Evaluating the Role of Chromohysteroscopy in Evaluation of Endometrial Pathology as a Cause of Abnormal Uterine Bleeding

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ABSTRACT

Background: The local application of stains or dyes during endoscopy is referred to as "chromoendoscopy" in an attempt to improve tissue identification, distinction, and diagnosis.

Objectives: To judge the value of chromohysteroscopy in identifying endometrial abnormalities that are too subtle for standard hysteroscopy to detect. The histopathology from routine endometrial sampling and chromohysteroscopy was compared.

Methodology: This interventional prospective study included 49 women with abnormal uterine bleeding. First of all, a 4 mm diameter hysteroscope was used to perform a diagnostic hysteroscopy. Between the 20th and 25th day of their menstrual cycle, patients were booked for blind endometrial sampling and chromohysteroscopy directed biopsies.

Results: Focal staining had higher sensitivity, specificity and accuracy 65.5%, 95% and 77.6% respectively, for detection of endometrial pathologies compared with diffuse staining. Focal dark pattern was significantly associated with, submucous myoma, endometrial hyperplasia, necrotic mass, endometritis, simple and complex endometrial hyperplasia with atypia and endometrial carcinoma.

Conclusion: The diagnostic precision of traditional hysteroscopy is enhanced with chromohysteroscopy. In cases of Abnormal Uterine Bleeding (AUB), it is a useful, affordable diagnostic for identifying endometrial diseases. **Keywords**: Chromohysteroscopy, Endometrial pathology, AUB.

INTRODUCTION

The impact of abnormal uterine bleeding on women, their families, and society at large is substantial when it comes to medical care. Over thirty percent of women will go for medical attention for this issue at some point in their reproductive life. In secondary health care, heavy menstrual bleeding and postmenopausal bleeding collectively make up the most prevalent gynecological presentations ⁽¹⁾.

Malignant tumors, uterine pathologies such as uterine leiomyomas, adenomyosis, and endometrial polyps, and cervical pathologies such as polyps, erosion, and cervicitis are among the conditions of the genital tract that can cause abnormal uterine bleeding ⁽²⁾.

Decreasing morbidity and mortality through successful therapy requires a precise evaluation. Numerous tests are accessible, such as the outpatient hysteroscopy, saline infusion sonography, transvaginal scan (TVS), and endometrial biopsy (EBx) ⁽³⁾.

In circumstances like these, endometrial biopsy is essential to the diagnosis and course of care. Hysteroscopic directed endometrial biopsy is regarded as the gold standard amongst endometrial biopsy techniques. However, other than in the event of endometrial polyps or submucous fibroid, it is challenging to identify aberrant locations during hysteroscopy ⁽⁴⁾.

The local application of stains or dyes during endoscopy is referred to as "chromoendoscopy" in an attempt to improve tissue identification, distinction, and diagnosis. Using dyes such as methylene blue, Lugol's solution, Congo red, and indigo carmine, this approach is utilized to identify areas that can be targeted for biopsy in gastrointestinal illnesses ⁽⁵⁾. Based on chromoendoscopy, a novel method called chromohysteroscopy is being developed to detect endometrial pathology and aid in the diagnosis of the reasons for irregular uterine bleeding. Regarding the staining substance and process, there is still no agreement. More research is required to determine the diagnostic accuracy and its function in hysteroscopy ⁽⁶⁾.

Chromohysteroscopy has been recommended as a means of increasing diagnostic precision in situations where the endometrium is not grossly abnormal ⁽⁷⁾.

The study attempted to assess the use of chromohysteroscopy in identifying endometrial alterations that are modest and may go unnoticed during regular hysteroscopy. The histopathology from routine endometrial biopsy and chromohysteroscopy was contrasted.

PATIENTS AND METHODS

This interventional prospective study was conducted at Obstetrics and Gynecology Department, Faculty of Medicine, Cairo University Maternity Hospitals from July 2023 until October 2023.

I. <u>Study population:</u>

We enrolled women attending at El Kasr Al Ainy – gynecological outpatient clinic - with the following criteria:

Inclusion criteria:

Women aging from 20 to 65 years, with a complaint of abnormal uterine bleeding as heavy menstrual bleeding, intermenstrual bleeding and post-menopausal bleeding were enrolled.

