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**Original Research Article**

# Comparison of chromohysteroscopy findings with histopathological findings in abnormal uterine bleeding

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## ABSTRACT

**Background:** Aim was to compare histological diagnosis of differently stained endometrial tissue on chromohysteroscopy.
**Methods:** A total of 80 patients diagnosed with AUB and satisfying the study design were included in the study. Hysteroscopy followed by chromohysteroscopy was done using 1% methylene blue. Staining patterns were observed and guided biopsies were taken from differently stained areas and sent for histopathology.
**Results:** On chromohysteroscopy, out of the 80 participants, 53 (66.3%) had focal staining and 27 (33.7%) had diffuse staining. The overall sensitivity, specificity, PPV and NPV of TVS in diagnosing uterine abnormalities was 51.7%, 45.1%, 34.9%, 62.2% respectively. The overall sensitivity, specificity, PPV and NPV for hysteroscopy were 96.6%, 41.2%, 48.3%, 95.5% respectively. The indices for chromohysteroscopy were as follows: sensitivity-69% for focal and 31% for diffuse staining, specificity-49.0% for focal staining and 69.7% for diffuse staining, PPV-43.5% for focal and 33.3% for diffuse staining, NPV-73.5% for focal staining and 62.3% for diffuse staining.
**Conclusions:** The idea of staining of endometrium and taking a guided biopsy is exciting and is undoubtedly, better than a blind sampling. However, subjecting all the patient of AUB to chromohysteroscopy in order to find a major histopathological difference is questionable and needs larger trials to reach to concrete decision.

**Keywords:** AUB, Chromohysteroscopy, Transvaginal ultrasound, Hysteroscopy, Histopathology, Diffuse staining, Focal staining

## INTRODUCTION

Abnormal uterine bleeding (AUB) refers to menstrual cycle anomalies that may affect the frequency, regularity, length and volume of flow. AUB might be classified as acute or persistent. Acute AUB is characterized by profuse bleeding and needs immediate management to prevent further blood loss. Acute AUB can occur independently or in conjunction with chronic AUB, which is defined by irregular menstrual bleeding for the majority of the preceding six months.[1]

Worldwide, the prevalence of AUB among women in the reproductive-age group is believed to range between 3% and 30%, with a peak occurrence around menarche and perimenopause.[2-4] While many studies focus exclusively on heavy menstrual bleeding (HMB), when irregular and intermenstrual bleeding are included, the prevalence increases to 35% or higher. However, it is difficult to determine the exact prevalence because many women may not seek treatment for their symptoms and while certain aspects of the diagnosis are objective, others are subjective.

Previously, AUB was diagnosed with blind conventional methods such as D and C, fractional endometrial biopsy and so on, but recently, diagnostic hysteroscopy with hysteroscopic guided biopsy has become the gold standard diagnostic tool for AUB.[7] Although hysteroscopy allows for better visualization of the uterine cavity and identification of intracavitary lesions, a normal endometrium during hysteroscopy does not guarantee endometrial cell integrity. Chromoendoscopy has been widely employed in gastrointestinal imaging to improve tissue characterization and differentiation and hence discover mucosal abnormalities. It is thus proposed, in this study, that chromohysteroscopy can detect endometrial disease in these seemingly normal locations.

## METHODS

The study was conducted on 80 patients in the Department of Obstetrics and Gynaecology, of a tertiary care institute at Bathinda, Punjab after getting approval from the ethics committee, Adesh university over a period of the 18 months. The study was carried out from March 2021 to October 2022.

After written informed consent and preop workup, all the cases underwent transvaginal sonography where uterine cavity was assessed using a GE logic P9, ultrasonography machine, the endometrial thickness (ET) was measured and a specific note made of any focal lesion seen in terms of impression of an endometrial polyp, submucous fibroid, intramural fibroid or suspicion of endometrial hyperplasia was made.

After giving appropriate anesthesia, hysteroscopy was done for visualization of uterine cavity and a specific note made on the endometrium and any abnormality, if detected.

