Interobserver Variability on Hysteroscopic Findings of Patients with Endometrial Hyperplasia

Mary Carmona MD, Gay Luz M. Talapian, MD, FPOGS and Marie Victoria Cruz-Javier, MD, FPOGS
Department of Obstetrics and Gynecology, St. Lukes's Medical Center Quezon City

Background: Endometrial hyperplasia is a common gynecologic disorder seen in the clinics. Among patients with endometrial hyperplasia, an estimated 5-10% have underlying malignancy hence early diagnosis and management is important. Hysteroscopy, regarded as the gold standard for diagnosing intrauterine abnormalities, enables accurate study of the endometrial surface as well as target eye biopsy during the same procedure. These eye-directed biopsies have a high accuracy in the hands of experienced operators, but accuracy of this technique is dependent on recognition of suspected endometrial pathology.[1]
Objective: The objective of this study is to ascertain inter-observer agreement in describing hysteroscopic findings among patients with endometrial hyperplasia.
Methodology: This is a prospective interobserver study of gynecologists from the Department of Obstetrics and Gynecology, St. Luke's Medical Center. Three invited, consenting gynecologists reviewed 22 hysteroscopy recordings with histologic diagnosis of normal endometrium or endometrial hyperplasia from the files of the section of Minimally Invasive Gynecologic Surgery. Then, evaluation of the hysteroscopy recordings was conducted using an assessment form containing questions about the quality of the recording, characteristics of the endometrium, and their diagnoses. The final outcome of this study is the inter-observer agreement among hysteroscopists in describing hysteroscopic findings of patients with endometrial hyperplasia.
Results: There is a wide gap in the interobserver agreement between hysteroscopists in describing hysteroscopic findings of patients with endometrial hyperplasia. However, the interobserver agreement was found to be substantial among participants in identifying the correct diagnosis.
Conclusion: A clear, systematic and standard way of identifying and describing hysteroscopic findings should be developed and instituted for use among hysteroscopists and hysteroscopy training programs. This will help in precisely identifying the areas where adequate sampling should be done.

Keywords: Endometrial hyperplasia, hysteroscopy, inter-observer agreement.

Introduction

Epidemiology of Endometrial Hyperplasia

Worldwide, uterine malignancy is the sixth most common malignancy affecting women and the fourth most common cancer in women in the United States.[2] In 2016, the projected number of cases is 60,050 patients, leading to 10,470 deaths. In the Philippines, it ranks 7th among the most common cancer sites in females. Endometrial hyperplasia is a well-known risk factor for endometrial carcinoma. In cases of simple hyperplasia without atypia, complex hyperplasia without atypia, simple hyperplasia with atypia, and complex hyperplasia with atypia, it is said that the risk of uterine malignancy is one, three, eight and twenty-seven percent, respectively. Significant morbidity and mortality can occur if endometrial hyperplasia is untreated with progression to cancer. In the Philippines, cancer of the uterus is the 13th

most common malignancy in both sexes and the 7th leading cancer among women.[2,3]

The 2014-revised WHO classification separates endometrial hyperplasia into two groups based upon the presence of cytological atypia (hyperplasia without atypia and atypical hyperplasia). It was reported that in patients with hyperplasia without atypia, there was a coexistent invasive endometrial carcinoma in their hysterectomy specimens in <1%. In patients with atypical hyperplasia / endometrioid intraepithelial neoplasia, 25-33% to as high as 59% in hysterectomy specimens have coexisting invasive endometrial carcinoma.[4]

