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Diagnosis of Endometrial Hyperplasia and Endometrial Cancer via Hysteroscopic Biopsy versus Dilatation and Curettage Biopsy

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ABSTRACT

Background: Endometrial cancer (EC) is the most common gynecological malignancy in high-income countries and the sixth most common cancer in women globally. In perimenopausal women, endometrial cancer and atypical endometrial hyperplasia (EH) are the most alarming etiology of abnormal uterine bleeding (AUB).

Objective: We aimed to assess the two standard tools for endometrial biopsy collection, namely dilatation and curettage (D & C) and hysteroscopy, regarding the sensitivity of results. **Methods:** An interventional study was conducted on 223 women complaining of AUB or an abnormal ultrasound scan. All patients were subjected to a trans-vaginal ultrasound scan as well as two biopsy specimens obtained by both hysteroscopy as well as D & C in the same setting. All specimens were assessed for EH and EC at the Armed Forces Medical Research Laboratories.

Results: Truly positive EH samples were higher in hysteroscopic biopsy compared to D & C biopsy (86.2 % and 68.9 %) and EC samples were truly positive in all hysteroscopic biopsies compared to only 88 % of D & C biopsies. Sampling failure was five times higher in D & C biopsy than in hysteroscopic biopsy (15 and 3 cases).

Conclusion: Hysteroscopic biopsy is more sensitive in diagnosing endometrial hyperplasia and endometrial cancer compared to dilatation and curettage biopsy and has a 5 times lower rate of sampling failure.

Keywords: Hysteroscopic biopsy, Dilatation and curettage biopsy, Endometrial hyperplasia, Endometrial cancer.

INTRODUCTION

Abnormal uterine bleeding (AUB) is defined as any deviation from the normal menstrual cycle in respect of regularity, frequency, volume, duration, or amount of bleeding during or in between periods for at least six months [(1)]. AUB is mainly encountered in peri- and post-menopausal women and attributes as a cause for 25 % of all gynecological surgeries. The aetiological reasons for AUB are mainly polyp, adenomyosis, leiomyoma, endometrial hyperplasia (EH), and endometrial cancer (EC) [(2)].

EH is a hyperplastic endometrial lesion with irregular gland size, increased glands, and increased glandular interstitial ratio. It is either EH without atypia or atypical EH, which could follow up further progress into EC [(3)].

EC is the most common gynecological malignancy in high-income countries and the sixth most common cancer in women globally [(4)]. It is associated with obesity and elevated estrogen levels but oral contraceptives lower the risk by 30-40 %. Over the past 30 years, the overall incidence of EC has increased by 132 %, with 417,000 new cases reported worldwide in 2020 [(5)]. EC mostly has an excellent prognosis as it is often diagnosed at an early stage in asymptomatic women, who present with an abnormal ultrasound scan and/or AUB [(6)]. Therefore prompting timely clinical evaluation and diagnosis through endometrial biopsy [(7)]. Targeted endometrial biopsies and histological examinations improve diagnostic accuracy and decrease false negative results [(8)].

The basic diagnostic intervention in AUB is endometrial biopsy via dilatation and curettage (D & C).

It is widely used due to its simplicity and low cost. However, some authors do not recommend blind curettage as it may lead to massive haemorrhage, secondary surgery, blood transfusion, and even hysterectomy [(9)].

On the other hand, over the last two decades, hysteroscopic biopsy has become the gold standard for obtaining endometrial biopsies as it is done under direct visualization of the entire uterine cavity. Hysteroscopic biopsy is minimally invasive and provides the opportunity for selective tissue removal for biopsy thus reducing the risk of complications [(10)].

The diagnosis of EH or EC depends on the pathological results of an endometrial biopsy sample. A false-negative result could lead to a missed diagnosis and therefore delay prompt treatment and intervention, leading to fatal outcomes. In this study, we aimed to assess whether hysteroscopic biopsy or D & C biopsy is superior in detecting EC and EH with or without atypia.

PATIENTS AND METHODS

This experimental study was conducted on 223 women complaining of perimenopausal bleeding or an abnormal ultrasound scan at the General Military Hospital in Alexandria, Egypt over 4 years (2020-2023).

