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ROLE OF OFFICE HYSTEROSCOPY IN EVALUATION OF PERIMENOPAUSAL BLEEDING PATIENTS ATTENDING OUTPATIENT GYNECOLOGIC CLINIC

By

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ABSTRACT

Background: Perimenopausal bleeding is a real clinical challenge facing gynecologists, which should indicate suspicion of endometrial malignant changes development and needs accurate evaluation of endometrium and uterine cavity.

Objective: To provide a clear understanding of the value of office hystroscopy as a diagnostic tool during assessment of women with perimemnopausal bleeding.

Patient and Methods: This prospective study included case records of 50 women with perimenopausal bleeding undergone office hysteroscopy and endometrial biopsy between 2017 and 2019 at Al Sayed Galal Hospital, Al-Azhar University, Cairo, Egypt.

Results: Sonographic findings of malignant or premalignant endometrium showed 25% sensitivity and 100% specificity for endometrial thickness ≥ 17 mm and 100% sensitivity and 58.7% specificity for endometrial thickness ≤ 10 mm. Sonographic findings of abnormal endometrial pathology showed 37.06% sensitivity and 100% specificity for endometrial thickness ≥10 mm and 88.24 % sensitivity and 57.14 specificity for endometrial thickness ≤ 7 mm. Hysteroscopic findings of malignant or premalignant showed 100% sensitivity and 76.09% specificity for endometrial thickness, 60% sensitivity and 93.48 specificity for endometrial polyp , 100% sensitivity and 100% specificity for endometrial mass and 50% sensitivity and 95.6% specificity for hypervascular endometrium .Hystroscopic findings of abnormal endometrial pathology showed 77.8% sensitivity and 92.7% specificity for thick endometrium , 80% sensitivity and 92.6% specificity for endometrial polyp , 22.2% and 100% specificity for endometrial mass, 22.2% sensitivity and 95.1% specificity for hypervascular endometrium.

Conclusion: Office hysteroscopy can be considered as a golden standard tool in diagnosis and management of perimenoipausal bleeding. It is valuable in assessment of endometrium and helpful in management planning.

Key words: Office Hysteroscopy, perimenopausal bleeding, gynecologic clinic.

INTRODUCTION

Perimenopausal bleeding is defined as any bleeding from genital tract which has any deviation from normal frequency, cyclicity, duration and amount of flow at or above 40 yrs. of age, approximately 20% of patients presenting to the gynaecologist have abnormal uterine bleeding and this proportion rises to 69%

during Perimenopausal age group *(Seshadri, (2016).*

Abnormal uterine bleeding is one of the most common clinical problems in gynecology. Up to 33% of women referred to gynecological outpatient clinics have this problem and the proportion rises more in peri- and postmenopausal women. This condition has enormous consequences with regard to social life, morbidity and clinical workload *(ACOG, 2012).*

Fibroids or polyps are the most common cause of anatomic AUB; Twenty to forty percent of women have fibroids. These women might present with abnormal bleeding, anemia, pain, and occasionally infertility *(Rashid et al., 2010).*

Clinical definition is the phase preceding the onset of menopause, general occurring around 40-45 years of age during which the regular cycle of women transitions to pattern of irregular cycles *(Nanda et al., 2013).*

There is a wide range of diagnostic modalities to delineate cause of Perimenopausal bleeding like dilatation and curettage, transvaginal ultrasonography, endometrial biopsy and hysteroscopy. Due to high accuracy and patient compliance, transvaginal sonography (TVS) allows detailed assessment of anatomical abnormalities of the uterus and endometrium *(Kotdawala et al., 2013).*

In addition, pathologies of the myometrium, cervix, tubes, and ovaries may be assessed. This investigative modality may assist in the diagnosis of endometrial polyps, leiomyomas, uterine anomalies, and generalized endometrial thickening associated with hyperplasia and malignancy *(Singh et al., 2013).*

The present study was designed to explore the role of office hysteroscopy in perimenopausal bleeding in patients attending outpatient gynecologic clinic.

PATIENTS AND METHODS

This study was a retrospective study involving case records of 50 women with perimenopausal bleeding undergone office hysteroscopy and endometrial biopsy between 2017 and 2019 at Al Sayed Galal Hospital, Al Azhar University, Cairo, Egypt.