Hysteroscopy and Diagnosis of Endometrial Hyperplasia

Hysteroscopy has high sensitivity (97.26%) and specificity (92%) in diagnosing endometrial abnormalities. Ianieri, et al.[5] developed a hysteroscopic risk scoring system to assist less experienced operators in differential diagnosis between non-pathological endometrium, non-atypical hyperplasia, complex atypical hyperplasia and well-differentiated adenocarcinoma. The scoring system showed a sensitivity and a specificity, respectively, of 77.1% and 80% for normal endometrium, 48.7% and 82.5% for non-atypical hyperplasia, 63.3% and 90.4% for atypical hyperplasia, and 95.4% and 98.2% for adenocarcinoma. Morphologic variables that show a statistically significant difference include diffuse and irregular endometrial thickening, presence of endometrial polyps, irregular color of the endometrium, presence of atypical vessels, crumbliness of endometrial neoformations during contact with the tip of the hysteroscope, or ease with which they bleed, presence of cerebroid neoformations and confirmation of hematometra. A study made by L.H. Uno, et al. in 1994[6] evaluated the morphologic hysteroscopic criteria leading to a diagnosis of endometrial hyperplasia and compared the accuracy with that of final histology. Results show that the presence of endometrial glands presenting a cystic pattern at hysteroscopy gave statistically significant results ($p<0.05$), with low sensitivity (15.79%), high specificity (97.29%) and a relative risk of 6.75. The positive predictive value of the study showed 64.54% and negative predictive value of 79.40%. M. Dueholm, et al. in 2015[7], studied the reproducibility of endometrial pathologic findings obtained on hysteroscopy, transvaginal sonography and gel infusion sonography in women with postmenopausal bleeding, including patients with endometrial hyperplasia. Pattern diagnosis of endometrial hyperplasia was found to be not reproducible by use of either ultrasound or hysteroscopy. There was also an increased observer bias toward the diagnosis of malignancy or hyperplasia using hysteroscopy in the large number of women with concomitant endometrial polyps. However, reliability of hysteroscopic findings may be influenced by the experience of the operator and by a lack of standard morphologic diagnostic criteria for endometrial hyperplasia. According to the study made by N. Bourdel, et al. in 2016[8], experience in hysteroscopy was studied if it would improve accuracy and inter-observer agreement in the management of abnormal uterine bleeding. The study concluded that sensitivity improves with observer's experience, but inter-observer agreement and reproducibility of hysteroscopy for endometrial malignancies are not satisfying no matter the level of expertise.

Accuracy of Hysteroscopy and Endometrial Hyperplasia

Reported hysteroscopic sensitivity for endometrial hyperplasia is 75.2% and specificity of 91.5%. In a study made by Gkrozou, et al.[9] asymptomatic patients and patients with abnormal uterine bleeding were examined and the authors reported a sensitivity, specificity, positive predictive value and negative predictive value for endometrial hyperplasia of 81%, 96%, 87% and 93%, respectively for the abnormal uterine bleeding group and sensitivity of 60% for the asymptomatic group. These values of sensitivity and specificity are reduced when hysteroscopy was performed by a less experienced operator, as shown in a study by De Marchi, et al.[10] In their study, it was shown that sensitivity and specificity for hyperplasia without atypia, atypical hyperplasia, and endometrial carcinoma were 60%, 9.09%, 70% (sensitivity) and 97%, 98%, 99.1% (specificity) respectively, when performed

by young residents with less than 201 performed hysteroscopies.

Hysteroscopic Findings in Endometrial Hyperplasia, Atrophy, Carcinoma

Endometrial Hyperplasia – abnormal proliferation of endometrial lining, encompasses the two histologic types (non-atypical and atypical / endometrioid intraepithelial neoplasia) and characterized by the following hysteroscopic changes:[11]

1. Increased endometrial thickness – proliferation of endometrial lining (flat thickening, plane thickening or polypoid thickening)

2. Non-homogenous endometrial regeneration – characterized by numerous regular filling defects of different sizes and separated by denser outlines

3. Increased vascularization – presence of increased number of aborescent or tree-like appearance of vessels that surrounds groups of glandular ostia

4. Presence of ciliated epithelium- focal or papillary mucosal projections of the endometrium

5. Presence of cystic dilatation – presence of irregularly-shaped, widened glandular openings with cystic-glandular formations approximately one millimeter in diameter

6. Presence of cystic spaces - characterized by numerous regular filling defects of different sizes and separated by denser outlines

7. Polypoid formations

8. Necrotic areas

9. Irregular arrangement of the glandular orifices

Atrophic Endometrium - endometrial mucosa that is thin and transparent, revealing the underlying vascular structures. There may be presence of hemorrhagic suffusion and petechiae; endometrium may be smooth, whitish and somewhat porcelain.

Endometrial Carcinoma - hysteroscopic pictures show a germinative one, with irregular, polylobate, friable projections that have a cerebroid pattern, usually necrotic and bleeds easily. Vascularization is irregular and bizarre. At times, a distinct zone between the neoplasia and normal endometrium can be seen.

Significance of the Project

The aim of this study is to evaluate the inter-observer agreement of gynecologists in St. Luke's Medical Center Quezon City on the hysteroscopic diagnosis of endometrial hyperplasia. It is hoped that the results of this study will help determine if a standardized method of describing hysteroscopic findings needs to be established for training purposes, creation of a diagnostic criteria for endometrial pathology and guide for performing a targeted biopsy.

