**Alieksieieva O. S., Lazurenko V. V., Vasylieva I. A., Afanasiev I. V., Kudin I. D., Harkavenko K.V. Features of ultrasound and dopplerometric endometry examination in autoimmune thyroiditis patients with abnormal uterine bleeding. Journal of Education, Health and Sport. 2022;12(1):539-550. eISSN 2391-8306. DOI http://dx.doi.org/10.12775/JEHS.2022.12.01.045**
**https://apcz.umk.pl/JEHS/article/view/43456**
**https://zenodo.org/record/7808666**

**The journal has had 40 points in Ministry of Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of December 1, 2021. No. 32343. Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical Culture Sciences (Field of Medical sciences and health sciences); Health Sciences (Field of Medical Sciences and Health Sciences).**

**Punkty Ministerialne z 2019 - aktualny rok 40 punktów. Załącznik do komunikatu Ministra Edukacji i Nauki z dnia 1 grudnia 2021 r. Lp. 32343. Posiada Unikatowy Identyfikator Czasopisma: 201159. Przypisane dyscypliny naukowe:Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu).**



**Received: 05.01.2022. Revised: 21.01.2022. Accepted: 31.01.2022.**

# FEATURES OF ULTRASOUND AND DOPPLEROMETRIC ENDOMETRY EXAMINATION IN AUTOIMMUNE THYROIDITIS PATIENTS WITH ABNORMAL UTERINE BLEEDING

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## Abstract

Abnormal uterine bleeding occurs in 10–30% of reproductive age women. Ultrasound examination is one of the most effective methods of diagnosing lesions of the pelvic organs while it has high sensitivity (96%), but low specificity (13.8%) in relation to endometrial lesions, the informativeness of ultrasound in the diagnosis of abnormal uterine bleeding ranges from 60 to 93.3%. It had been revealed revealed that the imbalance of thyroid hormones can have a direct effect on the endometrium. Thus, the analysis of ultrasound examinations data together with dopplerometric assessment of the blood flow of the internal genital organs in autoimmune thyroiditis patients with abnormal uterine bleeding is an urgent

task of modern gynecology. **The purpose** is to determine the features of ultrasound exanimation with Doppler assessment of the endometrium in autoimmune thyroiditis patients with abnormal uterine bleeding. **Materials and methods.** The patients' examinations were carried out from 2019 to 2022 We examined 120 patients, of whom 90 (75%) suffered from abnormal uterine bleeding and 30 (25%) did not have signs of gynecological and somatic pathology (control group). Abnormal bleeding patients average age was 36.3±3.2 years. The average age of bleeding and thyroid pathology women was 34.8±2.6 years, the control group average age was 30.7±2.9 years. **Results.** Echographic signs of endometrium structural changes were detected in 83 (92.2%) of abnormal nautoimmune bleeding women and in 7 (7.8%) women ultrasound signs of pathology were not detected. Significant differences were found when analyzing the results of ultrasonographic examination of patients with bleeding and bleeding + thyroid pathology. **Conclusion.** Ultrasound is an important method that contributes to a significant improvement in the diagnosis of isolated or combined benign uterine diseases in women with abnormal autoimmune bleeding at the background of thyroid pathology, and in most cases corresponds to the histological diagnosis.

**Key words: abnormal autoimmune bleeding; thyroid pathology; woman of reproductive age**

**Introduction.** Abnormal uterine bleeding (AUB) is considered to be changes in the menstrual cycle, which are associated with their increased volume, duration and frequency. It occurs in 10–30% of reproductive age women [1, 2, 3].

To determine the exact cause of AUB is a key element in achieving effective treatment. It is believed that ultrasound examination (USDE) is one of the most effective methods of diagnosing lesions of the pelvic organs, which has high sensitivity (96%), but low specificity (13.8%) in relation to endometrial lesions [ 5]. According to the data of literature, the informativeness of ultrasound in the diagnosis of AUB ranges from 60 to 93.3%.

