Prevalence of abnormal uterine bleeding according to new International Federation of Gynecology and Obstetrics classification in Chinese women of reproductive age
A cross-sectional study

Yu Sun, MSc[a], Yuzhu Wang, MSc[b], Lele Mao, PhD[c], Jiaying Wen, MSc[d], Wenpei Bai, MD[a],*

Abstract

The PALM-COEIN classification for causes of abnormal uterine bleeding (AUB) was proposed by the International Federation of Gynecology and Obstetrics (FIGO) in 2011, which has been gradually applied in the diagnosis of AUB in the past 2 years in China. However, there are no reports yet on the causes of chronic AUB among Chinese women with this new classification system.

The purpose of this study was to describe the prevalence of the causes of chronic AUB among Chinese women of reproductive age using the PALM-COIEN classification system.

This is a cross-sectional study. Beijing Shijitan Hospital, Capital Medical University.

A total of 1053 women aged 15 to 55 years with chronic AUB were evaluated between November 2016 and May 2017.

Prevalence of the causes of chronic AUB using the PALM-COEIN classification. AUB-O was the most frequent finding in women with chronic AUB, accounting for 608 (57.7%) cases. AUB-P was found in 171 (16.2%) women, AUB-L in 130 (12%) women, AUB-A in 52 (4.94%) women, AUB-E in 28 (2%) women, AUB-I in 23 (2%) women, AUB-M in 20 (1.9%) women, AUB-C in 10 (1%) women, and AUB-N in 10 (0.9%) women.

Ovulatory dysfunction (AUB-O) is the most common cause of AUB among the nonstructural causes. Endometrial polyps (AUB-P) are the most common among the structural causes, followed by uterine fibroids (AUB-L) and uterine adenomyosis (AUB-A).

Abbreviations: AUB = abnormal uterine bleeding, AUB-A = adenomyosis, AUB-C = coagulopathy, AUB-E = endometrial, AUB-I = iatrogenic, AUB-L = leiomyoma, AUB-M = malignancy and hyperplasia, AUB-N = not otherwise classified, AUB-O = ovulatory dysfunction, AUB-P = polyp, FIGO = International Federation of Gynecology and Obstetrics.

Keywords: Abnormal uterine bleeding, bleeding patterns, menstrual cycle, morbidity, PALM-COEIN classification

1. Introduction

Abnormal uterine bleeding (AUB) is the most common symptom of gynecological conditions, which is defined as any type of bleeding in which the duration, frequency, or amount is excessive for an individual patient.[1] AUB is regarded as a sign of possible uterine disease, including acute and chronic AUB. It is the most common symptom and main complaint among Chinese women of childbearing age in the gynecological clinic, accounting for 30% of gynecological outpatient clinics.[2] Previous studies have shown that the prevalence of AUB varies in different populations, with the overall prevalence fluctuating between 10% and 30%,[3,4] necessitating the use of a number of medical resources.[2,5,6] Owing to the confusion in and inconsistency of nomenclature, the lack of research and classification methods of various etiological criteria has hindered the research and management of AUB for quite a long time. The International Federation of Gynecology and Obstetrics (FIGO) published the consensus on the terms and definitions of normal and abnormal uterine bleeding in 2007. In 2011, a new nomenclature of AUB was introduced, and the terms uterine bleeding and excessive menstruation were cast aside.[7] The acronym PALM-COEIN is now being widely used for categorizing the causes of AUB (Fig. 1): polyp (AUB-P), adenomyosis (AUB-A), leiomyoma (AUB-L), malignancy and hyperplasia (AUB-M), coagulopathy (AUB-C), ovulatory dysfunction (AUB-O), endometrial (AUB-E), and iatrogenic and not otherwise classified (AUB-N). The "PALM" classification is structural and assessed visually (imaging and histopathological tests), whereas the "COEIN" classification is nonstructural.[8]

[a] Department of Obstetrics and Gynecology, Beijing Shijitan Hospital, Capital Medical University, [b] Department of Obstetrics and Gynecology, Tongzhou District Hospital of Integrated TCM & Western Medicine, [c] Department of Physiology and Pathophysiology, School of Basic Medical Sciences, Peking University Health Science Center, Beijing, [d] Department of Clinical Research Institute, Sichuan People's hospital of xiaojin county, Sichuan, China.