Included women in this study were within age range of 40 to 45 years old. The age of perimenopause was defined by ACOG as the phase leading up to the point of menopause that can last for up to 10 years. During perimenopause, shifts in hormone levels can affect the endometrium causing abnormal endometrial growth pattern. All women in this study were complaining of abnormal perimenopausal bleeding and didn’t take hormone replacement therapy and had no positive personal history of cancer of genital tract. Most of the women (39 women of the 50) in this study were suffering from comorbidities (diabetes mellitus, hypertension and chronic liver disease). These morbdidties have their influence on uterine and endometrial vascularity and may consequently affect the endometrial pattern and activity. Each patient underwent transvaginal ultrasound to define endometrial thickness, and all of the included patients had suspected endometrial pathology. Endometrial thickness was measured by calculating the

maximum distance between the two lines of the endometrium/myometrium interface in a sagittal scan. The 50 women in this study had no bleeding dyscarysis/ coagulopathy, e.g. platelet dysfunction, Von Willebrand and acute leukemia. All women were not taking anticoagulant drugs.

All study subjects have undergone hysteroscopy by usage of paracervical block (an anesthetic procedure used in obstetrics and gynecology, in which a local anesthetic is injected at a depth of 3–7 mm alongside the vaginal portion of the cervix in the vaginal fornices.) by administering lidocaine and endometrial biopsy was undertaken from all cases for histo-pathological examination, and .full clinical history and examination.

Statistical analysis:

Recorded data were analyzed using the statistical package for social sciences, version 20 (SPSS Inc., Chicago, Illinois, USA). Receiver operating characteristic curve (ROC) was used to assess the best cut off point with its sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and area under curve (AUC). The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant when $p \leq 0.05$.

RESULTS

Endometrial thickness range by sonographic assessment was (6-22) mm with Mean ± SD (10.5 ± 3.17) mm (Figure 1). By hysteroscopy, endometrial thickness was normal in 35 women (70%), while it was thick in 15 women (30%). Regarding hysteroscopic Endometrial Lesions, 45 women (90%) had no lesions, 3 women (6%) had endometrial polyp, 2 women had masses (4%). During evaluation of Endometrial Vascularity by hysteroscope, we found 46 women (92%) had normal endometrial vascularity, while we detected hypervascular endometrium in 4 women (8%). Concerning endometrial pathology, 7 women (14%) had atrophic endometrium, 34 women (68%) had proliferative endometrium, 7 women (14%) had simple endometrial hyperplasia without atypia, 1 woman (2%) had endometrial hyperplasia with atypia, and 1 woman (2%) had endometrial carcinoma **(Table 1)**.

Table (1): Sonographic, Hysteroscopic and Pathological Findings in Included Women

Sonographic Endometrial Thickness (mm)	
Range	6 – 22
Mean ± SD	10.5 ± 3.17
Hysteroscopic Endometrial Thickness	
Normal	35 (70%)
Thick	15 (30%)
Hysteroscopic Endometrial Lesion	
None	45 (90%)
Polyp	3 (6%)
Mass	2 (4%)
Hysteroscopic Endometrial Vascularity	
Normal	46 (92%)
Hypervascular	4 (8%)
Endometrial Pathology	
Atrophic	7 (14%)
Proliferative	34 (68%)
Simple Endometrial Hyperplasia without Atypia	7 (14%)
Endometrial Hyperplasia with Atypia	1 (2%)
Endometrial Carcinoma	1 (2%)

SD standard deviation
Data wer presented as range, mean ± SD; or frequency (percentage)

ROC curve revealed that there is statistical significant value of sonographic endometrial thickness as a predictor of malignant (endometrial carcinoma) or premalignant (endometrial hyperplasia with atypia) endometrial pathology in included women, as denoted by the significantly large area under the curve [AUC = 0.845, 95% CI (0.715 to 0.932), p value <0.001] **(Figure 1)**.