Exclusion criteria:

Women with established coagulation disorders, established thyroid disorders, fibroid uterus, hyperprolactinemia were excluded.

II. <u>Sampling Method "convenient targeted</u> <u>sampling":</u>

Using individuals who are "convenient" for the researcher is known as convenience sampling. There is absolutely no pattern in how these responders are found; they may be found by just approaching folks who are anywhere.

III. <u>Sample size:</u>

A total of 49 women were enrolled, after consenting each of them.

IV. <u>Sample size justification:</u>

By using Sample Size Calculator by Wan Nor Arifin, which is licensed under a Creative Commons Attribution-Non Commercial-ShareAlike 4.0 International License., the following criteria were considered for sample size calculation: Confidence level 95%, Precision \pm expected 0.15, The expected sensitivity 91.67%, The expected specificity 85.41%,

The prevalence of abnormal uterine bleeding 30%, Expected drop out: 0%

V. <u>Study interventions and procedures:</u>

1. In compliance with the criteria for inclusion and exclusion, patients experienced:

- a) Complete history taking, General examination with special emphasis on: Vital data (blood pressure, heart rate, temperature), BMI and signs of anemia.
- **b) Routine investigations** as complete blood count, liver function and kidney function tests and coagulation profile.
- c) Ultrasound examination: Transvaginal ultrasound measurements of endometrial thickness, uterine dimensions and detection of uterine lesions especially intrauterine messes.
- d) Participants were assigned for blind endometrial sampling and chromohysteroscopy directed biopsies: Between their menstrual cycls's 20th and 25th day. Initially, a 4 mm diameter hysteroscope was used to perform a diagnostic hysteroscopy.

Under general anesthesia, a fully assembled 6.5 mm Stryker hysteroscopy (*Stryker 502-740-081 Rev360*, *Germany*) with a 30° viewing angle was connected to a fiber-optic light source, the distending medium (0.9% sodium chloride solution) was inserted, and the video endocamera was inserted into the cervical cavity while the irrigating system was activated.

The patient underwent chromohysteroscopy if the endometrium appeared normal and had no visible lesions after a panoramic examination of the uterus. Using a reusable, sterile, 20-mL plastic syringe attached to the hysteroscope's inflow port, 10 ml of a 2% methylene blue coloring solution were injected into the uterus during chromohysteroscopy in order to paint the endometrium. To cleanse the endometrium, the distending media flow was restarted five minutes after the dye injection. To disperse and flush the dye, uterine distension with regular saline was restarted for a full minute.

For statistical simplicity, the endometrium's staining trend was then documented and classified as either light diffuse staining, dark focal/diffuse staining, or no staining completely. Regardless of the size or quantity of stained regions, blue staining over the cervical ostium was regarded as a favorable observation.

Under the hysteroscopic supervision, endometrial specimens were taken from stained (lightor dark-stained) regions. After this process, all uterine walls underwent formal endometrial curettage, and all endometrial biopsies were removed and submitted for histological analysis.

Consequently, by contrasting the outcomes of conventional tissue sample with chromohysteroscopy, the usefulness of chromohysteroscopy in assessing endometrial disease was established.

Study outcomes:

- **Primary outcome:** Value of adding methylene blue staining to conventional hystroscopic guided biopsy in identifying endometrial disease when abnormal uterine bleeding occurs.
- **Secondary outcomes:** any correlation between the pattern of staining and histopathological findings.

Ethical considerations:

The patients gave permission to take part in the research study prior to enrollment after being given a clear explanation of its purpose, scope, and potential outcomes. Throughout the whole research process, the Helsinki Declaration was applied. The approval of the Ethics Committee of the Faculty of medicine, Cairo University has been obtained.

Statistical analysis

Data analysis, or statistical procedures, were carried out using SPSS, version 23. For quantitative data, the statistical representation was given as mean \pm standard deviation $(\pm SD)$ and range, whilst frequency and percentage were utilized to characterize categorical data. Chi squared test was applied to compare categorical data. Calculation of accuracy measures was based the following formulas: on Sensitivity= $[a/(a+c)] \times 100$, Specificity= $[d/(b+d)] \times 100$, Positive predictive value (PPV)= $[a/(a+b)] \times 100$ & Negative predictive value (NPV)= $\left[\frac{d}{c+d}\right] \times 100$. A pvalue of less than 0.05 was considered statistically significant, and a p-value of less than 0.001 was considered statistically highly significant.



