

Table (2): Doppler findings of uterine artery among the studied cases

Characteristics		Mean±SD	Range	⌂p-value
Pulsatility index	**Baseline**	2.41±0.10	2.22–2.60	**<0.001***
	Month-3	2.26±0.13	1.98–2.48	
	Change	-0.15±0.05	-0.27–-0.06	
Resistance index	**Baseline**	0.92±0.06	0.82–1.02	**<0.001***
	Month-3	0.88±0.07	0.75–1.00	
	Change	-0.05±0.02	-0.09–-0.02	

Total=30. Change=month-3 – baseline, negative values indicate reduction. ^Independent t-test. ⌂Paired t-test. *Significant.

Table (3) reports the prevalence of HMB three months after IUCD insertion. It was observed in 8 out of 30 women (26.7%), which is consistent with literature reporting HMB in approximately 20–30% of copper IUCD users.

Table (3): HMB in month-3 among the studied cases

HMB	N=30	%
Positive	8	26.7%
Negative	22	73.3%

This comparative table (4) shows demographic variations between women who developed HMB and those who did not. While age, parity, time since delivery, and mode of delivery were statistically similar, **BMI was significantly higher** in the HMB group (29.6 vs. 27.2, $p = 0.020$).

Table (4): Comparison according to HMB regarding demographic characteristics

Characteristics		HMB		p-value
		Positive (Total=8)	**Negative (Total=22)**	
Age (years)		25.9±3.9	28.0±4.5	^0.241
BMI (kg/m²)		29.6±2.5	27.2±2.3	**^0.020***
Time since delivery (months)		3.0±0.5	3.1±1.0	^0.643
Parity		2.0 (2.0–3.0)	2.0 (1.0–3.0)	◊0.845
Mode of delivery	**Vaginal**	5 (62.5%)	13 (59.1%)	§0.999
	Cesarean	3 (37.5%)	9 (40.9%)	

Data described as Mean±SD, Median (1st –3rd Interquartiles) or number (%). ^Independent t-test. ◊Mann-Whitney test. §Fisher's Exact test. *Significant.

Table (5) highlights the key association between Doppler indices and HMB. Women who developed HMB had significantly **lower baseline and follow-up values of both PI and RI** compared to those who did not. Moreover, the magnitude of reduction in these indices over time was also greater in the HMB group.

Table (5): Comparison according to HMB regarding doppler findings of uterine artery

Characteristics		HMB		^p-value
		Positive (Total=8)	Negative (Total=22)	
Pulsatility index	Baseline	2.30±0.06	2.45±0.08	**<0.001***
	Month-3	2.09±0.08	2.32±0.09	**<0.001***
	Change	-0.21±0.03	-0.13±0.03	**<0.001***
	⌂p-value	**<0.001***	**<0.001***	
Resistance index	Baseline	0.86±0.04	0.94±0.04	**<0.001***
	Month-3	0.80±0.05	0.90±0.05	**<0.001***
	Change	-0.07±0.02	-0.04±0.01	**<0.001***
	⌂p-value	**<0.001***	**<0.001***	

Data described as Mean±SD. Change=month-3 – baseline, negative values indicate reduction. ^Independent t-test. ⌂Paired t-test. *Significant.

This ROC analysis evaluates the predictive accuracy of baseline PI and RI for identifying patients at risk for HMB. Both indices had excellent diagnostic performance, with **area under the curve (AUC)** values of 0.943 for PI and 0.898 for RI. A PI cut-off of ≤2.35 achieved 75% sensitivity and 95.5% specificity, indicating high discriminative power. Similarly, an RI cut-off of ≤0.89 also showed strong specificity and predictive value (Table 6).

Table (6): Diagnostic performance of baseline doppler findings of uterine artery in predcting HMB in month-3

Characters	Pulsatility index		Resistance index	
	Value	95% CI	Value	95% CI
AUC	0.943	0.860–1.000	0.898	0.771–1.000
p-value	**<0.001***		**<0.001***	
Cut point	≤2.35		≤0.89	
Sensitivity	75.0%	34.9%–96.8%	75.0%	34.9%–96.8%
Specificity	95.5%	77.2%–99.9%	90.9%	70.8%–98.9%
Diagnostic accuracy	90.0%	73.5%–97.9%	86.7%	69.3%–96.2%
Youden's Index	70.5%	39.2%–101.7%	65.9%	33.6%–98.2%
Positive predictive value	85.7%	42.1%–99.6%	75.0%	34.9%–96.8%
Negative predictive value	91.3%	72.0%–98.9%	90.9%	70.8%–98.9%

CI: Confidence interval. *Significant.

