VER
Vascular & Endovascular Review

A Study on the Role of Chromohysteroscopy in the Evaluation of Endometrial Pathology

Licia Chacko[1], Sarannya P Sasikumar[2], Nithin Paul E[3], Suneesh P J[4*]

[1]Senior resident, Department of Gynaecology, Amala Institute of Medical Sciences, Thrissur, Kerala, India
[2]Assistant Professor, Department of Gynaecology, Amala Institute of Medical Sciences, Thrissur, Kerala, India
[3]Assistant Professor, Department of Pathology, Amala Institute of Medical Sciences, Thrissur, Kerala, India
[4]Assistant Professor, Department of Plastic And Reconstructive Surgery, Government Medical College, Thrissur, Kerala, India
Corresponding author: Dr Suneesh P J,
Email. Id: suneeshpj@gmail.com

ABSTRACT

Chromohysteroscopy is an advanced technique that involves use of special dyes during hysteroscopy to enhance the visualization of endometrial abnormalities. However, its diagnostic value and clinical utility remain a subject of ongoing debate. This study aims to evaluate the effectiveness of chromohysteroscopy in diagnosing endometrial pathology versus conventional hysteroscopy.

Methods We include a group of 45 women presenting with complaints of infertility, heavy menstrual bleeding, Intermenstrual bleeding and Postmenopausal bleeding presented during a period of 12 months in the department of Obstetrics and Gynaecology, at a tertiary care centre, South India, from July 2022 to June 2023.

The first conventional hysteroscopy was done. Then, after instillation of methylene blue dye, hysteroscopic guided biopsies were obtained from stained and unstained areas. All three samples were sent for histopathological examination. Results were analysed and compared.

Results Chromohysteroscopy-guided endometrial biopsy (CHPE) identified 13 cases of endometrial pathology, whereas conventional hysteroscopic-guided biopsy detected seven cases and missed six. The diagnostic accuracy of CHPE in evaluating endometrial pathology was 77.8%, with a sensitivity of 71.4%, specificity of 78.9%, positive predictive value (PPV) of 38.5%, and negative predictive value (NPV) of 93.8%.

Conclusion In conclusion, chromohysteroscopy enhances the diagnostic efficacy of histopathology by facilitating targeted endometrial biopsy, even in the absence of macroscopic abnormalities. This technique provides a notable advantage over conventional methods, particularly in improving the detection of endometrial pathology. However, while it represents a significant advancement, chromohysteroscopy cannot be regarded as an absolute substitute for conventional biopsy techniques.

KEYWORDS: Chromohysteroscopy; Endometrial pathology; Hysteroscopy; Methylene blue dye; Targeted biopsy.

How to Cite: Licia Chacko, Sarannya P Sasikumar, Nithin Paul E, Suneesh P J, (2025) A Study on the Role of Chromohysteroscopy in the Evaluation of Endometrial Pathology, Vascular and Endovascular Review, Vol.8, No.6s, 314-319.

INTRODUCTION

Hysteroscopy has been the gold standard for direct visualization of the endometrial cavity, allowing targeted biopsies to improve diagnostic accuracy. However, conventional hysteroscopy has limitations in detecting subtle endometrial abnormalities, which has led to the development of chromohysteroscopy guided endometrial biopsy (CHPE), a technique that uses methylene blue staining to enhance lesion detection. In Endometrial hyperplasia not only inclines to endometrial carcinoma, its presentations-menorrhagia and menometrorrhagia, lead to emergency evaluation and care [1, 2]. Hysteroscopy technique facilitates adequate visualization of the cavity, accurate detection of intracavitary lesions, less hospitalization, reduced disability and rapid return to normal activity [3]. Chromohysteroscopy involves the application of stains or pigments to improve localization, characterization or diagnosis of lesions [11]

This study evaluates the diagnostic accuracy of chromohysteroscopy-guided endometrial biopsy (CHPE) compared to conventional hysteroscopy in detecting endometrial pathology.

MATERIALS AND METHODS

Study Design and Setting:

This prospective cross-sectional study was conducted over 12 months, from July 2022 to June 2023, in the Department of Obstetrics and Gynaecology at a tertiary care centre in South India. Ethical clearance was obtained from the institutional ethics committee, and written informed consent was obtained from all participants before enrolment in the study.