Figure (1): Hysteroscopic view showing dark patchy staining *(Kasr Alainy Operating room)*



Figure (2): Hysteroscopic view showing diffuse staining of endometrium (*Kasr Alainy Operating room*)

RESULTS

This study was conducted on 49 females who underwent chromohysteroscopy for evaluation of abnormal uterine bleeding.

Results of the current study were expressed in the following tables and figures:

Table (1): Our studied 49 females had a mean age of 42.80 ± 10.36 years and their mean BMI was 24.02 ± 3.42 . 46.9% had parity 1-2 and 44.9% had parity 3.

Table (1):	Descri	otive	data	of the	studied	population:
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	(N = 49)
Age, years	
Mean ± SD	42.80 ± 10.36
Range	30 - 64
Age group	
30-39 year	26 (53.1%)
40-49 year	9 (18.4%)
50-59 year	9 (18.4%)
>60 year	5 (10.2%)
BMI	
Mean ± SD	24.02 ± 3.42
Range	20 - 32
Parity	
Mean \pm SD	2.73 ± 0.88
Range	1 –5
Parity	
<3	23 (46.9%)
3	22 (44.9%)
>3	9 (18.4%)

*BMI: Body Mass Index *SD: Standard Deviation

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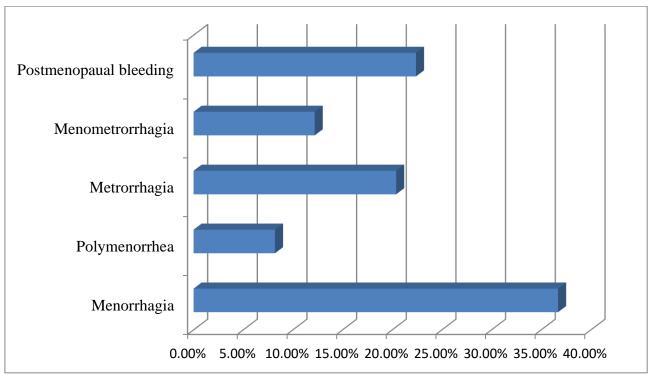