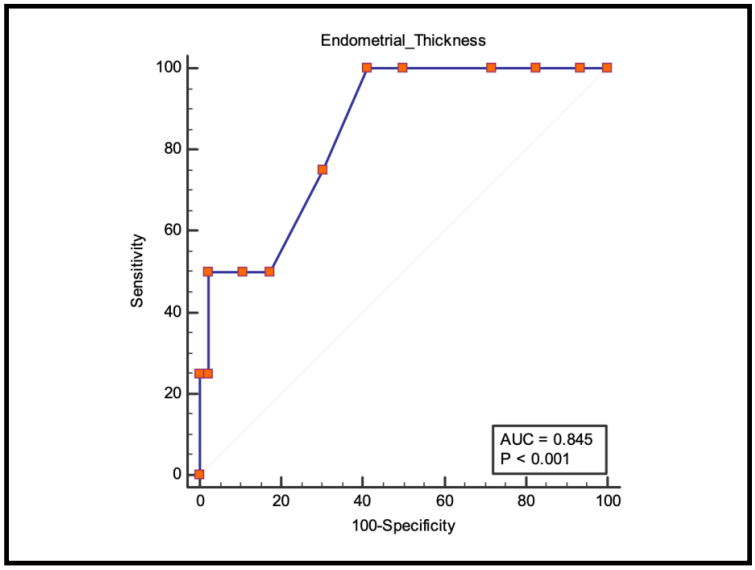

Figure (1): ROC Curve for Endometrial Thickness as a Predictor of Malignant or Premalignant Endometrial Pathology in Included Women

According to this ROC curve, and among included women, an endometrial thickness ≥ 17 mm was statistically significantly associated with malignant or premalignant endometrial pathology with a 100% specificity and an infinite LR+, while an endometrial thickness < 10 mm with associated with no malignant or premalignant lesion with a 100% sensitivity and a nil LR- and among included women, an endometrial thickness ≥ 10 mm was statistically significantly associated with abnormal endometrial pathology with a 100% specificity and an infinite LR+, while an endometrial thickness < 7 mm with associated with no abnormal endometrial pathology with a sensitivity of 88.24% and an LR- of 0.21**(Table 2)**.

Table (2): Validity of endometrial thickness as a Predictor of malignant, premalignant and abnormal endometrial pathology in included women

Sonographic endometrial Thickness	Sensitivity	Specificity	LR+	LR-
≥ 17 mm	25% (0.6 to 80.6)	100% (92.3 to 100)	∞	0.75 (0.4 to 1.3)
≤ 10 mm	100% (39.8 to 100)	58.7% (43.2 to 73)	2.42 (1.7 to 3.4)	0.0
≥ 10 mm	37.06% (29.8 to 64.9)	100% (59 to 100)	∞	0.53 (0.4 to 0.7)
≤ 7 mm	88.24% (57.5 to 96.7)	57.14% (29 to 69.3)	2.06 (0.9 to 4.9)	0.21 (0.07 to 0.6)

We studied the validity of different hysteroscopic findings in prediction of malignant (endometrial carcinoma) or premalignant (endometrial hyperplasia

with atypia) endometrial pathology in included fifty women. We found hysteroscopc thick endometrium as a predictor of malignant or premalignant endometrial pathology had 100% sensitivity, 76.09% specificity, LR+ 4-18, and nil LR-. Hysteroscopic endometrial polyp as a predictor had sensitivity of 60%, specificity of 93.48%, LR+ 0.0 and LR- 1.07. Hysteroscopic endometrial mass as a predictor had 100% sensitivity and 100% specificity, with infinite LR+ and LR- 0.0. Hysteroscopic hypervascular endometrium as predictor had sensitivity and specificity of 50% and 95.6% respectively, with LR+ 11.5 and LR- 0.52 and the validity of different hysteroscopic findings in prediction of abnormal endometrial pathology (endometrial hyperplasia with or without atypia; or endometrial carcinoma) in included women. As a predictor of abnormal endometrial pathology, hysteroscopic thick endometrium had sensitivity of 77.8%, specificity of 92.7%, LR+ 10.6 and LR- 0.24. Hysteroscopic endometrial polyp had 80% sensitivity, 92.6% specificity, nil LR+ and LR- 1.1. Hysteroscopic endometrial mass had sensitivity and specificity of 22.2% and 100% respectively, infinite LR+ and LR- 0.78. Hysteroscopic hypervascular endometrium as a predictor, had 22.2% sensitivity, 95.1% specificity, LR+ 4.6 and LR- 0.82 **(Table 3)**.