* Correspondence: Wenpei Bai, Department of Obstetrics and Gynecology, Beijing Shijitan Hospital, Beijing, Capital Medical University, Beijing 100038, China (e-mail: bwp66@163.com).
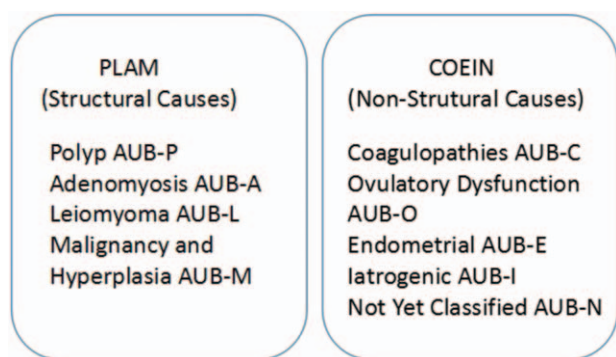
Figure 1. PALM-COIEN classfication.

The standard menstrual index includes 4 elements of menstrual bleeding: the frequency and regularity of the menstruation and menstrual cycle, the length of the period, duration of flow (days), and volume of monthly blood loss (milliliters). According to previous reports and international standards,[3,9–11] the criteria used in this study are shown in Table 1.[12] The bleeding pattern is an important basis for identifying the etiology of AUB and plays a crucial role in diagnosing such diseases. The diagnosis of AUB depends on the comprehensive assessment of the medical history, combined with blood tests and ultrasound or hysteroscopic examination. AUB without hysterectomy should be diagnosed on the basis of structural changes. Currently, there is no report from Chinese gynaecology clinics, on the analysis of the etiological components of chronic AUB based on the PALM-COEIN classification. Moreover, the bleeding patterns in various diseases are also worth analyzing. Therefore, this research provides the basis for clinical judgment in terms of AUB etiology and gynecological outpatient composition through a prospective observational study of Chinese women with chronic AUB and the analysis of various types of bleeding patterns in accordance with the FIGO classification system.

2. Materials and methods

We conducted a prospective study of patients with chronic AUB between November 2016 and May 2017 at Beijing Shijitan Hospital Gynaecological Clinic, Capital Medical University. The research project was reviewed and the human subject protection approval was given by the Ethics and Research Committee of Beijing Shijitan Hospital on May 21, 2016. All patients provided informed consent for the anonymous use of their data.

The subject inclusion criteria are as follows:

(1) Women aged 15 to 55 years
(2) Chronic AUB, including any of the following : menstrual cycle of <24 days; menstrual cycle of >38 days; irregularity of menses, cycle-to-cycle variation of >20 days during 12 months; duration of flow of >8 days; duration of flow of <4 days; volume of monthly blood loss >80 mL; volume of monthly blood loss <5 mL
(3) Signed informed consent to participate in this study.

The exclusion criteria are as follows:

(1) Acute AUB[1]
(2) Vaginal bleeding caused by pregnancy and pregnancy-related factors
(3) Vaginal bleeding caused by vaginitis
(4) Vaginal bleeding caused by cervical diseases
(5) Bleeding before menstruation
(6) Vaginal bleeding after menopause
(7) Use of drugs such as sex hormones for nearly 6 months.

This study adopted a questionnaire investigation method, following the principle of informed consent. Patient information, such as age, height, weight, menstrual history, menarche age, and medical and surgical history, and the relevant imaging examination and laboratory test results, including routine blood test, sex hormone, vaginal ultrasound, liver function, renal function, and hysteroscopic examination, were obtained. At the same time, a lecture and training on AUB-related concepts were conducted, and a menstrual record paper was distributed to the patients to be kept as a menstrual diary for 3 months. The menstrual diary should record abnormal menstruation (e.g., menstrual period cycle and duration, volume of monthly blood loss). After 3 months, the main causes of AUB were determined according to the medical history and physical and auxiliary examination results.

