ORIGINAL ARTICLE

Morphological study of Pipelle biopsy specimens in cases of abnormal uterine bleeding

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Abstract

Objective: To determine the frequencies of common morphological patterns of abnormal uterine bleeding on Pipelle biopsy specimen.

Methods: The cross-sectional study was conducted at PNS Shifa Hospital, Karachi, and comprised endometrial Pipelle biopsies of patients with abnormal uterine bleeding received between January 2013 and January 2014. Patient's age, marital status, parity and histopatholgical spectrum were recorded. SPSS 17 was used for data analysis.

Results: Of the 101 patients, 53(52.50%) presented with proliferative endometrium, 22(21.80%) had secretory endometrium, 13(12.9%) presented with chronic non-specific endometritis, 8(7.9%) had endometrial hyperplasia without atypia, and 5(5%) had endometrial hyperplasia with atypia. Besides, 86(85.1 %) were nulliparous; 15(14.9%) were parous; 92(91.1%) were married and 9(8.9%) were unmarried.

Conclusions: The most common morphological pattern was proliferative endometrium. Though Pipelle has its own limitations, it performed better when endometrial pathology was global rather than focal.

Keywords: Endometrial pathology, Abnormal uterine bleeding, Pipelle endometrial biopsy. (JPMA 65: 705; 2015)

Introduction

Menstrual problems account for much of the morbidity affecting up to one in five women at some point during their lifespan. Specifically, abnormal uterine bleeding is one of the most common debilitating menstrual problems. A study based on epidemiology of menstrual disorders in developing countries revealed that the prevalence of abnormal uterine bleeding (AUB) in developing countries, including Pakistan, is about 5-15%.[1] In the United Kingdom the annual frequency of general practitioner consultation rates for this condition is 31.0 per 100 women. The problem is common worldwide but the causes may vary from one region to another.[2] The aetiology of AUB includes a wide range of disorders that can be secondary to female genital tract pathology, pregnancy and pregnancy-related disorders, and systemic illnesses.[3] Spectrum of common pathologies that can be detected histologically in AUB include proliferative endometrium, secretory endometrium, chronic non-specific endometritis, endometrial hyperplasia without atypia and endometrial hyperplasia with atypia. Literature based on 20 observational and diagnostic studies reveals that prevalence of normal menstrual pattern is 30-50% in AUB.[3-9] It is also published that AUB has remained one of the most frequent indications for hysterectomy and in 40% cases no definite organic pathology is established.[10] In UK in the early 1990s it was estimated that at least 60% of women presenting with heavy menstrual bleeding would have a hysterectomy to treat the problem. There is significant morbidity associated with the procedure, reported up to 28/10,000 in National Health Service (NHS) hospitals of England and Wales per annum and even higher in our country.[11] These days hysterectomy is considered the last option to treat AUB in developed countries since there are many other minimally invasive surgical modalities available like endometrial ablation, thermal balloon therapy etc.[12-14] Since endometrium is the best accessible tissue for histopathological evaluation of uterine bleeding, several methods are used for endometrial sampling among which the dilatation of the cervix and curettage of the uterine cavity under general anaesthesia has long been the gold standard for the assessment of AUB. The method requires laboratory investigations, hospitalisation and carries the risks of general anaesthesia. Outpatient procedures are simple, inexpensive and avoid the need of general anaesthesia. One of these procedures is Pipelle endometrial sampling. Pipelle endometrial biopsy is considered a cheap and easy outdoor procedure.[15] Endometrial Pipelle was introduced in 1930 as an outpatient device to obtain an endometrial biopsy. It is a thin plastic suction tube, 3mm in diameter, with graduated markings designed to create a high vacuum without vacuum pump. It is mainly used in women with AUB who are from premenopausal or postmenopausal age groups. It is also suitable for women under 40 years of age with very low risk of developing endometrial carcinoma. Further investigations may be needed in high-risk symptomatic women. The procedure

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is very simple and convenient. Some patients may experience mild abdominal pain with some vaginal spotting for a short time after the procedure.[16]

The current study was planned to determine the frequencies of common morphological patterns of AUB on Pipelle biopsy specimen.

Materials and Methods

The cross-sectional study was conducted at PNS Shifa Hospital, Karachi, and comprised cases 20-60 years of age presenting with AUB between January 2013 and January 2014. The sample size was calculated to give the study 80% power to detect a frequency of 7% with the level of significance being 5%.[2] Convenient sampling was done. Patients with pregnancy-associated bleeding and biopsy with inadequate tissue were excluded. Patients' medical records were reviewed to collect parameters including age, marital status, parity and clinical presentation. After formalin fixation, sections were prepared from paraffin-embedded tissue blocks and stained with haematoxilin and eosin (H&E). Microscopic evaluation was done by three pathologists. Outcome variables were assessed in the light of clinical history. Data was recorded and analysed using SPSS 17. Frequency and percentages were calculated for marital status, parity and morphological patterns, including proliferative endometrium, secretory endometrium, endometrial hyperplasia with and without atypia and chronic endometritis. Effect modifiers like age, marital status and parity were controlled through stratification. Chi square test was applied to check the association between categorical variables. P value less than or equal to 0.05 was taken as significant.