Study Population and Sample Size

The study included 45 women aged 25–75 years presenting with abnormal uterine bleeding (AUB), heavy menstrual bleeding (HMB), postmenopausal bleeding (PMB), or infertility (including unexplained infertility, menstrual complaints, and recurrent

miscarriage). The sample size was calculated based on the sensitivity of chromohysteroscopy reported in earlier research by Taru Gupta et al., with a 95% confidence level and a 20% allowable error.

Inclusion and Exclusion Criteria:
Women with AUB, PMB, HMB, or infertility, as diagnosed through clinical, laboratory, or radiological evaluation, and willing to participate in the study were included. Patients with chronic kidney disease, known hypersensitivity to methylene blue or thiazides, or those who refused to participate were excluded.

Methodology:
Under general anaesthesia, hysteroscopy was performed using a 6.5 mm hysteroscope with a 30° viewing angle and glycine as the distending medium. The uterine cavity was initially inspected panoramically for gross pathology. If no obvious lesion was detected, a conventional hysteroscopic biopsy was performed. Subsequently, chromohysteroscopy was carried out using methylene blue dye. A 10 mL solution of 2% methylene blue dye diluted in 100 mL normal saline was instilled into the uterine cavity using a Leech-Wilkinson cannula. After five minutes, the cavity was lavaged, and the hysteroscope was reintroduced to observe the staining patterns of the endometrium.

Fig.1. Light staining in chromohysteroscopy guided endometrial biopsy

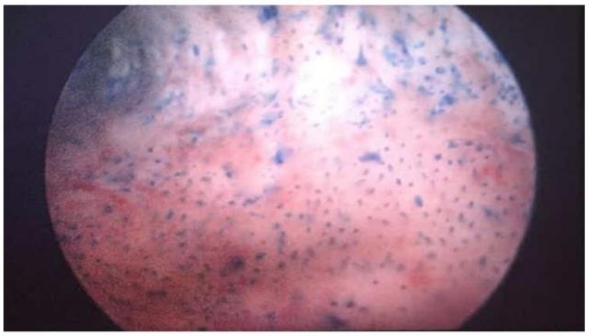


Fig. 2. Dark diffuse staining in chromohysteroscopy guided endometrial biopsy

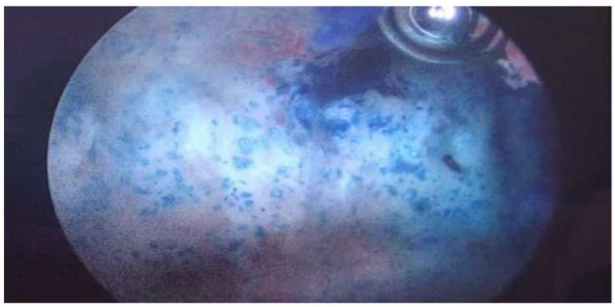
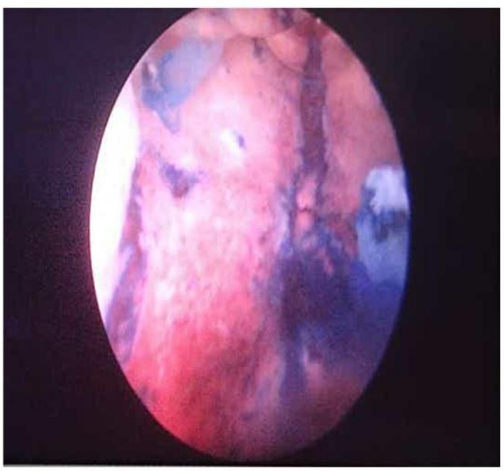


Fig. 3. Dark Focal staining in chromohysteroscopy guided endometrial biopsy



The staining patterns were classified as no staining, light staining (FIG. 1), or dark staining. Dark focal (FIG 3) or dark diffuse (FIG 2) blue staining above the cervical ostium, regardless of the size or number of stained areas, was considered a positive finding. Biopsy samples were obtained from areas showing dark or light staining under hysteroscopic guidance.

The data were analyzed to compare the histopathological outcomes of chromohysteroscopy-guided biopsy with conventional sampling.

