

Original article

Abnormal uterine bleeding in women of reproductive age: PALM-COEIN causes

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Abstract:

Objective: Abnormal uterine bleeding (AUB) is an often pathology in women of reproductive age. **Materials and methods.** The retrospective analysis of 336 patients with AUB was performed between 2017-2020. We analyzed the social and demographic data, reproductive function, somatic diseases, type and causes of AUB. **Results.** According to PALM-COEIN classification polyps were found in 13.39 % of patients, adenomyosis – 20.83 %, leiomyoma – 37.50 %, malignancy/hyperplasia – 14.29 %, ovulation disorders – 24.11 %, endometrial factor – 12.20 %, iatrogenic reason – 6.25 %. **Conclusion.** PALM-causes dominate over COEIN-etiological factors in the development of AUB in women of reproductive age. But, there are some differences in the rate of causes according to the age period.

Keywords: abnormal uterine bleeding; etiology; reproductive period.

*Bangladesh Journal of Medical Science Vol. 22 No. 04 October '23 Page : 809-814
DOI: <https://doi.org/10.3329/bjms.v22i4.67116>*

Introduction:

In recent years, the study of women's reproductive health has acquired particular importance. There have been changes in the structure of female genital diseases, new diseases have appeared, new methods of diagnosis and treatment have been improved. A woman's menstrual health is evidenced by her menstrual function. Menstruation takes place during the most active period of a woman's life. It is known that in millions of women menstruations impact their physical, psychological and social

status frequently and regularly ^{1, 2}. Understanding the deep mechanisms that are associated with both menstruation and menstrual disorders, in particular, abnormal uterine bleeding (AUB), will introduce an effective individual approach ³.

AUB occurs in nearly 30 % of women in reproductive age ^{4, 5} and is the often reason of hysterectomy ⁶. In 2011 the International Federation of Gynecology and Obstetrics (FIGO) presented the classification of causes of AUB according to which they are divided into two groups. The structural criteria (PALM)

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are P – polyp, A – adenomyosis, L – leiomyoma, M – malignancy and hyperplasia, non-structural criteria (COEIN): C – coagulopathy, O – ovulatory dysfunction, E – endometrial disorders, I – iatrogenic reasons and N – non otherwise classified factors ⁷.

The aim of the research was to analyze the structure of AUB reasons in women of reproductive age.

Materials and methods: We analyzed 336 cases of AUB in women of reproductive age. The information was got retrospectively from the medical cards of the patients who received medical care of AUB between 2017-2020. These persons formed the basic group. The control groups consisted of 50 healthy women without AUB. Inclusion criteria: age 18-45 years old, AUB, satisfactory specimen from the uterine cavity for histological study. Exclusion criteria: pregnancy.

The recommendations of FIGO were used for the diagnosis of AUB which determines that AUB is any deviations from the normal parameters of the menstrual cycle that includes frequency, duration, regularity and flow volume of the menstruation ⁷. Chronic and acute nongestational AUB, heavy menstrual bleeding (HMB) and intermenstrual bleeding (IMB) were determined according to the FIGO recommendations ⁷. The reasons for AUB were structured using PALM-COEIN classification ⁷.

The study was conducted in Kreminna multidisciplinary hospital of Kreminna district council (Ukraine) and confirmed by the Ethics commission (protocol N 1, 15.01.2018) in Shupyk Healthcare National Medical University of Ukraine following by the ethical standards of the Declaration of Helsinki (1964).

For statistical analysis the program Statistica 6.0 was used to assess the results. We calculated the parameters of descriptive statistics (mean, standard error of the mean); Mann-Whitney U test and the criterion χ^2 (Yates corrected Chi-square) were used to compare the data between groups.

Results:

The average age of the women in the basic group was 31.57 ± 0.33 years old, in the control one – 30.64 ± 0.86 . Most of the persons in both groups were 25-40 years old – 79.46 % and 74.00 % of individuals, respectively (table 1). The social characteristics were similar in the patients of both groups. The majority of the women with and without AUB lived in the city – 218 (64.88 %) and 35 (70.00 %), respectively, had official marriage – 288 (85.71 %) and 44 (88.00 %),

the intellectual type of occupation – 235 (69.95 %) and 38 (76.00 %).

