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TRANSVAGINAL ULTRASOUND DOPPLER ASSESSMENT OF SUBENDOMETRIUM BLOOD FLOW IN CASES OF EXCESSIVE MENSTRUAL BLEEDING AFTER INSERTION OF INTRAUTERINE CONTRACEPTIVE DEVICE

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ABSTRACT

Background: The intrauterine contraceptive device (IUCD) is one of the most used methods of contraception all over the world. The most important adverse effects related to copper intrauterine contraceptive device use are excessive uterine bleeding and menstrual pain. This study aimed to evaluate uterine artery and subendometrial blood flow in patients who are complaining of excessive menstrual bleeding after IUCD insertion. Patients and methods: Fifty-four women were included in this cross sectional case control study and they divided into group I (18 women) using copper intrauterine device (Tcu 380A) and complaining of menorrhagia; group II (18 women) using copper IUCD and not complaining of abnormal uterine bleeding and group III (18 women) who not using any contraceptive method and not complaining of abnormal uterine bleeding. Results: There is statistically significant difference between the studied groups regarding subendometrial RI and PI. On doing Turkey's HSD test, the difference is significant between group with IUD and manifested by excessive menstrual bleeding and the group with IUD and normal menstrual flow and control groups. RI was significantly higher in those with IUD and excessive menstrual flow and patients within this group had the lowest PI. The best cutoff of uterine PI in prediction of excessive menstrual bleeding if IUD inserted is ≤1.85 with area under curve 0.936, at which sensitivity 88.9%, specificity 88.9%, positive predictive value 94.1%, negative predictive value 80% and accuracy 88.9% ($p<0.05$).Conclusion: Uterine artery and subendometrial blood flow were increased in women with IUCD induced menorrhagia in comparison to women with copper IUCD and not complaining of abnormal bleeding and women without copper IUCD.

Keywords: Subendometrium Blood Flow; IUCD; Menstrual Bleeding

INTRODUCTION

Intrauterine devices (IUCDs) and contraceptive implants offer highly effective, safe, and long-acting reversible contraception without requiring routine effort from users to maintain effectiveness. In addition, women gain various non-contraceptive benefits during use and experience a rapid return to fertility upon discontinuation **(1).**

These methods do not depend on compliance or user adherence and do not require daily attention or use at the time of intercourse; hence, failure rates are low (1%) **(2)**.

Compared to women using short-acting reversible contraception (e.g., oral contraceptive pills, injectables, patches, or rings), LARC users generally report much

higher satisfaction and method continuation over time; 12-month continuation rates exceed 80% **(3)**.

Abnormal uterine bleeding (AUB) is the current preferred terminology to describe any aberration of menstrual volume, regulation, frequency, and duration according to the classification recommended by the International Federation of Gynecology and Obstetrics (FIGO) **(4).**

Transvaginal color Doppler sonography can be used to obtain flow velocity waveforms at any time during the menstrual period. Apparently there are complex relations between the concentration of ovarian hormones in peripheral blood and uterine artery blood flow parameters **(5)**.

Therefore, this study aimed to evaluate uterine artery and subendometrial blood flow in patients who are complaining of excessive menstrual bleeding after IUCD insertion.

PATIENTS AND METHODS

This cross sectional case control study was performed at Zagazig out patients clinic, during the period between February 2021andAugust 2021 Fifty fourwomen attending Gynecology and family planning outpatient clinic were included in the study.

Women were divided into three groups as follows: **Group (I):** included 18 women using copper T380 IUCD and complaining of menorrhagia. **Group (II)** included 18 women using CuT380 IUCD and not complaining of abnormal uterine bleeding. They attended the outpatient clinic complaining of vaginal discharge or inability to feel the threads of IUCD or requesting IUCD removal. **Group (III):** was a control group which included 18 women without IUCD who attended outpatient clinic complaining of vaginal discharge or requesting copper IUCD insertion and not complaining of abnormal uterine bleeding.

Inclusion and exclusion criteria:

Age of patients ranged from 25 to 40 years old. Regular menstrual cycle. Body mass index < 30 kg/m^2. While, Bleeding tendencies and general causes as Von Willebrand disease, Pregnancy and Patients on anti–coagulant and non-steroidal antinflammatory drugs.

Methods:

Detailed clinical history was taken from the patients with special consideration to age, parity, duration of IUCD insertion and history of other contraception before insertion of IUCD. Menstrual history before and after IUCD insertion was taken including duration and amount of menstrual flow, regularity and length of the cycle, intermenstrual bleeding or spotting contact bleeding. In addition, history of any drug intake, blood disease or any medical disorders were considered.

Clinical examination was done including general, abdominal and pelvic examination which included bimanual examination to detect any abnormal findings and speculum examination to detect the threads of the IUCD and exclude any local cause of bleeding as polyp and erosion.

