

## Role of Chromo Hysteroscopy in Evaluation of Endometrial Pathology in Female with Abnormal Uterine Bleeding.

Abdel-Halim.M.Nagy, Mohamed.A.Mohamed, Mohamed.A.El-Noury and Ibrahim.I.Swedan

Obstetrics and Gynecology Dept., Faculty of Medicine, Benha University

E-mail: abdelhalimnagy68@gmail.com

### Abstract:

**Background:** Abnormal hysteroscopy, laboratory testing, imaging, and other diagnostic procedures may all be necessary to determine the cause of abnormal uterine bleeding (AUB), which is defined as bleeding from the uterus that varies in frequency, regularity, length, or quantity as typically reported by the woman. The purpose of this study is to evaluate the value of chromo hysteroscopy in diagnosing and treating abnormal uterine bleeding in women. The Components and Procedures: Over the course of a year, 115 women with AUB problems were surveyed at the outpatient clinic of the Department of gynaecology and obstetrics at Benha University's department of medicine. Chromo hysteroscopy, performed with 5 ml of 1% methylene blue, was performed after conventional hysteroscopy. Distinct staining patterns seen. Staining that was concentrated in one area was termed positive, while staining that was more evenly distributed was regarded normal. These results were compared to those that had already been observed (on conventional hysteroscopy). Differentially stained regions were sampled for biopsies. The correlation between histopathology and hysteroscopic and chromo-hysteroscopic results was investigated. It was determined that chromo hysteroscopy had a high rate of success in diagnosing endometrial illness. The percentages for sensitivity (92.54%), specificity (83.33%), PPV (88.57%), and NPV (-92.54%) are as follows: (88.89 percent ). In addition to the 16 instances of atrophic endometritis, 28 cases of simple endometrial hyperplasia, 4 cases of atypical endometrial hyperplasia, and a new single case of endometrial cancer, the chromo hysteroscopy method resulted to the detection of 50 additional novel endometrial histopathologies. The diagnosis accuracy of traditional hysteroscopy for AUB is boosted by chromo hysteroscopy, as a result.

**Keywords:** Abnormal uterine bleeding, Dilatation and Curettage, Body mass index, chronic endometritis, Non-neoplastic endometrium

### 1. Introduction

Abnormal In the absence of pregnancy, abnormal uterine bleeding (AUB) is described as bleeding from the uterus that is different in frequency, regularity, length, or quantity. It is predicted that 30% of all women will be affected by AUB at some point in their life, with the highest frequency during the reproductive years. Diagnostic hysteroscopy with hysteroscopic guided biopsy has replaced previously used "blind" conventional techniques (such as D&C, fractional endometrial biopsy, etc.) in the assessment of AUB. A normal look of endometrium in standard diagnostic hysteroscopy does not guarantee the integrity of endometrial cells, but it does allow for good viewing of the uterine cavity and identification of intracavitary lesions.

In chromo hysteroscopy, stains or pigments are applied topically to enhance the characterisation of endometrial tissue, which aids in the detection of an endometrial lesion. Subtle endometrial alterations may not be seen during a routine hysteroscopy exam, however endometrial dyeing with 1% methylene blue may help highlight them. The study's goal was to assess the usefulness of endometrial dyeing during hysteroscopy as a novel and straightforward technique for assessing and diagnosing endometrial disease that may be

overlooked by standard hysteroscopy in the absence of macroscopic abnormalities.

### 2. Materials and methods

This study aims to identify the role of Chromo hysteroscopy in the evaluation of abnormal uterine bleeding by using a cross-sectional study design to collect data from 115 patients seen at the obstetrics and gynaecology outpatient clinic within the Faculty of Medicine at Benha University between August 2022 and July 2023. Cochran's formula for determining what constitutes a sufficient sample size was used.

