original article

Histopathological pattern of endometrial biopsies in patients with abnormal uterine bleeding in a tertiary referral hospital in Jordan

Eman Husssein Alshdaifat,[a] Sami Saif El-Deen Al-Horani,[b] Majd Mahmoud Al-Sous,[b] Afnaan Sharaf Al-Horani,[c] Fernas Emile Sahawneh,[a] Amer Mahmoud Sindiani[c]

From the [a]Department of Obstetrics and Gynecology, Yarmouk University, Irbid, Jordan; [b]Faculty of Medicine, Jordan University of Science and Technology, Irbid, Jordan; [c]Department of Obstetrics and Gynecology, Jordan University of Science and Technology, Irbid, Jordan

Correspondence: Dr. Eman Hussein Alshdaifat · Department of Obstetrics and Gynecology, Yarmouk University, Irbid 21163, Jordan · eman.shdaifat@yu.edu.jo · ORCID: https://orcid.org/0000-0003-2096-3165

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BACKGROUND: Abnormal uterine bleeding (AUB) is a symptom that deviates from the normal menstrual cycle. AUB is characterized by changes in the frequency, volume, and duration of the menstrual flow. The etiology of AUB, which varies with age, may be attributed to both structural and non-structural causes.

OBJECTIVES: Determine the histopathological pattern of endometrial biopsies in patients with AUB across different age and parity groups who have undergone dilation and curettage (D&C), along with the discrepancy between D&C and histopathological findings after hysterectomy.

DESIGN: Retrospective chart review

SETTING: Tertiary referral hospital

PATIENTS AND METHODS: We collected data on all patients diagnosed with AUB between January 2015 and December 2020. Histopathological findings of all D&C endometrial biopsy samples were examined after being categorized by age and parity groups. Sensitivity, specificity, positive predictive value, and NPV were calculated to evaluate the diagnostic accuracy of D&C.

MAIN OUTCOME MEASURES: Histopathological pattern of D&C endometrial biopsies by age and parity groups.

SAMPLE SIZE: 3233 patients.

RESULTS: Most patients were in the 18-39 year age group, with normal cyclical findings being the most common histopathological finding. Malignant lesions were observed in 42 patients with a majority being older than 50 years. In 13.3% (42/316) of patients, D&C failed to detect intrauterine disorder that was found on hysterectomy. The overall accuracy of D&C in determining the existence of normal versus pathological findings was 75.60%, the sensitivity was 72.90%, the specificity was 77.90%, the positive predictive value was 73.86% and the NPV was 77.05% in our patients.

CONCLUSION: Normal cyclic changes account for the highest proportion of histopathological findings. However, hyperplasia and malignancies are important causes of perimenopausal and postmenopausal bleeding. While the use of D&C as a sampling tool for AUB cases remains questionable, the use of D&C in diagnosing premalignant and malignant cases is highly effective.

LIMITATIONS: Single-center, retrospective design, incomplete medical records, and inter-rater reliability could not be determined.

CONFLICT OF INTEREST: None.

Abnormal uterine bleeding (AUB) is a symptom that deviates from the normal menstrual cycle. AUB involves changes in frequency, volume, and duration of the menstrual flow.[1] In postmenopausal women, it is defined as any bleeding after 1 year of menstrual cessation.[2] The prevalence of this symptom is difficult to determine, as women may not seek treatment and physicians may depend on the patient's subjective perception of symptoms which fails to meet objective criteria. Around 10%-30% of reproductive-age women experience heavy menstrual bleeding, making the estimated prevalence of AUB, a broader term, exceed 10%-30%. The true impact of AUB is seen in subscales that measure the physical and emotional role functioning, hence impeding work productivity and other daily activities.[3]

The etiology of AUB varies with age; the first step is to exclude pregnancy-related causes by means of a patient history and the presence of the β-subunit of human chorionic gonadotropin.[4] After excluding pregnancy, a thorough investigation using the PALM-COEIN classification proposed by The International Federation of Gynecology and Obstetrics (FIGO) focuses on causes by structural pathologies (Polyps, Adenomyosis, Leiomyomas, and Malignancy or atypical endometrial hyperplasia [PALM]) while the "COEIN" causes are non-structural and are diagnosed by a wider approach of clinical assessment, history, and sometimes laboratory tests (Coagulopathies, Ovulatory disorders, primary Endometrial disorders, Iatrogenic and Not otherwise classified; COEIN).[5]