Objective

The objective is to evaluate interobserver variability in describing hysteroscopic findings of patients with endometrial hyperplasia among hysteroscopists from the Department of Obstetrics and Gynecology of St. Luke's Medical Center Quezon City.

Methods

The protocol was sent to the ISRC for approval and Institutional Ethics Review Committee (IERC) of the Research and Biotechnology Group for ethical clearance. Hysteroscopy procedures were performed in a standardized manner, using a 5-mm outer diameter, continuous flow hysteroscope with 30 degree direction of view (Storz). Cases chosen for the study must be: women belonging to the reproductive age group, had undergone hysteroscopy at St. Luke's Medical Center Quezon City with a corresponding histologic diagnosis of normal endometrium and endometrial hyperplasia. The recordings were edited in such a way that every recording starts at the entrance into the uterine cavity and ends just before leaving the outer ostium of the cervix. Then

the charts of the chosen recordings including the operative technique and histopathological reports were obtained from the medical records section. Patient identifiers of chosen recordings, charts and histopathology reports were removed to uphold patient confidentiality. Instead, a code was used to reconcile recordings and chart data. Data were saved in one computer , with password only available to the researcher. An expert hysteroscopist was invited to view the recordings and evaluate the data collection form for the purposes of standardization.

Three hysteroscopists from the Department of Obstetrics and Gynecology of St. Luke's Quezon City were invited to participate in the study. Informed consent was discussed. The study was commenced once informed consent form was signed. The selected video recordings were then shown one by one to the study participants. Demographics of the observers such as the level of medical specialization, years of experience performing hysteroscopy, and number of hysteroscopies performed were recorded. Evaluation of the hysteroscopy recordings was conducted using an assessment form (Appendix 1). The assessment form was created by the researcher/s and evaluated by an expert hysteroscopist. This form contained questions about the quality of the recording, characteristics of the endometrium and their diagnoses. The participant observer was asked to describe the video recordings and answer the checklist based on their individual assessment of the recordings. The observers were blinded regarding the medical history of the patients in the video recordings. Individual evaluation findings of each participant as well as final diagnosis of the video were not revealed. Only the investigators and the expert hysteroscopist knew the final diagnosis.

Inclusion Criteria and Exclusion Criteria

This study included hysteroscopy video recordings of patients with diagnoses indicated in the histopathological report as normal endometrium (includes benign endometrial tissues, atrophic endometrium, proliferative / secretory endometrium) and endometrial hyperplasia (includes atypical or non-atypical hyperplasia). Excluded from the study were hysteroscopy video recordings of patients diagnosed with endometrial hyperplasia but with concomitant pathologies indicated on the histopathological report.

Description of Outcome Measures

The primary study outcome was the inter-observer agreement among hysteroscopists from the Department of Obstetrics and Gynecology of St. Luke's Medical Center Quezon City in describing hysteroscopic findings of patients with endometrial hyperplasia.

Data Analysis and Statistical Evaluation

Data were encoded in Microsoft Excel and statistical analysis was performed using SPSS. The inter-observer agreement is expressed as the intraclass correlation coefficient (ICC). The ICC is an approximation of the overall weighted kappa values. Kappa is a measure of agreement above or below what is expected to be the agreement by chance. A kappa value (or ICC) of <0.20 represents poor agreement, 0.21-0.40 fair agreement, 0.41-0.60 moderate agreement, 0.61-0.80 substantial agreement, and a value of 0.81-1.00 indicates almost perfect agreement. A linear mixed model was used to ensure that observer agreement was not be influenced by the quality of a record. The estimated variance of the recordings of the highest quality was compared with the estimated variance of the recordings of the lowest quality, making use of the z-test. A higher estimated variance is associated with a higher ICC and therefore higher observer agreement. A p-value of <0.05 will be considered statistically significant.

The descriptive statistics was determined by means of the SPSS 12.0 frequency, descriptives and crosstabs procedures. For the comparison between means, t-test was performed with SPSS 12.0.

