

A Histopathological Study of Endometrium in Abnormal Uterine Bleeding: A Retrospective Study

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Abstract--- *Background: Abnormal uterine bleeding (AUB) is a common gynecological complaint associated with considerable morbidity and significantly affects the patient's family, personal and social life. The study aimed to analyze the histomorphological patterns of endometrium in patients presenting with AUB and also to determine the incidence of AUB in various age groups.*

Methods: *This type of research is a descriptive study with a cross-sectional approach. Data was taken from medical records of the patients with a diagnosis of Abnormal Uterine Bleeding by dilatation and curettage and then by a histopathological laboratory examination at the K.R.M.T Wongsonegoro Hospital Semarang, Indonesia.*

Results: *A total of 87 cases were analyzed. The patient's age ranged from 19-68 years old. Body Mass Index (BMI) divided three groups: Normal weight 27%, overweight 35.6% and obese 36.8%. Endometrial hyperplasia was the most common histopathological finding and was seen in 29.9% of patients, followed by irregular shedding 24.13%, disorder proliferative pattern 17.24%, proliferative with glandular and stromal breakdown 9.19%, Progestin effect 6.89%. Statistical test results with chi-square relationship between BMI with histopathological features is $p = 0.290$.*

Conclusion: *Statistical test results showed no relationship between age and BMI with histopathological results. We found that hyperplasia endometrium is the commonest cause of abnormal uterine bleeding.*

Keywords--- *Abnormal Uterine Bleeding, Curettage, Endometrial Hyperplasia.*

I. INTRODUCTION

Abnormal uterine bleeding (AUB) is a disorder that often occurs. By definition, AUB is a range of symptoms, such as heavy menstrual bleeding.^{1,2} Involve more blood loss (> 7days or > 80 mL) during menses (menorrhagia, or hypermenorrhagia), intermenstrual bleeding (occur frequently and irregularly between menses /metrorrhagia) and a combination of heavy and prolonged menstrual bleeding (menometrorrhagia).^{3,4} Menstrual disorders which were previously described as dysfunctional uterine bleeding, are now more appropriately referred to as AUB. The terminology of AUB was established by the International Federation of Gynecology and Obstetrics (FIGO), called

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the PALM-COEIN classification system.¹PALM indicates structural causes: polyp, adenomyosis, leiomyoma, and malignancy, and COEIN indicates non-structural causes: coagulopathy, ovulatory dysfunction, endometrial, iatrogenic, and not yet classified.⁵ PALM indicators can be examined visually (imaging and histopathology) and COEIN is a non-structural cause.¹Thus, a curettage is the methods to determine the etiology of AUB, based on PALM-COEIN classification. Our main concern is to determine and excluding the possibilities of malignancy, especially on perimenopause women. If cancer or hyperplasia that tends to be malignant were found from the curettage, it needs special oncology-based treatment.

AUB are common conditions that affect 14-25% or one-third of women in reproductive age, that fill affects them physically, socially, emotionally, quality of life.¹ Women with abnormal bleeding have a lower quality of life than the one with none. AUB leads to loss of productivity, and surgical intervention may be needed.⁶ Also, it is the most common cause of iron deficiency in developed countries and chronic illnesses in developing countries.⁷ According to the previous study, the prevalence of AUB varies on every population, but it is fluctuating between 10% and 30%.² In the UK, this condition made approximately 800.000 women seek for help.¹ In India, the prevalence of AUB is around 17.9%.⁶

The bleeding pattern is used for identifying the etiology of AUB and it also contributing to diagnose secondary comorbidities.² The standard menstrual index consists of 4 elements from menstrual bleeding, which are the frequency and regularity of menstruation and menstrual cycle, duration of the cycle, flow's duration, and volume of blood loss monthly. The volume of blood loss is affected by uterus contraction, vascular tone, hemostatic function. Normal menstruation has a frequency of 24-38 days, with a duration of 4,5-8 days, and the volume of blood loss of 5-80 ml every cycles.³

Acute AUB is defined as the amount of uterine bleeding that does not require any immediate intervention to prevent blood loss of reproductive age who are not currently pregnant. AUB is said to be chronic when there is abnormal uterus corpus bleeding in terms of quantity, regularity, and/or onset that has existed from the previous 6 months.^{2,3}

Our goal is to determine the underlying pathologies of AUB, whether is it dysfunctional or organic lesions, especially hyperplasia that could lead to neoplasm (adenocarcinoma). Malignant disease is one of our country's main health problems. In Indonesia, particularly in our city, Semarang, there has not been any study about AUB. We felt that it is really important to map out AUB's underlying disease to lower the incident rate and improve our health service to treat cancerous disease. We also tried to explain and find any diseases that precedent AUB to improve patients' quality of life.