Results

Of the 101 patients, 56(55.40%) were in the reproductive age group between 18-39 years, 33(32.70 %) were in the perimenopausal age group between 40-50 years, and

Table-1: Morphological pattern according to age (n=101).

Morphological Pattern	Age (Years)				
	18-39	40-50	>51	Total	P-Value
Proliferative Endometrium	29(54.71%)	19(35.84%)	05(9.45%)	53(52.50%)	0.63
Secretory Endometrium	16(72.74%)	03(13.63%)	03(13.63%)	22(21.80%)	0.09
Endometrial Hyperplasia Without atypia	02(25%)	05(62.50%)	01(12.5%)	08(7.90%)	0.14
Endometrial Hyperplasia With Atypia	0(0%)	03(60%)	02(40%)	05(5.00%)	0.02
Chronic Endometritis	09(69.20%)	03(23.10%)	01(7.70%)	13(12.90%)	0.56
Total	56(55.44%)	33(32.67%)	12(11.88%)	101(100%)	0.04

Table-2: Morphological pattern according to parity (n=101).

Morphological Pattern	Parity			
	Parous	Nulliparous	Total	P-value
Proliferative Endometrium	48(90.56%)	05(9.44%)	53(52.50%)	0.10
Secretory Endometrium	17(77.27%)	05(22.73%)	22(21.80%)	0.24
Endometrial Hyperplasia Without atypia	06(75%)	02(25%)	08(7.90%)	0.40
Endometrial Hyperplasia With Atypia	04(80%)	01(20%)	05(5.00%)	0.74
Chronic Endometritis	11(84.62%)	02(15.38%)	13(12.90%)	0.95
Total	86(85.15%)	15(14.85%)	101(100%)	0.546

Table-3: Morphological pattern according to marital status (n=101).

Morphological Pattern	Marital Status			
	Married	Unmarried	Total	P-value
Proliferative Endometrium	48(90.56%)	05(9.43%)	53(52.50%)	0.84
Secretory Endometrium	18(81.81%)	04(18.19%)	22(21.80%)	0.08
Endometrial Hyperplasia Without atypia	08(100%)	0(0%)	08(7.90%)	0.35
Endometrial Hyperplasia With Atypia	05(100%)	0(0%)	05(5.00%)	0.47
Chronic Endometritis	13(100%)	0(0%)	13(12.90%)	0.22
Total	92(91.08%)	09(8.92%)	101(100%)	0.299

12(11.90 %) were in the postmenopausal age group >51 years. The overall mean age was 39.66±7.70 years (range: 25-58 years).

Proliferative endometrium was found in 53(52.50%) cases, secretory endometrium 22 (21.80%), endometrial hyperplasia without atypia in 8(7.9%), endometrial hyperplasia with atypia in 5(5%) and chronic endometritis in 13(12.9%).

Out of 53 cases of proliferative endometrium 29(54.71%) were between 18-39 years, while 19(35.84 %) were between 40-50 years and 5(9.34%) were >51 years.

Out of 22 cases of secretory endometrium, 16(72.72%) were between 18-39 years, 3(13.63%) were between 40-50 years and 3(13.63%) were >51 years.

Out of 13 cases of chronic endometritis, 9(69.23%) were between 18-39 years, 3(23.07 %) were between 40-50 years and 1(7.69 %) was >51 years.

Out of 8 cases of endometrial hyperplasia without atypia, 2(25%) were between 18-39 years and 05(62.5%) were between 40-50 years and 1(12.5%) was >51 years. Out of 5 cases of endometrial hyperplasia with atypia, no cases were seen between 18-39 years, 03(60%) were between 40-50 years and 2(40 %) were >51 years (p=0.04) (Table-1).

Further, 86(85.1%) women were parous and 15(14.9%) were nulliparous (p=0.54) (Table-2).

Finally, 92(91.1%) women were married and 09(8.9%) were unmarried (p=0.29) (Table-3).

Discussion

Endometrial diseases rank among the most common gynaecological disorders that affect women globally. These diseases cut across all age groups and contribute significantly to increased maternal morbidity and mortality. Most females with endometrial diseases present with AUB. AUB is excessive, erratic, or irregular bleeding usually associated either with hormonal disturbance or intrauterine pathology. Thus, AUB justify the need for urgent diagnosis. This is so because of the wide range of histopathological patterns of endometrium diseases. These lesions range from simple endometrial hyperplasia to more complex disorders, including endometrial carcinoma. Majority of these lesions can only be diagnosed by sampling the endometrium. Endometrial biopsy and curettage are two most important sampling methods for definitive diagnosis of the lesions.