Timing of ultrasound scanning and Doppler evaluation:

Ultrasoundexamination and Doppler assessment of subendometerium blood flow, right and left uterine arteries were carried out between days 7-10 of the cycle.

Technique of transvaginal ultrasound and Doppler examination:

The woman were instructed to empty the urinary bladder before examination. The uterus and adnexa were initially visualized using conventional B mode ultrasound toexclude any uterine or ovarian pathology. The probe was turned 90 degree at the level of cervix to bring its transverse section and the flow velocity wave forms of the

main uterine artery were obtained on right and left sides at the level of the inner cervical os just beside the cervix. When three systolic peaks of equal heights were visualized, the image was frozen on display screen and sonographic printout is taken for further analysis. Doppler indices of the main right and left uterine arteries were measured and mean was obtained. The probe was swipe up to visualize mid-sagittal view and the flow velocity wave forms of the Subendometerium.

Equipment:

The ultrasound equipment used was a Voluson 730 system with 6-9 MHz transvaginal transducer.

Doppler study was performed upon:

1) The right and left uterine arteries.
2) Sub-endometrial blood flow.

The Doppler indices, which wereused are the pulsatility index (PI; A-B/mean) and the resistance index (RI; A-B/A), in which A was the maximum (systolic)Doppler frequency shift; Bwas the minimum (diastolic) Dopplerfrequency shift; and the mean represented the average Doppler frequency shift. Three waveforms werestudied for the sub-endometrial blood flow, right and left uterine arteries.

Statistical analysis:

Data performed using the software SPSS (Statistical Package for the Social Sciences) version 20. Quantitative variables were described using their means and standard deviations. Categorical variables were described using their absolute frequencies and were compared using chi square and Fisher exact test when appropriate. Kolmogorov-Smirnov (distribution-type) and Levene (homogeneity of variances) tests, independent sample t test were used. Kruskal wallis test and Turkey HSD were used. p value of one way ANOVA test was <0.05. ROC curve was used to calculate performance of cutoff of certain marker in diagnosis of health problem. The level statistical significance was set at $P<0.05$. Highly significant difference was present if $p\leq0.001$.

RESULTS

The present study showed a statistically non-significant difference between the studied groups regarding parity or mode of delivery **(Table 1)**. There is statistically non-significant association between duration of IUD insertion and occurrence of heavy menstrual flow among the studied patients **(Table 2)**.

There is statistically significant difference between the studied groups regarding subendometrial RI and PI. On doing Turkey's HSD test, the difference is significant between group with IUD and manifested by excessive menstrual bleeding and the group with IUD and normal menstrual flow and control groups. RI was significantly higher in those with IUD and excessive menstrual flow and patients within this group had the lowest PI **(Table 3)**.

The best cutoff of sub-endometrial PI in prediction of excessive menstrual bleeding if IUD inserted is ≤1.74 with area under curve 0.845, at which sensitivity 88.9%, specificity 75%, positive predictive value 64%, negative predictive value 93.1% and accuracy 79.6% ($p<0.05$) **(Table 4 & Figure 1)**.

The best cutoff of uterine PI in prediction of excessive menstrual bleeding if IUD inserted is ≤1.85 with area under curve 0.936, at which sensitivity 88.9%, specificity 88.9%, positive predictive value 94.1%, negative predictive value 80% and accuracy 88.9% ($p<0.05$) **(Table 5 & Figure 2)**.

Table (1): Comparison between the studied groups regarding obstetric data:

Parameter	Groups			Test	
	IUD with excessive bleeding group	IUD without excessive bleeding group	Control group	KW/χ^2	p
	N=18 (%)	N=18 (%)	N=18 (%)		
Parity:					
Median	3	3	1	3.613	0.164
Min – max	2 – 4	2 – 4	0 – 5		
Mode of delivery	11 (61.1)	8 (44.4)	11 (68.8)	MC	0.37
NVD	7 (38.9)	9 (50)	5 (31.2)		
CS	0 (0)	1 (5.6)	0 (0)		
CS after NVD					

KW Kruskal Wallis test MC Monte Carlo test χ^2 chi square test

Table (2) Association between duration of IUD and excessive menstrual bleeding:

Duration (year)	IUD w		Test	
	With excessive menstrual bleeding	With average menstrual bleeding	t	p
	N=18	N=18		
Mean ± SD	4.222 ± 2.686	4.167 ± 1.85	0.062	0.951
Range	0.5 – 10	2 – 8		

t independent sample t test

Table (3) Comparison between the studied groups regarding sub-endometrial Doppler:

Parameter	Groups			Test	
	IUD with excessive bleeding group	IUD without excessive bleeding group	Control group	F	p
	N=18 (%)	N=18 (%)	N=18 (%)		
RI:					
Mean ± SD	0.79 ± 0.14	0.66 ± 0.19	0.5 ± 0.12	7.939	0.001**
Min – max	0.54 – 0.98	0.31 – 0.89	0.42 – 0.79		
Turkey's HSD	P_1 0.038*	P_2 0.346	P_3<0.001**		
PI:					
Mean ± SD	1.45 ± 0.3	2.0 ± 0.62	2.09 ± 0.32	5.616	0.006*
Min – max	1.0 – 1.87	1.32 – 3.05	1.18 – 2.7		
Turkey's HSD	P_1 0.001**	P_2 0.815	P_3<0.001**		

**p≤0.001 is statistically highly significant *p<0.05 is statistically significant F One way ANOVA test

Table (4) Performance of subendometrial RI in prediction of excessive bleeding if IUCD inserted among the studied participants:

cutoff	AUC	Sensitivity	Specificity	PPV	NPV	Accuracy	P
≤1.74	0.845	88.9	75	64	93.1	79.6%	0.001**

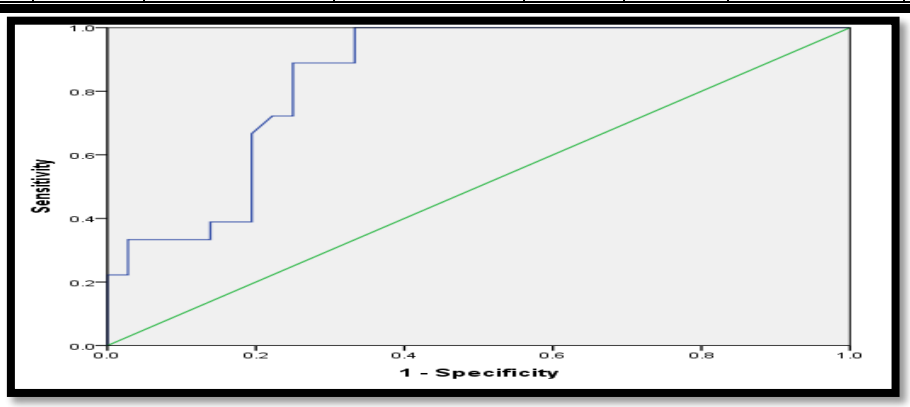

Figure (1) ROC curve showing performance of subenodometrial RI in prediction of excessive bleeding if IUCD inserted among the studied participants

Table (5) Performance of uterine PI in prediction of excessive bleeding if IUCD inserted among the studied participants:

cutoff	AUC	Sensitivity	Specificity	PPV	NPV	Accuracy	P
≤1.855	0.936	88.9	88.9	94.1	80	88.9%	0.001**

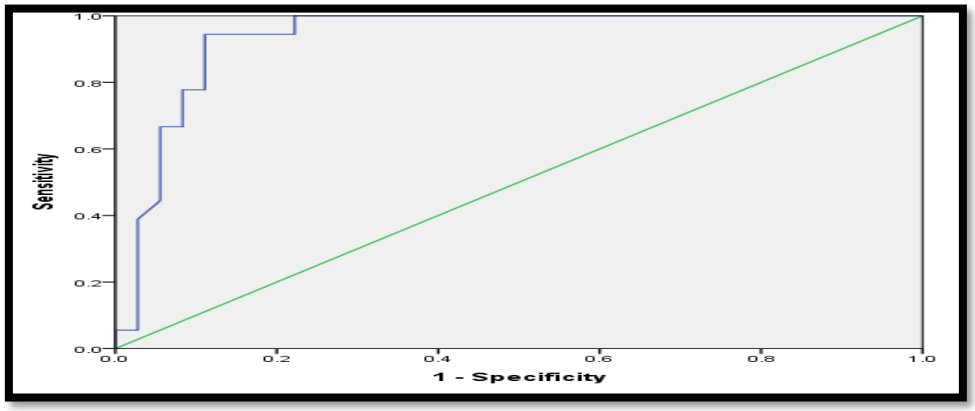

Figure (2) ROC curve showing performance of uterine artery PI in prediction of excessive bleeding if IUCD inserted among the studied participants

DISCUSSION:

An intrauterine contraceptive device (IUCD) is one of the most frequently used methods for birth control around the world. However, menorrhagia is among its side effects. Menorrhagia may cause iron deficiency anemia and usually ends by removing the IUCD in the first year after its insertion in many cases **(6).**

This cross sectional case control study to assess uterine artery, subendometrial microvascularization indices in relation to heavy menstrual bleeding as a predictor the risk of bleeding after IUCD insertion.