The formula for determining the SS is as follows:  $SS = Z^2 \times (P \times (1-P)) / E^2$  Z= value of Z (e.g. 1.96 for 95 percent confidence level). A sample size of 91.9 percent was determined by using the formula  $P = \text{proportion of respondents who made a selection, expressed as a decimal}$  (Al-Ani et al, 2018). The decimal form of the standard error formula is E. (e.g., .05). Using the above criteria, a sample size of 115 patients would be considered minimal. Women with occasional heavy bleeding, rarely heavy bleeding, heavy menstrual bleeding despite therapy, and women with chronic intermenstrual bleeding were also included in the research. Patients with acute or chronic cervicitis or PID, as well as those using hormonal contraception, a

copper intrauterine device (IUD), or hormone replacement therapy (HRT) were not included.

Questions of Morality: Before patients participated in the trial, they provided informed written permission. Information such as the study's objective, location, methodology, and participants' willingness to have their anonymized data published were provided. All participants were guaranteed of the privacy of their findings.

A complete medical history was taken from each patient: period history, sexual history, family history, medical history, obstetrical history, contemporary method of birth control, and social history. In addition to any coagulopathies, cancer, or endocrine problems that you may already be aware of. Checking of the usuals (blood pressure, body mass index, etc.) Pallor, hormonal abnormalities. After that, we'll do a full physical, including an abdominal and a local checkup. In addition to a complete blood count and urine or serum quantitative human chorionic gonadotropin (HCG), thyroid stimulating hormone (TSH), prolactin, follicle stimulating hormone (FSH), luteinizing hormone (LH), estradiol, luteal phase progesterone, free androgens, and a pelvic ultrasound may be performed. Index.

If no abnormalities were discovered during a routine hysteroscopy, 5cc of methylene blue 1 percent was injected into the uterine cavity. Staining patterns in the uterine cavity were observed. Cases in which there was a single or more dark blue stains above the internal cervical ostium were judged positive (group I). A hysteroscopically guided biopsy was performed on the darkly stained endometrium, and a second hysteroscopically guided biopsy was performed on the lightly stained endometrial. Cases in whom a random biopsy was performed and the endometrium showed diffuse light blue staining were classified as group II. Histopathological analysis using Hematoxylin and Eosin stain was performed on the various specimens, which were stored in labelled vials of 10% formalin.

### 3. Analysis Based on Statistics

Using the Social Science Statistical software programme, we cleaned, processed, and tallied the data we gathered. Statistics including means, standard deviations, one-way analysis of variance, pairwise and multiple correlation and regression were utilised. All given p-values were two-tailed, and a significance level of p 0.05 was significant.

### 4. Results

Group I comprised seventy individuals with chromo hysteroscopy showing localised regions of dark staining surrounded by lighter parts. Histopathological investigations were performed

on samples collected from both heavily and lightly stained regions, with the following findings: Eight cases (11.4%) were found to have non-neoplastic, non-inflammatory endometrium; eighteen patients (25.7%) were found to have atrophic endometritis; two patients (2.9%) displayed endometrial carcinoma; 32 patients (45.7%) were found to have simple endometrial hyperplasia without atypia; four patients (5.7%) were found to have complex endometrial hyperplasia with atypia; and six cases (8.6 In Table 1, we see that 82.9% of patients with diffuse light-stained areas had non-neoplastic, non-inflammatory endometrium, 2.9% had atrophic endometritis, 1.4% had endometrial carcinoma, 5.7% had simple endometrial hyperplasia without atypia, and 0% had complex endometrial hyperplasia with or without atypia Of the 45 patients in Group II, 88.9 percent had NNE, 2.2% had atrophic endometritis, and 8.9 percent had simple endometrial hyperplasia. Table 2.