Dilation and curettage (D&C) is a surgical procedure that scrapes the endometrial lining for diagnostic and therapeutic indications. After a diagnosis of miscarriage or post-partum, D&C is one treatment option to relieve bleeding symptoms as it immediately evacuates and cleans the uterus from retained products of conception (RPOC).[6] Also, D&C is used in diagnosing ectopic pregnancy and differentiates it from a miscarriage, which is fatal if not detected early on.[7] In a non-gravid context, D&C retrieves specimens from patients with AUB to evaluate the endometrial lining. Patients at risk of atypical hyperplasia or carcinoma are selected for endometrial sampling to detect any histopathological atypia.[8] It is recommended that endometrial sampling be considered for all women in the perimenopausal age group and above.[9] Persistent AUB that is unexplained or not treated requires a uterine evaluation by endometrial sampling along with a uterine imaging modality.[9]

The efficacy of D&C as a sampling tool has been questioned.[10] Drawbacks include obtaining scant tissue, and not covering the entire endometrium. It is important to keep the patient's history in mind when interpreting the histopathological reports by D&C to avoid both over- and under-treatment of patients. In these AUB cases D&C is indicated. In this study, we aimed to describe the histopathological findings of all patients who underwent this procedure in our institution, regardless of the cause of AUB during a 6-year period. We further investigated the accuracy of D&C by comparing it to a subsequent hysterectomy specimen.

PATIENTS AND METHODS

This retrospective chart review assessed the histopathological patterns of endometrium obtained from patients presenting with AUB in the department of obstetrics and gynecology along with the pathology department at a tertiary center (King Abdullah University Hospital (KAUH), Ar-Ramtha, Jordan) from January 2015 to December 2020. All patients who underwent uterine biopsy using D&C for any indication, including pregnant patients during the study period, were included in the study. All other forms of endometrial biopsies (Pipelle) were excluded.

Biopsy was done in inpatient settings by either D&C under hysteroscopy or dilation and evacuation (D&E). In D&C, the cervix is dilated after passing the sound to know the length and direction of the uterus. In D&E, the cervix is already dilated. Once sufficient dilation has occurred, the sharp end of the curette is passed and the anterior, posterior wall, two lateral walls, and finally, the fundus of the uterus are curetted and the specimen was collected in a container containing 10% formalin and sent to the pathology lab for processing. Pathology slides were then prepared by fixing the endometrial tissues in 10% formalin. The paraffin-embedded tissues were sectioned and then stained with hematoxylin and eosin stain. Sections were studied by pathologists, under the light microscope.

Demographic data, parity, gestational age if pregnant, the indication, and histopathological findings were all collected from medical records. Patients were stratified by age groups (18-39, 40-49, and ≥50 years), and by parity status (nulliparous and multiparous). For statistical analyses, IBM SPSS, version 23 (Armonk, New York, United States: IBM Corp) was used for data processing and data analysis. Descriptive measures including mean, standard deviation, median, interquartile range (IQR), and minimum and maximum values are used to present quantitative variables. Numbers and percentages are presented for categorical variables. To evaluate the diagnostic accuracy, the D&C histological findings, which are considered the current

best practice, were matched to the histological findings from the hysterectomy specimens. Then the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated. This study was approved by the Institutional Review Board of Jordan University of Science and Technology (JUST)/ KAUH (47/139/2021). Patient consent was waived as this retrospective chart review involved electronic medical records review and analysis on de-identified data. Patient data privacy and confidentiality were maintained as this study was conducted in compliance with the ethical standards per Helsinki declaration.[11]

RESULTS

Between January 2015 and December 2020, 3233 cases presenting with AUB who had undergone D&C were included in the study. Overall, the age of the patients ranged from 19 years to 86 years. The median age was 41 years with an interquartile range of 16 years (25th to 75th percentiles, 34-48 years) (**Table 1**). The youngest patients (n=5, 19 years) presented with two cases of proliferative phase endometrium, and three cases of products of conception (normal pregnancy). The oldest patient (n=1, 86 years) presented with an inactive endometrium. The maximum number of patients presented in the age group 18-39 years (n=1412, 43.7%), followed by 40-49 years (n=1125, 34.8%) and ≥50 years (n=696, 21.5%).