Table (3): Validity of Hysteroscopic Findings as a Predictor of malignant, premalignant and abnormal endometrial Pathology in Included Women

	Sensitivity	**Specificity**	**LR+**	**LR-**
Malignant or Premalignant Endometrial Pathology				
Hysteroscopic Thick Endometrium	100% (39.7 to 100)	76.09% (61.2 to 87.4)	4.18 (2.5 to 7.01)	0.0
Hysteroscopic Endometrial Polyp	60% (0.0 to 84.19)	93.48% (82.1 to 98.6)	0.0	1.07 (0.99 to 1.6)
Hysteroscopic Endometrial Mass	100% (15.8 to 100)	100% (91.7 to 100)	∞	0.0
Hysteroscopic Hypervascular Endometrium	50% (6.9 to 93.2)	95.6% (85.2 to 99.5)	11.5 (2.2 to 61.3)	0.52 (0.19 to 1.4)
Abnormal Endometrial Pathology				
Hysteroscopic Thick Endometrium	77.8% (39.9 to 97.2)	92.7% (80.1 to 98.5)	10.6 (3.4 to 33.4)	0.24 (0.07 to 0.8)
Hysteroscopic Endometrial Polyp	80% (0.0 to 63.6)	92.6% (80.1 to 98.5)	0.0	1.1 (0.99 to 1.2)
Hysteroscopic Endometrial Mass	22.2% (2.8 to 60.1)	100% (91.4 to 100)	∞	0.78 (0.5 to 1.1)
Hysteroscopic Hypervascular Endometrium	22.2% (2.8 to 60.1)	95.1% (83.5 to 99.4)	4.6 (0.7 to 28.2)	0.82 (0.57 to 1.2)

DISCUSSION

Perimenopausal bleeding is a real clinical challenge facing gynecologists, which should indicate suspicion of endometrial malignant changes development and needs accurate evaluation of endometrium and uterine cavity. Although uncommon, endometrial polyps may be the potential origin of the malignancy *(Balik et al., 2013* and *Acmaz et al., 2014).* Thus, many tools are arising to reveal the best diagnostic approach and the appropriate management protocol of perimenopausal bleeding. Clinical trials and researches are investigating the accuracy, sensitivity and specificity of these different diagnostic tools, and comparing them with each other, to find the best and the most accurate one *(Giannella et al., 2014* and *Shor et al., 2019).*

Office hysteroscopy did not require hospitalization and anesthesia, which reduced the cost making it an inexpensive choice. It can be performed on an outpatient basis or as a day case procedure with high acceptability and satisfaction from patients *(Khrouf et al., 2014).*

In the present study, 34% were free, with no comorbidities while the rest (66%) had comorbidities, 24% had hypertension, 26% had diabetes mellitus and 16% had chronic liver disease.

There was a statistical significance of sonographic endometrial thickness as a predictor of endometrial malignant/ premaliganat pathological changes. Endometrial thickness > 17mm was significant statistically associated with malignant/ premalignant endometrial pathology with 100% specificity and 25% sensitivity. On the other hand, endometrial thickness between 10-17 mm was significant statistically associated with endometrial pathology, with 100% specificity, while endometrial thickness < 7 mm was associated with no endometrial pathology with sensitivity 0f 88.24%.

In the present study, office hysteroscopic assessment of endometrium revealed 90% women had no endometrial lesion, 6% women had endometrial polyps and 4% women had masses. Hystroscopic detection of thick endometrium had 77.8% sensitivity and 92.7% specificity. In addition, *Gkrozou et al. (2015)* reported that office hystroscopy in diagnosing both endometrial polyps and masses had both sensitivity and specificity of more than 95%. As a predictor of malignant/ premalignat endometrial changes, hysteroscopic detection of thick endometrium had 100% sensitivity and 76.09% specificity.

Regarding endometrial polyps, our calculated specificity of detecting them by office hysteroscopy was 92.6%, while its sensitivity was 80%. Also, hysteroscopic detection of them had 93.48% specificity in prediction of malignant/premalignant endometrial changes, and 60% sensitivity. Office hysteroscpy had 22.2% sensitivity and 100% specificity in detecting endometrial masses, but it had both sensitivity and specificity of 100% in prediction of malignant/premalignant endometrial changes. Another study by *Shor et al. (2019)* revealed 100% sensitivity and 98.7% specificity of hysteroscopy in diagnosing endometrial polyps and masses.

Pennant et al. (2017) documented similar findings in their study of the value of hysteroscopic exploration for abnormal

uterine bleeding. They described diagnostic hysteroscopy as a basic tool allows precise diagnosis of endometrial lesions as polyps and masses. Furthermore, *Spadoto-Dias et al. (2016)* found office hysteroscopy a sensitive tool to diagnose endometrial polyps and masses and reported its higher sensitivity when compared to curettage in diagnosing these benign endometrial lesions.