II. METHODS

A total of 87 endometrial samples resulting from curettage were histopathologic examination in the pathology laboratory of K.R.M.T. Wongsonegoro General Hospital, Semarang.

This type of research is using a descriptive-analytic method with a cross-sectional approach. The data was taken from medical records of patients with a diagnosis of Abnormal Uterine Bleeding by curettage and then by

histopathological examination treated at K.R.M.T. Wongsonegoro General Hospital period January 2017 - December 2017. Data analysis was performed by t-test using SPSS 21.

Sample selection by consecutive sampling is that all subjects who meet the study criteria were included in the study, which was carried out by looking at the patient's medical records by curettage on the indication of abnormal uterine bleeding and then histopathological examination at the K.R.M.T Wongsonegoro General Hospital for the period January 2017 – December 2017. This study was approved by our Ethical Committee and we already got the ethical clearance with references number 070/4801/2019.

III. RESULTS

The study conducted with 87 endometrial samples presented with abnormal uterine bleeding. The main outcomes revealed that 55 cases out of 87 cases presented with dysfunctional uterine bleeding, and the remaining presented with an organic lesion.

Table 1: Functional Lesion Lead to Abnormal Uterine Bleeding

Functional lesion	
Irregular shedding	21 (38.19%)
Simple endometrial hyperplasia	15 (27.27%)
Proliferation with glandular and stromal -breakdown	10 (18.18%)
Progestin effect	6 (10.91%)
Abnormal secretion	3 (5.45%)
Total	55 (100%)

Table 2: Organic Lesions Lead to Abnormal Uterine Bleeding

Organic Lesions	
Non-atypical endometrial hyperplasia	26 (81.26%)
Adenocarcinoma	3 (9.38%)
Endometrial atrophy	1 (3.12%)
Chronic endometritis	1 (3.12%)
Adenomyosis	1 (3.12%)
Total	32 (100%)

The study showed that irregular shedding of the endometrium is the most common cause of the dysfunctional uterine problem, and endometrial hyperplasia is the most common cause of the organic lesions of the uterus. We found that adenocarcinoma could be the main problem of abnormal uterine bleeding caused by organic lesions.

Table 3: Distribution of Different Endometrial Patterns in Different Age Groups

Histopathological diagnosis	< 40	40 – 55	>55	Total
Adenocarcinoma	1	2	0	3 (3.44%)
Non-atypical endometrium-hyperplasia	8	17	1	26 (29.88%)
Abnormal secretory phase	2	1	0	3 (3.44%)
Simple endometrial-hyperplasia	6	9	0	15 (17.24%)
Proliferative with glandular and stromal breakdown	6	4	0	10 (11.49%)
Irregular shedding	8	12	1	21 (24.13%)
Progestin effect	2	4	0	6 (6.89%)
Adenomyosis	1	0	0	1 (1.14%)
Atrophy endometrium	0	1	0	1 (1.14%)
Chronic endometritis	1	0	0	1 (1.14%)
Total	35	50	2	87 (100%)

In the age group 40-55 years old, 50 cases were found. The most common histopathological in this group was non-atypical endometrium hyperplasia and we found no case of chronic endometritis. In the age group over 55 years old, we only found 2 cases, which are irregular shedding and non-atypical endometrium hyperplasia.

Table 4: The Relation Between Ages and Body Mass Index to Pathologic Anatomy Studies on Abnormal Uterine Bleeding

Variable	Hyperplasia	Carcinoma	Others	Total N (%)	p- value
Age					0.740
< 40	8	1	26	35 (40.22)	
40-55	17	2	29	48 (55.17)	
>55	1	0	3	4 (4.59)	
BMI					0.290
Normal weight	6	0	18	24 (27.58)	
Overweight	13	1	17	31 (35.63)	
Obese	7	2	23	32 (36.78)	

The results were calculated with chi-square. It showed that there is no significant relationship between age and BMI to histopathology patterns of women with abnormal uterine bleeding.

