

Evaluation of PALM-COEIN Classification with Abnormal Uterine Bleeding in Turkish Women

Anormal Uterin Kanamalı Türk Kadınlarında PALM-COEIN Sınıflandırmasının Değerlendirilmesi

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ABSTRACT

Objective: In 2011, the International Federation of Gynaecology and Obstetrics working group on menstrual disorders has introduced a new classification system called "PALM-COEIN" in the interest of abnormal uterine bleeding (AUB). The aim of the study was to evaluate the new classification and to compare with former classical terminology for AUB. **Material and Methods:** This retrospective study was performed in Gynaecology Clinic of Zekai Tahir Burak Women Health Care, Training and Research Hospital in Ankara, Turkey, between February 2015 and February 2016. The study was assessed including premenopausal women without proven chronic disease. Each case has been examined in terms of anatomical structure, physical examination and pelvic ultrasonography. Endometrial samples and hysterectomy specimens were obtained for histopathological investigation if applicable. Possible underlying causes were categorised according to the new classification system. **Results:** The study included 437 premenopausal women who presented with complaints of abnormal uterine bleeding. The people who complained of general sources of bleeding have categorized with classical terminology and examined under the name of hypermenorrhoea, menorrhagia, metrorrhagia, menometrorrhagia including polyps, leiomyoma uteri, adenomyosis, hyperplasia, iatrogenic causes, unopposed estrogen, malignancy, cervical polyp, hormone imbalance, infection of cervix and problems linked to birth control pills and intrauterine devices. Cases which has categorized with PALM-COEIN classification system demonstrated the results as 175 (40%) polyp, 93(21.3%) adenomyosis, 153 (35%) leiomyoma, 16 (3.7%) malignancy and hyperplasia. **Conclusion:** There is a general inconsistency in the classification of abnormal uterine bleeding. As a result of existing several causes and possibility of coexisting different pathologies in a patient, evolution of a consistent and universally accepted categorization would be an important step to be understood for these complicated cases. Another necessity for the use of a new-generally accepted and known classification system is to facilitate the communication between clinicians and clarify the targeted populations which would be evaluated in clinical researches. It is clear that this new classification system will promote the communication with patients. Widespread adoption of the PALM-COEIN system will light the way to the development of new treatment modalities of AUB.

Keywords: Abnormal uterine bleeding; classification; dysfunctional uterine bleeding; menstrual disorders

ÖZET

Amaç: 2011 yılında International Federation of Gynaecology and Obstetrics working group on menstrual disorders (FIGO) anomal uterin kanama ile ilgili "PALM-COEIN" olarak adlandırılan yeni bir sınıflandırma sistemini oluşturmuştur. Çalışmamızın amacı, yeni sınıflandırma sisteminin incelenmesi ve anormal uterin kanama için kullanılan klasik terminoloji ile karşılaştırılmasıdır. **Gereç ve Yöntemler:** Çalışmamız retrospektif olarak Şubat 2015-Şubat 2016 tarihleri arasında Zekai Tahir Burak Kadın Sağlığı Eğitim ve Araştırma Hastanesi jinekoloji kliniği'nde yapılmıştır. Çalışma bilinen kronik hastalığı olmayan premenopozal kadınları içermektedir. Çalışmaya dahil edilen her hasta anatomik yapı, fizik muayene ve pelvik ultrasonografi ile değerlendirilmiştir. Uygun ise endometrial örnekler ve histerektomi materyalleri histopatolojik inceleme için alınmıştır. Altta yatan olası sebepler yeni sınıflandırma sistemine göre kategorize edilmiştir. **Bulgular:** Çalışma anomal uterin kanama şikayeti olan premenopozal 437 kadını içermektedir. Genel olarak kanama şikayeti olan hastalar klasik terminolojiye göre leiomyoma uteri, polip, adenomyozis, hiperplazi, iatrojenik nedenler, karşılanmamış östrojen, malignite, servikal polip, hormonal bozukluklar, servikal enfeksiyon, ve doğum kontrol hapları ve intrauterin araçları da içeren doğum kontrol yöntemlerine bağlı sebepler olmak üzere farklı sebepler için hipermenore, menoraji, metrorroji ve menometrorroji başlıkları altında gruplandırıldı. PALM-COEIN sınıflandırmasına göre hastalarda 175 (%40) polip, 93 (%21,3) adenomyozis, 153 (%35) leiomyoma, 16 (%3,7) malignite ve hiperplazi saptandı. **Sonuç:** Anormal uterin kanamanın sınıflandırmasında genel bir tutarsızlık vardır. Bir hastada birçok nedenin ve farklı patolojilerin birlikte bulunabilmesi sebebi ile tutarlı ve universal olarak kabul gören bir sınıflandırma sistemi karışık vakaların da anlaşılması için önemli bir adım olacaktır. Diğer bir gereklilik ise: Genel olarak kabul gören ve bilinen bir sınıflandırma sistemi klinisyenler arasındaki iletişimi geliştirecek ve klinik araştırmalarda incelenmesi hedeflenen kitleyi açıklığa kavuşturacaktır. Ayrıca yeni sınıflandırma sisteminin hastalar arasındaki iletişimi güçlendireceği de açıktır. PALM-COEIN sisteminin yaygın kullanımı anormal uterin kanamanın yeni tedavi modalitelerine de ışık tutacaktır.

