Color Doppler Ultrasound Assessment of the Uterine and Intraovarian

Arteries Blood Flow in Cases of Menorrhagia

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ABSTRACT

Background: Menorrhagia (menstrual bleeding >80 ml per period) is one of the most common problems in gynecology. Menorrhagia is a menstrual period with excessively heavy flow and falls under the larger category of abnormal uterine bleeding (AUB).

Objectives: To use the transvaginal color Doppler to study the blood flow in the uterine and intraovarian arteries in patients with menorrhagia. To add more to the service of Doppler ultrasound in Aswan University Hospital.

Patients and methods: This is a cross sectional observational study which was done in the Department of Obstetrics and Gynecology, Aswan University Hospital. The study included 100 ladies. Fifty women came complaining of menorrhagia and another 50 women were regularly menstruating with normal cycles.

Results: There was a highly statistically significant difference in the Doppler indices of both the right and left uterine arteries between the cases of menorrhagia and the control group. There was no statistically significant difference in the Doppler indices of the right and left intraovarian arteries between the cases of menorrhagia and the control group. There was a strong positive correlation between the uterine volume and Doppler indices of the uterine arteries in cases of menorrhagia while only positive correlation with pulsatility index in regularly menstruating women.

Conclusion: Vascular changes may play an important role, in the occurrence of menorrhagia, so the use of the transvaginal color Doppler to study the blood flow in the uterine and intraovarian arteries is a useful adjuvant diagnostic tool.

Keywords: Menorrhagia, Color Doppler Ultrasound, Uterine and Intraovarian Arteries Blood Flow.

INTRODUCTION

Abnormal uterine bleeding can be caused by structural abnormalities in the reproductive tract, anovulation, bleeding disorders, hormone issues (such as hypothyroidism) or cancer of the reproductive tract. Initial evaluation aims at figuring out pregnancy status, menopausal status, and the source of bleeding ⁽¹⁾. Approximately 53 in 1000 women are affected by AUB ⁽²⁾.

Although new diagnostic methods improved the clinical triage of menorrhagia, approximately half of the cases show no underlying pathology ⁽³⁾. Vascular changes may play an important role, but remain poorly studied.

Transvaginal Doppler is a non-invasive method for studying changes of blood flow which may highlight the underlying pathology in cases with menorrhagia. Studies with transvaginal sonography (TVS) coupled with color Doppler have shown that the uterine artery pulsatility index (PI), measuring arterial flow impedance ⁽⁴⁾, is higher in amenorrhoeic and climacteric than in menstruating women ⁽⁵⁾. On the other hand, PI is reduced by hormone replacement therapy and the restoration of cyclic withdrawal bleeding ⁽⁵⁾.

Moreover, women with menorrhagia induced by an intrauterine device (IUD) have lower PI values than those without menorrhagia, with or without IUD ⁽⁶⁾. These data imply a possible association between uterine blood flow and menstrual blood loss (MBL).

Treatment depends on the cause, severity, and interference with quality of life. ⁽⁷⁾. Initial treatment often involves contraceptive pills. Surgery can be an effective second line treatment for those women whose symptoms are not well-controlled ⁽⁸⁾.

AIM OF THE WORK

- 1. To use the transvaginal color Doppler to study the blood flow in the uterine and intraovarian arteries in patients with menorrhagia.
- 2. To find if Doppler can differentiate between dysfunctional and organic causes.
- 3. To add more to the service of Doppler ultrasound in Aswan University Hospital.
- 4. To find the relation between the endometrial thickness, uterine volume and uterine and Intraovarian blood flow in cases of menorrhagia.

PATIENTS AND METHODS

Sitting: Department of Obstetrics and Gynecology, Aswan University Hospital. Device Used: GE Voluson S8 Ultrasound. **Type of study**: cross sectional observational study. **Sample size:** The sample size was set as 100 ladies. Fifty women came complaining of menorrhagia at the Department of Obstetrics and Gynecology, Aswan University Hospital. The patients were divided in categories according to the cause and diagnosis. Another 50 women were regularly menstruating with normal cycles.

Inclusion criteria:

- 1. Regularly menstruating women with menorrhagia ⁽¹⁾.
- 2. Age between 20 and 45 years,
- 3. Hormonal treatment has not been taken at least 2 months before the study.
- 4. Non-steroidal anti-inflammatory has not been taken 24 h before the examination.

Exclusion criteria:

- 1. Acyclic bleeding (metrorrhagia).
- 2. Receiving anti-coagulant.
- **3.** Receiving hormonal treatment.
- 4. Using IUD either hormonal or non-hormonal.
- 5. Patients with bleeding tendency or thrombophilia.