The vast majority of AUB patients are women of reproductive age. It is noted that the most common cause of their AUB is structural disorders, in particular polyps and leiomyomas; ovulatory dysfunction and endometrial lesions are also common. Among women of peri- and postmenopausal age, AUB is etiologically caused mainly by organic lesions, in particular, hyperplastic states or endometrial cancer.

The frequency and prevalence of hyperplastic processes of reproductive organs, in particular, the uterus, remains at a high level. Thus, the incidence of polyps tends to increase with age and is 8–35%.

The study of the pathogenetic aspects of hormonal regulation influence, changes in reproductive function and the development of lesions of the reproductive system revealed that the imbalance of thyroid hormones can have a direct effect on the endometrium.

Thus, the analysis of USDE data together with dopplerometric assessment of the blood flow of the internal genital organs in autoimmune thyroiditis (AIT) patients with AUB is an urgent task of modern gynecology.

**The purpose** is to determine the features of USDE with Doppler assessment of the endometrium in AIT patients with AUB.

**Materials and methods.** The patients' examinations were carried out from 2019 to 2022 at the clinical base of the Department of Obstetrics and Gynecology No. 2 of the Kharkiv National Medical University in the Kharkiv Regional Perinatal Center as a part of the "Regional Clinical Hospital". To achieve the purpose and fulfill the set tasks, we examined 120 patients, of whom 90 (75%) suffered from AUB and 30 (25%) did not have signs of gynecological and somatic pathology (control group).

Verification of AUB was carried out according to the recommendations of the International Federation of Obstetricians and Gynecologists (FIGO, 2011). AUB patients were divided into two clinical groups (main and comparison), the presence of thyroid glad pathology was taken into account. The first (main) group consisted of 60 women with AUB and thyroid pathology, the second group (comparison) included 30 patients with AUB. Verification of TG diseases was carried out together with an endocrinologist. The scope of the examination and the choice of treatment tactics were carried out in accordance with the order of the Ministry of Health of Ukraine dated April 13, 2016 No. 353 (Unified clinical protocol "Abnormal uterine bleeding").

The control group consisted of 30 women without somatic and gynecological pathology.

All patients signed an informed consent for examination and treatment during hospitalization. The examinations made were carried out with respect for human rights, in accordance with Ukrainian bioethics legislation. In addition to a general clinical and laboratory examination, all AUB patients underwent an USDE of the internal genital organs on the day of admission to the hospital. In the control group patients the blood flow were evaluated on the 3rd-5th day of the menstrual cycle.

Ultrasound examination and dopplerometry were performed on a TOSHIBA (CANON) XARIO 200 device using transabdominal (PVU-375BT, 3.6-9.2 MHz/convex), transvaginal (PVU-781VTE, 4-9 MHz/convex) sensors according to a standard protocol to

clarify the state of the internal genital organs.

During USDE the position of the uterus and its overall size was determined, the structure of the myometrium was assessed, the presence of structural changes, e. g. leiomatous nodes, their size and localization, polyps of the endometrium and cervical canal, endometrial hyperplasia was detected; adenomyosis sonographic signs were determined also. During uterine cavity examination, its shape and content were determined, and the thickness of the median uterine cavity was measured. Biometry of the ovaries was performed according to their maximum length and width in the same perspective. When evaluating the follicular apparatus, the following parameters were taken into account: the number of follicles in the maximum echographic section along the length, the maximum diameter of the follicles, the presence of volumetric formations, their sizes. After the biometry of the uterus and ovaries, color Doppler mapping was performed followed by a qualitative and quantitative assessment of the blood flow velocity curves in the uterine, arcuate, radial and basal arteries of the endo- and myometrium. Uterine arteries were visualized at the level of the isthmus of the uterus before the entry of the vessel into the myometrium, arcuate arteries - in the outer, radial arteries - in the middle third of the myometrium, basal arteries - on the line separating the myometrium and endometrium or immediately below it.