Figure (3): Presenting symptom of the studied population

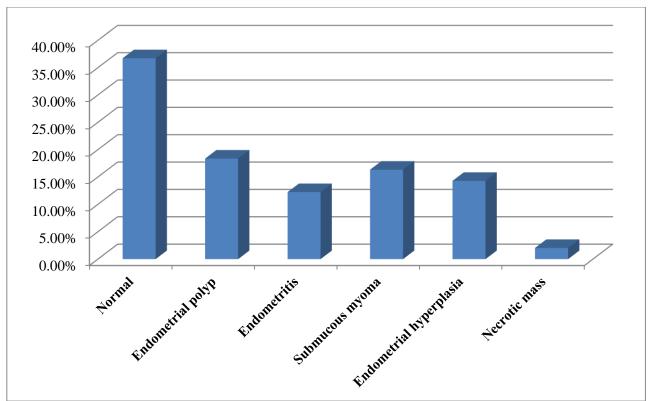


Figure (4): Hysteroscopy findings of the studied population

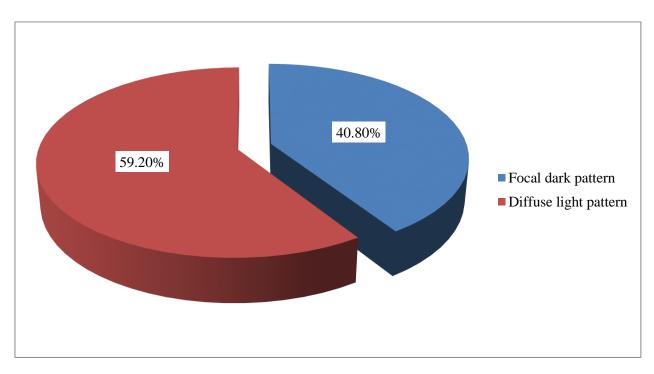


Figure (5): Staining pattern of the studied population

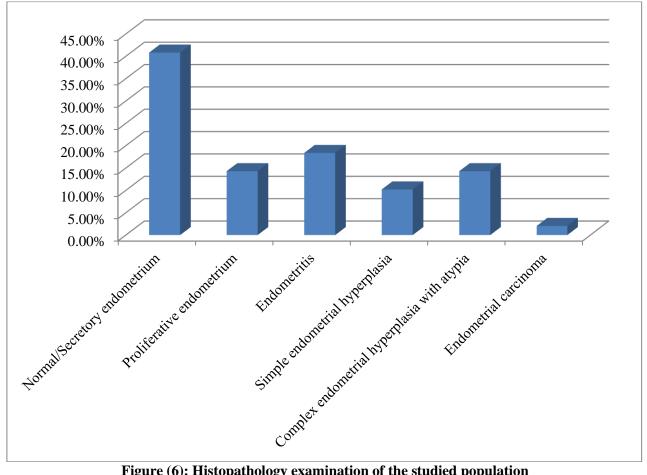


Figure (6): Histopathology examination of the studied population

Table (2): Among our studied 49 females, diffuse light staining pattern was significantly associated with normal hysteroscopy and endometritis while focal dark staining pattern was significantly associated with, submucous myoma, endometrial hyperplasia and necrotic mass.

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Table (2). Association between	Πγριει υρευργ ΠΠα	ings and stanning pattern	I OI IIIE SIUUIEU POPUIAIIOII

	Focal dark pattern N=20		Diffuse light pattern N=29		chi square test	
Hysteroscopy findings	N	%	N	%	X^2	P-value
Normal	0	0%	18	62.1%	22 720	-0.001
Endometrial polyp	4	20%	5	17.2%		
Endometritis	1	5%	5	17.2%		
Submucous myoma	7	35%	1	3.4%	32.729	< 0.001
Endometrial hyperplasia	7	35%	0	0%		
Necrotic mass	1	5%	0	0%		

There was statistically significant agreement between hysteroscopy findings and staining pattern of the studied population (Kappa -0.211, P-value 0.002)

Table (3): Among our studied 49 females, diffuse light staining pattern was significantly associated with normal/secretory endometrium and proliferative endometrium while focal dark pattern was significantly associated with endometritis, simple endometrial hyperplasia, complex endometrial hyperplasia with atypia and endometrial carcinoma.

Table (3):	Association between histopathology findings and staining pattern of the studied population

	Focal dark pattern N=20		Diffuse light pattern N=29		chi square test	
Histopathology findings	Ν	%	Ν	%	x2	P-value
Normal/Secretory endometrium	1	5%	19	65.5%		
Proliferative endometrium	1	5%	6	20.7%		
Endometritis	6	30%	3	10.3%		
Simple endometrial hyperplasia	4	20%	1	3.4%	29.928	< 0.001
Complex endometrial hyperplasia with atypia	7	35%	0	0%		
Endometrial carcinoma	1	5%	0	0%		

There was statistically significant agreement between histopathology findings and staining pattern of the studied population (Kappa -0.172, P-value 0.008)

Table (4): Focal staining has sensitivity of 65.5% and specificity of 95% for detection of endometrial pathologies while diffuse staining has sensitivity of 34.5% and specificity of 5% for detection of endometrial pathologies.

Table (4):	Diagnostic accuracy of chromohysteroscopy staining in detection of endometrial pathologies

	total	endometrial pathology	sensitivity%	specificity%	PPV	NPV	accuracy
Focal dark pattern	20	19	65.5%	95%	95%	65.5%	77.6%
Diffuse light pattern	29	10	34.5%	5%	34.4%	5%	22.4%

DISCUSSION

A hysteroscopy is advised for a direct and indepth examination of the endometrium. When it comes to detecting and treating submucous myomas, adhesions, and polyps that are microscopic endometrial diseases, this method is the best. Conventional hysteroscopy normality does not guarantee endometrial integrity ⁽⁸⁾.

During traditional hysteroscopy, chromohysteroscopy involves endometrial dying with methylene blue dye. When using traditional hysteroscopy to visualize the uterus, if it looks normal, the uterus gets colored to check for endometrial abnormalities ⁽⁹⁾.

Based on the staining sequence, patients are categorized. A diffuse light blue stain is seen as typical. Irrespective of the size and quantity of stained regions, focal or diffuse dark blue staining above the internal cervical ostium is regarded as a good observation. The endometrial pathology is identified by the final histology report ⁽¹⁰⁾.