Two ml of 1% methylene blue diluted with 8 ml of normal saline was pushed into the uterine cavity using a 5 mm Karman's cannula. After waiting for 5 min hysteroscopy was repeated.

Note was made of staining patterns and guided biopsy were taken from normal and abnormal areas of staining. Biopsy samples taken were sent for histopathological examination.

The findings were noted on a master chart and tests of statistical analysis were applied using SPSS.

## RESULTS

In our study, out of 80 participants maximum belonged to age group of 41-50 year (43) and least (3) in the age group of <30 years with mean age of participants as 42.7±6.9 years. Majority of our participants (n=38) had parity of more than 3 followed by 2 (n=27) with only 1 nulliparous. According to BMI, majority of participants (n=52) were normal weight, 23 were overweight and 1 obese with mean BMI of 23.7±2.9 kg/m$^2$ in my study.

Out of the 80 participants, a maximum of 24 (29.6%) had regular cycles with HMB followed by 16 (19.8%) patients who had IMB. The least common clinical presentation was regular cycles with light menstrual bleeding i.e. in 8 (10%) patients as shown in Figure 1.

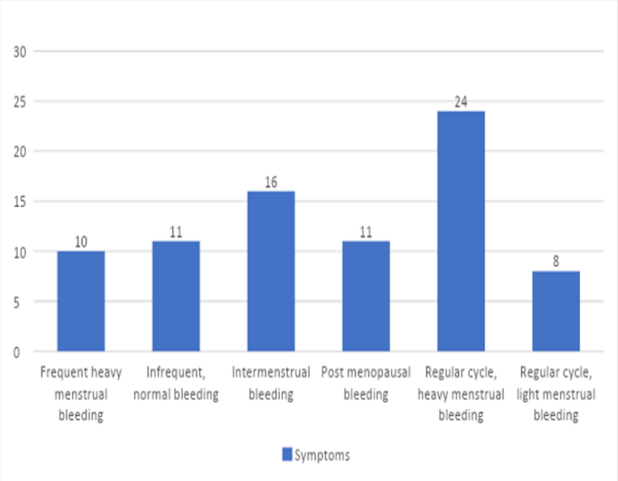


**Figure 1: Distribution of participants according to symptoms.**

The mean duration of menstrual bleeding in the study participants was 4.6±3.3 days with mean of 3.0±2.4 pads used per day. Out of 80 participants, TVS findings in 37participants came out normal, with mean endometrial thickness of 6.9±1.9 mm, 19 participants had adenomyosis, 9 had fibroid and 9 participants had a polyp.

On chromohysteroscopy, out of the 80 participants, 53 (66.3%) had focal staining and 27 (33.7%) had diffuse staining. Out of the 53 focally stained endometrium, 22 participants in the dark staining were found to be in proliferative phase and 36 participants with light staining were found to be in proliferative phase on histopathological examination, 15 participants were reported to have polyp on dark staining and secretory phase was found in 12 participants on light staining as shown in Table 1.

**Table 1: Histopathological findings on focal staining, (n=53).**

| Findings | Dark stained | Light stained |
|---|---|---|
| **Atrophic endometrium** | 2 | 2 |
| **Endometrial hyperplasia** | 2 | 2 |
| **Endometritis** | 1 | 1 |
| **Proliferative endometrium** | 22 | 36 |
| **Secretory endometrium** | 11 | 12 |
| **Polyp** | 15 | 0 |

Out of 27 diffusely stained endometrium 14 had proliferative endometrium, 4 had secretory endometrium,

3 had endometrial hyperplasia, 2 had endometritis as shown in Table 2.

**Table 2: Histopathological findings on diffuse staining.**

| Findings | N |
|---|---|
| **Atrophic endometrium** | 4 |
| **Endometrial hyperplasia** | 3 |
| **Endometritis** | 2 |
| **Proliferative endometrium** | 14 |
| **Secretory endometrium** | 4 |
| **Polyp** | 0 |
| **Total** | 27 |

Out of 23 abnormal histopathological findings, 18 were detected on focal staining and 5 were detected on diffuse staining as shown in Table 3.