Endometrial biopsy revealed a normal cyclical pattern of the endometrium in the majority of the patients forming 57.7% of cases (n=1867) including proliferative endometrium (n=1066, 57.1%), and secretory endometrium (n=801, 42.9%). The second most common finding was pregnancy-related abnormal bleeding which accounted for 566 (17.5%) of cases, including products of conception (normal pregnancy) in 560 of the patients (98.9%), partial molar pregnancy in three patients (0.5%), complete molar pregnancy in two patients (0.4%) and Arias-Stella reaction in only one patient (0.2%). The least common finding was atrophic endometrium in 19 patients (**Table 1**).

Reproductive age group (18-39 years)

Among the 1412 cases in the 18-39 years age group, the predominant pattern noted was functional endometrium (n=810, 57.4%) among which proliferative phase endometrium was the most common finding (n=422, 52.1%) followed by secretory phase endometrium (n=388, 47.9%) (**Table 1**). The second most common finding was pregnancy-related patterns (n=441, 30.9%), with products of conception (normal pregnancy) being the most common finding among this pattern (n=427, 99.1%) followed by partial molar pregnancy (n=2, 0.5%) and complete molar pregnancy (**Figure 1**) (n=2, 0.5%). Malignant lesions were the least common finding with only two patients having endometrioid adenocarcinoma (**Figure 2**).

Perimenopausal age group (40-49 years)

Among the 1412 cases in the 40-49 years age group, the predominant pattern noted was functional endometrium pattern (n=740, 65.8%) among which proliferative phase endometrium was the most common finding (n=422, 57.0%) followed by secretory phase endometrium (n=318, 43.0%) (**Table 1**). The second most common finding was benign lesions (n=121, 11.4%), with benign endometrial polyps being the most common finding among the lesions (n=160, 99.4%) followed by leiomyoma (n=1, 0.5%). Malignant lesions were the least common finding with four patients (80.0%) having endometrioid adenocarcinoma and only one patient presenting with serous carcinoma (20.0%).

Postmenopausal age group (≥50 years)

Among the 696 cases in the ≥50 years age group, the predominant pattern noted was functional endometrium pattern (n=317, 45.5%) among which proliferative phase endometrium was the most common finding (n=222, 70.0%) followed by secretory phase endometrium (n=95, 30.0%) (**Table 1**). The second most common finding was benign lesions (n=184, 26.4%), with benign endometrial polyps being the most common finding among the lesions (n=182, 98.9%) followed by leiomyoma (n=2, 1.1%). Pregnancy-related patterns were the least common finding with only two patients having products of conception (normal pregnancy) .

Nulliparous group

Among the 536 in the nulliparous group, the predominant pattern noted was the functional endometrium pattern (n=361, 67.4%); among which proliferative phase endometrium was the most common finding (n=201, 55.1%) followed by secretory phase endometrium (n=160, 44.3%) (**Table 2**). The second most common finding was pregnancy-related patterns (n=441, 30.9%), with products of conception (normal pregnancy) being the only finding among this pattern (n=70, 100%). The least common finding was atrophic endometrium in 3 patients.

Multiparous group

Among the 2696 cases in the multiparous group, the predominant pattern noted was the functional

Table 1. Demographic and clinical characteristics by age group (n=3233).