Seventy instances (group I) had focused dark stained regions on chromo hysteroscopy, whereas 45 cases (group II) did not (group II). Table 3. Sixty-two out of the 70 patients who had localised regions of black staining confirmed abnormal histopathology. Of the 45 patients who had diffuse light staining in chromo hysteroscopy, 40 had normal results, indicating a positive predictive value of 88.57 percent. This resulted in an 88.89 percent negative predictive value. Microscopic investigation revealed endometrial abnormalities in 67 of the patients. When examined with chromo hysteroscopy, 62 of the women had localised regions of dark staining. This meant that chromo hysteroscopy has a sensitivity of 92.54 percent. Forty-eight individuals received negative results on histopathology tests, and chromo hysteroscopy found no localised black staining in those women's uteruses. According to these results, chromo hysteroscopy has an 83.33 percent specificity.comprised seventy individuals with chromo hysteroscopy showing localised regions of dark staining surrounded by lighter parts. Histopathological investigations were performed on samples collected from both heavily and lightly stained regions, with the following findings: Eight cases (11.4%) were found to have non-neoplastic, non-inflammatory endometrium; eighteen patients (25.7%) were found to have atrophic endometritis; two patients (2.9%) displayed endometrial carcinoma; 32 patients (45.7%) were found to have simple endometrial hyperplasia without atypia; four patients (5.7%) were found to have complex endometrial hyperplasia with atypia; and six cases (8.6 In Table 1, we see that 82.9% of patients with diffuse light-stained areas had

non-neoplastic, non-inflammatory endometrium, 2.9% had atrophic endometritis, 1.4% had endometrial carcinoma, 5.7% had simple endometrial hyperplasia without atypia, and 0% had complex endometrial hyperplasia with or without atypia. Of the 45 patients in Group II, 88.9 percent had NNE, 2.2% had atrophic endometritis, and 8.9 percent had simple endometrial hyperplasia. Table 2.

Seventy instances (group I) had focused dark stained regions on chromo hysteroscopy, whereas 45 cases (group II) did not (group II). Table 3. Sixty-two out of the 70 patients who had localised regions of black staining confirmed abnormal histopathology. Of the 45 patients who had diffuse light staining in

chromo hysteroscopy, 40 had normal results, indicating a positive predictive value of 88.57 percent. This resulted in an 88.89 percent negative predictive value. Microscopic investigation revealed endometrial abnormalities in 67 of the patients. When examined with chromo hysteroscopy, 62 of the women had localised regions of dark staining. This meant that chromo hysteroscopy has a sensitivity of 92.54 percent. Forty-eight individuals received negative results on histopathology tests, and chromo hysteroscopy found no localised black staining in those women's uteruses. According to these results, chromo hysteroscopy has an 83.33 percent specificity.%. Table 3.

**Table (1)** Histopathological findings in group I.

Histopathology	Group I N = 70			
	Darkly stained areas		Lightly stained areas	
	No	%	No	%
NNE	8	11.4	58	82.9
Atrophic endometritis	18	25.7	2	2.9
Endometrial carcinoma	2	2.9	1	1.4
Simple endometrial hyperplasia without atypia	32	45.7	4	5.7
Complex endometrial hyperplasia with atypia	4	5.7	0	0.0
Complex endometrial hyperplasia without atypia	6	8.6	0	0.0

**Table (2)** Histopathology of diffuse lightly stained areas in group II.

Histopathology	Group II N = 45	
	Lightly stained areas	
	No	%
NNE	40	88.9
Atrophic endometritis	1	2.2
Simple endometrial hyperplasia	4	8.9

**Table (3)** Numerical data of Chromo Hysteroscopy in detection of abnormal endometrial pathologies missed by hysteroscopy.

Histopathology	Dark stained areas (group I)	No focal dark stain (group II)	Total number
	Number	Number	
Abnormal histopathologic findings	62	5	67
Normal findings	8	40	48
Total	70	45	
Sensitivity	92.54%		
Specificity	83.33%		
Positive predictive value (PPV)	88.57%		
Negative predictive value (NPV)	88.89%		

- The total number of cases: 115
- True +ve test results: 62 cases.
- False +ve test results: 8 cases.
- True -ve test results: 40 cases

-False –ve test results: 5 cases.

### 5. Discussion

The majority of female patients present with symptoms of abnormal uterine bleeding (AUB). Endometrial illnesses, whether malignant or benign, all have early clinical symptoms that increase the likelihood of a prompt diagnosis and successful treatment. Ninety percent of women with endometrial cancer only have vaginal bleeding, thus this symptom should always be thoroughly examined.