**Table 3: Comparison between diffuse and focal staining.**

| Comparison | Diffuse staining | Focal staining | Total |
|---|---|---|---|
| **Normal HPE** | 22 | 35 | 57 |
| **Abnormal HPE** | 5 | 18 | 23 |
| **Total** | 27 | 53 | 80 |

The statistical analysis of this showed that sensitivity, specificity, PPV and NPV of focal staining to detect uterine pathology was found 69.0%, 49.0%, 43.5% and 73.5% respectively with sensitivity, specificity, PPV and NPV of diffuse staining to detect uterine pathology was found 31.0%, 64.7%, 33.3%, and 62.3% respectively.

## DISCUSSION

Current study was an observational study aimed to evaluate the comparison between chromo hysteroscopy finding with histopathological findings in AUB. A total 80 participants were included in the present study.

For statistical analysis, the participants were divided into two age groups, above 40 years and below 40 years.

In our study, mean age of study participants was 42.7±6.9 years with minimum age of 22 years and maximum age of 60 years. Out of the 80 participants, the majority of them i. e., 53.75% (43) belonged to 41-50 years of age, followed by 32.50% between 31-40 years of age, 10 % in the age group >50 years and the least i.e.3.75% in ≤30 years of age.

Haider et al conducted a similar study on 35 patients of AUB with an average age of 39.5±8.5 years, with the majority of cases falling between the age of 35 and 50 years.[8]

The study population was again divided on the basis of parity and it was found that, 38 participants (47.5%) belonged to parity ≥3 followed by 27 (33.3%) had parity 2. In our study, mean height, weight and BMI of study participants was 160.7±12.8 cm, 62.8±8.5 kg and 23.7±2.9 kg/m$^2$ respectively. The majority of them i.e. 65% (52) were normal weight, followed by 28.75% were overweight, 5% were underweight and the least i.e. 1.25% were obese according to BMI classification.

Chaturvedi et al conducted a prospective study including 27 women with AUB with an average age of 29.18±7.29 years which is quite low as compared to our study population. However, they did not comment anything about the parity status.[9]

El-Faissal et al conducted a similar trial, enrolling 50 women with postmenopausal (PMB). Thereby, the average age being 57.5 years (range 42-72 years), while the parity ranged between 1 and 6, with an average of 3.4.[10]

In our study, out of the 80 participants, 24 (29.6%) had complaint of regular cycles, HMB followed by 16 (19.8%) patients who had IMB. Other symptoms were infrequent, normal bleeding (13.6%), PMB (13.6%), frequent HMB (12.3%) and regular cycle, light menstrual bleeding which was found in 10.0% cases.

Also, the mean duration of symptoms among the participants was 12.1±10.0 months, mean duration of menstrual bleeding among the participants was 4.6±3.3 days, mean number of the pads used per day was 3.0±2.4 pads/ day and mean duration of gap between 2 cycle among the participants was 28.6±09.2 days. 35 patients also reported passage of clots during menstrual cycle.

Haider et al discovered that the majority of the patients i. e., 60% had the HMB. Only two patients (5.7%) had PMB.[8]

The histopathology of chromohysteroscopy-guided endometrial biopsy was compared to that of conventional endometrial sampling by Gupta et al.[11] There were 24 HMB cases, 9 cases of IMB, 7 PMB cases, 15 infertility cases, 2 failed IUI cases and 3 recurrent spontaneous abortions (RSA) instances in this study group of 60 women.