2.1. Definitions and diagnostic criteria

Acute AUB is defined as an episode of bleeding that is of sufficient quantity requiring immediate intervention to prevent further blood loss in a woman of reproductive age who is not pregnant. Chronic AUB is defined as bleeding from the uterine corpus which is abnormal in duration, volume, and/or frequency and has been present for the majority of the last 6 months.[13,14] The definition of AUB in the study is based on the medical terms recommended by FIGO in 2011, as shown in Table 1. Diagnostic criteria and procedures for AUB are based on the 2011 FIGO guidelines. The diagnosis of "PALM," the cause of structural change, was confirmed by imaging techniques or histopathological methods. In addition, the diagnosis of uterine "COEIN," without disease of structural change, was confirmed by imaging technologies or histopathological methods on the basis of organic disease combined with sex hormone and blood coagulation laboratory tests. Meanwhile, for any one or more causes associated with AUB, only the first diagnosis or the most likely diagnosis of AUB is included.

These findings and diagnoses were recorded in an MS Excel spreadsheet and coded and analyzed using Stata statistical

Table 1

Suggested "normal" limits for menstrual parameters in the mid-reproductive years[12].

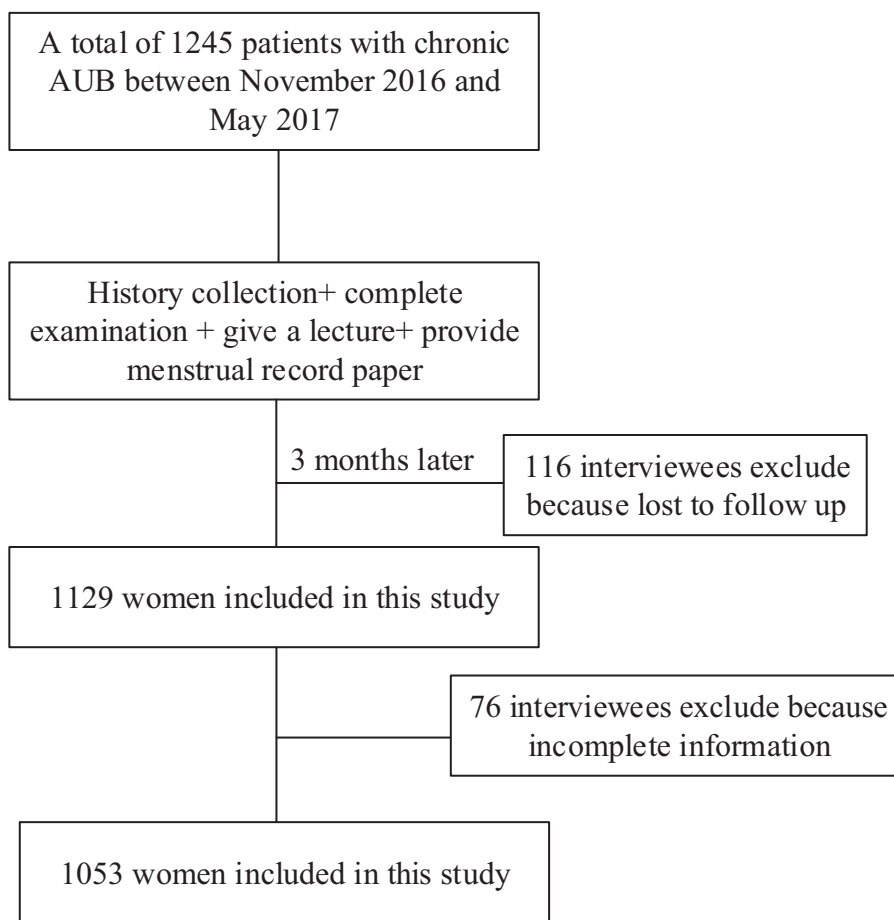| Clinical dimensions of menstruation and menstrual cycle	Descriptive terms	Normal limits
Menstruation and menstrual cycle		(5–95th percentiles)
Frequency of menses, days	Frequent	<24
	Normal	24–38
	Infrequent	>38
Regularity of menses, cycle to cycle variation during 12 months, days	Absent	No bleeding
	Regular	Variation > 2–20 days
	Irregular	Variation > 2–20 days
Duration of flow, days	Prolonged	>8.0
	Normal	4.5–8.0
	Shortened	<4.5
Volume of monthly blood loss, mL	Heavy	>80
	Normal	5–80
	Light	<5

Figure 2. A flowchart showing patients through the study.

software SPSS 20.0. The count data are expressed as a percentage.