Thus, this investigation was carried out with the intention of comparing the histopathology acquired from chromohysteroscopy with conventional endometrial sample, as well as assessing the value of chromohysteroscopy in identifying minute endometrial alterations that may go unnoticed during ordinary hysteroscopy.

This experimental prospective research, which involved 49 women, aimed to assess the value of chromohysteroscopy in identifying endometrial abnormalities that are too subtle for conventional hysteroscopy. The histopathology from routine endometrial sampling and chromohysteroscopy were compared.

Diffuse light staining pattern was significantly associated with normal hysteroscopy as well as endometritis while diffuse light pattern was significantly associated with submucous myoma, endometrial hyperplasia and necrotic mass among our study population. This highlights a significant agreement between hysteroscopy findings and staining pattern in the studied population.

A harmless dye with a higher propensity for hyperplastic and inflammatory endometrium is methylene blue. When combined with hysteroscopy, it serves as a useful tool to spot unseen unwell areas during the procedure while avoiding injury and does not involve complex equipment or clinical expertise to use (11).

Regarding chromohysteroscopy staining diagnostic efficacy in identifying endometrial abnormalities, our study revealed that focal staining has sensitivity of 65.5% and specificity of 95% for detection of endometrial pathologies while diffuse staining has sensitivity of 34.5% and specificity of 5% for detection of endometrial pathologies.

According to **Yadav** *et al.*, hysteroscopy had a specificity of 90.59% and a PPV of 33.32 and 87.50

for anticipating diffuse endometrial alterations, whereas chromohysteroscopy had a sensitivity of 80.00% for identifying endometrial diseases ⁽¹¹⁾.

According to our research, hysteroscopy can diagnose diffuse endometrial lesions only to a limited extent but is highly accurate in detecting large intrauterine abnormalities (fibroid, polyp). A biopsy is necessary for excluding any pathology since hyperplastic endometrium on hysteroscopy may be mistaken for late secretory endometrial. This is consistent with a sizable meta-analysis conducted by **Clark** *et al.*, which found that hysteroscopy has a reasonable diagnostic accuracy for endometrial illness. Since it is less accurate in identifying diffuse endometrial disease, additional testing could be necessary to validate the diagnosis ⁽¹²⁾.

In a retrospective research conducted by **Lasmar** *et al.* to confirm the effectiveness of hysteroscopy in cases of endometrial hyperplasia and carcinoma in patients with (AUB), this was further demonstrated. Sixteen of the 4054 hysteroscopies that were followed by biopsy had endometrial hyperplasia that was confirmed by HPE. However, the sensitivity, specificity, PPV, and NPV of the hysteroscopy were 56.3%, 89.1%, 48.0%, and 92.0%, respectively, with an accuracy of 72.7% in identifying hyperplasia ⁽¹³⁾.

During hysteroscopy, 18 (36.73%) of the women in our study had a normal endometrium (NE). The term "negative hysteroscopic view" was coined by Loffer and refers to the following: a well-visible uterus cavity, no structural abnormalities, and a uniformly thin, homogenous endometrium that seems to be thick without variation. Using an instrument or the pointed tip of a hysteroscope to poke through the endometrium, endometrial thickness was measured. According to their research, tissue sampling doesn't significantly improve the diagnosis if the negative view characteristics are met, with the exception of endometritis patients, which hysteroscopy could overlook ⁽¹⁴⁾.

However, the notion of negative hysteroscopic perspective is called into doubt in our research. As among our studied 49 females, hysteroscopic examination showed endometrial polyp in 18.37%, submucous myoma in 16.33%, endometrial hyperplasia in 14.29%, and endometritis in 12.24% and necrotic mass in 1 case (2%) while the remaining 36.73% appeared normal. Also, 40.8% showed focal dark staining, and 59.2% showed diffuse light staining pattern in chromohysteroscopy. Thus, if simply hysteroscopy had been performed, these cases might have gone unnoticed. Hysteroscopy cannot detect the microscopic alterations caused by endometritis, and hyperplastic alterations are readily mistaken for late secretory endometrium, resulting in an under- or overdiagnosis of endometrial alterations. Furthermore, the technique of measuring endometrial thickness by using a device to indent the endometrium is highly subjective and prone to inaccurate findings. Therefore, the idea of methylene blue staining was introduced to improve hysteroscopy's reliability in identifying minute endometrial abnormalities that may go undetected ⁽¹⁴⁾.