		18-39 (n=1412)	40-49 (n=1125)	≥50 (n=696)
Age (years)	41 (16)	33 (7)	45 (7)	53 (7)
Functional endometrium	1867	810	740	317
Proliferative phase	1066 (57.1)	422 (52.1)	422 (57.0)	222 (70.0)
Secretory phase	801 (42.9)	388 (47.9)	318 (43.0)	95 (30.0)
Inflammatory endometrium	48	17	24	7
Acute endometritis	5 (10.4)	2 (11.8)	2 (8.3)	1 (14.3)
Chronic endometritis	42 (87.5)	15 (88.2)	21 (87.5)	6 (85.7)
Endometrial tuberculosis	1 (2.1)	0 (0.0)	1 (4.2)	0 (0.0)
Endometrial atrophy	19	0	2	17
Atrophic endometrium	19 (100)	0 (0.0)	2 (100)	17 (0.0)
Endometrial hyperplasia	27	6	4	17
Simple hyperplasia without atypia	9 (33.3)	2 (33.3)	1 (25.0)	6 (35.3)
Simple hyperplasia with atypia	4 (14.8)	1 (16.7)	0 (0.0)	3 (17.6)
Complex hyperplasia without atypia	4 (14.8)	0 (0.0)	2 (50.0)	2 (11.8)
Complex hyperplasia with atypia	10 (37)	3 (33.3)	1 (25.0)	6 (35.3)
Benign lesions	456	111	161	184
Benign endometrial polyp	453 (99.3)	111 (100)	160 (99.4)	182 (98.9)
Leiomyoma	3 (0.7)	0 (0.0)	1 (0.6)	2 (1.1)
Malignant lesions	55	2	5	48
Endometrioid adenocarcinoma	42 (76.4)	2 (100)	4 (80.0)	36 (75.0)
Serous carcinoma	7 (12.7)	0 (0.0)	1 (20.0)	6 (12.5)
Mixed mullerian tumor	5 (9.1)	0 (0.0)	0 (0.0)	5 (10.4)
Endometrial stromal neoplasm	1 (1.8)	0 (0.0)	0 (0.0)	1 (2.1)
Pregnancy related	566	441	123	2
Products of conception (Normal pregnancy)	560 (98.9)	437 (99.1)	121 (98.4)	2 (100)
Partial molar pregnancy	3 (0.5)	2 (0.5)	1 (0.8)	0 (0.0)
Complete molar pregnancy	2 (0.4)	2 (0.5)	0 (0.0)	0 (0.0)
Arias-Stella reaction	1 (0.2)	0 (0.0)	1 (0.8)	0 (0.0)
Miscellaneous	195	25	66	104
Inactive endometrium	60 (30.8)	4 (16.0)	23 (34.8)	33 (31.7)
Hormonal effect	33 (16.9)	6 (24.)	14 (21.2)	13 (12.5)
Autolyzed endometrium	1 (0.5)	0 (0.0)	0 (0.0)	1 (1.0)
Unidentified/Inadequate	101 (51.8)	15 (60.0)	29 (43.9)	57 (54.8)

Data are n (%) except for age (median and interquartile range)

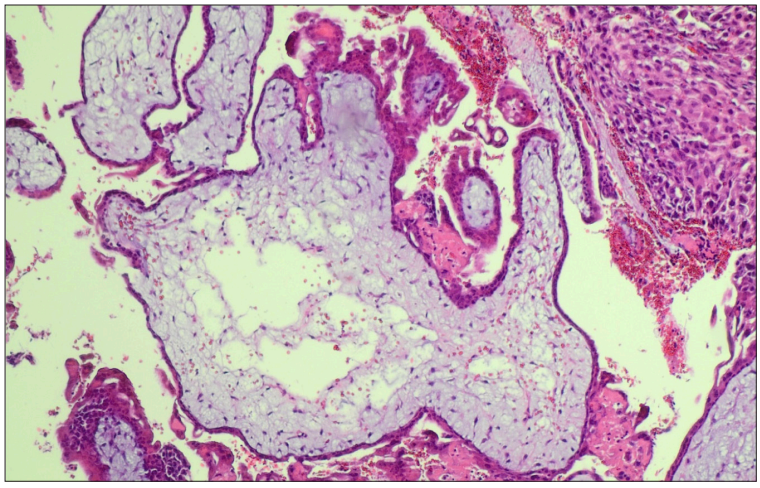

Figure 1. This is a microscopic examination at medium power of a complete hydatidiform mole showing markedly hydropic villi with cistern formation. This biopsy exhibits circumferential trophoblastic hyperplasia.