3. Results

The flow chart is shown in Figure 1. A total of 1245 women were initially included, 76 of them were excluded because of difficulties in determining the diagnosis because of lack of complete information. After 3 months, 116 patients did not complete the menstrual diary. After excluding these women, the total number of interviewees was 1053 (84.6%). The average age of women who met the inclusion criteria was 35.9±9.3 years. The mean body mass index was 23.5± 3.9 (Fig. 2).

3.1. The etiological composition of chronic AUB

The prevalence of the cause of chronic AUB using the PALM-COEIN classification is shown in Table 2. Structural cause of chronic AUB accounts for 35.42% of cases, whereas nonstructural cause of chronic AUB accounts for 64.58% of cases. AUB-O was the most frequent finding in women with chronic AUB, accounting for 608 (57.7%) cases. AUB-P was found in 171 (16.2%) women, AUB-L in 130 (12%) women, AUB-A in 52 (4.94%) women, AUB-E in 28 (2%) women, AUB-I in 23 (2%) women, AUB-M in 20 (1.9%) women, AUB-C in 10 (1%) women, and AUB-N in 10 (0.9%) women.

3.2. Bleeding patterns

The bleeding patterns of women with AUB-O, AUB-P, AUB-L, and AUB-A are shown in Table 3. Menstruation was absent in 14% of women with AUB-O. A total of 63% of women with AUB-O have irregular menstruation, with infrequent menses

Table 2

Distribution according to final diagnosis.

AUB classification	No. of patients	%
PLAM	373	35.42%
AUB-P	171	16.24%
AUB-A	52	4.94%
AUB-L	130	12.35%
AUB-M	20	1.90%
COIEN	680	64.58%
AUB-C	11	1.04%
AUB-O	608	57.74%
AUB-I	23	2.18%
AUB-E	28	2.66%
AUB-N	10	0.95%
Total	1053	100%

The diagnosis was confirmed. AUB-O was the most common cause of abnormal uterine bleeding and was confirmed in 57.7% of cases. AUB-P (16.2%) and AUB-L (12%) were the second and third most common cause observed. AUB-A was the fourth common case of abnormal uterine bleeding. AUB-E, AUB-I, AUB-M, AUB-C, and AUB-N were the other causes observed. AUB-A = adenomyosis, AUB-C = coagulopathy, AUB-E = endometrial, AUB-I = iatrogenic, AUB-L = leiomyoma, AUB-M = malignancy and hyperplasia, AUB-N = not otherwise classified, AUB-O = ovulatory dysfunction, AUB-P = polyp

Table 3

The bleeding patterns of women with AUB-O, AUB-P, AUB-L, and AUB-A.

		AUB-O	AUB-P	AUB-L	AUB-A
Regularity of menses	Absent	14% (85/608)	0	0	0
	Regular	23% (140/608)	89% (152/171)	75% (98/130)	77% (40/52)
	Irregulay	63% (383/608)	11% (19/171)	25% (35/130)	23% (12/52)
Frequency of menses	Frequent	15% (92/608)	24% (40/171)	18% (24/130)	6% (3/52)
	Normal	51% (312/608)	61% (106/171)	70% (86/130)	82% (43/52)
	Infrequent	34% (204/608)	15% (25/171)	12% (20/130)	12% (6/52)
Duration of flow	Prolonged	33% (201/608)	44% (76/171)	44% (57/130)	42% (22/52)
	Normal	44% (267/608)	53% (91/171)	48% (63/130)	60% (31/52)
	Shortened	23% (140/608)	2% (4/171)	8% (10/130)	0
Volume of month blood	Heavy	7% (44/608)	13% (22/171)	51% (66/130)	17% (9/52)
	Normal	71% (430/608)	80% (137/171)	49% (64/130)	83% (43/52)
	Light	22% (134/608)	7% (12/171)	0	0