According to our research, the efficacy of diffuse staining in detecting endometrial diseases was 34.5% with a 5% specificity. The prediction of diffuse endometrial disease by chromohysteroscopy was 80.00%, 96.47%, 80.00%, and 96.47%, representing sensitivity, specificity, positive predictive value, and negative predictive value respectively. Our findings concur with those of **Schatz** *et al.*, who determined that chromohysteroscopy's overall diagnostic performance for identifying novel histopathologies overlooked by conventional hysteroscopy was 93.2% in terms of sensitivity, 87.8% in terms of specificity, 91.6% in terms of positive predictive value, and 90% in terms of negative predictive value ^{(5).}

Additionally, as stated by **Singh and Singh**, there was a statistically significant difference (p = 0.006) between the accuracy of diagnosis of stained tissue specimens and endometrial aspiration in detecting endometrial disease. Five (45.4%) of the 11 instances with endometrial pathology, in their study, had no abnormalities found on conventional hysteroscopy. This demonstrated that in 45.5% of cases, chromohysteroscopy improved the diagnostic precision of hysteroscopy ⁽⁷⁾.

In our study, histopathology examination in showed endometritis 18.37%. proliferative endometrium and complex endometrial hyperplasia with atypia in 14.29% for each, simple endometrial hyperplasia in 10.29%, and endometrial carcinoma in 1 case (2%) while the remaining 40.82% demonstrated normal/secretory endometrium. Diffuse light staining pattern was significantly associated with normal /secretory endometrium and proliferative endometrium while **focal** dark pattern was significantly associated with endometritis, simple endometrial hyperplasia, complex endometrial hyperplasia with atypia and endometrial carcinoma. There was statistically significant agreement between histopathology findings and staining pattern of the studied population.

Mansour and Mohamed conducted research to assess the efficacy of endometrial coloring in the detection of endometritis when gross abnormalities are not present during hysteroscopy. Pathology was identified in 7.3% of patients with light-stained endometrial, whereas inflammatory endometrium was identified in 43.6% of patients with dark-stained endometrium. As a result, endometritis could be diagnosed with greater sensitivity (70%) when darkstained endometrium was used, along with specificity (80.8%), negative predictive value (92.6%), and positive predictive value (43.7%) ⁽¹⁵⁾.

Singh and Singh identified 4 cases of chronic endometritis and two cases of T.B. endometritis on dark staining sixty individuals of AUB (sensitivity 100%), which provided additional credence to our results (7).

Kucuk and Safali et al. discovered that chromohysteroscopy had a 69.2% sensitivity, 74% specificity, 40.9% positive predictive value, and 90.2% negative predictive value for endometritis among women with recurrent IVF failure (16).

Our findings are consistent with a research conducted by Schatz et al. on AUB patients in the perimenopausal age group. 28 (90.3%) of the 31 cases of simple hyperplasia were identified only through the use of dark staining on chromohysteroscopy (5).

Methylene blue colonoscopy greatly aided in the prompt identification of intraepithelial neoplasia, especially of flat lesions, and the evaluation of the magnitude of disease progression in patients with ulcerative colitis, according to one such study conducted by **Kiesslich and Neurath** (17).

In agreement with our findings, **Gupta** *et al.* found that chromohysteroscopy discovered more endometrial abnormalities patients than blind endometrial samples and could identify endometrial disease that was overlooked by conventional hysteroscopy. In assessing endometrial pathology, chromohysteroscopy-guided endometrial sampling demonstrated 86.67% diagnostic efficacy, 91.67% sensitivity, 85.41% specificity, 61.12% PPV, and 97.61% NPV (P < 0.001)^{(9).}

Compared to traditional blind fractional curettage, **El-Faissal and Kamel's** use of chromohysteroscopy in 50 postmenopausal women resulted in the diagnosis of three additional cases of endometritis, two additional cases of endometrial hyperplasia, but no cases of endometrial cancer ⁽¹⁸⁾.

According to **Singh and Singh**, the stained tissue's diagnostic potential was noticeably greater (p = 0.005) than that of the uncolored biopsy and endometrial aspirations ⁽⁷⁾.