In present study, we found 92% had normal hysteroscopic endometrial vascularity, while 8% had hypervascular endometrium. The sensitivity of hysteroscopic hypervascular endometrium as a predictor of benign endometrial lesion was 22.2%, while the specificity was 95.1%. As a predictor of malignat/premalignat endometrial pathology, hysteroscopic hypervascular endometrium had a sensitivity of 50% and a specificity of 95.6%, denoting higher specificity. *Dias et al. (2014)* concluded that postmenopausal bleeding and endometrial hypervascularity along with vascular atypia at diagnostic hysteroscopy showed a greater association with endometrial cancer.

Shor et al. (2019) studied prediction of malignant endometrial polyps by hysteroscopic features, and they stated that hysteroscopic findings of increased vascularity of endometrial polyps may suggest the diagnosis of malignant polyps. Similar to our findings, they reported higher specificity than sensitivity for hysteroscopic hypervascular endometrial as a predictor of malignant/premalignant endometrial changes.

In this study, we diagnosed atrophic endometrium in 14%, proliferation endometrium in 68%, simple endometrial hyperplasia without atypia in 14%, endometrial hyperplasia with atypia in 2%, and endometrial carcinoma in 2%. Concerning the woman with endometrial carcinoma and the other one with simple endometrial hyperplasia with atypia, they were both correctly observed and diagnosed in a preliminary form visualized by the operators, and none of the biopsies obtained during hysteroscopy were eventually revealed to be benign in histopathological study. Thus, we reported that office hysteroscopy is valuable in detecting endometrial carcinoma and endometrial hyperplasia with atypia. Additionally, *Trojano et al. (2018)* reported 66.7% sensitivity and 100% specificity of hysteroscopy in diagnosing endometrial hyperplasia, while in diagnosing endometrial carcinoma they reported sensitivity and specificity of 100% and 98.6% respectively.

Gkrozou et al. (2015) studied the accuracy of hysteroscopy in diagnosing endometrial carcinoma, and they concluded that hysteroscopic procedures have a high accuracy for detecting endometrial carcinoma. However they reported moderate diagnostic accuracy for endometrial hyperplasia and they explained that as endometrial hyperplasia does not appear with a specific hysteroscopic presentation.

Bourdel at al. (2016) stated that due to lack of morphological diagnostic criteria for endometrial malignant pathologies, hysteroscopic reliability may be influenced by the experience of the operator. They found that sensitivity improves with the observer's experience, but inter-observer agreement and reproducibility of hysteroscopy for

endometrial malignancies are not satisfying no matter the level of expertise. Therefore, an accurate and complete endometrial sampling is still needed.

However, prior research studies did not show conclusive determination of the accuracy of the histological malignancy grade in a biopsy obtained at outpatient hysteroscopy in comparison to the final pathology result obtained at hysterectomy. As malignant lesions have tendency to bleed during examination, it is possible that the outpatient hysteroscopic procedures are ended prematurely in comparison to inpatient hysteroscopy, which overwhelms the visual challenges by higher fluid pressure and better instrumental tools *(Hoshino et al., 2017)*.

CONCLUSION

It appears that office hysteroscopy can be considered as a golden standard tool in diagnosis and management of perimenoipausal bleeding. It is valuable in assessment of endometrium and helpful in management planning.

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دور المنظار الرحمى المكتبى فى تقييم حالات نزيف ما قبل انقطاع الدورة فى المرضى المترددين على العيادة الخارجية لأمراض النساء

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خلفية البحث: يُعتبر نزيف ما قبل انقطاع الطمث أحد التحديات الإكلينيكية التى تواجه أطباء التوليد وأمراض النساء، وهو يشير إلى الاشتباه في وجود بعض التغيرات أو الأورام الخبيثة في بطانة الرحم ويحتاج إلى تقييم دقيق لبطانة الرحم وتجويف الرحم.

الهدف من البحث: تهدف هذه الدراسة إلى توفير فهم واضح لقيمة منظار الرحم كأداة تشخيصية أثناء تقييم السيدات اللاتى يُعانين من نزيف ما قبل انقطاع الطمث.