Benefits of the Study

In developing countries such as the Philippines, the burden of endometrial cancer often besets women in any societal classification. Endometrial hyperplasia not only predisposes to endometrial carcinoma, its presenting clinical symptoms (heavy menstrual bleeding, post menopausal bleeding) often lead to emergency and outpatient

evaluations. Hysteroscopy as the gold standard of evaluating endometrial abnormalities is the first step in diagnosing endometrial hyperplasia. To the best knowledge of the researcher, there are no current guidelines or standard way as to how hysteroscopists describe endometrial findings and make their operative diagnoses. Knowing the interobserver agreement among hysteroscopists may confirm if standardization of describing endometrial characteristics is actually needed. This study may also be a guide for future researchers in the creation of diagnostic criteria or a hysteroscopic risk scoring for endometrial pathologies. There is, however, no direct benefit to the study subjects.

Results

Three gynecologists invited to participate reviewed 22 hysteroscopy video recordings were all consultants of the department. Among the observers, the mean number of hysteroscopies performed was 30 cases per year and the average year of experience with performing hysteroscopy was 14.25 years.

Table 1. Characteristics of participants

Characteristics of participants	
Level of specialization: Consultants	3
Years of experience	14.25 ± 4.8
Number of hysteroscopies performed	30 ± 17.3

Note: Data are given as mean ± SD

Inter-observer Agreement

The inter-observer agreement was calculated for the features of the endometrium seen, the diagnosis, and quality of recording. The Kappa Coefficient or ICC was calculated and interpreted as the following: <0.20 indicates poor agreement, 0.21 to 0.40 fair agreement, 0.41 to 0.60 moderate agreement, 0.61 to 0.80 substantial agreement, and 0.81 to 1.00 excellent agreement.

Excellent agreement was noted between observers when presented with hysteroscopy recordings of endometrium with features of no abnormalities (ICC 0.91), increased endometrial thickness (ICC 0.78), increased vascularization (ICC 0.85), presence of cystic dilatation (ICC 0.78), and polypoid formations (ICC 0.83). Substantial agreement between observers was seen when non-homogenous endometrial regeneration was observed (ICC 0.63). However, in features such as presence of ciliated epithelium, necrotic areas and irregular arrangement of glandular orifices, only fair agreement was noted (ICC 0.59, 0.43, 0.41, respectively).

The inter-observer agreement between the three gynecologists for the correct diagnosis of the hysteroscopy recordings seen was found to be substantial, with an ICC of 0.61.

Table 3 shows the level of inter-observer agreement and corresponding ICC values for the assessment of different features of the endometrium

Table 4 illustrates the number of correct diagnoses of each observer based on the final histopathological report. Resulting p-value of 0.036 suggests that there is a significant difference on the percentage of correct diagnoses.

Table 2. Level of overall observer agreement expressed in ICC*

	ICC	Interpretation
No abnormalities	0.9144	Excellent
Increased endometrial thickness	0.7752	Excellent
Non-homogenous endometrial regeneration	0.6255	Substantial
Increased vascularization	0.8451	Excellent
Presence of ciliated epithelium	0.5903	Fair
Presence of cystic dilatation	0.7836	Excellent
Polypoid formations	0.8303	Excellent
Necrotic areas	0.4273	Fair
Irregular arrangement of glandular orifices	0.4141	Fair
Correct Diagnosis	0.6085	Substantial

*ICC, intraclass correlation coefficient (equivalent to overall weighted k)

Table 3. Level of inter-observer agreement and corresponding ICC values for the assessment of different features of the endometrium

No abnormalities

	ICC	95% CI	Strength of Agreement
Consultant 1 vs 2	0.4634	-0.13 to 1.00	Moderate
Consultant 1 vs 3	0.7755	0.36 to 1.00	Good
Consultant 2 vs 3	0.6452	0.01 to 1.00	Good

Increased endometrial thickness

	ICC	95% CI	Strenght of Agreement
Consultant 1 vs 2	0.4634	-0.13 to 1.00	Moderate
Consultant 1 vs 3	0.433	0.07 to 0.79	Moderate
Consultant 2 vs 3	0.1539	-0.12 to 0.43	Poor

Non-homogenous endometrial regeneration

	ICC	95% CI	Strength of Agreement
Consultant 1 vs 2	0.0888	-0.03 to 0.21	Poor
Consultant 1 vs 3	0.3384	0.06 to 0.61	Fair
Consultant 2 vs 3	-0.0476	-0.36 to 0.27	Poor

Increased vascularization

	ICC	95% CI	Strength of Agreement
Consultant 1 vs 2	0.4211	0.10 to 0.74	Moderate
Consultant 1 vs 3	0.5299	0.18 to 0.88	Moderate
Consultant 2 vs 3	0.4086	-0.00 to 0.82	Moderate