Singh *et al.* conducted a second study in 2016 on 50 cases of irregular uterine bleeding; however, they used toluidine blue instead of methylene blue as the stain. There was no statistically significant difference in the sensitivity, NPV, and diagnostic accuracy of endometrial aspiration (75%, 92.6%, 94% respectively), unstained biopsy (83.3%, 95%, and 96% respectively), or stained biopsy (83.3%, 95%, 96% respectively)^{(19).}

38 individuals with irregular uterine bleeding were enrolled by **Alay** *et al.* in 2014, and chromohysteroscopy using methylene blue solution was performed. They claimed that there was no statistically significant difference between the BES, uncolored, and stained samples. The lack of significance of the outcome may have resulted from the fact that in our investigation, we collected biopsy samples from both light- and dark-stained regions of distinct patients, and we contrasted them using blind endometrial biopsies ⁽²⁰⁾.

Chopra *et al.* assessed infertile women to determine the diagnostic precision of chromohysteroscopy. In contrast, biopsy from a lightstained site revealed chronic endometritis in 5.35% (3 out of 56) cases and normal endometrium in the remaining 94.65% of cases. Histopathology of biopsy samples from dark-stained areas revealed endometritis in 50% of cases (22 out of 44) and normal endometrium in 50% of cases (22 out of 44). The following values indicate the diagnostic efficacy of chromohysteroscopy: sensitivity = 88%, specificity = 70.66%, PPV = 50%, and NPV = 94.6%. They came to the conclusion that, in cases of infertility, chromohysteroscopy is an easy and reliable method of identifying endometrial disease ⁽¹⁰⁾.

It has been said that hysteroscopy is well accepted. Only 6% of patients had non-pain adverse reactions, such as nausea and vomiting, according to **Teran-Alonso** *et al.* ^{(21).}

Many factors, such as differences in research methodology, outcomes, sample size, and the general health of the individuals under investigation at the period of recruitment, were cited by the vast majority of research papers that disagreed with what we found.

One of the study's strengths is that no patients were lost while it was being conducted. This was the first study conducted at Cairo University Hospitals to histopathology acquired by contrast the chromohysteroscopy with traditional endometrial sample, as well as to test the value of chromohysteroscopy in detecting subtle endometrial alterations that may go unnoticed during routine hysteroscopy. Anything possible was made to make sure that all data were captured and that solely accurate data were included in the data analysis. All testing, study measures and evaluations of research findings were carried out by the same personnel.

However, it's crucial to remember that the research in question had several restrictions. In comparison to the study's findings, there were fewer instances and a lower number of participants as the research was carried out in one hospital. Furthermore, the study was not typical of any one community and there was a significant risk of publication bias due to its lack of multicentricity.

The present study can contribute to the body of literature and offer some insight into future prospective studies with bigger samples, as chromohysteroscopy is thought to be capable to distinguish endometrial pathology that may be omitted when using conventional hysteroscopy and detect more cases of endometrial pathology than blind endometrial testing.

CONCLUSION

Our research demonstrates that chromohysteroscopy enhances the diagnostic precision of traditional hysteroscopy. In cases of AUB, it is a useful, low-tech diagnostic for identifying endometrial disease.

Focal staining had higher sensitivity, specificity and accuracy of 65.5%, 95% and 77.6% respectively, for detection of endometrial pathologies compared with diffuse staining. Focal dark pattern was significantly associated with, submucous myoma, endometrial hyperplasia, necrotic mass, endometritis, simple and complex endometrial hyperplasia with atypia and endometrial carcinoma.

Authors of this manuscript state that:

1) the paper is not under consideration elsewhere,

2) none of the paper's contents have been previously published and

3) all authors have read and approved the manuscript.