AUB-A = adenomyosis, AUB-L = leiomyoma, AUB-O = ovulatory dysfunction, AUB-P = polyp

accounting for 34% of cases. About 56% of these women had changes in the flow duration. Only 7% of these women experienced heavy menstrual bleeding (HMB). A total of 89% of women with AUB-P had regular menstruation. HMB accounted for 36.8% (63/171) of cases. About 44% of these women had a prolonged duration of flow. Of these women, 80% have menstruation in the normal range. A total of 13% of women with AUB-P have HMB. The main bleeding pattern of women with AUB-L is HMB and prolonged flow duration. The regularity of menstrual cycle was 75%. About 51% of women had HMB and 44% had a prolonged flow duration. The main bleeding pattern of women with AUB-A was a prolonged flow duration, accounting for 40% of cases. Regular menstrual cycle accounted

for 77% and HMB accounted for 17% of cases. There was no change in the flow volume in 83% of women.

3.3. The age distribution of women with AUB

The 4 categories of AUB diseases with the highest prevalence among different age groups are shown in Figure 3. The age distribution of women with AUB-O is shown in Figure 3A. The main prevalence was between the age of 20 and 34; the highest was 19.9% at 25 to 29 years followed by 18% at 30 to 34 years, 16.6% at 20 to 24 years, and 11.3% at 45 to 49 years. The age distribution of women with AUB-P is shown in Figure 3B. The main prevalence was between the age of 25 and 49; the highest
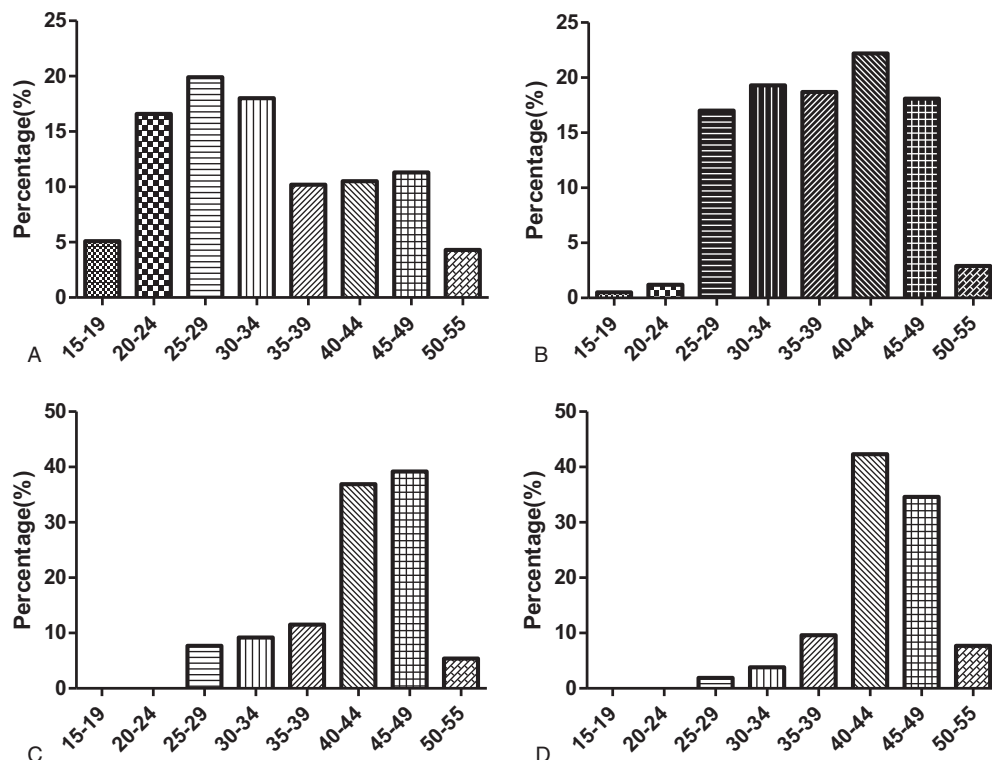