Presence of ciliated epithelium

	ICC	95% CI	Strength of Agreement
Consultant 1 vs 2	0.1316	-0.27 to 0.53	Poor
Consultant 1 vs 3	0.0494	-0.35 to 0.45	Poor
Consultant 2 vs 3	0.3265	-0.25 to 0.91	Fair

Presence of cystic dilatation

	ICC	95% CI	Strength of Agreement
Consultant 1 vs 2	0.4211	0.00 to 0.84	Moderate
Consultant 1 vs 3	0.4762	0.17 to 0.78	Moderate
Consultant 2 vs 3	0.1539	-0.05 to 0.36	Poor

Polypoid formations

	ICC	95% CI	Strength of Agreement
Consultant 1 vs 2	0.4954	0.11 to 0.88	Moderate
Consultant 1 vs 3	0.6973	0.38 to 1.00	Good
Consultant 2 vs 3	0.1619	-0.27 to 0.59	Poor

Necrotic areas

	ICC	95% CI	Strength of Agreement
Consultant 1 vs 2	-0.0784	-0.21 to 0.05	Poor
Consultant 1 vs 3	0.2326	-0.21 to 0.68	Fair
Consultant 2 vs 3	-0.0845	-0.23 to 0.06	Poor

Irregular arrangement of glandular orifices

	ICC	95% CI	Strenght of Agreement
Consultant 1 vs 2	0.0000	0.00 to 0.00	Poor
Consultant 1 vs 3	0.0571	-0.03 to 0.15	Poor
Consultant 2 vs 3	0.0000	0.00 to 0.00	Poor

Table 4. Number of correct diagnoses per observer

	O1	O2	O3	p value
Number of correct diagnoses	17	15	8	0.0369
Percentage (%)	77.3	68.2	36.4	

Discussion

The present study demonstrates that the inter-observer agreement in describing the features seen in hysteroscopic recordings of patients with endometrial hyperplasia is variable. When the gynecologists were presented with hysteroscopy video recordings of endometrium with no abnormalities, agreement was noted to be excellent. This was also true for hysteroscopic recordings of patients with endometrial hyperplasia with endometrial features of increased endometrial thickness, increased vascularization, presence of cystic dilatation and polypoid formations. There was substantial agreement noted when endometrial feature of non-homogenous endometrial regeneration was shown. When features such as presence of ciliated epithelium, necrotic areas and irregular arrangement of glandular orifices were shown, there

was only fair agreement between the observers. The study also shows that the inter-observer agreement in the correct diagnosis (normal endometrium or endometrial hyperplasia) was substantial (ICC 0.60).

Hysteroscopy with targeted endometrial biopsy is the gold standard used to investigate patients with abnormal uterine bleeding. Logically, it is of importance that a hysteroscopist is able to identify pathological endometrial features for which a biopsy is required. The hysteroscopic appearance of endometrial hyperplasia is extremely varied. As shown in this study, there are features of endometrial hyperplasia that had excellent inter-observer variability, however there are also some features that only had fair agreement. Therefore, results of interobserver agreement among each observer is varied, though collectively, it is classified as substantial interobserver agreement. This may demonstrate that subjectivity lies within each observer. Is there a correlation between the length and/or the quality of training each observer had? The study was only limited to describing hysteroscopic findings. This study did not take into account the correlation of previous training, how each observer differs in conducting a hysterocopic procedure to the way each one describes his finding.

Conclusion

The agreement between hysteroscopists on describing hysteroscopic findings of patients with endometrial hyperplasia was varied. While the results show that the observers were able to substantially diagnose endometrial hyperplasia, the descriptions of each characteristic findings are of equal importance. This implies that for hyperplastic features such as presence of ciliated epithelium, necrotic areas and irregular arrangement of glandular orifices, some hysteroscopists may not be able to identify such as pathological. For this study, these findings have implication in the most important step during hysteroscopy, which is identifying the pathological endometrial features for targeted biopsy. Hence, development of a clear and standard method to identify hysteroscopic findings is warranted, which can serve as a guide for targeted biopsies.

Recommendation

Future areas for research may include looking into factors that may contribute to the inter-observer variability findings in this study. Another recommendation for future researches should be the development of a standardized way to describe features of endometrial hyperplasia, and implementing such standards among hysteroscopy training programs.