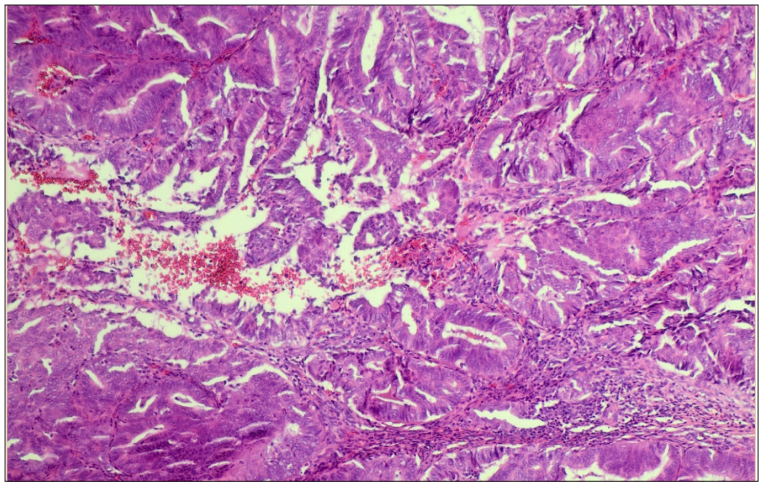

Figure 2. This image of FIGO grade 1 endometrioid carcinoma illustrates its complex architecture composed of confluent fused glands, and little intervening stroma. This biopsy exhibited glandular growth predominantly with <5% nonsquamous solid components.

endometrium pattern (n=1506, 55.9%) among which proliferative phase endometrium was the most common finding (n=865, 57.4%) followed by secretory phase endometrium (n=641, 42.6%) (**Table 2**). The second most common finding was pregnancy-related patterns (n=496, 18.4%), with products of conception (normal pregnancy) being the most common finding among the pattern (n=490, 96.8%) followed by partial molar pregnancy (n=3, 0.6%), complete molar pregnancy (n=2, 0.4%) and Arias-Stella reaction in one patient only (n=1, 0.2%). The least common finding was atrophic endometrium in 16 patients.

Pre-hysterectomy curettage diagnostic accuracy

The pathologic findings of patients who had undergone hysterectomy (n=316) following diagnostic D&C showed normal endometrium in 183 women; 103 had proliferative endometrium and 80 had secretory endometrium. Benign lesions were observed in 52 patients; 51 had benign polyps and one had leiomyoma. Malignant lesions were observed in 42 patients; 34 had endometrioid endometrial cancer, 6 had serous carcinoma and 2 had mixed Müllerian tumor (carcinosarcoma). After the hysterectomy, 181 women presented with normal endometrium; 102 had proliferative endometrium and 79 had secretory endometrium. Benign neoplastic lesions were observed in 27 patients; 27 had benign polyps and one case of leiomyoma upon D&C was confirmed to be a benign polyp. Malignant lesions were observed in 43 patients; 33 had endometrioid endometrial cancer, 7 had serous carcinoma and 3 had mixed Müllerian tumor (carcinosarcoma). In 13.29% (42/316) of patients, D&C failed to detect the intrauterine disorder that was found on hysterectomy. The characteristics of the diagnoses vs normal findings is shown in **Table 3**.

FIGO tumor grading of endometrioid adenocarcinoma

Thirty-four (10.2%) D&C histological reports showed endometrioid adenocarcinoma. However, 30 (9.03%) were confirmed to be endometrioid adenocarcinomas on the final histology following hysterectomy. Of the 30 patients diagnosed with endometrioid adenocarcinoma upon D&C, 17 were grade 1, 9 were grade 2, and 4 were grade 3. Upon hysterectomy, 14 reports showed grade 1 tumors, 12 reports showed grade 2 tumors, and 4 reports showed grade 3 tumors. Upon hysterectomy, (4 of the 17) grade 1 tumors upgraded to grade 2, (1 out of the 9) grade 2 tumors upgraded to grade 3 and (1 out of the 9) grade 2 tumors downgraded to grade 1, and (1 out of the 4) grade 3 tumors downgraded to grade 2. The remaining D&C endometrioid adenocarcinoma reports (4/34) were confirmed upon hysterectomy to be 1 case of serous carcinoma, 1 case of mixed Müllerian tumor (carcinosarcoma), 1 case of atrophic endometrium, and 1 report showed proliferative phase endometrium (**Table 4**).