DISCUSSION

The most serious side effect of copper IUCD is increased menstrual bleeding by 30 to 50%, sometimes with cramping. Iron deficiency anemia might result from the volume of menstrual blood. These changes result in the removal of 4–15% of IUCDs during the first year following implantation [6,7]. The cause of the severe monthly bleeding in women on IUCD was clarified by the increased endometrial prostaglandin production, which raises vascular permeability, platelet activity, vascularity, and other possible processes. Another possibility is that the IUCD promotes fibrinolysis because it damages the capillary plexus [6].

Assessing the Doppler ultrasound usefulness in the prediction and follow-up of copper 380 IUCD-induced excessive menstrual bleeding was emphasized as a primary area of interest since abnormal uterine bleeding following IUCD insertion constitutes a significant issue and may be linked to consequences [8].

This study was done and aimed to assess HMB related to copper IUCD using initial uterine artery Doppler indices, RI and PI.

This prospective study was conducted at tertiary care hospital at Ain Shams University Maternity hospitals from February 2024 to November 2024 and performed on total 30 women seeking long-acting contraception with IUCDs.

IUDs are widely used, but their association with HMB has prompted significant research into predictive markers, particularly Doppler indices.

The study provided an in-depth evaluation of HMB associated with copper IUCDs by utilizing uterine artery Doppler indices, specifically PI and RI. It adopted a prospective design and included a well-defined cohort of young women aged 20–40years, seeking long-acting contraception without prior hormonal treatment for at least 3 months.

Regarding Demographic data, our study revealed that the mean age of participants was 27.5years, with a mean BMI of 27.9 kg/m², suggesting a predominance of women within a healthy reproductive age range. The majority (60%) had vaginal deliveries, while 40% underwent cesarean

sections. These baseline characteristics established a uniform cohort for analyzing Doppler changes and menstrual bleeding outcomes.

This population was comparable to that of **Sweed *et al.*** [9] who conducted a prospective cohort study that included a larger sample of 110 women to investigate the role of Doppler velocimetry of the uterine artery and endometrial and sub-endometrial vascularization indices in predicting HMB induced by copper IUDs and reported a mean age of 27.6 years with a BMI of 24.2 kg/m², and that of **Özbay & Şanlıkan** [10] who conducted a prospective study involved 55 women to assess the predictive value of uterine and arcuate artery Doppler indices for HMB with participants had a mean age of 28.75 years.

Attia *et al.* [11] conducted a prospective clinical study that enrolled 100 women to evaluate the predictive value of baseline uterine artery Doppler indices for HMB before and after IUD insertion, with follow-ups at three and six months and included women aged 20–40 years, with an average age of 28.01 years, and **Fouda *et al.*** [12] carried out a prospective clinical trial with ninety-three women to find out if elevated uterine artery blood flow, measured through PI and RI, was associated with IUD-induced bleeding and had similar age distributions. These similarities enhance the comparability of findings across studies. A unique feature of our study was the significant relationship observed between BMI and HMB, which other studies did not emphasize to the same extent. This insight underscores the role of body composition in vascular parameters and HMB risk.

Regarding Doppler findings, our findings demonstrated significant reductions in uterine artery PI and RI three months post-IUD insertion. Baseline values of PI≤2.35 and RI≤0.89 showed strong predictive capabilities for HMB, with PI decreasing from 2.41 ± 0.10 at baseline to 2.26 ± 0.13 at three months and RI reducing from 0.92 ± 0.06 to 0.88 ± 0.07. These reductions reflect alterations in uterine artery hemodynamics, indicative of vascular adaptation following IUCD placement.

These results were in line with **Attia *et al.*** [11] who reported PI≤2.02 and RI≤0.83 as predictive, with sensitivity and specificity values above 93%. Similarly, **Fouda *et al.*** [12] identified PI ≤ 2.07 and RI ≤ 0.7 as optimal cutoffs, demonstrating sensitivity of 84.4% and specificity of 83.3%.