Appendix

1. Data collection form

ASSESSMENT FORM: INTER-OBSERVER AGREEMENT STUDY ***Video No.*** _____

Observer No:

Current level of medical specialization: ☐ Resident ☐ Fellow ☐ Consultant
Place of training of minimally invasive procedures: _____
Number of months or years of training: _____

Years of experience with performing hysteroscopy: ☐ <5 years ☐ 5-10 years ☐ 11-15 years ☐ >15 years

Estimated total number of hysteroscopies performed per year: _____

Hysteroscopy recording assessment

Quality of recording:	☐ Good	☐ Intermediate	☐ Poor
Symmetrical uterus:	☐ Yes		☐ No
Left tube os visualized:	☐ Yes		☐ No
Right tube os visualized:	☐ Yes		☐ No
Features seen:			
No abnormalities	☐ Yes		☐ No
Increased endometrial thickness	☐ Yes		☐ No
Non-homogenous endometrial regeneration	☐ Yes		☐ No
Increased vascularization	☐ Yes		☐ No
Presence of ciliated epithelium	☐ Yes		☐ No
Presence of cystic dilatation	☐ Yes		☐ No
Polypoid formations	☐ Yes		☐ No
Necrotic areas	☐ Yes		☐ No
Irregular arrangement of glandular orifices	☐ Yes		☐ No

Diagnosis:
- ☐ No Endometrial Pathology
- ☐ Endometrial Polyp
- ☐ Endometrial Hyperplasia
- ☐ Endometrial Malignancy
- ☐ Others, specify _____

References

1. Garuti G, Cellani F, Garzia D, Colonnelli M and Luerti M. Accuracy of hysteroscopic diagnosis of endometrial hyperplasia: A retrospective study of 323 patients. J Min Inv Gynecol 12 (3): 247-53.
2. Lentz GM, Lobo RA, Gershenson DM and Katz VL. Comprehensive Gynecology Sixth Edition. Elsevier. 2012.
3. Laudico A, Medina V, Lumague M, Mapua C, Redaniel M, Valenzuela F, et al. 2010 Philippine Cancer Facts and Estimates. Philippine Cancer Society, Department of Health. Philippine Cancer Society, Inc.
4. Smit JG, Kasius JC, Eijkemans MJ, Veersema S, Fatemi HM, Santbrink van EJ, et al. The international agreement study on the diagnosis of the septate uterus at office hysteroscopy in infertile patients. Fertility and Sterility American Society of Reproductive Medicine 2013; 99 (7).
5. Ianieri MM, Staniscia T, Pontrelli G, Sardo A, Manzi FS, Recchi M, et al. A new hysteroscopic risk scoring system for diagnosing endometrial hyperplasia and adenocarcinoma. J Min Inv Gynecol 2016; 23 (5).
6. Uno L, Sugimoto O, Carvalho F, Bagnoli V, Fonseca A and Pinotti J. Morphologic hysteroscopic criteria suggestive of endometrial hyperplasia. Int J Gynecol Obstet 1995; 49: 35-40.
7. Dueholm M, Hjorth ID, Secher P, Jorgensen A and Ortoft G. Reproducibility of endometrial pathologic findings obtained on hysteroscopy, transvaginal sonography, and gel infusion sonography in women with postmenopausal bleeding. J Min Inv Gynecol 2015; 22 (6): 1036-44.
8. Bourdel N, Modaffari P, Tognazza E, Pertile R, Chauvet P, Botchorishivilli R, et al. Does experience in hysteroscopy improve accuracy and inter-observer agreement in the management of abnormal uterine bleeding? Surg Endosc 2016; 30 (12): 5558-64.
9. Gkrozou F, Dimakopoulos G, Vrekoussis T, Lavasidis L, Koutlas A, Navrozoglou I, Stefos T, Paschopoulos M. Hysteroscopy in women with abnormal uterine bleeding: a meta-analysis on four major endometrial pathologies. Arch Gynecol Obstet. 2015; 291(6):1347-54. doi: 10.1007/s00404-014-3585-x. Epub 2014 Dec 19.
10. De Marchi F, Fabris AM, Tommasi L, Nappi L, Saccardi C, Litta P.Accuracy of hysteroscopy made by young residents indetecting endometrial pathologies in postmenopausal women. Eur J Gynaecol Oncol 2014; 35(3): 219-23.
11. Mencaglia L, Cavalcanti de Albuquerque Neto L and Arias Alvarez R. Manual of Hysteroscopy Diagnostic, Operative and Office Hysteroscopy. Firenze, Italy: Endo Press Publisher.