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REFERENCES

- 1. Turan G, Bahat P, Aydın A *et al.* (2018): Evaluation of platelet-rich plasma injection activity in the treatment of abnormal uterine bleeding. *Turkish Journal of Obstetrics and Gynecology*, *15*(4): 222.
- 2. 2.Gentry-Maharaj A, Karpinskyj C (2020): Current and future approaches to screening for endometrial cancer. *Best Practice and Research Clinical Obstetrics and Gynaecology*, 65: 79-97.
- **3. Dreisler E, Kjer J (2019):** Asherman's syndrome: Current perspectives on diagnosis and management. *International Journal of Women's Health*, *11*: 191-198.
- Cappellini D, Comin-Colet J, de Francisco A et al. (2017): Iron deficiency across chronic inflammatory conditions: International expert opinion on definition, diagnosis, and management. American Journal of Hematology, 92(10): 1068-1078.
- 5. Schatz F, Guzeloglu-Kayisli O, Arlier S *et al.* (2016): The role of decidual cells in uterine hemostasis, menstruation, inflammation, adverse pregnancy outcomes and abnormal uterine bleeding. *Human reproduction update*, 22(4), 497-515.
- 6. Wang K, Okoro N, Prasad G et al. (2011): Endoscopic evaluation and advanced imaging of Barrett's esophagus. *Gastrointestinal Endoscopy Clinics of North America*, 21(1): 39-51.
- Singh N, Singh B (2013): Chromohysteroscopy—A new technique for endometrial biopsy in abnormal uterine bleeding (AUB). *Open Journal of Obstetrics and Gynecology*, 3(05): 11-14. doi: 10.4236/ojog.2013.35A1003.
- 8. Vitale S, Haimovich S, Riemma G et al. (2021): Innovations in hysteroscopic surgery: Expanding the meaning of "in-office". *Minimally Invasive Therapy and Allied Technologies*, 30(3): 125-132.
- **9.** Gupta T, Singh S, Verma A *et al.* (2019): Role of chromohysteroscopy in evaluation of endometrial pathology using methylene blue dye. *The Journal of Obstetrics and Gynecology of India*, 69: 363-368.
- **10.** Chopra K, Trivedi S, Patra S et al. (2017): Diagnostic accuracy of chromohysteroscopy in women with unexplained infertility. International Journal of Reproductive Contraception, Obstetrics and Gynecology, 6(7):2955–2959.
- **11. Yadav S, Nanda S, Malhotra V** *et al.* (2021): Role of chromohysteroscopy in patients of abnormal uterine bleeding. *Indian Journal of Gynecologic Oncology, 19*: 1-6.
- 12. Clark T, Stevenson H (2017): Endometrial polyps and abnormal uterine bleeding (AUB-P): What is the

relationship, how are they diagnosed and how are they treated? *Best Practice and Research Clinical Obstetrics and Gynaecology*, 40: 89-104.

- **13.** Lasmar R, Paulo R, Oliveir M et al. (2016): Validation of hysteroscopic view in cases of endometrial hyperplasia and cancer in patients with abnormal uterine bleeding. *Journal of Minimally Invasive Gynecology, 13*: 409–412.
- *14.* Loffer F (2019): Hysteroscopy with selective endometrial sampling compared with D&C for abnormal uterine bleeding: the value of a negative hysteroscopic view. *Obstetrics and Gynecology*, *73*: 16–20.
- **15. Mansour H, Mohamed A (2011):** Value of endometrial dyeing in diagnosis of endometritis in absence of macroscopic abnormality during hysteroscopy. *Middle East Fertility Society Journal, 16*: 83–6.
- **16.** Kucuk T, Safali M (2008): "Chromohysteroscopy" for evaluation of endometrium in recurrent in vitro failure. *Journal of Assisted Reproduction and Genetics*, 25:79– 82.

- **17. Kiesslich R, Neurath M (2014):** Surveillance colonoscopy in ulcerative colitis: magnifying chromoendoscopy in the spotlight. *Gut*, *53*: 165–7.
- **18.** El-Faissal Y, Kamel A (2014): The value of chromohysteroscopy in the assessment of postmenopausal vaginal bleeding. *Journal of Clinical Gynecology and Obstetrics*, 3(1): 35–41.
- **19.** Singh N, Agarwal G, Singh U *et al.* (2016): Role of Chromo-hysteroscopy with toluidine blue in diagnosing endometrial pathology after 40 years of age. *Journal of Medical and Surgical Pathology*, *1*(2): 1–18.
- **20.** Alay A, Usta T, Ozay P *et al.* (2014): Comparison of two modalities: a novel technique, 'chromohysteroscopy', and blind endometrial sampling for the evaluation of abnormal uterine bleeding. *Journal of Obstetrics and Gynaecology Research*, 40(5): 1407–1414.
- **21. Teran-Alonso MJ, De Santiago J, Usandizaga R** *et al.* (2014): Evaluation of pain in office hysteroscopy with prior analgesic medication: a prospective randomized study. *European Journal of Obstetrics and Gynecology and Reproductive Biology, 178*: 123–127.