Haggag *et al.* [7] carried out a prospective longitudinal analytical study that enrolled 160women to compare Doppler indices across groups and establish optimal cutoff values for predicting AUB, emphasizing the differences in vascular flow patterns between bleeding and non-bleeding cohorts and observed that uterine artery PI and arcuate vessel RI were significantly lower in women with abnormal bleeding. Their reported optimal cutoff for arcuate vessel RI (≤ 0.49) achieved a sensitivity of 87.5% and specificity of 80%. **Özbay & Şanlıkan** [10] corroborated these trends, showing significantly lower uterine and arcuate artery indices in women with HMB, with baseline PI averaging 2.3 in the HMB group. This consistency across studies highlights the predictive value of Doppler indices.

Our study revealed that HMB occurred in 26.7% of participants (8 out of 30) by the three-month mark. A comparison between participants with and without HMB revealed notable differences. Women with HMB had a significantly higher BMI (29.6 ± 2.5 vs. 27.2 ± 2.3, p = 0.020). However, other demographic factors, including age, parity, and mode of delivery, showed no significant differences. Doppler indices also differed significantly between the two groups. Baseline PI was lower in the HMB group (2.30±0.06 vs. 2.45±0.08, p<0.001), as was the three-month PI (2.09 ± 0.08 vs. 2.32 ± 0.09, p < 0.001). The change in PI was greater in women with HMB (-0.21±0.03 vs. -0.13±0.03, p<0.001).

Similar trends were observed for RI, with lower baseline and three-month values in the HMB group and a more pronounced reduction (-0.07 ± 0.02 vs. -0.04 ± 0.01, p < 0.001). However, our study uniquely underscores the longitudinal changes in indices over three months, linking their predictive value to both baseline measurements and follow-up trends. This dynamic approach adds depth to the static assessments prevalent in prior studies.

In our study, the incidence of HMB was 26.7% of participants developed HMB within three months of IUD insertion. This incidence was lower than the 38.2% reported by **Sweed *et al.*** [9] and the 43.6% observed by **Özbay & Şanlıkan** [10]**.**

Attia *et al.* [11] reported a higher incidence of 48%, likely due to their larger sample size and inclusion criteria. **Fouda *et al.*** [12] observed HMB in approximately 34.4% of their participants. These variations in incidence may reflect differences in study populations, diagnostic criteria, and follow-up durations.

Similarly, **Elsayed *et al.*** [8] conducted prospective study included 120 women seeking insertion of the Copper 380 IUD to evaluate Doppler ultrasound indices—including uterine artery PI, RI, and endometrial vascular indices—in predicting and monitoring IUD-induced excessive menstrual bleeding and reported negative correlations between uterine artery PI and RI and the occurrence of HMB, with significant declines post-insertion.

Elsayed *et al.* [8] extended their analysis to sub-endometrial indices like vascularization index (VI) and vascularization flow index (VFI), which were positively correlated with HMB.

Regarding Diagnostic Performance and Predictive Accuracy, the diagnostic capabilities of baseline Doppler indices in predicting HMB were robust. The PI at a cut-off of ≤2.35 showed high specificity (95.5%) and negative predictive value (91.3%), with an AUC of 0.943 (p < 0.001). The RI,

with a cut-off of ≤0.89, exhibited similar specificity (90.9%) and NPV (90.9%), with an AUC of 0.898 ($p < 0.001$). Both indices demonstrated strong diagnostic performance, suggesting their utility in identifying women at risk of developing HMB after IUCD insertion. These findings suggest that Doppler measurements taken prior to IUCD insertion can serve as effective tools for anticipating HMB risk, potentially guiding contraceptive counseling and management.

These results are consistent with **Sweed *et al.*** [9] who demonstrated that endometrial VFI (≥0.18) and sub-endometrial VI (≥3.75) showed high sensitivity (83% and 77%, respectively) and specificity (85% and 80%, respectively) for predicting HMB.