IV. DISCUSSION

Evaluation of patients with abnormal uterine bleeding and identifying those with dysfunctional uterine bleeding is achieved with a combination of the following: history, physical examination, laboratory evaluation, USG, and endometrial sampling. Abnormal uterine bleeding is one of the commonest complaints leading to endometrial sampling by endometrial biopsy or curettage. Examination of endometrial curettage is a challenge to practicing pathologists, largely due to the wide range of morphologic patterns resulting from the normal and abnormal change, exogenous hormones, infections, and intrauterine tumors.

Based on the characteristics of the overall histopathological results from our study we found that the highest number was non-atypical endometrial hyperplasia (29.88%), followed by irregular shedding (24.13%) and simple endometrial hyperplasia (17.24%). Whereas the research conducted by Gerald Dafe Forae et al in 2013, the most number was complex endometrial hyperplasia (27.7%), followed by proliferative (22.5%) and hyperplasia simplex (19.9%).⁸

Endometrial Hyperplasia

Endometrial hyperplasia (EH) is a condition in which the lining of the uterus or endometrium is abnormally thick. The most common symptom of endometrial hyperplasia is abnormal uterine bleeding, such as menorrhagia, menometrorrhagia.^{10,11}

According to WHO, endometrial hyperplasia are classified into simple hyperplasia, complex hyperplasia, simple atypical hyperplasia, complex atypical hyperplasia.¹¹⁻¹³ In our study 87 patient was diagnosed by biopsy, 17,24% (15 cases) patient was diagnosed with simple hyperplasia and non-atypical hyperplasia 29,88% (26 cases). According to the KH Allison study with 2.601 specimens reviewed, 70,31% was diagnosed with simple hyperplasia and 11,07% cases are atypical hyperplasia.¹⁴ In James V's study in 241 control patients had index biopsies 27,8% in simple hyperplasia and 14,1% in atypical hyperplasia.¹³

Simple hyperplasia is characterized by benign proliferation of endometrial glands with low risk of progression to endometrial carcinoma. Atypical hyperplasia has the greatest risk in the progression of endometrial carcinoma.^{11,12} Woman with atypical hyperplasia were 14 times more likely develop to carcinoma than non-atypical EH.¹³ EH peak incidence was founded in the early 60's woman, which simple hyperplasia was 142 among 100.000 women per years, complex hyperplasia 213 among 100.000 women per years, and atypical hyperplasia 56 among 100.000 women per years.¹¹

Adenocarcinoma

From our experiment, there are only 9.35% of the total sample of abnormal uterine bleeding that suffers from adenocarcinoma. This correlates with the study conducted by GawronIetal,¹⁵ Jairajpur et al,¹⁶ and Snehkiran et al¹⁷ where endometrial cancer in premenopausal women was detected in only 0,9%1, 5%, and 19,1% respectively of total samples. As we know, there are many cases of endometrial cancer as it is the fourth most common malignancy that women after breast, lung, and colorectal cancer. The mortality increases by 8% for the past 20 years, and it is most common in women age 63, with 90% of cases occurred in women age more than 50 years.¹⁷ Although there are lots of cases of abnormal uterine bleeding, the tendency of endometrial carcinoma is low, as we could see from all of the studies.

Multiple risk factors that could cause endometrial carcinoma like endogenous factors such as obesity, nulliparity, women age > 52 years, unopposed estrogen, and others.¹⁸ Most women with it have symptoms of abnormal uterine bleeding; this includes irregular menstrual bleeding, spotting, and bleeding between menstrual periods. For postmenopausal women, any bleeding is abnormal.¹⁹

Endometrial cancer was diagnosed by endometrial biopsy, dilatation and curettage, and hysteroscopy. It is also supported by physical examination and a transvaginal ultrasound exam. The treatment for adenocarcinoma is total hysterectomy with bilateral salpingo-oophorectomy. Radiation and chemotherapy also play a role in treatment.¹⁸ We only found a few numbers of adenocarcinoma in this study, probably due to early hysterectomy before the progression becomes malignant.

Irregular Shedding

In our study, we found 24.13% of irregular shedding cases out of our entire population. Eight patients of irregular shedding aged below 40, twelve patients aged between 40 to 55 years old, and one patient aged above 55 years old. In the previous study, there were 2.35% cases of irregular shedding out of their entire population in abnormal uterine bleeding.¹⁶ Irregular shedding was the most founded in our functional issues group.