Ultrasound, saline sonohysterography, and D&C endometrial biopsies are standard procedures for the investigation of abnormal uterine bleeding (AUB) in postmenopausal and menopausal women. D&C operations, particularly in industrialised nations, are declining in importance in the examination of abnormal uterine bleeding due to the rise in popularity of hysteroscopy and outpatient sampling methods. Because it "sees" and "decides" the reason of abnormal uterine bleeding, hysteroscopy is rapidly replacing blind curettage. This is so because a doctor can see into the uterus and curettage the affected region. The uterine ovum is, in reality, an eye. On the other hand, hysteroscopy may miss localised endometrial hyperplasia or even early endometrial cancer.

In fact, hysteroscopy has a negative predictive value of >90% when no structural abnormalities is seen in a fully visible uterine cavity and the endometrium looks uniformly thin and homogenous (Ebstein et al, 2001). Endometrial hyperplasia, endometritis, and endometrial cancer are all examples of diffuse endometrial diseases, and hysteroscopy's accuracy in detecting them is debatable. Atypical lesions may go undetected by visually guided biopsy. The endometrium is not an absorptive epithelium under normal conditions, and structural disruption to the cells facilitates passage of methylene blue dye into the cells, as observed by Marconi et al., Kucuk and Safali.

This investigation used methylene blue dying as a novel technique called "chromo hysteroscopy" for hysteroscopy-guided endometrial sampling to identify endometrial abnormalities that are not visible during a standard hysteroscopy and are responsible for abnormal uterine bleeding in reproductive-aged, perimenopausal women.

A careful history, in-depth general and local examination, and transvaginal sonographic assessment revealed no underlying medical or anatomical abnormalities in any of the 115 patients who presented with complaints of abnormal uterine bleeding in this investigation.

Patients were classified into Group I (those with positive focal dark staining) and Group II (those without such staining) (without focal dark staining). One randomly biopsied specimen from each participant in Group II was submitted together with two specimens from Group I (one from the darkly stained regions and the other from the remainder of the endometrium) for histopathological evaluation. Table (1) shows 62 histological abnormalities in hysteroscopically guided specimens from the focal dark stained regions that were previously deemed normal by conventional hysteroscopy in Group II. Atrophic endometritis was found in 18 instances (25.7%), simple endometrial hyperplasia was found in 32 cases (45.7%), complex endometrial hyperplasia was found in 6 cases (8.6%), and atypia was found in 4 cases (5.7%). includes 2 more instances showing obvious malignant alterations, but only 8 demonstrating NNE (as opposed to INE).

Additionally, 55 (80.6%) new histopathologies were diagnosed only in the focal darkly stained areas, with an increased sensitivity for the diagnosis of atrophic endometritis (16 new cases) and simple endometrial hyperplasia (28 new cases) missed by the conventional hysteroscopic view, as well as 4 cases of atypical endometrial hyperplasia, 6 cases of complex endometrial hyperplasia without atypia and a new single case of endometrial carcinoma diagnosed only by chromo hysteroscopy (1). This, while being statistically insignificant, is very valuable and substantial, as seen in table, with values of 92.54% sensitivity, 83.33% specificity, 88.57% positive predictive value, and 88.89% negative predictive value (3).

Similar histology was observed in stained biopsy, unstained biopsy, and endometrial aspiration in 48 percent of cases with normal endometrium and in 32 percent of cases with hormonal disturbance, as compared to a study performed by (Singh N. and Singh B., 2013) using chromo hysteroscopy with methylene blue dye in 60 women with AUB. In eight of the eleven instances where endometrial illness was suspected, the diagnosis was confirmed by a biopsy of stained tissue. Stained tissue biopsy was substantially more accurate than endometrial aspiration and unstained tissue biopsy in detecting endometrial pathology ( $p=0.006$ ). The diagnostic accuracy of hysteroscopy is improved by chromo hysteroscopy in roughly half of the cases; five of these 11 patients showed no abnormalities or suspicious lesions on diagnostic hysteroscopy.