After determining the localization of the vessel, the blood flow velocity curves were recorded using colour Doppler mapping. For this, a stable image of the curves was obtained during at least three cardiac cycles. A 100 Hz filter was used to eliminate low-frequency signals from moving vessel walls. The total power of ultrasonic radiation did not exceed 100 $mW/cm^2$.

For the qualitative analysis of the spectral curves of blood flow velocities, the following indicators were evaluated: A — maximum systolic velocity, B — end diastolic velocity, C — average velocity, SDR — systolic-diastolic ratio, IR — resistance index, PI — pulsation index. The systolic-diastolic ratio, the resistance index, and the pulsation index reflect the vascular resistance of the peripheral part of the vascular bed, the increase of which is characterized mainly by a decrease in the diastolic component of the spectral curve and is accompanied by an increase in the numerical values of the indices link.

The digital material was processed statistically using the standard package of statistical programs "STATISTICA 10.0" and "MS Excel" on a personal computer Intel Core i5, 2.5 GHz, 8 GB RAM HP. Arithmetic mean (M), mean square deviation and errors of the mean (m) were calculated. Under the condition of normal distribution of values, the study groups were compared using the Student's test (t). When analyzing values that did not

correspond to a normal distribution, non-parametric criteria were used, in particular the Mann-Whitney test, the Pearson $\chi 2$ test. The dependence between traits was calculated by determining the Pearson correlation coefficient (r). Multiple correlation, regression, dispersion and discriminant analyzes were conducted. To test the null hypothesis, the level of significance was assumed to be equal to 0.05. $p<0.05$ was taken as the level of statistical significance.

**Results and discussion.** At the time of examination the AUB patients average age ranged from 20 to 49 years old and averaged 36.3±3.2 years. The average age of AUB and TP women was 34.8±2.6 years, the control group average age was 30.7±2.9 years.

Echographic signs of endometrium structural changes were detected in 83 (92.2%) of AUB women and in 7 (7.8%) women ultrasound signs of pathology were not detected.

Significant differences were found when analyzing the results of ultrasonographic examination of patients with AUB and AUB + AIT The ultrasound picture of hyperplastic processes was distinguished by pronounced polymorphism, but the heterogeneity of the structure of the endometrium was most often encountered - in 74.4% of the women under examination, among AUB women who had concomitant thyroid pathology, it occurred in 48 patients (80%), in the group of women only with AUB it was found in 19 (63.3%) women, and was characterized by a change in the median M-echo, the thickness of which was more than 12-14 mm in the first phase of the menstrual cycle, an inhomogeneous structure, increased echogenicity, the presence of fine linear and point inclusions, increased blood flow and a decrease in the resistance index during dopplerography.

The position of the uterus in retroflexio occurred in 15 women with AUB + AIT and was found in 5 examined women only with AUB, which amounted to 25% and 16.7%, respectively. In the control group it was detected in 4 (13.3%) patients. In 15 cases (25%) in the group with AUB+AIT and in 5 (16.7%) cases in the group with only AUB, asymmetry of the thickness of the mucous membrane of the front and back walls of the uterus was noted. Expansion of the uterine cavity due to an-/hypoechoic content was observed in 25 (41.7%) and 12 (40%) cases ($p<0.05$) of women with AUB+AIT and a group of AUB women, respectively, and took place either due to the presence of clinical signs of bleeding or bleeding itself. It should be noted that no such changes were found either in the endometrium or in the myometrium in the control group women.