DISCUSSION

AUB usually peaks in the 4th-5th decade as the physiologic phenomenon of menopausal transition takes place.[12,13] Anovulatory cycles in women approaching menopause begin with the loss of ovarian follicular activity and manifest as menstrual irregularities.[14] This

Table 2. Demographic and clinical characteristics by parity (n=3233).

		Nulliparous (n=536)	Multiparous (n=2696)
Age (years)	41 (16), 19-86	33 (13), 19-82	43 (13), 19-86
Functional endometrium	1867	361	1506
Proliferative phase	1066 (57.1)	201 (55.1)	865 (57.4)
Secretory phase	801 (42.9)	160 (44.3)	641 (42.6)
Inflammatory endometrium	48	4	44
Acute endometritis	5 (10.4)	0 (0.0)	5 (11.4)
Chronic endometritis	42 (87.5)	4 (100.0)	38 (86.4)
Endometrial tuberculosis	1 (2.1)	0 (0.0)	1 (2.3)
Endometrial atrophy	19	3	16
Atrophic endometrium	19 (100)	3 (100.0)	16 (100.0)
Endometrial hyperplasia	27	8	19
Simple hyperplasia without atypia	9 (33.3)	3 (37.5)	6 (31.6)
Simple hyperplasia with atypia	4 (14.8)	1 (12.5)	3 (15.8)
Complex hyperplasia without atypia	4 (14.8)	1 (12.5)	3 (15.8)
Complex hyperplasia with atypia	10 (37)	3 (37.5)	7 (36.8)
Benign lesions	456	67	389
Benign endometrial polyp	453 (99.3)	67 (100.0)	386 (99.2)
Leiomyoma	3 (0.7)	0 (0.0)	3 (0.8)
Malignant lesions	55	12	43
Endometrioid adenocarcinoma	42 (76.4)	10 (83.3)	32 (74.4)
Serous carcinoma	7 (12.7)	1 (8.3)	6 (14.0)
Mixed mullerian tumor	5 (9.1)	1 (8.3)	4 (9.3)
Endometrial stromal neoplasm	1 (1.8)	0 (0.0)	1 (2.3)
Pregnancy related	566	70	496
Products of conception (Normal pregnancy)	560 (98.9)	70 (100.0)	490 (98.8)
Partial molar pregnancy	3 (0.5)	0 (0.0)	3 (0.6)
Complete molar pregnancy	2 (0.4)	0 (0.0)	2 (0.4)
Arias-Stella reaction	1 (0.2)	0 (0.0)	1 (0.2)
Miscellaneous	195	11	183
Inactive endometrium	60 (30.8)	4 (36.4)	55 (30.1)
Hormonal effect	33 (16.9)	2 (18.2)	31 (16.9)
Autolyzed endometrium	1 (0.5)	0 (0.0)	1 (0.5)
Unidentified/Inadequate	101 (51.8)	5 (45.5)	96 (52.5)

Data are n (%) except for age (median interquartile range and minimum-maximum)

Table 3. Diagnostic accuracy of D&C versus histopathological findings after hysterectomy (n=277).

	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Accuracy
Normal vs pathologic	72.9	77.9	73.86	77.05	75.60
Premalignant (endometrial hyperplasia)	81.82	97.92	75.00	98.60	96.77
Malignant	100	99.3	97.56	100	99.45
Premalignant and malignant	96.15	97.24	92.59	98.6	96.95

Values are percent.

Table 4. Comparison between D&C and hysterectomy endometrioid adenocarcinoma grading.