Attia *et al.* [11] demonstrated even higher specificity (100%) for PI and RI, with AUC values of 0.971 and 0.949, respectively with slightly lower sensitivity, while **Elsayed *et al.*** [8] confirmed the predictive role of both uterine and sub-endometrial indices. Similarly, **Fouda *et al.*** [12] reported significant diagnostic accuracy with AUC values of 0.829 for PI and 0.804 for RI. Our findings of a diagnostic accuracy of 90% for PI and 86.7% for RI further support the utility of these indices in clinical practice.

CLINICAL IMPLICATIONS

Our study provides a practical and clinically relevant framework for predicting HMB associated with copper IUDs. By identifying baseline uterine artery PI and RI as significant predictors of HMB, clinicians can utilize Doppler ultrasound as a non-invasive tool to assess vascular changes before IUD insertion. The high specificity of these indices allows for effective risk stratification, enabling early intervention or alternative contraceptive counseling. This predictive capability may reduce the incidence of adverse outcomes, enhance patient satisfaction, and support personalized contraceptive care. Furthermore, integrating Doppler evaluations into routine IUD assessments could refine management protocols and improve overall reproductive health outcomes.

STRENGTHS OF THE STUDY

The study boasts several strengths. One of the key advantages is the focused approach, which simplifies the diagnostic process by emphasizing the utility of uterine artery Doppler indices. This straightforward framework is both clinically actionable and easy to implement in practice. Additionally, the longitudinal design, with follow-ups conducted three months post-IUD insertion, provides critical insights into the temporal dynamics of vascular changes and their correlation with HMB.

The study's robust diagnostic accuracy, with PI and RI cutoffs showing over 90% specificity, underscores the reliability of the findings. Moreover, the inclusion of a homogeneous sample—young, healthy women aged 20–40 years—ensures minimal confounding factors, thereby strengthening the internal validity of the results.

LIMITATIONS

Despite its advantages, the study has several limitations that should be considered. First, the relatively small sample size of 30 participants may limit the generalizability of the findings. To confirm these findings across various demographics and healthcare environments, larger, more varied populations are required. Also, the study focuses solely on copper IUCDs, leaving the applicability of Doppler indices in predicting HMB associated with other types of contraceptives unexplored. Finally, while the Doppler indices provide valuable diagnostic insights, their practical integration into routine clinical workflows may require further standardization and training.

CONCLUSION

Our study underscores the significant role of uterine artery Doppler indices in predicting HMB in women using copper IUDs. The observed reductions in PI and RI three months post-IUD insertion highlight their diagnostic value, with baseline indices demonstrating high specificity and diagnostic accuracy. These findings affirm the utility of Doppler ultrasound as a cost-effective and non-invasive diagnostic tool, enabling healthcare providers to proactively identify and manage women at risk for HMB. The study also emphasizes the importance of early risk stratification in improving clinical outcomes and enhancing patient satisfaction with contraceptive choices.

Based on the findings, the study recommends the incorporation of uterine artery Doppler measurements into pre-IUCD insertion evaluations, particularly for women with risk factors for HMB. Further research with larger, more diverse cohorts is essential to validate the results and expand their applicability. Studies comparing Doppler indices in different types of contraceptives, such as hormonal IUCDs, could provide a broader understanding of their clinical utility.

Author Contributions

- **Concept and design:** Ahmed Mohamed Mamdouh; Mohamed Abdulhameed Mohamed Nasr Eldeen; Mohamed Waheed Soliman El-Molla; Amr Saad Mahmoud Ahmed
- **Acquisition, analysis, or interpretation of data:** Ahmed Mohamed Mamdouh; Mohamed Abdulhameed Mohamed Nasr Eldeen; Mohamed Waheed Soliman El-Molla; Amr Saad Mahmoud Ahmed
- **Drafting of the manuscript:** Ahmed Mohamed Mamdouh; Mohamed Abdulhameed Mohamed Nasr Eldeen; Mohamed Waheed Soliman El-Molla; Amr Saad Mahmoud Ahmed

- **Critical review of the manuscript for important intellectual content:** Ahmed Mohamed Mamdouh; Amr Saad Mahmoud Ahmed
- **Supervision:** Ahmed Mohamed Mamdouh; Mohamed Abdulhameed Mohamed Nasr Eldeen; Amr Saad Mahmoud Ahmed

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