This agrees with what has been found in earlier research. Several authors, including Safali (Sensitivity -69.20 percent , specificity - 74.00 percent , positive predictive value - 40.90 percent and negative predictive value -90.20 percent ). Authors Abd El-Moneim et al (sensitivity of 93.20 percent , specificity of 87.80 percent , a positive predictive value of 91.60 percent and a negative predictive value of 90.00 percent . ). Hoda The accuracy of chromo hysteroscopy for the diagnosis of endometrial illness was evaluated by Mansour et al. (sensitivity 70%, specificity 80%, positive predictive value 43.70%, and negative predictive value 92.60%).

Table 2 shows that in group II, normal, pathology-free endometrium is clearly suggested by diffuse light blue staining without localised dark patches. As for the validity of the test, the findings are mostly in accordance with (Mansour H and Mohammed M., 2011), with the exception of the fact that most of the patients in group II (40 cases, 88.9 percent) revealed a non-neoplastic non inflammatory histology in their specimens.for diagnosis of endometritis.

## 6. Conclusion

It was that research found that chromo hysteroscopy significantly improved the diagnostic and exclusion accuracy of conventional hysteroscopy for endometrial disorders. Evaluation of individuals with abnormal uterine bleeding requires both hysteroscopy and histopathology for proper diagnosis and therapy..

## 7. Recommendations

If mini-Hysteroscopy using a small calibre of hysteroscopic sheath ( 3.6 mm in outer diameter) may further simplify the use of hysteroscopy in the office setting; this technique would be a wonderful screening tool for cases of abnormal uterine bleeding, avoiding the need for general anaesthesia while providing a higher sensitivity compared to more traditional methods of hysterotomy. In situations of atypical endometrial hyperplasia (diagnosed solely by D&C biopsy), chromo hysteroscopy may be useful in making a final diagnosis so that a more extensive surgical treatment or at least postoperative supplementary therapy is not missed. Expanded research is required to draw firmer conclusions and possibly routine use of endometrial dying in cases of abnormal uterine bleeding, and future modifications, such as the use of small calibre mini-hysteroscopies and new vital stains like toluidine blue, would

refine and improve the accuracy of the technique.bleeding.

**Financial support and sponsorship:** Nil.

**Conflicts of interest:** There are no conflicts of interest.

## References

- [1] Al-Ani, S., El-Gamal, H., Abd-El-Salam, M., Ghanem, R. (2018). Role of diagnostic hysteroscopy and histopathology in evaluation of abnormal uterine bleeding. *The Egyptian Journal of Hospital Medicine*, 72(7), 4765-4771. doi: 10.21608/ejhm.2018.10109
- [2] Alay, A., Usta, T. A., Ozay, P., Karadugan, O., & Ates, U. (2014). Comparison of two modalities: a novel technique, 'chromohysteroscopy', and blind endometrial sampling for the evaluation of abnormal uterine bleeding. *The journal of obstetrics and gynaecology research*, 40(5), 1407–1414. <https://doi.org/10.1111/jog.12341>El-Faissal, Y. M., & Kamel, A. M. (2014). The value of chromohysteroscopy in the assessment of postmenopausal vaginal bleeding. *Journal of Clinical Gynecology and Obstetrics*, 3(1), 35-41.
- [3] Critchley, H. O. D., Babayev, E. and Bulun, S. E. (2020). Menstruation: science and society. *American journal of obstetrics and gynecology*, 223(5), 624–664. <https://doi.org/10.1016/j.ajog.2020.06.004>
- [4] Davis E, Sparzak PB. 2022. Abnormal Uterine Bleeding. In: StatPearls. StatPearls Publishing, Treasure Island (FL); PMID: 30422508.
- [5] Dr Shimona Agarwal. (2019). To evaluate the role of chromo hysteroscopy in abnormal uterine bleeding. *International Journal of Medical Science And Diagnosis Research*, 3(2). Retrieved from <https://www.ijmsdr.com/index.php/ijmsdr/article/view/253>.
- [6] Genovese, F., Di Guardo, F. and Monteleone, M. M. (2021). Hysteroscopy as An Investigational Operative Procedure in Primary and Secondary Infertility: A Systematic Review. *International journal of fertility & sterility*, 15(2), 80–87. <https://doi.org/10.22074/IJFS.2020.134704>.