Anahtar Kelimeler: Anormal uterin kanama; sınıflandırma; disfonksiyonel uterin kanama; menstrüel düzensizlik

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Abnormal uterine bleeding (AUB) is generally defined as abnormal bleeding from the uterus in terms of regularity, volume, frequency, or duration and occurs in the absence of pregnancy.^{1,2} AUB can be classified as acute or chronic. Acute AUB implies an episode of heavy uterine bleeding which is severe and would probably require immediate intervention to prevent hemodynamic instability.² Chronic AUB, which defines abnormal uterine bleeding continues for previous 6 months, occurs in approximately 10 to 35 percent of women.^{3,4} Patients who present with acute AUB should be evaluated in three stages: 1) Assessing rapidly the clinical condition and vitals, 2) Determining the possible etiology of the bleeding, 3) Choosing the most appropriate treatment. Chronic heavy or prolonged uterine bleeding can result in anemia, interfere with daily activities, and raise concerns about uterine cancer but occasionally an exacerbation of chronic AUB is severe enough to necessitate emergency medical care.

Initial evaluation of the patient with acute AUB should provide a serious assessment for signs of hypovolemia, anemia and potential hemodynamic instability. In case of hemodynamically instability and hypovolemia, intravenous access with at least one or two large intravenous lines should be initiated rapidly for blood transfusion and clotting factor replacements. After the initial assessment and stabilization, the probable etiology of acute AUB should be evaluated to choose the most appropriate and effective treatment strategy.

The etiologies of acute and chronic AUB are multifactorial and can be classified under the name of same reasons. The Menstrual Disorders Working Group of the International Federation of Gynecology and Obstetrics (FIGO) revealed a classification system and revised terminology for the etiologies of AUB, which has been approved by the International Federation of Gynecology and Obstetrics' executive board and also promoted by the American College of Obstetricians and Gynecologists.^{2,5} The aim of this new classification system was avoiding poorly responded or confusing terms used previously to define AUB (eg, menorrhagia, menometrorrhagia, polimenorrhea,

oligomenorrhea). This system classified the etiologies of AUB as "related to uterine structural abnormalities" and "unrelated to uterine structural abnormalities". Under these basic headers AUB categorized following the acronym PALM-COEIN: **P**olyp, **A**denomyosis, **L**eiomyoma, **M**alignancy and hyperplasia, **C**oagulopathy, **O**vulatory dysfunction, **E**ndometrial, **I**atrogenic, and **N**ot otherwise classified.

Determining the etiology of the uterine bleeding is essential to choose the most appropriate and effective treatment strategies for individual patients. General inconsistency in the classification used to describe AUB has been admitted as the main reason to create this classification system which was approved by FIGO. Another necessity for the use of a new-generally accepted and known classification system is to facilitate the communication between clinicians, investigators and also patients. This system may clarify the targeted populations which would be evaluated in clinical researches. Widespread adoption of the PALM-COEIN system will light the way to the development of new treatment modalities and researches of AUB.

MATERIAL AND METHODS

The descriptive cross-sectional study was conducted in Gynaecology Clinic of a tertiary referral hospital, Zekai Tahir Burak Women Health Care, Training and Research Hospital in Ankara, Turkey, between February 2015 and February 2016.

The study was planned as a retrospective study and we did not apply for ethical committee approval. The Institutional review board approved the study protocol (4/27/2016*19).