المرضى وطرق البحث: شملت هذه الدراسة المستقبلية سجلات حالة لـ 50 سيدة مصابة بنزيف ما قبل سن اليأس وخضعت لعملية تنظير الرحم وأخذ خزعة من بطانة الرحم بين عامي 2017 و 2019 بمستشفى السيد جلال، جامعة الأزهر، القاهرة، مصر.

نتائج البحث: أظهرت نتائج الدراسة وجود دلالة إحصائية لسُمك بطانة الرحم بالموجات فوق الصوتية كأحد عوامل التنبؤ بظهور أورام خبيثة في بطانة الرحم أو قبل الولادة. وكان هناك ارتباط ذو دلالة إحصائية بين سُمك بطانة الرحم الأكثر من 17 ملم وبين ظهور الأورام الخبيثة ما قبل السرطانية ببطانه الرحم بخصوصيه 100٪ وحساسية 25٪. ومن ناحية أخرى، كان سمك بطانة الرحم بين 10-17 ملم مرتبطًا إحصائيًا بعلم أمراض بطانة الرحم بخصوصية 100٪، في حين أن سمك بطانة الرحم <7 مم كان مرتبطًا بعدم وجود أمراض بطانة الرحم بحساسية 88,24٪. في الدراسة الحالية، كشف تقييم الرحم بالمنظار لبطانة الرحم أن 90٪ لم يكن لديهن آفة بطانة الرحم، و6٪ كان لديهن سلائل بطانة الرحم، وكان لدى 4٪ تعانين من كتل ورمية. وكان الكشف عن الرحم من بطانة

الـــرحم الســـميكة حساســـية 77,8٪ وخصوصـــية 92,7٪ خصوصـــية. كمتنبـــئ بـــالأورام الخبيثـــة للحمـــل، كـــان الكشـــف عـــن الـــرحم مـــن بطانـــة الـــرحم الســـميكة 100٪ حساســـية و76,09٪ خصوصـــية. فيمـــا يتعلـــق بـــأورام بطانـــة الـــرحم، كانـــت خصوصـــيتنا المحســـوبة لاكتشـــافها عـــن طريـــق تنظيـــر الـــرحم 92,6٪، فـــي حـــين كانـــت حساســـيته 80٪. وكـــان الكشـــف عـــن تنظيـــر الـــرحم بخصوصـــية 93.48٪ فـــي التنبـــؤ بظهـــور أورام بطانـــة الـــرحم وحساســـية 60٪. وبالمثـــل، كـــان لتنظيـــر الـــرحم فـــي مكتبنـــا فـــي دراســـتنا حساســـية 22,2٪ وخصوصـــية 100٪ فـــي الكشـــف عـــن كتـــل بطانـــة الـــرحم، ولكـــن كـــان لـــه حساســـية وخصوصـــية بنســـبة 100٪ فـــي التنبـــؤ بظهـــور أورام خبيثـــة مـــا قبـــل الســـرطان ببطانـــة الـــرحم. وكـــان للكشـــف عـــن بطانـــة الـــرحم الســـميكة حساســـية 77,8٪ وخصوصـــية 92,7٪. وقـــد وجـــد أن 92٪ لـــديهن تكـــون طبيعـــى للأوعيـــة الدمويـــة بطانـــة الـــرحم، فـــي حـــين أن 8٪ مـــن النســـاء كـــن يعـــانين مـــن فـــرط الأوعيـــة الدمويـــة ببطانـــة الـــرحم. وكانـــت حساســـية بطانـــة الـــرحم تحـــت الـــرحم بالمنظـــار كمتنبـــئ بآفـــة بطانـــة الـــرحم الحميـــدة 22,2٪ بينمـــا كانـــت الخصوصـــية 95.1٪. كمتنبـــئ بـــأورام خبيثـــة ببطانـــة الـــرحم، وكـــان لبطانـــة الـــرحم تحـــت الـــرحم بالمنظـــار حساســـية 50٪ وخصوصية 95,6٪ مما يشير إلى خصوصية أعلى.

الاســـتنتاج: يمكـــن اعتبـــار تنظيـــر الـــرحم المكتبـــى أداة قياســـية ذهبيـــة فـــي تشـــخيص وعـــلاج نزيـــف مـــا قبـــل الطمـــث. كمـــا أنـــه أداة قيمـــة فـــي تقيـــيم بطانـــة الـــرحم ومفيـــد فـــي التخطيط للعلاج.