RESULTS

Out of 45 cases,24 cases had complaints of heavy menstrual bleeding, nine had intermenstrual bleeding, seven had postmenopausal bleeding, and five cases were of infertility. The mean age of cases was 41 years. After Chromohysteroscopy staining, the pattern of the endometrium was noted. It was grouped as light-stained endometrium (Group 1) (n=34, 75.6 %) and dark-stained endometrium (Group 2) (n=11, 24.4 %). Dark staining (Group 2) was further subdivided into 'Dark Focal' (Group 2A) (n=9) and 'Dark Diffuse' (Group 2B) (n=2).

In our study, 22 (48.9%) participants were in the age group of ≤ 40 years, 19 (42.2%) were 41-60 years, and 4 (8.9%) were > 60 years. As per complaints, 24 (53.3%) of cases were HMB, 9 (20.0%) of cases were IMB, 7 (15.6%) of cases were PMB, and 5 (11.1%) of cases were Infertility. Based on endometrial thickness, about 70% (n=24) showed light staining (FIG 1) in patients with ET <12 and about 30% (n=10) showed light staining in patients with ET >12. In cases of dark staining, about 33% (3 out of 9) showed dark focal staining (FIG 2) in patients with ET <12 and 66% (6 out of 9) showed dark focal staining in patients with ET >12. Whereas 50% patients showed dark diffuse staining (FIG 3) in patients with ET > 12 (1 out of 2)

On Conventional Endometrial Sampling, 32 (71.1%) cases were reported as secretory endometrium, 6 (13.3%) were Proliferative, 5 (11.1%) were endometritis, 1 (2.2%) was Hyperplasia without Atypia, and 1 (2.2%) was Hyperplasia with Atypia. On chromohysteroscopy-guided endometrial biopsy (CHPE), 26 (57.8%) cases were reported as secretory endometrium, 6 (13.3%) were Proliferative, 9 (20.0%) were endometritis, 2 (4.4%) were Hyperplasia without Atypia, and 2 (4.4%) were Hyperplasia with Atypia.

In our study, 34 (75.6%) cases showed light-stained endometrium and 11 (24.4%) cases showed dark-stained endometrium. Among 11 dark-stained endometriam 9 (81.8%) cases were dark focal and 2 (18.2%) were dark diffuse.

Distribution of light staining and dark staining (Table 1)

Type of staining	Secretary	Proliferative	Endometritis	Hyperplasia with atypia	Hyperplasia without atypia	Carcinoma	Total
Light staining	25	4	4	0	1	0	34
Dark staining							
II A Focal	0	3	4	2	0	0	9
II B diffuse	1	0	0	0	1	0	2

Distribution of light staining

Only about 14.7% cases of light staining endometrium detected an abnormal endometrium.ie, 85.3% of light staining showed normal endometrium. 1 case of Hyperplasia with atypia detected in light staining was diagnosed as Endometritis in BES.
Dark staining CHPE detected cases of endometrial pathology (4 endometritis, 2 hyperplasia without atypia,1 hyperplasia with atypia,1 secretory endometrium,3 proliferative endometrium).

Distribution of dark staining

Out of 9 cases of dark focal staining, 66.66% showed abnormal endometrial pathologies. And out of 2 cases of dark diffuse staining, 50% cases showed abnormal endometrial pathologies.

Here, conventional, detected 18 cases of secretory endometrium, 4 cases of proliferative endometrium, and 2 cases of endometritis. No cases of hyperplasia with atypia, hyperplasia without atypia or carcinoma were detected in BES.
In CHPE 15 cases of secretary endometrium, 4 cases of proliferative endometrium, 4 cases of endometritis, and 1 case of hyperplasia with atypia were detected.

Comparison between CHPE and Conventional hysteroscopy in detecting endometrial pathologies based on complaints (Table 2)

Type of Bleeding	**Secretary**	**Proliferative**	**Endometriosis**	**Hyperplasia with atypia**	**Hyperplasia without atypia**	**CA Endometriculam**
HMB						
Conventional	18	4	2	0	0	0
CHPE	15	4	4	0	1	0
IMB						
Conventional	5	1	1	1	1	0

CHPE	2	1	3	2	1	0
PMB						
Conventional	4	1	2	0	0	0
CHPE	4	1	2	0	0	0

Comparison between CHPE and Conventional in detecting endometrial pathologies in HMB
Here, hyperplasia with atypia, shown in CHPE, was detected as endometritis in Conventional.
In conclusion, abnormal endometrial pathologies in HMB are better detected by CHPE than Conventional. But hyperplasia with atypia was detected in light staining rather than dark staining in CHPE. This may be due to dilution of methylene blue. In Conventional, 5 cases of secretory endometrium, 1 case of proliferative endometrium, 1 case of endometritis, 1 case of hyperplasia with atypia, and 1 case of hyperplasia without atypia were detected. While in CHPE 2, cases of secretory endometrium, 1 case of proliferative endometrium, 3 cases of endometritis, and 2 cases of hyperplasia without atypia were detected; 1 case of hyperplasia with atypia was detected.