Intervention: All patients were subjected to the following:

- A detailed history including parity, contraceptive method, menstrual pain, regularity of cycles from all women.
- Careful pelvic examination to identify uterine size and position.
- Patients were scheduled for TVS at the proliferative phase preferably during the 2nd or 3rd day of the cycle.

Transvaginal ultrasonography (TVUS): to

- Measure the uterine size (length, anteroposterior and transverse diameter).
- Endometrial thickness was identified by measuring the distance in mm between the two basal layers of anterior and posterior uterine wall.
- Uterine volume, the volume was calculated by measuring the maximum length and anteroposterior and transverse diameters of the uterine corpus, and using the formula for the volume of a prolate ellipsoid: $V = 0.52 \times (L \times AP \times T)$.
- If there is myoma and its size.
- The presence of adenomyosis.
- Any uterine pathology.

Transvaginal pulsed Doppler (TVPD) on uterine arteries:

- Ultrasound examination was done using an ultrasound duplex system. This duplex system combines B-mode imaging (linear and sector probes) and bidirectional pulsed colored Doppler technique with real time spectral analysis. The high pass filter was set on 125 Hz. All examinations were performed at the beginning of a menstrual cycle (day 2 or 3).

- Doppler examination was done using 7.5 MHz transvaginal probe with pulsed and color Doppler facilities. Color Doppler was used to identify vessels of interest and served as a guide for pulsed Doppler velocimetry studies.
- The patients were examined in the dorsal lithotomy position. The transducer was inserted into a condom with a coupling jelly. The transducer was inserted into the vaginal fornix with the aid of lubricating jelly and directed along the paracervical area. In each case, flow velocities were obtained from both main uterine arteries at the level of internal os.
- The image then was frozen including at least three waveform signals. Color flow mapping and pulsed Doppler measurements were performed on ovarian stromal blood vessels once normal pelvic findings were confirmed. Areas of maximum color intensity, representing the greatest Doppler frequency shifts, were selected for pulsed Doppler examinations. Blood flow velocity waveforms were detected and recorded. We tried to get angles between the pulsed Doppler beam and the vessel close to zero or as low as possible.
- Then calculations of PI, RI and S/D ratio for both uterine and intraovarian arteries.
- All examinations were performed between 10.00AM 1:00 PM to reduce the effect of circadian variation in PI ⁽⁹⁾.
- Dilatation and curettage biopsy were done in suspicious cases.

Study outcomes:

- 1. Comparison between the Doppler finding in the cases of menorrhagia and normally menstruating women.
- 2. Gained experience in the use of Doppler and introduce it as a service in Aswan University Hospital.

Ethical aspect: All the regulation of the ethical committee of the Faculty of Medicine was followed. Each patient had private file with nondisclosure policy at data presentation where all presented data didn't contain any personal information specifying the identity of any of the patients. All the patients had clear verbal and written description about the study. Only those who consented to participate after descriptions were enrolled in the study.

Statistical analysis

The collected data were revised, coded, tabulated and introduced to a PC using Stat view using Apple Macintosh. Quantitative variables are expressed as mean, SD, and range or as median and interquartile range (IQR) in cases of nonparametric variables. Qualitative variables were expressed as frequencies and percent. **Student t test** and **Mann Whitney** test were used to compare a continuous variable between two study groups. P-value <0.05 was considered statistically significant.

RESULTS

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Table	(1).	Chincar	char acteristic	01	Cases	01	menorrhagia	anu	control.

Variable	Cases (Menorrhagia) N = 50	Control (Regularly menstruating) N = 50	P value
Age (Years):			
Mean <u>+</u> SD	42.54 <u>+</u> 6.33	27.68 <u>+</u> 8.21	0.0001
Range	24 - 52	16 - 43	0.0001
Parity :			
Mean <u>+</u> SD	3.6 <u>+</u> 1.67	0.9 <u>+</u> 1.2	0.0001
Range	0 - 7	0 - 5	0.0001
Duration of marriage:			
(Years):	21.5 ± 7.20	7 46 5 08	
Mean <u>+</u> SD	$\frac{21.3 \pm 7.29}{5.22}$	/.40 <u>+</u> 5.98	0.0001
Range	5 - 35	1 - 19	

This table shows the clinical characteristics of cases and control, showing that there was a highly statistically significant difference between both groups regarding age, parity and duration of marriage.

Variable	Right uterine artery in cases (Menorrhagia) N = 50	Right uterine artery in control (Regularly menstruating), N = 50	P value
S/D:			
Mean <u>+</u> SD	4.95 <u>+</u> 1.62		
Range	2.83 - 11.14	00	
Resistance index:			
Mean <u>+</u> SD	0.77 <u>+</u> 0.07	1 <u>+</u> 0	0.0001
Range	0.56 - 0.91	1 - 1	
Pulsatility index:			
Mean+SD	1.73 <u>+</u> 0.39	4.33 ± 0.92	0.0001
Range	.78 - 2.52	2.27 - 6.23	

Table (2): Doppler blood flow in right uterine arteries in cases of menorrhagia and control groups.