The increasing use of Pipelle and other methods of biopsy not necessitating general anaesthesia has resulted in greater numbers of specimens with scant tissue, resulting in problems in assessing adequacy and in interpreting artefactual changes, some of which appear more common with outpatient biopsies. We planned this study to observe frequencies of common morphological spectrum of abnormal uterine bleeding by Pipelle biopsy specimen in Karachi as no such study has been done previously in the region before. There is scant data about the usefulness of this procedure. In our study 56(55.40%) cases were between 18-39 years, 33(32.70%) were between 40-50 years and 12(11.9%) were >50 years of age. Majority were married, 92(91.1%) and 86(85.1%) were multiparous. The frequency of morphological pattern on histopathological examination reveals that 53(52.50%) were with proliferative endometrium, 22(21.80%) had secretory endometrium, 13(12.9%) had chronic endometritis, 8(7.9%) had endometrial hyperplasia without atypia and 5(5%) had endometrial hyperplasia with atypia. One study[17] upon analysis of histopathology reports of Pipelle biopsy revealed secretory endometrium in 38.88% cases, proliferative endometrium in 34.92%, atrophic endometrium in 4.76%, adenomatous hyperplasia and carcinoma endometrium was in 5.55% cases. Endometritis was reported in 7.14% of cases. Among 126 patients, majority (38.09%) were in age group 35-45 years. The age group 46-55 was next in line. Analysis of parity distribution showed that majority of women were multipara (52.37%) i.e. parity $\geq$2. Only 4.76% cases were nullipara. In another study proliferative endomentrium was reported in 33%, cystic hyperplasia in 25% cases.[18] The results of present study also correspond with another study from Pakistan, where on analyzing the histopathology results of the samples 34% were showing proliferative endometrium.[19] Proliferative phase endometrium was reported in 42% by another study.[20] One study[21] showed that out of 119 specimens of endometrium that were analysed 73.94% cases were from peri-menopausal age group. The most common presenting complaint was menorrhagia (48.86%) followed by post-menopausal bleeding (26.05%). In peri-menopausal age group, proliferative endometrium (35.22%) was the predominant histopathological pattern followed by endometrial hyperplasia (23.86%). Atrophic endometrium (25.80%) was the most frequent finding followed by endometrial hyperplasia (19.35%) in post-menopausal age group. A study[22] analysed 2295 endometrial samples from women presenting with AUB from January 1995 to June 2008 and noted that the commonest histopathological diagnosis was secretory endometrium in 571(24.9%) cases, followed by proliferative endometrium in 498(21.7%), endometrial polyp in 227(9.9%), disordered proliferative endometrium

in 200(8.7%), simple cystic hyperplasia in 160(7%), chronic endometritis in 134(5.8%), inactive endometrium in 126(5.5%), atrophic endometrium in 70(3.1%), uterine malignancies in 41(1.8%), complex hyperplasia without atypia in 33(1.4%) and finally complex hyperplasia with atypia in 15(0.7%) cases. In the study, 202(9.6%) samples did not contain endometrial tissue and were considered insufficient for diagnosis. Uterine malignancies and complex hyperplasia with atypia were more common in the age group of 52 years and older, and were seen in 3.3% and 1.2% respectively.

Upon histopathological examination of the endometrium, one study[23] showed various histological patterns in AUB. Patterns of normal cyclical endometrium (proliferative and secretory phases) were the most common and seen in 165 (40.94 %) cases. They were also the predominant patterns seen in all the three age groups. Upon evaluation of the endometrium, another study[24] revealed various patterns on histopathology, functional causes accounted for majority of the diagnosis. Secretory endometrium seen in 71(32.4%) cases was the most common. While proliferative endometrium on histopathology was the second most common diagnosis seen in 67(30.5%) patients. Endometrial hyperplasia was seen in 24(10.9%) cases out of which simple hyperplasia without atypia was seen in 19, complex hyperplasia without atypia in 4 and complex hyperplasia with atypia in 1 case. The other diagnoses, which accounted for the rest of the functional causes of atypical uterine bleeding, were disordered proliferative endometrium 15(6.8%) cases, and luteal phase defects 3(1.3%).

Pipelle endometrial sampling was cost-effective and a safe procedure; it is widely used in the investigation of reproductive, peri-menopusal and post-menopausal women with AUB. It is a highly sensitive method for detection of abnormal changes in the endometrium; though it has its own limitations: it performs better when endometrial pathology is global rather than focal. In high-risk women, an additional method can be required to confirm the diagnosis. A combination of Pipelle and ultrasound can achieve high diagnostic accuracy. Hysteroscopy is the definitive investigation for AUB in cases where the diagnosis of other assessment methods remains uncertain.

Conclusion

The most common morphological pattern was proliferative endometrium. Although age was directly associated with more progressive endometrial lesions found in peri- and post-menopausal age groups such as endometrial hyperplasia, but hyperplastic changes were seen in women as young as 25 years, thus making it essential to investigate in women younger than 35 years of age. Though Pipelle has its own limitations, it performs better when endometrial pathology is global rather than focal.

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