In thyroid pathology patients ultrasound examination revealed a significant increase (by 1.5 times; $p<0.05$) of the endometrium thickness and, accordingly, of its volume (see Table 1). Retention cystic formations were found in 15% of AUB+AIT women, in contrast to

the corresponding values in women without AIT, which were detected in 3 (10%) of women. The most significant parameter, which is a criterion for the formation of risk groups for the occurrence of endometrial hyperplasia, is the volume of the endometrium and its ratio to the volume of the uterine body (UV). It should be noted that in 13 (26.7%) AUB +AIT women, and in 5 (16.7%) AUB women, the thickness of the endometrium exceeded 14 mm, and in 7 (11.7%) women with AMC+ AIT and 4 (13.3%) patients with AMC only, the endometrium was relatively thin - up to 4-5 mm.

As for the patients of the control group, their M-echo thickness was on average 5.4 ± 2.1 mm, and the index >8 mm and <3 mm was not noted ($p<0.05$). The percentage ratio of the volume of the endometrium to the volume of the uterus between the parameters of the main group and the control one showed significant differences, where the specified ratio in the control group was smaller than in AUB group ($p<0.05$), and in the AUB +AIT women it was significantly higher than the group of women only with AUB.

*Table 1*

**Average values of thickness, volume of endometrium and uterus M±m, n=120**

| Parameters | I group, AUB+AIT n=60 | II group, AUB n=30 | Control, n=30 |
|---|---|---|---|
| M-echo thickness, mm | 14,9±0,3 * | 10,2±0,2 * | 5,4 ±0,2 |
| V endometrium, cm3 | 3,9±0,2 * | 3,5±0,2 * | 2,5±0,1 |
| V of uterus, cm3 | 60,8±7,2 * | 55,5±5,6 * | 40,5±3,2 |
| V endometrium / V uterus, % | 11,3 | 10,6 | 9,4 |

*Note:* the difference is significant relative to the data of the control group, $p<0.05$.*

The presence of polyp-like formations in the uterine cavity was detected in every second among the total number of AUB women (46 or 51.1% patients). Among them the largest number were for AUB + AIT women - 35 patients (58.3%), while there were 11 (36.7%) women with only AMC, respectively.

Polyps were visualized in the form of oval or rounded formations with increased echogenicity, a more uniformed echo structure, clear contours and a vascular pedicle. On average, their size varied from 3 to 20 mm, and was 7.3±4.2 mm in AUB only group, and 6.6±3.5 mm in AUB + AIT women. Significant differences between the size of polyps in the group of the women under examination were not found. This type of pathological changes

was absent in the control group.

In 24 patients (40%) of the AUB+AIT group and 14 women (46.7%) with AUB, a significant, uneven increase in the echo density of the uterine walls without a significant vascular component was determined, and that was considered as the presence of adenomyosis. In the norm echo-density of the walls is low, while in adenomyosis uneven areas of medium and high density are more often detected. The transition-connective zone in adenomyosis on ultrasound images was characterized by a jagged contour in combination with excessive thickening of the uterine mucosa and the predominance of proliferative processes in the endometrium. In 32 (26.7%) women under examination, the structure of the myometrium was determined by zones of increased or decreased echogenicity with the presence of a capsule and clear contours and corresponded to the structure of leiomatous nodes of various locations and sizes.

We noted the presence of leiomyomas in 25 (41.7%) AUB + AIT patients and in 5 (16.7%) patients who had only AUB. The presence of submucosal nodes with centripetal growth, a clear capsule and heterogeneous echo-structure were detected in 8 (13.3%) and 2 (6.7%) women from the AUB+AIT and AUB groups, respectively. As for the characteristics of echo parameters of the myometrium in the control group, in all cases it was quite homogeneous without signs of leiomatous growth and pathological inclusions. In the patients under examination the presence of combined pathology was observed in almost every second patient.

Doppler parameters of the patients under examination are presented in tables 2, 3, 4, 5.