Table 1. Baseline parameters of the patients

Parameter	Basic group (n=336)		Control group (n=50)	
	Abs.	%	Abs.	%
<i>Age (years):</i>				
18-24	28	8.34	8	16.00
25-40	267	79.46	37	74.00
40-45	41	12.20	5	10.00
<i>Residence of:</i>				
City	218	64.88	35	70.00
Village	118	35.12	15	30.00
<i>Marriage status:</i>				
The marriage is registered	288	85.71	44	88.00
The marriage is unregistered	27	8.04	4	8.00
Lonely	6	1.79	-	-
Divorced	15	4.46	2	4.00
<i>Education:</i>				
Higher	132	39.28	22	44.00
Secondary special	178	52.98	22	44.00
School	26	7.74	6	24.00
<i>Type of occupation:</i>				
Intellectual	235	69.94	38	76.00
Physical	101	30.06	12	24.00
<i>BMI:</i>				
Underweight	4	1.19	1	2.00
Normal	244	72.62	38	76.00
Overweight	64	19.05	11	22.00
Obesity I	22	6.55	-	-
Obesity II	2	0.59	-	-

The average meaning of the body mass index (BMI) was 23.44 ± 0.17 kg/m² in the women in the basic group and 22.90 ± 0.34 kg/m² in control persons. Every fourth patient with AUB (88 (26.19 %) persons) and every fifth woman without AUB (11 (22.00 %) individuals) was overweight or obese I, II.

The average age of the menarche onset in patients with AUB was 12.77 ± 0.05 years and in women without AUB – 12.70 ± 0.13 . The menstrual cycle became regular at once after menarche in 37 (11.01 %) and 4 (8.00 %) persons, respectively, in 6-12 months after menarche – in most of the women (267 (79.47 %) and 44 (88.00 %)), in 1-2 years – in 32 (9.52 %) та 2 (4.00 %) individuals.

The rate of gynecological diseases was higher in patients with AUB (table 2). 157 patients (46.73 %) in the basic group complained about algodysmenorrhea that was in 1.80 times more compared to the control persons ($\chi^2=6.77$, $p=0.002$), uterine myoma – in 18.75 times, ($\chi^2=23.26$, $p<0.001$), endometriosis and premenstrual syndrome – 10.42 ($\chi^2=9.07$, $p=0.003$), and 2.51 times $\chi^2=9.90$, $p=0.002$), respectively. 67 (19.94 %) women in the basic group had AUB before.

Table 2. Gynecological and reproductive data of the women

Parameter	Basic group (n=336)		Control group (n=50)	
	Abs.	%	Abs.	%
<i>Disorders of menstrual cycle:</i>				
Abnormal uterine bleeding	67	19.94*	-	-
in anamnesis	157	46.73*	13	26.00
Algo/dysmenorrhea	3	0.89	-	-
Amenorrhea				
Chronic salpingitis and oophoritis	98	29.17	13	26.00
Uterine myoma	126	37.50*	1	2.00
Ovary cyst	57	16.96	5	10.00
Endometriosis	70	20.83*	1	2.00
Infertility	4	1.19	-	-
Polycystic ovary syndrome	5	1.49	-	-
Premenstrual syndrome	135	40.18*	8	16.00
Cervical intraepithelium neoplasia I-II	6	1.79	1	2.00
Chronic cervicitis and cervical erosion	66	19.64	6	12.00
Abscess of the Bartholin's gland	2	0.59	-	-
<i>Pregnancy:</i>				
- none	14	4.17	3	6.00
- one	152	45.24*	31	62.00
- two	133	39.58*	11	22.00
- three and more	37	11.01	5	10.00
<i>Labor:</i>				
- none	24	7.14	5	10.00
- one	170	50.60	29	58.00
- two	121	36.01	15	30.00
- three and more	21	6.25	1	2.00

Parameter	Basic group (n=336)		Control group (n=50)	
	Abs.	%	Abs.	%
Artificial abortion	27	8.04	3	6.00
Spontaneous miscarriage	18	5.36	2	4.00
Missed abortion	8	2.38	1	2.00
Ectopic pregnancy	2	0.59	-	-

Note: * – significant difference between indicators of two groups ($p<0.05$)

The rate of gynecological operations in patients with AUB was more in 4.02 times (27 (8.04 %) individuals) than in women without AUB (1 (2.00 %) person). In the basic group the indications for the operations were: uterine myoma (14 (4.17 %) women), ectopic pregnancy (2 (0.59 %)), polycystic ovarian syndrome (1 (0.30 %)). In 10 (2.98 %) patients in the basic group and one (2.00 %) individual in the control group the surgery was because of ovarian cysts. Besides this, small gynecological procedures (curettage, polypectomy, surgical excision of the abscess of the Bartholin's gland) had 41 (12.20 %) persons with AUB versus 2 (4.00 %) controls.