Figure 3. Represents the age distribution of abnormal uterine bleeding. (A) AUB-O distribution with age. (B) AUB-P distribution with age. (C) AUB-L distribution with age. (D) AUB-A distribution with age.

was 22.2% at 40 to 44 years followed by 19.3% at 30 to 34 years, 18.7% at 35 to 39 years, and 2.9% at 50 to 55 years. The prevalence of AUB-A increased by the age (Fig. 3D). The prevalence rate was 42.3% among women aged 40 to 44 years and 34.6% in women aged 45 to 49 years. The lowest prevalence was 0 in women aged 15 to 24 years. The incidence of AUB-L was similar to that of AUB-A (Figure 3C), and the prevalence rate increased with age. The prevalence rate in women aged 45 to 49 was 39.2% and in women aged 40 to 44 years was 36.9%. The prevalence rate of women aged 50 to 55 years was significantly reduced to 5.4%.

3.4. Comment

AUB is the most common symptom of gynecological conditions, and its etiology is complicated. Owing to the lack of unified definitions, the description of menstrual symptoms and the lack of uniform standards have led to difficulties in conducting clinical research. It was not until 2011 that FIGO came up with the PALM-COEIN classification system, which divided AUB into structural and nonstructural cause. In China, physicians have gradually begun to use the PALM-COEIN classification in diagnosing AUB. However, there is still no report of AUB in Chinese women using the PALM-COEIN classification. This study, for the first time, conducted clinical research on the etiology of AUB based on the new classification, which was developed by FIGO, and provided the Chinese data of AUB etiology. This study investigated the etiology of AUB in Chinese women through a prospective observational study. This study has found that the nonstructural cause is the main cause of AUB in Chinese women, with AUB-O being the most prevalent (57.7%). The results are similar to previous literature, and ovulatory dysfunction was found to be the most common cause of AUB.[15,16] The study found that the main bleeding pattern of women with AUB-O was a changing menstrual cycle. About 63% of these women have irregular and infrequent menstruation, whereas 14% have amenorrhea. Consistent with previous studies, a changing menstrual cycle is the most important hemorrhage pattern for those with AUB-O.[16] The reason for this is the ovulatory dysfunction caused by the malfunction of the hypothalamic-pituitary-ovarian axis. The hypothalamic-pituitary-ovarian axis fails to develop the necessary hormonal feedback to result in ovulation and a subsequently stable endometrium. The clinical manifestations are irregular menstrual cycle, irregular menstruation, and even amenorrhea. Although there are still a few women who do not undergo ovulation, they may experience bleeding periodically. In the absence of ovulation, a corpus luteum does not develop and the ovary fails to secrete progesterone. This results in continual endometrial proliferation without progesterone withdrawal-induced shedding and bleeding, which manifests as periodic breakthrough bleeding. Some populations can be expressed as measured changes and extended periods. In this study, women with AUB-O were found to have an extended duration of menstrual period (33%) and HMB (7%). AUB-O is mainly prevalent between ages 20 and 34; however, the prevalence rate gradually decreased between ages 45 and 49, which may be related to most women undergoing menopausal transition during this period along with a decline in ovarian function.

An endometrial polyp is a common gynecological disease. Its incidence is not exactly known, as the clinical manifestations of endometrial polyps are not obvious. According to previous studies, the prevalence rate of endometrial polyps fluctuates from 7.8% to 34.9%.[17–19] AUB is the most common clinical manifestation of endometrial polyps. Previous studies have reported that in both premenopausal and postmenopausal women, AUB was the most common symptom, with an incidence of up to 68%.[20] Approximately 10% to 40% of women with AUB have endometrial polyps, and the severity of the symptoms was not related to the diameter, location, and number of polyps.[21] This study found that AUB caused by endometrial polyps accounted for 16.2% of case, slightly lower than that reported by Clark et al, that is, AUB caused by AUB-P was 20%~30%.[22–24] This study found that AUB-P is the most common etiology of AUB organic disease, and its main bleeding pattern is a prolonged duration of flow and HMB, whereas the regularity of menstrual cycles is usually not affected.