S/D: systolic diastolic ratio

This table shows that there was a highly statistically significant difference in the Doppler indices of the right uterine artery between the cases of menorrhagia and the control group.

Table (3): Doppler blood flow in left uterine arteries in cases of menorrhagia and control gr

Variable	Left uterine artery in cases (Menorrhagia) N = 50	Left uterine artery in control (Regularly menstruating), N = 50	P value
S/D:			
Mean <u>+</u> SD	5.19 <u>+</u> 1.56	~	
Range	2.38 - 8.33	ω	
Resistance index:			
Mean <u>+</u> SD	0.77 ± 0.08	1 <u>+</u> 0	0.0001
Range	0.58 -0 .88	1 - 1	
Pulsatility index:			
Mean <u>+</u> SD	1.82 <u>+</u> 0.49	4.34 <u>+</u> 0.95	0.0001
Range	0.78 - 3.37	2.2 - 6.22	

S/D: systolic diastolic ratio

This table shows that there was a highly statistically significant difference in the Doppler indices of the left uterine artery between the cases of menorrhagia and the control group.

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Variable	Right intraovarian artery in cases (Menorrhagia) N = 50	Right intraovarian artery in control (Regularly menstruating) N = 50	P value
S/D:			
Mean <u>+</u> SD	6.22 <u>+</u> 1.51	6.31 <u>+</u> 2.67	NS
Range	2.29 - 8.6	2.11 - 13.5	
Resistance index:			
Mean <u>+</u> SD	0.84 ± 0.08	0.77 <u>+</u> 0.12	NS
Range	0.56 - 0.92	0.53 - 0.93	
Pulsatility index:			
Mean <u>+</u> SD	2.69 <u>+</u> 0.91	2.59 <u>+</u> 0.76	NS
Range	0.93 - 4.61	0.73 - 3.41	

S/D: systolic diastolic ratio

This table shows that there was no statistically significant difference in the Doppler indices of the right intraovarian artery between the cases of menorrhagia and the control group.

Table (5): Dop	pler blood fl	ow in left	t intraovarian	arteries in o	cases of men	orrhagia and	l control grou	ıp.

Variable	Left intraovarian artery in cases (Menorrhagia) N = 50	Left intraovarian artery in control (Regularly menstruating) N = 50	P value
S/D:			
Mean <u>+</u> SD	6.72 <u>+</u> 2.64	6.69 <u>+</u> 2.63	
Range	2.29 - 13	2.29 - 13	NS
Resistance index:			
Mean <u>+</u> SD	0.82 ± 0.09	0.82 ± 0.09	
Range	0.56 - 0.92	0.56 -0. 92	NS
Pulsatility index:			
Mean+SD	2.63 <u>+</u> 0.96	2.62 <u>+</u> 0.96	
Range	0.94 - 4.68	0.93 - 4.61	NS

S/D: systolic diastolic ratio

This table shows that there was no statistically significant difference in the Doppler indices of the left intraovarian artery between the cases of menorrhagia and the control group.

Table (6): Correlation between uterine volume and Doppler indices.

	r ²	Р
Menorrhagia N=50		
S/D	0.05	0.01
RI	0.01	0.001
PI	0.01	0.001
Control N=50		
S/D	0.72	NS
RI	0.69	NS
PI	0.03	0.01

S/D: systolic diastolic ratio RI: resistance index PI: pulsatility index

There is a strong positive correlation between the uterine volume and Doppler indices of the uterine arteries in cases of menorrhagia while only positive correlation with pulsatility index in regularly menstruating women.

DISCUSSION

In our study we found that the menorrhagia group had a highly statistically significant older age, higher parity and longer duration of marriage than normally menstruating group, which is agreed with the finding of **Tokyol** *et al.* ⁽¹⁰⁾ **and Shapley** *et al.* ⁽¹¹⁾.

In this study the uterine volume was significantly higher in cases of menorrhagia which may be due to multiparty and the associated increase in the uterine volume and increased vascularity in some cases and the presence of some pathology (leiomyoma in some cases and adenomyosis in some others).

Also the endometrial thickness was significantly higher in cases of menorrhagia which attributed to associated hormonal disturbance leading to increased thickness and vascularity. This is in accordance with the finding of **Aleem** *et al.* ⁽¹²⁾ who found that endometrial thickness had better sensitivity and specificity to discriminate between benign and malignant or normal and pathologic endometrium.