Abnormal transvaginal ultrasound scan: Transvaginal ultrasonography is a common tool for the screening of atypical EH and EC in asymptomatic women and/or women presenting with vaginal bleeding. Studies showed that an endometrial thickness of $\geq$14 mm increased the relative risk of atypical EH or EC by 3-fold relative to women below the cut-off [(11)].

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Inclusion criteria: Age group between 42 to 85 years (premenopausal or menopausal) presenting with vaginal bleeding or an abnormal transvaginal ultrasound scan.

Exclusion criteria: Patients who had vaginal bleeding caused by endometrial polyps or myoma diagnosed by transvaginal ultrasonography.

History taking: All patients were asked about age, gravidity, timing, and severity of perimenopausal bleeding.

Clinical evaluation: All patients were subjected to a trans-vaginal ultrasound by an experienced ultra-sonographer and endometrial thickness of $\geq$14 mm and/or a deformed endometrial border was considered abnormal trans-vaginal ultrasound.

Grouping: Hysteroscopic biopsy group (n=120): Patients were subjected to hysteroscopic biopsy first and followed by a D & C biopsy in the same setting.
D & C biopsy group (n=103): Patients were subjected to D & C biopsy first and followed by hysteroscopic biopsy in the same setting.

Hysteroscopic biopsy: Hysteroscopic biopsy was performed before D & C biopsy in group 1 and after D & C biopsy in group 2. If lesions were visible, direct biopsies from the lesions were taken and random biopsies were taken if no lesion was visible. A Karl Storz Hopkins Telescope 30^0, 2 mm, 26 cm was used with continuous flow and working channel.

D & C biopsy: D & C biopsy was performed after hysteroscopic biopsy in group 1 and before hysteroscopic biopsy in group 2.

Pathological evaluation: All patients included in the study had two biopsy specimens obtained by both hysteroscopy as well as D & C. All specimen were assessed for EH and EC at the Armed Forces Medical Research Laboratories.

Ethical approval: All patients were subjected to informed written consent before participating in the study. This study was approved by the Ethics Committee of the General Military Hospital and it is in accordance to the Declaration of Helsinki.

Statistical analysis: Data were managed and analysed using statistical software SPSS version 25.

RESULTS

The histological results of the total sample (n=223) showed that 29 patients had endometrial hyperplasia (16 simple, 9 complex, and 4 atypical hyperplasia) and 25 patients had endometrial cancer. Hysteroscopic biopsy alone revealed that only 25 patients had endometrial hyperplasia (14 simple, 8 complex, and 3 atypical hyperplasia) 25 patients had endometrial cancer and 3 patients had atrophic endometrium.

Four patients with endometrial hyperplasia were missed. On the other hand, dilatation and curettage alone revealed that only 20 patients had endometrial hyperplasia (12 simple, 6 complex, and 2 atypical hyperplasia) 22 patients had endometrial cancer and 15 patients had an atrophic endometrium. Nine patients with endometrial hyperplasia and 3 patients with endometrial cancer were missed (Table 1).

Table (1): Histological diagnosis of the samples obtained by hysteroscopic biopsy versus dilatation and curettage (n=223)

Histological diagnosis	Hystero-scopic biopsy	D&C	Hysteroscopic and D & C biopsy
Endometrial hyperplasia	25	20	29
Simple	14	12	16
Complex	8	6	9
Atypical	3	2	4
Endometrial Cancer	25	22	25
Insufficient material	3	15	0
No Pathology	170	166	169

The histological results obtained by hysteroscopic biopsy alone showed satisfactory results as endometrial hyperplasia was in 86.2 % truly positive and only in 13.8 % falsely negative, and more importantly, endometrial cancer was truly positive in 100 % of cases and no cases were falsely negative (Table 2).

Table (2): Histological diagnosis of the sample obtained by hysteroscopic biopsy alone (n=223)

	True Positive	False Negative
Endometrial hyperplasia	25 (86.2%)	4 (13.8%)
Simple	14 (87.5%)	2 (12.5%)
Complex	8 (88.9%)	1 (11.1%)
Atypical	3 (75%)	1(25%)
Endometrial Cancer	25 (100 %)	0

The histological results obtained by dilatation and curettage alone showed that endometrial hyperplasia was only 68.9 % truly positive and 31.1 % falsely negative. Moreover, endometrial cancer was truly positive in only 88 % and falsely negative in 12 % of cases (Table 3).