Uterine fibroids is a common disease in women, with a high incidence of 70%~80%,[25] and >50% of women with uterine fibroids are asymptomatic.[26] However, there are still some women with uterine fibroids who manifest AUB and iron deficiency anemia because of chronic loss of blood.[27] AUB symptoms often co-exist with fibroma, but the relationship between AUB and fibroma is still unclear. In many women, uterine fibroids may only co-exist with AUB, but they are not considered as the main factor that causes AUB. The symptoms of AUB are more related to the location and size of the myoma, and the incidence of AUB-L is closely related to the increase in endometrial surface area because of uterine fibroids.[28] There is still lack of data on the proportion of AUB-L in AUB. The study has found that uterine fibroids were the first to be diagnosed as a cause of abnormal uterine hemorrhage by 12%. Previous studies had indicated that AUB caused by AUB-L was more severe and the incidence is 14%~25%.[29,30] However, our study has found that the bleeding pattern of women with AUB-L was mainly HMB, which accounted for 51% and 44% of length-period prolongation, and the menstrual cycle was regular. Previous study suggested that uterine myoma and endometrial causes of bleeding are associated with increased surface area and brittleness of the blood vessels, resulting in endovascular blood flow increase to overcome platelet aggregation.[28,31] In addition, AUB-L was associated with age.[32,33] The study found that the incidence of AUB-L increased with age, reaching a peak between 45 and 49 years.

Uterine adenomyosis is one cause of AUB and the incidence of AUB-A is 20% to 35%.[34–36] Previous study has rarely reported AUB caused by uterine adenomyosis, currently the criterion standard for the diagnosis of uterine adenomyosis for pathological diagnosis, but the diagnostic method has inevitable limitations. Therefore, the prevalence of AUB-A in AUB is not clear. AUB-A was diagnosed by imaging examination and combined with medical history taking and laboratory tests. AUB-A was found to be 4.94% in AUB. The main bleeding pattern is a prolonged duration of flow, accounting for 42% of cases, followed by HMB, accounting for 17% of cases. It may be associated with increased uterine surface area because of increased uterine volume.[37,38] The prevalence of AUB-L increased with age, with a peak of 42.3% between 40 and 44 years. Subsequently, it was 34.6% at 45 to 49 years and 9.6% at 35 to 40 years.

3.5. Strength and limitation

This study investigates the etiology of AUB in Chinese women through observational studies and provides data for the etiology of Chinese gynecological outpatients based on the new

classification. At the same time, we analyzed the bleeding pattern and age distribution of the 4 diseases with the highest prevalence of AUB. However, there is still a limitation for this research: it has a small sample size. Considering the statistics, the bleeding pattern may not be able to accurately reflect the characteristics of the disease; so, there is still a need to further increase the sample size in future studies to support the findings.

4. Conclusion

AUB is a common symptom of gynecological conditions, which seriously affects the quality of life of women. Currently, there is no report on the study of the etiology of a new classification of gynecological conditions in China. This study has found that AUB-O is the most common cause of AUB in 15- to 55-year-old Chinese women. The most frequent bleeding pattern is a changing menstrual cycle, sometimes accompanied by an increase in the volume of flow or prolonged periods. AUB-P is the most common cause of structural changes, and the most common manifestation is a prolonged period followed by an increase in volume. The prevalence rates of AUB-L and AUB-A rank third and fourth, respectively. Their major bleeding patterns are increased by the amount of HMB and the extension of period, respectively, and they are associated with age, with the highest prevalence between 40 and 49 years.

Author contributions

Data curation: Yuzhu Wang, Jiaying Wen.
Formal analysis: Lele Mao.
Investigation: Yu Sun.
Methodology: Yu Sun.
Supervision: Wenpei Bai.
Writing – original draft: Yu Sun.
Writing – review & editing: Wenpei Bai.

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