Comparison between CHPE and Conventional in detecting endometrial pathologies in IMB
Here, CHPE detected a greater number of abnormal endometrial pathologies than Conventional. One case of Hyperplasia without atypia, which was missed in Conventional, was detected in CHPE. And in the dark staining category, dark focal detected 2 cases of hyperplasia without atypia and dark diffuse detected 1 case of hyperplasia with atypia, which makes CHPE a better option in detecting abnormal endometrial pathologies.

In Conventional, we detected 4 cases of secretory endometrium, 1 case of proliferative endometrium and 2 cases of endometritis. While in CHPE, there also detected 4 cases of secretory endometrium, 1 case of proliferative endometrium, and 2 cases of endometritis were detected.

Comparison between CHPE and Conventional in detecting endometrial pathologies in PMB
Light staining showed all secretory endometrium, and dark focal staining showed both proliferative and endometrial pathologies. Here, not many differences were seen between CHPE and Conventional. This may be due to a smaller number of PMB cases in our study.

In infertility cases, both CHPE and Conventional showed secretory endometrium only. This may be due to fewer cases of infertility in our study.

Distribution of the histopathology obtained from chromohysteroscopy (CHPE) and Conventional endometrial sampling. (Table 3)

CHPE	**Conventional Endometrial Sampling**					**Total**
	Secretory	**Proliferative**	**Endometritis**	**Hyperplasia without Atypia**	**Hyperplasia with Atypia**	
Secretory	25	0	1	0	0	26
Proliferative	1	4	1	0	0	6
Endometritis	5	2	2	0	0	9
Hyperplasia without Atypia	1	0	0	1	0	2
Hyperplasia with Atypia	0	0	1	0	1	2
Total	32	6	5	1	1	45

On chromohysteroscopy-guided endometrial biopsy (CHPE), 26 cases were reported as secretory endometrium, while on conventional endometrial sampling, 32 cases were reported as secretory endometrium. Hence, conventional missed 6 cases of endometrial pathology and reported them as secretory. CHPE detected 6 cases of proliferative endometria, while conventional detected 4 cases of proliferative endometria, 2 cases of proliferative as secretory endometrium (n=1) and endometritis (n=1). CHPE detected 9 cases of endometritis as compared to conventional, which detected only 5 cases. This suggests that conventional reports 5 cases of endometritis as secretory endometrium and 2 cases of endometritis as proliferative. Two cases of dark focal staining were reported as proliferative endometria on CHPE, which was reported as endometritis on conventional. Two cases of hyperplasia without atypia were picked up by CHPE, and only 1 case was picked up by conventional. Therefore, 1 case was missed by the conventional method and reported as normal endometrium (secretory). Two cases of hyperplasia with atypia were picked up by CHPE, but conventional picked up 1 case only. Conventional hysteroscopic guided endometrial sampling detected 7 cases of endometrial pathology (5 endometritis, 1 hyperplasia without atypia and 1 hyperplasia with atypia). Detection of

endometrial cancer was not detected in both CHPE and Conventional hysteroscopic-guided endometrial sampling.
Comparison between the histopathology obtained from chromohysteroscopy (CHPE) and Conventional hysteroscopic-guided endometrial sampling. CHPE detected 13 cases of endometrial pathology, while conventional detected 7 cases of endometrial pathology and missed 6 cases. Thus, the diagnostic accuracy of chromohysteroscopy in evaluation of endometrial pathology was 77.8% with sensitivity of 5/7=71.4%, specificity of 30/38=78.9%, PPV of 5/13=38.5% and NPV of 30/32=93.8%. No statistically significant difference was determined in the comparison of biopsy samples obtained from methylene blue-stained and blind biopsy (> 0.05).