The analysis of reproductive function presented that the number of primigravida women among patients with AUB was 1.37 times lower compared to the women without AUB ($\chi^2=4.26$, $p=0.04$), and multigravida – 1.58 times higher (170 (50.59 %) versus 16 (32.00 %) patients, respectively; $\chi^2=5.31$, $p=0.02$). However, there was no difference between women in both groups regarding the number of births and the negative pregnancy outcomes (artificial abortion, miscarriage, missed abortion, ectopic pregnancy).

Noteworthy is the fact that the rate of the persons with extragenital pathology in the basic group (162 (48.21 %) patients) was in 1.51 times higher than in the control one (16 (32.00 %) women; $\chi^2=3.98$, $p=0.046$). 30 (8.93 %) women with AUB had two somatic diseases versus the absence of such persons without AUB. Extragenital pathology in patients with AUB was mainly represented by diseases of the gastrointestinal tract, which were diagnosed in 72 (21.43 %) women, chronic pathology of the urinary system – 41 (12.20 %) patients, arterial hypertension I-II – 26 (7.74 %), varicose veins of lower extremities I-II – 21 (6.25 %), thyroid pathology – 11 (3.27 %). The rate of other somatic diseases was less than 1 %. Whereas in women without AUB, the most frequent extragenital pathology was represented by chronic

diseases of the gastrointestinal tract and amounted to 10.00 % (5 patients), 4 (8.00 %) persons had chronic pathology of the urinary system, 1 (2.00 %) – arterial hypertension.

The majority of the patients in the basic group had chronic AUB – 313 (93.15 %), 23 (6.85 %) women were diagnosed acute AUB, HMB was diagnosed in 74 (22.02 %) persons.

The most frequent complaints of patients in the basic group were prolonged menstruations (38.09 %) and IMB (41.37 %; table 3). 87 (25.89 %) women had irregular periods, 67 (19.94 %) – frequent periods. Among 143 persons with IMB 118 (35.11 %) of them had IMB regularly during the last six months, mostly in the middle of the menstrual cycle (71 (21.13 %) patients). Only 21 (6.25 %) women complained of rare cases of this type of menstrual cycle disorder.

Table 3. The characteristics of the menstrual cycle in the patients with abnormal uterine bleeding (n=336)

Parameter of the menstrual cycle	Abs.	%
Frequency:		
Normal	264	78.57
Frequent	67	19.94
Infrequent	5	1.49
Duration of menstrual bleeding:		
Normal	208	61.91
Prolonged	128	38.09
Regular menstrual cycle	249	74.11
Irregular menstrual cycle	87	25.89
Flow volume:		
Normal	217	64.59
Light	45	13.39
Heavy	74	22.02
Intermenstrual bleeding, total:	139	41.37
Random	21	6.25
Cyclic:	118	35.11
- early cycle	12	3.57
- mid cycle	71	21.13
- late cycle	35	10.42
Unscheduled bleeding on progestin, estrogen gonadal steroids	21	6.25

According to the anamnesis, clinical examination of patients, ultrasound of the pelvic organs, results of hysteroscopy and the histological study of the specimens from the uterine cavity, it was found that the structural causes (PALM) of AUB prevailed relative to the number of non-structural ones (table 4). Two factors of AUB development were found in

45 patients. Taking into account that the total number of etiological factors of AUB was 432, structural causes amounted to 289 (66.90 %) cases, and non-structural – 143 (33.10 %). It was found that the largest frequency of structural causes were uterine leiomyoma (126 (37.50 %) women), endometrial hyperplasia (48 (14.29 %) patients) and endometrial polyp (45 (13.39 %) persons), among non-structural – disorders ovulation (81 (24.11 %) individuals).