Grade (G)	D&C	Hysterectomy	Upgraded	Downgraded
G1	17	14	4 (23.5%) to Grade 2	-
G2	9	12	1 (11.1%) to Grade 3	1 (11.1%) to Grade 1
G3	4	4	-	1 (25.0%) to Grade 2
Total	30	30	5 (16.67%)	2 (6.67%)

Grade 1: 5% or less of tumor tissue is solid tumor growth. The cancer cells are well-differentiated.
Grade 2: 6%–50% of tissue is solid tumor growth. The cancer cells are moderately differentiated.
Grade 3: More than 50% of tissue is solid tumor growth. The cancer cells are poorly differentiated.

diagnosis is reached after excluding all the possible causes, including an endometrial biopsy to exclude structural lesions. In our study, the reproductive age group was the most frequently encountered group, but this is attributed to the wider range of age (18-39) as well as the therapeutic indication of D&C (to remove products of conception) compared to the peri-menopausal age group (40-49).

AUB in women of reproductive age is mainly caused by pregnancy-related complications unless proven otherwise.[15] The incidence of structural uterine lesions like polyps, hyperplasia, and particularly endometrial cancers, increases with age.[16] Polyps were more common in postmenopausal (11.8%) than premenopausal women (5.8%) ($P<.01$).[17] The incidence of endometrial cancer follows that of atypical hyperplasia, both peak in women aged (55-64).[18] A classification, other than the one proposed by the WHO, suggested the term "endometrial intraepithelial neoplasia" (EIN) to replace the WHO term atypical hyperplasias.[19]

Lesions of atypical hyperplasia, specifically the complex type, have a high concurrent cancer rate and a potential to turn cancerous; 30%-45% of complex atypical hyperplasia will progress to cancer if left untreated.[20] Kurman et al[21] found progression to carcinoma in ~25% of endometrial hyperplasia with atypia; Trimble et al[20] found that 39% of the removed uteri had adenocarcinoma, with 33% having myometrial invasion. A conservative management should be considered only after thorough assessment of the patient's condition. Therefore, we should always rule out any dangerous pathology in patients in the perimenopausal age group with AUB. Endometrial biopsy is indicated for younger patients with risk factors like obesity, diabetes, with cycle irregularities, and diagnosed with polycystic ovarian syndrome (PCOS).[4,22] Cases of persistent AUB unresponsive to treatment are also sampled in reproductive-age women.[9] AUB due to infections, medications, and anovulation can be encountered throughout the timeframe and is not directly related to age.

Nulliparous women were less likely to present with AUB than multiparous women; this is also seen in other studies.[23,24] Parity status does not predispose women to a greater risk of AUB because AUB is a common morbidity in the perimenopausal age group when most women have completed their child-bearing phase. The inherent effect of parity is linked to estrogen-driven endometrial pathologies, like hyperplasia and cancer.[25] The progesterone effect in parous women counteracts the circulating estrogen that stimulates endometrial growth. Therefore, nulliparity increases estrogen

exposure which drives endometrial proliferation and predisposes to endometrial cancer. The risk significantly increases when the parity status is two or less.[25]

Hysterectomy is a permanent solution to alleviate bleeding symptoms (heavy menstrual bleeding) and is satisfactory in selected patients.[9] It is also a treatment option for patients with uterine pathologies such as cancer. The histopathological reports obtained from hysterectomy specimens are of great diagnostic value; they are used as a reference standard to evaluate the accuracy of other sampling techniques.[26,27] Many studies have reported the flaws of D&C as a sampling tool.[10] In almost 60% of the D&C procedures, less than half of the uterine cavity is curetted,[27] so lesions can be missed. Focal intracavitary lesions as polyps, submucosal fibroids, focal hyperplasia, and localized neoplasia are best managed by hysteroscopy that could otherwise be missed by D&C.[28] In the Bettocchi study, D&C failed to detect 62.5% of the intrauterine disorders, specifically the focal lesions.[10]

The discrepancy rate in detecting polyps was high in our study and others. D&C can miss up to 50%-85% of focal intracavitary pathology yielding a false-negative D&C result.[29,30] On the other hand, D&C yields a false-positive result for detecting focal lesions as its invasive nature might alter the polyp.[31] D&C is also a traditional method to remove polyps; although less popular after improved diagnostic procedures emerged, it is still used by gynecologists.[32] The discrepancy could be due to undetected polyps by D&C, or D&C sampling altering the polyp, or D&C was a polypectomy procedure.