- [7] Haider, A., Bano, I. and Sabzposh, N. A. (2019). Role of chromohysteroscopy in detection of endometrial pathology in abnormal uterine bleeding. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*, 8(3), 916-921.
- [8] Manchanda, R., Valenti, G. and Rathore, A. (2022). Distension media delivery systems in hysteroscopy: past, present and future. *Minimally invasive therapy & allied technologies: MITAT: official journal of the Society for Minimally Invasive Therapy*, 31(1), 1-12.  
<https://doi.org/10.1080/13645706.2020.1763402>.
- [9] Mansour, H., & Mohamed, M. A. (2011). Value of endometrial dyeing in diagnosis of endometritis in the absence of macroscopic abnormalities during hysteroscopy. *Middle East Fertility Society Journal*, 16(1), 83-86.
- [10] Munro, M. G., Critchley, H. O. D. and Fraser, I. S. (2018). The two FIGO systems for normal and abnormal uterine bleeding symptoms and classification of causes of abnormal uterine bleeding in the reproductive years: 2018 revisions. *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics*, 143(3), 393-408.  
<https://doi.org/10.1002/ijgo.12666>
- [11] Nanjundeswaraswamy, T. S., & Divakar, S. (2021). Determination of sample size and sampling methods in applied research. *Proceedings on Engineering Sciences*, 3(1), 25-32.
- [12] Nees, L. K., Heublein, S. and Steinmacher, S. (2022). Endometrial hyperplasia as a risk factor of endometrial cancer. *Archives of gynecology and obstetrics*, 306(2), 407-421.  
<https://doi.org/10.1007/s00404-021-06380-5>
- [13] Ozturk, M., Ercan, C. M. and Dede, M. (2012). Toluidine blue staining in the diagnosis of endometrial pathologies: a preliminary study before chromohysteroscopy. *European journal of obstetrics, gynecology, and reproductive biology*, 160(2), 191-195.  
<https://doi.org/10.1016/j.ejogrb.2011.10.013>.
- [14] Singh, G., & Puckett, Y. (2022). Endometrial Hyperplasia. In *StatPearls*. StatPearls Publishing.
- [15] Singh, N., & Singh, B. (2013). Chromohysteroscopy—A new technique for endometrial biopsy in Abnormal Uterine Bleeding (AUB).
- [16] Singh, N., Agarwal, G. & Jaiswar, S. P. (2016). Role of Chromohysteroscopy with toluidine blue in diagnosing endometrial pathology after 40 years of age. *J Med Surg Pathol*, 1(2), 1-18.
- [17] Sun, Y., Wang, Y. & Bai, W. (2018). Prevalence of abnormal uterine bleeding according to new International Federation of Gynecology and Obstetrics classification in Chinese women of reproductive age: A cross-sectional study. *Medicine*, 97(31), e11457.  
<https://doi.org/10.1097/MD.00000000000011457>.
- [18] Umranikar, S., Umranikar, A., & Cheong, Y. (2010). Hysteroscopy and hysteroscopic surgery. *Obstetrics, Gynaecology & Reproductive Medicine*, 20(6), 167-173.
- [19] Vijay, A., Koothan, V., & Baskaran, M. V. (2019). Efficacy of Chromohysteroscopy for Evaluation of Endometrial Pathologies in Abnormal Uterine Bleeding. *Journal of South Asian Federation of Obstetrics and Gynaecology*, 11(5), 302.
- [20] Vitale, S. G., Watrowski, R. & Angioni, S. (2022). Abnormal Uterine Bleeding in Perimenopausal Women: The Role of Hysteroscopy and Its Impact on Quality of Life and Sexuality. *Diagnostics (Basel, Switzerland)*, 12(5), 1176.  
<https://doi.org/10.3390/diagnostics12051176>