DISCUSSION

Diagnostic hysteroscopy with hysteroscopic-guided biopsy is thought to be the gold standard diagnostic tool for evaluation of AUB.

Sangham Jha et al. Study [4] reported that chromohysteroscopy had a significantly higher diagnostic accuracy (92%) for detecting endometrial pathology compared to conventional hysteroscopy (8). The sensitivity and specificity of chromohysteroscopy were 94.12% and 90.9% respectively.

Abdel-Halim et al.'s study [5] is a prospective study and reported a high specificity (83.33%) and sensitivity (92.54%) in diagnosing endometrial pathology, particularly in cases of AUB. This suggests that incorporating chromohysteroscopy could lead to more accurate diagnoses and targeted treatments.

Yahia et al. [7] in 2014 used chromohysteroscopy in 50 postmenopausal women, which led to the diagnosis of three more cases of endometritis, two more cases of endometrial hyperplasia, but none of endometrial carcinoma as compared to standard blind fractional curettage. In our study, out of 7 cases with postmenopausal bleeding, 3 showed dark staining in chromohysteroscopy with no detection of endometrial pathology other than endometritis on histopathology.

Singh and Singh [8] reported a 72.2% detection rate from stained biopsies, significantly better than unstained and aspirated samples. Both studies conclude that chromohysteroscopy offers better diagnostic accuracy, especially for subtle or focal lesions, and serves as a valuable adjunct to conventional hysteroscopy.

Alay et al. [9] in 2014 enrolled 38 patients with abnormal uterine bleeding. The study showed comparable outcomes, whereas our study reinforces its potential clinical superiority by offering more diagnostic clarity and application across varied gynecological complaints.

Chopra et al [10] studied the efficacy and diagnostic accuracy of staining in infertility patients. In this Light-staining pattern was seen in 56 cases, and 44 cases had dark staining. Histopathology of biopsy tissue from these dark-stained areas showed endometritis in 50% (22 out of 44 cases) and normal endometrium in 50% (22 out of 44) cases, while biopsy from light-stained areas showed chronic endometritis in 5.35% (3 out of 56) cases, and the remaining 94.65% had normal endometrium. Diagnostic accuracy of chromohysteroscopy was the following sensitivity = 88%, specificity = 70.66%, PPV = 50%, NPV = 94.6%. They concluded that chromohysteroscopy is a simple and effective technique for diagnosing endometrial pathology in cases of infertility.

Taru Gupta etal [6] studied 60 women with complaints of infertility, failed IUI, IMB, and PMB. On CHPE, 36 Cases (60%) were reported as secretory endometrium, while on conventional, 42 (70%) cases were reported as secretory endometrium. Hence, the conventional method missed 6 cases. In our study, CHPE reported 26 cases (57.77%) as secretory endometrium, whereas conventional reported 32 cases (71.11%) of secretory endometrium. Here, conventional missed 6 cases. Both CHPE and conventional methods detected an equal number of proliferative endometria in both studies. In Taru Gupta, 4 cases (6%) of Hyperplasia without atypia were picked up by CHPE and 3 cases 5% picked up by conventional (Which was reported as secretory) in our study. 2 cases (4%) of Hyperplasia without atypia were picked up by CHPE and only 1 case picked up by conventional (2%). 2 cases of Hyperplasia with atypia were picked up by CHPE, but conventional picked 1 case only (1%) whereas in our study, 2 cases of Hyperplasia with atypia (4%) were picked up by CHPE but conventional picked 1 case only (2%). No endometrial carcinoma was detected in our study. Whereas in Taru Gupta, the detection of endometrial carcinoma was the same in both CHPE and conventional. In Taru Gupta, CHPE detected 11 cases (18.3%) of endometritis as compared to conventional, which detected only seven cases (11.6%), whereas in our study, CHPE detected nine cases (20%) of endometritis as compared to conventional, which detected only five cases (11.11%).

The diagnostic accuracy of CHPE in Taru Gupta in evaluation was 86.677% with a sensitivity of 91.67%, a specificity of 85.4% with a PPV of 61.12%, NPV of 97.61% ($p<0.001$). but in our study, the diagnostic accuracy of chromohysteroscopy was 77.8% with a sensitivity of 71.4%, specificity of 78.9% with PPV of 38.5%, and NPV of 93.8%. Aleena et al. [12] also concluded that CHPE is an efficacious tool for detecting pathology.