*Table 2*

**Doppler parameters of blood flow velocity curves in uterine arteries**

| Doppler parameters | AUB+AIT (n=60) | AUB (n=30) | Control (n=30) |
|---|---|---|---|
| PI | 2.64 ± 0.27 | 2.79 ± 0.28 | 3.02 ± 0.13 |
| RI | 0.85±0.04 | 0.99±0.02 | 1.92±0.7 |
| SDR | 7.99±1.53 | 8.64±2.13 | 9.89±0.79 |
| Maximal diastolic velocity | 27.45±3.86 | 28.14±2.95 | 29.32±3.88 |
| Final diastolic velocity | 4.05±0.21 | 3.56±0.43 | 2.95±0.35 |
| Average velocityC | 9.54±1.28 | 9.21±1.75 | 8.98±1.56 |

*Note: In comparison with the indicators of the control group p >0.05*

In AUB patients at the background of AIT, in contrast to AUB women, the following features of blood flow in the uterine arteries were found, namely, the end-diastolic and average blood flow velocity were higher than similar indicators in women with only AUB,

and even greater in the control group of women. However, the maximum systolic blood flow velocity in patients with AIT and AUB was lower, in contrast to similar indicators in women without thyroid pathology. In the control group women these indicators were within normal values and reliably higher than in the main group women. In addition, in AIT group reduced resistance to blood flow was more noted, as evidenced by a decrease of the systolic-diastolic ratio, pulsation indices and resistance. Uterine arteries by colour Doppler mapping were detected in 100% of the patients, both the main and control groups.

As can be seen from the data presented in Table 3, the following characteristics of blood flow in arcuate arteries were found in patients with AUB+AIT, in contrast to the group of patients with only AUB and the control group indicators: end-diastolic, maximum systolic and average blood flow velocities were higher than the corresponding indicators in AUB women and even higher in comparison with control group. In contrast to the control group results a more reduced blood flow resistance was observed, which was manifested by a decrease in the systolic-diastolic ratio, indices of resistance and pulsation. However, these differences turned out to be statistically insignificant. Detection of arcuate arteries by CDM in women with AUB alone was 70.2%, in AUB + AIT patients it was 74.6%, in the control group it equalled to 69.8%.

*Table 3*

**Doppler parameters of velocity curves in arcuate arteries**

| Doppler parameters | AUB+AIT (n=60) | AUB (n=30) | Контрольна група (n=30) |
|---|---|---|---|
| PI | 1.19±0.04 | 2.25±0.08 | 2.56±0.43 |
| RI | 0.93±0.03 | 0.88±0.06 | 0.79±0. 04 |
| SDV | 4.40±0.41 | 4.87±0.34 | 5.10±0.42 |
| Maximal diastolic velocity | 10.65±0.61 | 11.12±1.33 | 8.82±1.15 |
| Final diastolic velocity | 2.95±0.59 | 2.49±0.34 | 2.34±0.78 |
| Average velocity | 3.23±0.95 | 3.71±0.72 | 3.91±0.52 |

*Note. When compared with the indicators in the control group: p >0.05*

The features of blood flow found in AUB + AIT women compared with only AUB patients and control group are given in table 4.

In the radial arteries the value of the final velocity of diastole blood flow in AIT women (the main group) and those without thyroid gland pathology did not differ significantly, but were significantly higher than in control group women; maximum systolic

and average blood flow velocity also did not differ significantly, but were significantly higher than similar indicators in women of the control group; accordingly, blood flow resistance did not have significant differences in women of the main group, but according to the control group of women, it was lower, which was manifested by a significant decrease in the systolic-diastolic ratio, indices of resistance and pulsation.