Table (3): Histological diagnosis of the sample obtained by dilatation and curettage (n=223)

	True Positive	False Negative
Endometrial hyperplasia	20 (68.9%)	9 (31.1%)
Simple	12 (75%)	4 (25%)
Complex	6 (66.7%)	3 (33.3%)
Atypical	2 (50%)	2 (50%)
Endometrial Cancer	22 (88%)	3 (12%)

DISCUSSION

Endometrial hyperplasia (EH) and endometrial cancer (EC) affect women in the peri- and post-menopausal phases of life and lead to poor quality of life. Endometrial biopsy is the inevitable diagnostic tool, but the means are different [(12)].

We aimed to assess the two standard tools for endometrial biopsy collection, namely D & C and hysteroscopy, regarding the sensitivity of results.

The current study showed that inadequate samples were five times higher in D & C endometrial biopsy than in hysteroscopic biopsy, 15 and 3 cases, respectively. **Piatek *et al.* [(13)]** also reported a high rate of sampling failure via D & C endometrial biopsy in a retrospective cohort. The study assessed the rate of endometrial sampling failure and factors affecting the quality of specimens obtained for pathological examination by D & C endometrial biopsy. Inadequate samples were found in 88 cases of the 556 examined cases of D & C endometrial biopsy. The study suggested that D & C endometrial biopsy did not guarantee adequate specimen sampling.

The current study showed that truly positive EH samples were higher in hysteroscopic biopsy compared to D & C biopsy, 86.2 % and 68.9 %, respectively. Moreover, atypical EH showed the highest false negative values in both procedures. Similar results were reported in a retrospective study that evaluated the correlation between the histological diagnoses of atypical EH obtained through hysteroscopic biopsy or D & C and the definitive histological evaluation after hysterectomy. The study showed that diagnostic accuracy of hysteroscopic biopsy was higher than D & C with diagnostic coincidence in cases of 87 % and 14 %, respectively [(14)].

The current study showed that EC was truly positive in all biopsies obtained via hysteroscopy compared to only 88 % of biopsies obtained via D & C reflecting a higher accuracy of hysteroscopic biopsy than D & C biopsy in detecting EC. **Sardo *et al.* [(15)]** also reported that Endometrial biopsy under direct hysteroscopic visualization was associated with a higher rate of sample adequacy compared to blind sampling. However, hysteroscopic visualization only detected 82 % of EC, and like in our study statistical significance was not reached (p=0.06). Our findings are consistent with the findings of a meta-analysis, which showed that endometrial biopsy via hysteroscopy was the targeted biopsy method with the highest diagnostic accuracy (Level A) in patients with suspected endometrial malignancy. The meta-analysis only recommended D & C biopsy when hysteroscopic biopsy was unavailable (Level B) [(11)].

A cross-sectional study done by **Utida *et al.* [(16)]** assessed the pathological diagnosis of malignancy and the costs of both techniques. The study enrolled 45 women with AUB or postmenopausal bleeding who underwent endometrial biopsy using both techniques. Both techniques had a high accuracy for EC (100% agreement between the two procedures) but the cost was 27 times higher in hysteroscopic biopsy [(16)]. Recent studies on women with AUB concluded that besides its tendency to cause pain, blind D & C scrapes up to 50 % of the uterine wall and thus missing nearly 10 % of EC (false-negative EC diagnoses) [(17)].

LIMITATIONS

Our study had several limitations, such as the "selective outcome reporting", since we only reported the histological diagnosis and excluded other outcomes e.g. incidence of hysterectomy surgeries, definitive histological evaluation after hysterectomy, quality of life after diagnosis and mortality due to EC. These long-term effects could be further followed up and demonstrated in order to address the limitations of the current study.

CONCLUSION

Hysteroscopic biopsy is more sensitive in diagnosing endometrial hyperplasia and endometrial cancer compared to dilatation and curettage biopsy and has a 5 times lower rate of sampling failure.

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