In a similar study done by Chaturvedi et al (n=27) 40.74% had only AUB, 44.44% had AUB combined with infertility and the remaining 14.82% had AUB with infertility with unsuccessful IUI.[9]

Kucuk et al and Mansour et al discovered that inflammatory cells absorbed more methylene blue, aiding in the diagnosis of unexplained endometritis.[7,13]

Cicinelli et al presented three criteria for establishing a hysteroscopic diagnosis of chronic endometritis: hyperemia, stromal edema and micro polyps and histopathologically by the presence of: superficial stromal

edema, increased stromal density and inflammatory stromal infiltration with lymphocytic and plasma cells predominance.[12]

***Comparison of chromohysteroscopy, TVS and hysteroscopic findings with histopathological***

All the patients in the study underwent an ultrasonography by vaginal route. Out of the 80 participants, 24 (30%) participants had enlarged uterus, 16 (20%) were found to have globular uterus and 7 (8.8%) participants had endometrial polyp. Mean endometrial thickness on TVS among participants was found to be 6.9±1.9 mm. On hysteroscopy, it was found that 19 (23.8%) participants had adenomyosis followed by 13 (16.3%) patients who had polyp and 11 (13.8%) patients had fibroid on hysteroscopy. No abnormality was observed in 22 (27.5%) participants. On chromohysteroscopy,53 (66.3%) had focal staining and 27 (33.7%) had diffuse staining on chromohysteroscopy. Among these 53 participants who had focal staining, 22 patients (41.5%) in dark staining had proliferative endometrium and 36 (67.9%) in light staining had proliferative endometrium followed by 15 (28.3%) participants who had polyp on dark staining and 12 (22.6%) patients had secretory endometrium on light staining in histopathological findings. Hence it was observed that in the present study, 37 participants had normal findings on TVS, 22 were found to have normal findings on hysteroscopy while histopathology showed normal findings in 51.

In our study, out of the 29 patients in when uterine abnormality was detected on histopathology, 15 were polyp, 6 was AE, 5 were endometrial hyperplasia and 3 were EM in order, it was found that 20 participants showed focal staining on chromohysteroscopy. Applying the test of statistical analysis showed that sensitivity, specificity, PPV and NPV of focal staining to detect uterine pathology was found 69.0%, 49.0%, 43.5% and 73.5% respectively and while that of diffuse staining to detect uterine pathology was found to be 31.0%, 64.7%, 33.3%, and 62.3% respectively. It is important to note that all the cases of polyps took a focal staining pattern on chromohysteroscopy.

**Table 4: Comparison of statistical analysis of different studies.**

| Authors | Year | Sample size (n) | Statistical analysis | | | | Remarks |
|---|---|---|---|---|---|---|---|
| | | | Sensitivity | Specificity | PPV | NPV | |
| **Haider et al[8]** | 2019 | 35 | 69.2 | 74 | 40.9 | 90.2 | |
| **Mansour et al[13]** | 2011 | 57 | 70 | 80.8 | 43.7 | 92.6 | |
| **Singh et al[14]** | 2013 | 60 | - | - | - | - | Diagnostic ability-higher (p=0.006) |
| **Saleh et al[15]** | 2012 | 100 | 93.2 | 87.8 | 91.6 | 90 | |
| **Chaturvedi et al[16]** | 2019 | 27 | 100 | 91.30 | 66.67 | 100 | |
| **El-Faissal et al[17]** | 2014 | 50 | 93.755 | 27.77 | 69.76 | 71.42 | Post menopausal women |
| **Vijay et al[18]** | 2019 | 50 | 76 | 89 | 71 | 92 | |
| **Agarwal et al[19]** | 2019 | 60 | 85.7 | 84.8 | 95.1 | 63.2 | |
| **Chopra et al[20]** | 2017 | 100 | 88 | 70.66 | 50 | 94.6 | Infertility patients |
| **Current study** | - | 80 | 69 | 49 | 43.5 | 73.5 | |
| | | | 31 | 69.7 | 33.3 | 62.3 | |

## CONCLUSION

The idea of staining of endometrium and taking a guided biopsy is exciting with the colour vision inside the uterus. It is undoubtedly, better than a blind sampling. However, the study could not find statistically significant difference between HPE of differently stained endometrium. If darkly stained polyps are not counted separately (as they can be easily identified on plain hystero as well). Hence, subjecting all the patient of AUB to chromohysteroscopy in order to find a major histopathological difference remains questionable. Thus, larger studies with different dyes are required to reach to concrete decision.

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