Table 4. The causes of abnormal uterine bleeding in the patients of the basic group (n=336)

Cause	Abs.	%
Polyp	45	13.39
Adenomyosis	70	20.83
Leiomyoma	126	37.50
Malignancy/hyperplasia	48	14.29
Ovulation disorders	81	24.11
Endometrial	41	12.20
Iatrogenic	21	6.25

Among 126 cases of uterine leiomyoma in most of the patients (81 (24.11 %) persons), fibroids (Lo) did not lead to deformation of the uterine cavity, and the rate of women with one submucosal node (L_{SM}) was 13.39 % (45 individuals).

It should also be noted that 31 (9.23%) patients with AUB re-applied for medical care during the last 6 months. 13 persons of them did not follow the schedule and regimen of previously prescribed hormonal treatment; in 8 patients the prescribed hormone therapy was not effective. 13 women did not get treatment because they refused to take previously prescribed hormonal drugs to correct the menstrual cycle and prevent AUB. There were no incidences of coagulopathy, cancer (only the presence of endometrium hyperplasia) and non-otherwise classified causes of AUB in our study. We found some difference in the structure of reasons of AUB according to the age (table 5).

Discussion:

Most of the scientists prefer the new classification of causes of AUB (PALM-COEIN) which takes into account the etiological factor ^{8,9,10}. A lot of researches demonstrate that structural causes dominate over the non-structural ones. Thus, in patients 18-45 years old the rate of structural reasons (PALM) was 60 % versus nonstructural (COEIN) – 40 % ⁴; in women after 40 years old and till one year after menopause the frequency of PALM-causes was 50.23 % ⁸. The most common etiological factor of AUB was uterine

Table 5. The structure of the causes of abnormal uterine bleeding according to age

Cause	Age, years				
	till 25 (n=28)	26-30 (n=76)	31-35 (n=89)	36-40 (n=102)	41-45 (n=41)
Polyp	4 (14.29)	10 (13.16)	8 (8.99)	9 (8.82)	14 (34.15)
Adenomyosis	4 (14.29)	13 (17.11)	21 (23.59)	28 (27.45)	4 (9.76)
Leiomyoma	-	14 (18.42)	38 (42.70)	48 (47.06)	26 (63.41)
Malignancy/hyperplasia	-	6 (7.89)	12 (13.48)	18 (17.65)	12 (29.27)
Ovulation disorders	19 (67.85)	32 (42.11)	20 (22.47)	10 (9.80)	-
Endometrial	1 (3.57)	9 (11.84)	17 (19.10)	12 (11.76)	2 (4.88)
Iatrogenic	-	-	4 (4.49)	15 (14.71)	2 (4.88)

leiomyoma – in different studies its prevalence is 30 %⁹ – 53.7 %¹⁰, adenomyosis is on the second place – 23.5 %¹⁰ – 29.66 %⁹. Among the non-structural components of the causes of AUB in women of the reproductive period the most spread is ovulatory dysfunction – 37.6 %¹⁰. But nevertheless, one should not forget about the infrequent causes of AUB, for example, chorionic carcinoma¹¹ and cavernous haemangioma¹².

The results of our study are consistent with data from other scientists. Thus we found that the rate of PALM-causes is 66.90 %, COEIN – 33.10 %. Leiomyoma was the most spread etiological factor of AUB – 37.50 %. But in the age till 25 years old non-structural causes dominated (67.85 % of persons had ovulation disorder). It should be mentioned, that the frequency of structural causes (leiomyoma, hyperplasia and polyp) increased with the age and was the highest after 40 years old, and ovulation disorders – decreased. The maximum rate of adenomyosis was in women 26-40 years old, ovulation disorders – till 25, endometrial

factor – 31-35 years. The prevalence of HMB in our research (22.02 %) corresponded to other studies that indicates it at the level 18.2 %¹³ – 22.5 %¹⁴.

Conclusion: In the women of the reproductive period the most of the causes for AUB have structural character. But, there are some differences in rate of etiological factors according to the age.

Prospect for further research is to study the structure of causes of abnormal uterine bleeding in women with chronic psychoemotional stress.

Source of funding. None

Conflict of interest. None declared

Author's contribution: Data gathering: Fedosiuk K.

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