The current study is in harmony with **Al-Araji et al. (7)** included 58 women divided into two groups: the control group 30 women without IUCD and the 2nd group 28 women with copper coated IUCD. Their age mean of

(28.7± 6.5) years. And the parity is ranging between (0-8) with a mean of (2.9± 2.1), and both groups were comparable with no statistically significant difference.

Our results in agree with the study by **El-Mazny et al. (8)** revealed 47 (39.2%) had menorrhagia after IUD insertion (group A), whereas 73 (60.8%) had no menorrhagia (group B). They found no significant difference in the clinical characteristics, age (P=0.273) and parity (P=0.387) between the two groups.

A prior prospective observational study was performed by **Mansour et al. (6)** on 60 cases at family planning outpatient clinics in the maternity hospital, Ain Shams University for insertion of an IUCD were categorized into two research groups: Research group 1 (30 cases) no menorrhagia and research group 2 (30 cases) presence of menorrhagia. There was no statistically significant difference among the two research groups concerning the demographic data.

A possible mechanism explaining the association of the PI of uterine artery with menstrual blood loss may be that women with menorrhagia show a significant increase in endothelial cell proliferation, reflecting disturbed angiogenesis. It is possible that there are also other vascular abnormalities resulting from disturbed angiogenesis. In abnormal vessels, poor contractibility and dysfunction of the haemostatic system may cause menorrhagia and decreased impedance **(9).**

In agreement with us, **Jarvela et al. (10)** evaluated the effects of a copper IUCD on uterine artery blood flow in 21 women with regular menstrual cycles using copper IUCDs. In patients with increased IUCD-related pain during menstruation (n = 5), however, there was a decrease in the PI after IUCD insertion. They concluded that the copper IUCD does not induce any major changes in the resistance of uterine artery blood flow, although during menstruation in patients with increased menstrual pain after IUCD insertion, there seems to be a decrease in the uterine artery PI (**Järvelä et al., 1998)**.

Frajndlich et al. (11) also observed that women who had abnormal bleeding had a significantly lower PI and RI of the uterine arteries when compared with control subjects. They concluded that when the PI of the uterine arteries is greater than 2.00, women might be at higher risk for development of IUCD induced bleeding.

Similarly, **Mohamed and Abdel Hakim (12)** conducted on 60 patients referred to the gynecology outpatient clinic for insertion of an IUCD (Cu T-380A), the patients were classified into two groups: Group (1): 30 cases not complaining of menorrhagia. Group (2) included 30 cases complaining of menorrhagia. A highly significant difference between the two studied groups regardinguterine artery resistance index after 3 months of IUCD insertion. They found highly significant difference between the two studied groups regarding uterine artery pulsatility index after 3 months of IUCD insertion**.**

This study was in line with **Al-Araji et al.(7)** found that in women with IUCD induced heavy menstrual loss, the blood flow indices of the uterine arteries are much lower (PI was 1.78) when compared with the women without menorrhagia, with or without IUCD (PI > 2).

Likewise, **Yigit et al. (13)** reported that women using IUCD with increased bleeding scores had significantly lower PI values compared with those without increased bleeding scores, PI values being lower than 2 in the former group.

Furthermore **Munro et al. (14)** assessed and evaluated the PI and RI of uterine arteries in 68 study subjects, involving 44 cases using intrauterine contraceptive device and 24 control study subject not using a contraceptive method. Both the PI and RI were statistically significantly lower in cases with IUCD- triggered bleeding than in those using IUCD and not complaining of abnormal vaginal bleeding **(Munro et al., 2011)**.

In line with our study, Ninety-three women were examined by **Fouda et al**. **(15)** and divided into three groups. Group I; included 32 women using CIUD (TCu-380A) and complaining of menorrhagia, group II; included 30 women using CIUD with normal menstrual flow and group III which was a control group. They used the ROC curves to detect the optimum cutoff of PI and RI for discrimination between women with CIUD-induced abnormal uterine bleeding and women using CIUD with normal menstrual bleeding. The ROC curves reveal that PI>2.07 has sensitivity 84.4% and specificity 83.3% in detecting women with CIUD-induced abnormal uterine bleeding and RI>0.7 has sensitivity 78.1% and specificity 80% in detecting women with CIUD-induced abnormal uterine bleeding**.**

In contrast, **El-Mazny et al. (8)** measured PI and RI of uterine arteries and subendometrial in 120 women before and three months after the copper IUD insertion, concluded that it was not predictive for menorrhagia. Their studyas a prospective studydepended only on the number of cases of menorrhagia among all the cases with IUCD, the number of menorrhagia cases in their study, forty seven cases may not express the whole population.

CONCLUSION:

Uterine artery and subendometrial blood flow were increased in women with IUCD induced menorrhagia in comparison to women with copper IUCD and not complaining of abnormal bleeding and women without copper IUCD.

No Conflict of interest.

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