Irregular shedding is a term that pictures an abnormal condition of menstrual blood flow. It will become prolonged and profuse blood during the menstrual period. It is diagnosed with a curettage method and histopathology examination of the endometrial tissue. The curettage of the entire uterus should be done within five days or more after the onset of menstruation. In the normal uterus, the surface of the endometrium should be regenerated, it could be seen from the microscopic examination. However, if the regeneration process is not fully complete or even not found, it means irregular shedding of the endometrial lining. From the previous study, the bleeding occurs in the secretion phase, specifically in corpus luteum, that occurs before it should be happening. It is

shown by a basal temperature indicator. Progesterone levels did not decline during this phase. Thus, the bleeding continues where it should have been stopped.²⁰

Endometrial Atrophy

We found one case (2%) of endometrial atrophy from the age group of 40-55 years that leads to AUB. From other studies, they also found one case (0.71%).¹⁷ and another study found three cases ranging from the age group 41-50 years (2.19%) and four cases ranging from age group 51- 60 years (8.88%).²¹ The definitive pathology from endometrial atrophy is still undetermined until now. It is suggested that there are correlations between vascularization anatomy or abnormal mechanism of the hemostatic. Blood vessels easily injured due to the thin-walled veins.

Chronic Endometritis

The chronic endometritis case was founded in our study (1.14%). In previous studies, it was found that chronic endometritis was also had a few percentages in histological findings. Previous studies found three cases (2.3%),¹⁷ seventeen cases (4.16%),²¹ and two cases (2%).²² Endometrial pathology is one of the causes of AUB (AUB-E in PALM-COEIN classification). Chronic endometritis is observed with biopsy or curettage, especially when AUB manifested.

Adenomyosis

Based on our study, we found only 1.14% of total samples that were diagnosed with adenomyosis. This correlates with the study by Bhosie et al,²³ where 5% with abnormal uterine bleeding turned out to be adenomyosis. Compared to other studies by Rizvi et al,²⁴ the result is different from us, where adenomyosis was found in 46,34% samples; where they conclude that adenomyosis was found to be the commonest cause of abnormal uterine bleeding. Several risk factors contribute to adenomyosis, including age were between 40-50 years old and multiparity. Other factors such as smoking, tamoxifen treatment remain controversial.²⁵

Progestin Effect

In our study, there are 6.89% of total samples have a histopathological diagnosis of progestin effect. No absolute data hasn't been found in other studies. Women who used progestin contraceptive methods that have abnormal uterine bleeding is treated with supplemental estrogen to stabilize the endometrium, or using Non-steroidal anti-inflammatory drugs to decrease endogenous prostaglandins if the bleeding still exist.²⁶

Proliferation with A glandular and Stromal Breakdown

Ten patients were identified with a proliferative disorder with a glandular and stromal breakdown (11.49%). Six of them were aged below 40 and the remaining were aged between 40-55 years old. Endometrial glandular and stromal breakdown (EGBD) is recognized by the pattern of stromal collapse as well as the disrupted glands. With breakdown and bleeding, fragmented glands lose the stroma that should be present between intact glands.²⁷ In Japan study by Norimatsu Y, during 7 years period 144 cases for which histopathological diagnoses were obtained following endometrial curettage. Thirty-two cases of EGBD (patients aged 30-67, average 49.6%) was founded.²⁸

Abnormal Secretion

The Abnormal secretory phase leads to AUB. We found three cases out of the entire population (3.44%). In

previous studies, they found 66% that manifested in various bleeding pattern.¹⁵ Another study found only six cases (4.7%) secretory disorder that leads to AUB. Abnormal secretion is one of the functional issues. The bleeding occurs because of the dysfunctional issue of ovulatory cycle.²¹

V. CONCLUSION

Endometrial biopsy and curettage were done to diagnose women with abnormal uterine bleeding, which is the most common symptom found located in Semarang, Indonesia. The histopathological patterns in abnormal uterine bleeding have various results from normal to malignancy. From our study, we concluded that hyperplasia endometrium is the commonest cause of abnormal uterine bleeding. Hyperplasia has tended to be malignant, but in reality, the incidence of adenocarcinoma is low.

Conflicts of Interest

The authors affirm no conflicts of interest in this study.

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