CONCLUSION

45 patients with complaints of AUB, PMB, HMB and infertility were evaluated in our study. Both blind biopsy and chromohysteroscopy evaluation on the same patient were done. In this study, we concluded that chromohysteroscopy improves the diagnostic efficacy of histopathology in targeting endometrial biopsy. But there is no sufficient data to suggest that CHPE will be able to replace conventional hysteroscopy as a gold standard in detecting endometrial pathologies.[13] This guided biopsy

helps to diagnose endometrial pathology in the absence of macroscopic abnormalities, making better advantage over the conventional method, but not an absolute alternative.

Conflict of interest: Nil

REFERENCES

1. A. Golan, M. Siedner, M. Bahar, et al., High-output left ventricular failure after dextran use in an operative hysteroscopy, Fertil. Steril. 54 (1990) 939–941. doi: 10.1016/s0015-0282(16)53962-4.
2. S. Padubidri, N. Daftary, Shaw's Textbook of Gynaecology, 16th ed., Reed Elsevier India Pvt. Ltd., 2015. ISBN: 978-81-312-3672-7.
3. L. Speroff, M.A. Fritz, Clinical Gynecologic Endocrinology and Infertility, 8th ed., Lippincott Williams & Wilkins, Philadelphia, 2011, pp. 591–604.
4. S. Jha, S. Singh, J.B. Singh, Enhancing endometrial pathology detection: chromohysteroscopy vs. conventional hysteroscopy in infertility evaluation, Middle East Fertil. Soc. J. 28 (2023) 31. https://doi.org/10.1186/s43043-023-00157-3.
5. M. Mohamed, M. El-Noury, I. Sayed, A. Abdel-Halim, Role of chromo hysteroscopy in evaluation of endometrial pathology in females with abnormal uterine bleeding, Benha J. Appl. Sci. 8 (2023) 11–16. https://doi.org/10.21608/bjas.2023.232405.1236.
6. T. Gupta, S. Singh, A.K. Verma, Role of chromohysteroscopy in evaluation of endometrial pathology using methylene blue dye, J. Obstet. Gynaecol. India 69 (2019) 363–368. https://doi.org/10.1007/s13224-019-01233-3.
7. Y.M. El-Faissal, A.M. Kamel, The value of chromohysteroscopy in the assessment of postmenopausal vaginal bleeding, J. Clin. Gynecol. Obstet. 3 (2014) 35–41, doi: http://dx.doi.org/10.14740/jcgo209w.
8. N. Singh, B. Singh, Chromohysteroscopy—A new technique for endometrial biopsy in abnormal uterine bleeding (AUB), Open J. Obstet. Gynecol. 3 (2013) 11. DOI: 10.4236/ojog.2013.35A1003
9. A. Alay, T.A. Usta, P. Ozay, et al., Comparison of two modalities: a novel technique, 'chromohysteroscopy', and blind endometrial sampling for the evaluation of abnormal uterine bleeding, J. Obstet. Gynaecol. Res. 40 (2014) 1407–1414. doi: 10.1111/jog.12341.
10. K. Chopra, S.S. Trivedi, S. Patra, Diagnostic accuracy of chromohysteroscopy in women with unexplained infertility, Int. J. Reprod. Contracept. Obstet. Gynecol. 6 (2017) 2955–2959. DOI: https://doi.org/10.18203/2320-1770.ijrcog20172915
11. Vijay A, Koothan V, Baskaran MV. Efficacy of Chromohysteroscopy for Evaluation of Endometrial Pathologies in Abnormal Uterine Bleeding. J South Asian Feder Obst Gynae 2019; 11(5):301–304.
12. Haider, A., Bano, I., Sabzposh, N. A., & Arif, S. H. (2019). Role of chromohysteroscopy in detection of endometrial pathology in abnormal uterine bleeding. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*, *8*(3), 916–920. https://doi.org/10.18203/2320-1770.ijrcog20190857
13. Kaur, A., Bedi, M., Singh, P., Lamba, P., Kaur, H., & Suri, V. (2024). Comparison of chromohysteroscopy findings with histopathological findings in abnormal uterine bleeding. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*, *13*(4), 890–894. https://doi.org/10.18203/2320-1770.ijrcog20240782