The study included 437 reproductive aged (25-45 years) premenopausal women coming to outpatient clinic with complaints of abnormal uterine bleeding presented with unpredictable, irregular, excessive duration, abnormal volume, and/or abnormal frequency of menses and intermenstrual bleeding were incorporated to the study. Each patient has been examined in terms of anatomical structure, physical examination and pelvic ultra-

sonography. Endometrial samples and hysterectomy specimens were obtained for histopathological investigation if applicable. Possible underlying causes were categorised according to the new classification system. Women with bleeding as a result of cervical causes were excluded. "Coagulopathy" was named for all cases with several defects of coagulation. "Iatrogenic" category was characterized by any hormone or steroid intake. "Ovulatory dysfunction" is considered as the condition manifesting in some combination of unpredictable timing of bleeding and a variable amount of flow. Hypermenorrhea was used to define excessive menstrual bleeding with soaking more than one pad or tampon in an hour; menorrhagia was used to describe the condition when the menses are prolonged and associated with heavy bleeding, metrorrhagia was used to define increased duration of menstrual flow beyond 7 days and irregularly continues during the cycle and menometrorrhagia was used to describe heavy, prolonged and irregular bleeding.

Data was analyzed by SPSS version 16 and descriptive statistics were presented as frequencies and percentages.

RESULTS

The study included 437 women who presented with complaints of abnormal uterine bleeding. The people who complained of general sources of bleeding has categorized with classical terminology and examined under the name of hypermenorrhea, menorrhagia, metrorrhagia and menometrorrhagia (Table 1). Hypermenorrhea, menorrhagia, metrorrhagia and menometrorrhagia were used to explain bleeding patterns of the causes including polyps, leiomyoma uteri, adenomyosis, hyperplasia, iatro-

genic causes, unopposed estrogen, malignancy, cervical polyp, hormone imbalance, infection of cervix and problems linked to birth control pills and intrauterine devices. Polyps are presented with hypermenorrhea, menorrhagia, metrorrhagia and menometrorrhagia in different cases. 44% of polyps were presented with hypermenorrhea, 9.7% of polyps were presented menorrhagia, 10.8% of polyps were presented with metrorrhagia and 35.4% of polyps were presented with menometrorrhagia (Table 1). 66.6% of adenomyosis were presented with hypermenorrhea, 12.9% of adenomyosis were presented menorrhagia, 6.4% of adenomyosis were presented with metrorrhagia and 13.9% of adenomyosis were presented with menometrorrhagia (Table 1). Leiomyomas were presented with hypermenorrhea, menorrhagia, metrorrhagia and menometrorrhagia with a frequency of 40.5%, 0.6%, 6.5% and 52% respectively (Table 1). Malignancies were mostly presented with hypermenorrhea (37.5%) and menometrorrhagia (37.5%). Iatrogenic causes were presented hypermenorrhea and menometrorrhagia with a frequency of 30% and 40% respectively (Table 1). Cases which has categorized with PALM-COEIN classification system demonstrated the results as 175 (40%) polyp, 93 (21,3%) adenomyosis, 153 (35%) leiomyoma, 16 (3,7%) malignancy and hyperplasia (Table 1). When we look at the subclassification of leiomyomas, submucozal leiomyoma 26.79% and others 73.21 were established (Table 2).

DISCUSSION

The study was undertaken to define the causes of AUB based on PALM-COEIN classification and to correlate the clinical and histopathological features

TABLE 1: Cases which has categorized with classical terminology and PALM-COEIN classification system.

PALM-COEIN System	Hypermenorrhea	Menorrhagia	Metrorrhagia	Menometrorrhagia
P (Polyp) (n=175)	77 (44%)	17 (9.7%)	19 (10.8%)	62 (35.4%)
A (Adenomyosis) (n=93)	62 (66.6%)	12 (12.9%)	6 (6.4%)	13 (13.9%)
L (Leiomyoma uteri) (n=153)	62 (40.5%)	1 (0.6%)	10 (6.5%)	80 (52%)
M (Malignancy) (n=16)	6 (37.5%)	3 (18.7%)	1 (6.2%)	6 (37.5%)
O (Others) (n=190)	132 (69.4%)	16 (8.4%)	5 (2.6%)	37 (19.4%)
I (Iatrogenic) (n=10)	3 (30%)	2 (2%)	1 (1%)	4 (40%)

TABLE 2: Leiomyoma subclassification.

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Leiomyoma subclassification (n=153)	%35.01
Submukozal (n=41)	26.79%
0 (n=2)	
1 (n= 5)	
2 (n=34)	
Other (n=112)	73,21%

to be able to figure out the precise etiology of AUB for appropriate management of AUB.