Aleem et al. (12) and Khanna et al. (13) found transvaginal color and pulsed Doppler that sonography of endometrium have a possible role in reducing number of dilation and curettage procedure. They did a prospective study on 42 postmenopausal patients with pathological endometrium. These patients underwent TVS for endometrial thickness (cut-off value of 8 mm), rates of visualization and density of uterine, myometrial (peritumoral) and endometrial (intratumoral) vessels were used to assess and correlate with endometrium pathology. Resistive index and pulsatility index values of these studied vessels of endometrial carcinoma were significantly lower than those for endometrial hyperplasia. In 80% of cases of endometrial carcinoma, dense vascularity was found in myometrium.

Fibroid was found in 8 cases (16% of cases with menorrhagia) which in agreement with the finding of **Stovall** ⁽¹⁴⁾, who found that fibroid was found in about 20% of cases with menorrhagia and **Cramer and Patel** ⁽¹⁵⁾ who found more incidences in the hysterectomy specimens. This can be explained by the finding that the myometrium in leiomyomatous uteri showed an increase in the venous plexus, especially at the edge of the leiomyomas ⁽¹⁶⁾.

Early studies also noted an increased vascular supply to leiomyomas; fibroids are very vascular, containing thick walled muscular vessels. This dysregulation of normal vascular function in leiomyomas may be attributed to abnormalities in expression of angiogenic growth factors and their receptors ^(16, 17). In a recent study, blood flow and angiogenic gene expression was investigated in fibroid, perifibroid and distant myometrium. Blood flow in tissue around leiomyomas was higher than within the leiomyoma, although there was heterogeneity.

Adenomyosis was found in 7 cases (14% of cases with menorrhagia) which in agreement with the finding of **Naftalin** *et al.* ⁽¹⁸⁾, who found that adenomyosis was found in about 20% of cases with menorrhagia.

The uterine blood flow was significantly higher and the Doppler indices were significantly lower in cases of menorrhagia in comparison to the normally menstruating women. This is in accordance with the findings of **Lakhani and Hardiman** ⁽¹⁹⁾. They demonstrated that uterine vascular resistance, measured as the pulsatility index (PI), is lower in women with menorrhagia associated with fibroids than in healthy controls.

Also these findings are in agreement with the findings of **Momtaz** *et al.* ⁽⁶⁾ who found that women with menorrhagia induced by an intrauterine device (IUD) have lower PI values than those without menorrhagia, with or without IUD. These data imply a possible association between uterine blood flow and menstrual blood loss (MBL).

To the best of our knowledge this is the first study, that studied the blood flow in the intraovarian vessels in cases of regularly menstruating women and in women with menorrhagia, and we found no statistically significant difference between both groups. This is mostly due to that the changes which occurred in the blood flow in cases of menorrhagia did not affect the intraovarian blood vessels.

Previous study compared the blood flow in the intraovarian vessels in cases of normally and regularly menstruating women and women with polycystic ovarian syndrome and found that Doppler indices were statistically significantly decreased in women with polycystic ovarian syndrome mostly due to neoangiogenesis/⁽²⁰⁾.

There was a strong "positive correlation between the uterine volume and Doppler blood flow and strong negative correlation with the Doppler indices of the uterine arteries in cases of menorrhagia while only positive correlation with pulsatility index in regularly menstruating women. This could be explained by increasing the uterine volume; the blood flow increased and the Doppler indices decreased due to decreasing the vascular resistance.

Strength of the study:

- 1. It is an outpatient procedure easily to be done and did not need surgical intervention.
- 2. It can differentiate between some pathology as myoma from localized adenomyosis.
- 3. It can decrease the surgical intervention by endometrial thickness and blood flow.

Limitations of the study:

- 1. Lack of a histopathology gold standard.
- 2. The fact that premenopausal women with abnormal uterine bleeding may present with an endometrial thickness that is inherently difficult to evaluate because it may be affected by exogenous or endogenous sex hormones.
- 3. It needs a bigger number of patients to study the different groups with different pathology.

CONCLUSIONS

- Vascular changes may play an important role, in the occurrence of menorrhagia, so the use of the transvaginal color Doppler to study the blood flow in the uterine and intraovarian arteries is a useful adjuvant diagnostic tool.
- The use of color Doppler transvaginal ultrasonography (CDTU) of the endometrium is an important part of the evaluation of women presenting abnormal uterine bleeding (AUB). It is fairly sensitive, specific, non-invasive, lowcost procedure with good patient acceptability. In patients with AUB, ultrasound-based triage has become widely accepted.
- The role of color Doppler sonography to discriminate between benign and malignant endometrial condition in women presenting with abnormal bleeding and thickened endometrium is not conclusive, but it can help in the diagnosis.
- Color Doppler transvaginal ultrasonography would result in a significant reduction of endometrial biopsy or curettage.

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