The hyperplastic endometrium portrays a wide array of histologic changes, ranging from benign lesions treated completely by hormones to persistent ones that later turn malignant.[33,34] A six-month prospective study concluded that initial hyperplastic endometrium (except for atypical complex hyperplasia) mostly undergoes regression with the samples obtained by D&C at intervals.[35] In our study, three lesions regressed into normal histology whereas two lesions progressed, one of which was an atypical complex hyperplasia on D&C and adenocarcinoma on the final pathology. The time span between the initial D&C and the final hysterectomy in our study ranged from 3 weeks to 13 months.[19] Two patients were downgraded to tumor negative to show a normal endometrium in one and an atrophic endometrium in the other. The lesions were minimally localized and removed entirely by D&C. Another two cases were endometrioid adenocarcinoma on D&C whereas on hysterectomy one was a Müllerian carcinoma, the other was a serous carcinoma. D&C detected an endometrial malignancy, but the histopathological morphology was misidentified.

The specificity for detecting both premalignant and malignant lesions is high (97.92%), whereas the sensitivity is slightly lower (81.82%). A positive test result by D&C, in our case, is accurate and believable but D&C is not as accurate to rule out these lesions and needs confirmation. Looking at the reliability of D&C at detecting malignant lesions alone, the sensitivity was 100%, specificity was 99.3%, a positive predictive value was 97.56% and a NPV was 100%. We follow the conclusion of Barut et al, considering D&C to be the current best practice, especially for the high sensitivity, specificity, NPV, PPV, and accuracy for the diagnosis of malignant endometrial pathologies.[36]

We compared the FIGO grades results obtained from D&C with that of hysterectomy to assess the concordance rate. Grade I/II tumors (low-grade tumors) were the frequently encountered grade,[37] the early manifestations of symptoms (like bleeding) urge the patients to seek immediate care.

The difference in grade in our study was by one, which is common and reported in other studies.[38,39] The variation seen could be due to inter-observer differences, specifically when it comes to discriminating whether the pathology report is a grade I or II. Scholten et al studied the reports of 253 patients with endometrial carcinoma stages I-III, the original pathology was 21%, 57%, and 22% Grade 1, 2, and 3 tumors, respectively, compared with the after-review reports 67%, 8%, and 25% Grade 1, 2, and 3 tumors, respectively.[40] Grade III tumors have the highest concordance rate[41] as they are histologically distinct from the low grade (Grade I-II).[42] In addition, the scarce material sometimes obtained by D&C influences the judgment of the final grade when compared to the greater tissue volume obtained from hysterectomy.[39] Therefore, pre-surgical D&C is a useful tool to identify the presence of cancer rather than determining its true risk.

Other endometrial sampling techniques like the Pipelle were compared with D&C; one study found that the difference between NPV of D&C and Pipelle was not statistically significant, whereas the PPV of D&C (100%) was superior to the Pipelle (86%). Both techniques have limitations, like inaccuracy in detecting focal lesions, but the Pipelle is patient friendly as it causes less pain, and is more cost effective as it can be done in an outpatient setting.[43]

Age helps to narrow the possible causes of AUB, whereas parity status does not. As a woman ages, structural lesions become a more common cause and pregnancy-related issues follow an inverse trend, becoming less common. A woman with postmenopausal

bleeding should be investigated in a manner to rule out cancer; an insufficient endometrial sample warrants further investigation. D&C, in our experience, was a reliable device to sample the endometrial lining to detect malignant lesions and to determine its presence rather than the true risk it poses.

The study was not without limitations. The retrospective design limits data when it comes to presentation, duration of symptoms before presentation and the time between presentation and procedure. We also did not address inter-observer differences as our medical records did not report whether different pathologists read different samples throughout the timeframe; thus, we could not assess the inter-rater reliability among pathologists in this study. Future studies should consider and overcome these limitations in their study designs. Also, further studies comparing Pipelle with conventional D&C are recommended.

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Authors' contribution

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

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