Defining the possible etiological condition is the most important milestone in effective management of AUB. The treatment modalities differs according to the patients, clinicians' experiences, causes of bleeding and respond to the medical treatment. Common interpretation of results of several clinical studies aiming to determine epidemiology, etiology, treatment and prognosis of AUB was prevented due to the lack of consistency in the classification. Dysfunctional uterine bleeding was used under the name of any kind of irregular uterine bleeding that occurs in the absence of recognizable pelvic pathology, general medical disease, or pregnancy.⁶ "Dysfunctional uterine bleeding (DUB)" now an useless term as the women classified in this category in the past actually fall in FIGO categories of a varying combination of coagulopathy, disorder of ovulation, or endometrial pathologies considered as "unrelated to uterine structural abnormalities".⁷

Polyps are defined combination of ultrasound (including saline infusion sonography) and hysteroscopic imaging with or without histopathology.⁸ Although the most of polyps are asymptomatic, the contribution to AUB of polyps varies from 3.7% to 65%.⁹ In the present study, 27.4% of women with AUB was found to have polyps resulting in AUB. It is also important to exclude polypoid-appearing endometrium as this appearance may be a variant of normal estrogen effected endometrium.⁸

The diagnostic criteria for adenomyosis have traditionally been based on histopathologic evaluation of the depth of "endometrial" tissue into my-

ometrium especially in hysterectomy specimens.¹⁰ This feature is a substantially limiting factor for the requirement of diagnosis of adenomyosis. In this system diagnostic criteria based on both sonography and magnetic resonance imaging (MRI) were used.^{11,12} The ratio of adenomyosis in our study was 14.5% similarly to the study of Qureshi et al. with 15.4% adenomyosis as a cause of AUB.⁷

Most leiomyomas (fibroids) are asymptomatic, and frequently is not considered as a cause of AUB. Leiomyomas are classified in a subclassification system including submucozal and other leiomyomas.¹³ This system ensures the common language between clinicians leading to appropriate management. In the recent study we have found the leiomyomas accounting 24% correlatively to the study of Mishra et al.¹⁴ Leiomyomas are the most common cause of AUB in literature.^{7,15} Leiomyomas can be subclassified based on the site as submucosal (L-SM) and others (L-O). Submucosal type constituted 26.79% of leiomyomas in the present study, similar to Arnold et al. study.¹⁶ It was thought that submucous fibroids distort the cavity and more likely to cause heavy menstrual bleeding (HMB).¹⁷

Endometrial hyperplasia which is abnormal proliferation of endometrial glands is a cause of AUB and its progression to endometrial carcinoma is also a serious cause of AUB.¹⁸ AUB-M was seen in 2.5% of cases, similar to Qureshi et al study and Mishra et al. study.^{7,14}

Although coagulopathies are reported to be found 13% of women presenting with AUB, our study had no cases with diagnosed coagulopathies and also no endometrial pathologies. Ovulatory dysfunction was the most common cause of AUB (29.8%) in the present study and Arnold et al found ovulatory dysfunction 17.2% of cases.¹⁶

Most of the unscheduled bleedings are related to exogenous hormone therapy or drugs effecting hormones.⁹ Medications like anticonvulsants, hormonal steroids and antipsychotics can cause hormonal instability which can result in AUB. Intrauterine contraceptive device (IUD) may cause low grade endometritis that induces AUB.⁹ Iatrogenic causes are in charge of 1.56% of AUB in recent study.

In our study, the cases were categorized according to positive results of endometrial samples, hysterectomy specimens if possible, ultrasonographic findings and laboratory results. Endometrial samples do not rule out possible adenomyosis or myoma uteri. There can be one or more underlying causes together and it is not possible to be sure about the certain cause of AUB without performing the same diagnostic tests (hysterectomy specimens, coagulation parameters, imaging methods and detailed anamnesis of medication and diseases) for all cases. These are the weak points of our study.

Consequently, further studies are needed to show the causes of AUB according to PALM-

COEIN system. This analysis will enable us to have a better understanding of classification of etiologic factors to develop appropriate management strategies for the treatment of AUB.

There is no conflicts of interest in connection with this paper, and the material described is not under publication or consideration for publication elsewhere. We also confirm that all the research meets the ethical guidelines, including adherence to the legal requirements of the study country.

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