Table 4

**Doppler indicators of blood flow velocity curves in radial arteries**

| DI | AUB+AIT (n=60) | AUB (n=30) | Control group (n=30) |
|---|---|---|---|
| PI | 0.87±0.02*** | 0.97±0.02*** | 1.16±0.02 |
| RI | 0.49±0.01** | 0.54±0.01** | 0.64±+0.01 |
| SDV | 2.60±0.15** | 2.70±0.15** | 3.09±0.13 |
| MDV | 13.04±1.23* | 16.04±1.23* | 9.62±2.04 |
| FDV | 5.15±0.30*** | 4.93±+0.30*** | 2.87±0.14 |
| ADV | 9.48±0.50*** | 8.95±0.50*** | 5.11±0.62 |

*Note. When compared with indicators in the control group: * - p < 0.05; ** - p < 0.01; *** - p < 0.01.*

Detection of radial arteries by CDM in the control group was 55.1%, in AUB women it was 65.4%, and AIT patients with AUB – 66.1%.

The features of basal arteries blood flow were compared with those in AUB women, AUB + AIT and control group women.

*Table 5*

**Dopplerometric indicators of velocity curves blood flow in basal arteries**

| DI | AUB+AIT (n=60) | AUB (n=30) | Control group (n=30) |
|---|---|---|---|
| PI | 0,81±0,02*** | 0,65±0,02*** | 1,01±0,02 |
| RP | 0,59±0,02** | 0,61±0,02** | 0,68±0,02 |
| SDV | 1,99±0,07 * | 2,05±0,07 * | 2,11±0,14 |
| MDV | 11,79±1,15*** | 9,82±1,15*** | 6,92±1,32 |
| FDV | 5,97±0,54 * | 4,33±0,54 * | 2,49±0,90 |
| ASD | 6,78±0,45 | 5,95±0,45 | 4,32±0,55 |

*Note. When compared with indicators in the control group: * - p <0.05; ** - p <0.01; *** - p < 0.001*

The values of the final diastolic blood flow velocity in women with AUB + AIT were slightly higher than in AUB women, and almost twice exceeded these values in control group women; maximum systolic and average blood flow velocity in women with AUB and AUB +AIT did not differ significantly, but were significantly higher than similar indicators in women of the control group; it was noted that in women with and without thyroid pathology,

blood flow resistance was lower than in women of the control group, as evidenced by a significant decrease in the ratio of systolic-diastolic, resistance and pulsation indexes.

Basal arteries according to CDM were detected in 38.8% of the control group patients, in AUB +AIT women it was 60.3%, and constituted 54.5% in only AUB women.

Regarding the analysis of the sonographic characteristics of the venous collectors of the small pelvis, varicose veins of the small pelvis were found in 3% of the control group women, 15.5% of AUB women and in 26.9% of patients with AUB + AIT, where an increase in the average diameter of the veins by 1 .6 times took place, different from the results of the control group ($p<0.05$).

The results obtained show the increase of blood flow hemodynamic disturbances in the organs of the small pelvis. In AUB patients with concomitant thyroid pathology the presence of adequate blood flow in the endo-myometrium was noted only in a quarter of cases and signs of pronounced venous stasis were revealed in almost half of the observations. This requires a differentiated approach to the selection of therapeutic tactics aimed to improve blood flow and reduce venous blood flow in the pelvis.

So, myo- and endometrium blood flow indicators do not differ significantly either in AUB + AIT or only AUB women but in comparison with control group women there is a decrease of vascular resistance indexes in radial and basal arteries which evidences blood flow increase in the areas mentioned.

The objective diagnostic criterion of AUB in every woman was endometrium biopsy by hysperoresectoscopy and further histological test.

The analysis of echographic picture shows that the latter is a valuable method contributing to significant improvement of uterine pathology and in majority of cases corresponds to the results of histology. The specificity of this method was 86.5%, and its accuracy was 73%.

Thus, it is advisable to carry out an USDE with the assessment of Doppler parameters for all patients with symptoms of AUB to determine the ultrasonographic signs of pathological changes in the endometrium and to choose treatment tactics.

**Conclusion.** Ultrasound is an important method that contributes to a significant improvement in the diagnosis of isolated or combined benign uterine diseases in women with AUB at the background of AIT, and in most cases corresponds to the histological diagnosis. The specificity of this method was 86.5%, and its accuracy was 73%.

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