

Role of Hysteroscopy in Recurrent Pregnancy Loss

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Abstract

Background: Because its cause is frequently unclear, recurrent pregnancy loss (RPL) ranks among reproductive medicine's most challenging and distressing subspecialties. In 10–50% of cases, uterine variables (both inherited and acquired) have a role. When it comes to assessing the endometrial cavity, hysteroscopy is considered the gold standard due to its ability to directly observe the endometrium.

Aim: The purpose of this study is to analyze the efficacy of hysteroscopy in detecting uterine abnormalities in women who experience repeated miscarriages.

Subjects and methods: From October 2023 through April 2024, one hundred women who experienced recurrent first-trimester miscarriages were included in this prospective cohort study at Al-Hussein University Hospital's hysteroscopy Unit, Obstetrics and Gynaecology Department. Diagnostic hysteroscopy was performed on all patients after their periods had ended, typically between three and six months after the abortion.

Results: In 53.0% of cases where first-trimester miscarriages (MRs) occurred again, an abnormal hysteroscopic examination was detected. Uterine septum was the most prevalent congenital uterine abnormality, occurring in 20% of cases. Uterine polyp(s) were the most common acquired abnormality, occurring in 11% of cases.

Conclusion: It is possible to do hysteroscopy as an outpatient procedure without numbing the patient, and the procedure is safe, sensitive, and dependable.

Keywords: Hysteroscopy; Recurrent pregnancy loss (RPL)

1. Introduction

For women and their families, the insoluble experience of repeatedly trying to conceive only to have the pregnancy end in miscarriage or recurrent pregnancy loss (RPL) is a difficult and distressing condition.¹

A still-valid definition of RM is three or more consecutive miscarriages. However, according to the American Society for Reproductive Medicine (ASRM), diagnostic workup should begin after the second pregnancy failure, and the three-miscarriage threshold should be considered solely for epidemiological and statistical purposes.²

Even while up to half of pregnancies have occasional pregnancy loss, only around five percent of couples will receive a diagnosis of

RPL. About half of all cases of RPL have no known etiology.³

Both frequent and infrequent miscarriages might have a wide variety of causes. Hereditary abnormalities are the leading cause of RPL, accounting for more than half of all instances. Some examples of these abnormalities include whole chromosome abnormalities (e.g., trisomy, monosomy, triploidy, etc.), partial chromosome abnormalities (e.g., macro- and microdeletions and insertions, unbalanced translocations), disorders affecting a single gene (e.g., micro-RNA defects and changes in gene function reflecting epigenetic changes) and single genes (e.g., exons, introns, and promoter regions). The uterine cavity can have either a hereditary or an acquired component, and either might lead to recurrent miscarriages.⁴

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Historically, patients have had to endure more expense and risk due to the utilization of abdominal or laparoscopic procedures for surgical repairs. As safer and more advanced surgical tools have been developed, the hysteroscope has become an essential tool for the diagnosis and treatment of RPL in patient management.⁵

The researchers in this study set out to determine how often and what kinds of uterine abnormalities can be detected using hysteroscopy in RPL patients.

2. Patients and methods

Participants enrolled in this prospective cohort study ranged in age from 2023 to 2024 and came from the Obstetrics and Gynaecology clinic at Al-Hussein University Hospital. Each participant had a chain reaction of three or more recurrent miscarriages without a known cause.

Inclusion criteria:

Patients must be between the ages of 18 and 45 and not pregnant. They must have the presence of three or more pregnancy-related MRs in a row before the 20-week mark, a transvaginal ultrasound scan that appears normal, normal levels of progesterone during the luteal phase, and all of the husband's spermograms to be within normal limits.

Exclusion criteria:

The following groups of women were not eligible to participate: those who had undergone a therapeutic abortion, those who had a proven cause for RPL, those who had a recent or acute pelvic infection, those who were pregnant or thought to be pregnant, those who were known to carry balanced chromosomal anomalies, those who had uncontrolled or previously undiagnosed endocrinological diseases like hypothyroidism or diabetes, and those who refused to participate.

Sampling Method "Convenient targeted sampling":

Researchers use respondents who are "convenient" for them in convenience sampling. There is no set procedure for gathering these respondents; anyone can be approached in this way. Most people mistake this idea for "random sampling" since it implies that people are being stopped "at random" (i.e., randomly). A convenience sample, on the other hand, is incredibly biased, in contrast to the proper definition of random sampling, which typically leads to a statistically balanced selection of the population.

Ethical considerations:

Both the OB/GYN department's council and the Faculty of Medicine's Research Committee at Al-Azhar University in Cairo gave their clearance to this study. They were asked to provide their informed permission.

Study interventions and procedures:

During their prenatal checkup, we were able to collect information about the mother's demographics and other personal traits.

Patients were evaluated using a digital ultrasonic diagnostic imaging system and an ultrasound machine equipped with a 2-5 MHz curved array vaginal transducer. The evaluation included a thorough history taking of clinically significant events, surgical history, a general physical examination, and routine laboratory investigations. Two-dimensional transvaginal ultrasounds were performed to evaluate the uterus and adnexa.

Diagnostic hysteroscopy:

Preoperative Preparation

In order to identify any co-morbidities, the patient's medical history and physical examination were carefully reviewed. Ideally, the operation would have taken place after menstruation had stopped, during the proliferative period of the menstrual cycle. Each patient was given a different dosage of general anaesthetic based on their pain threshold and amount of fear. With their legs in adjustable stirrups, the patient was placed in the dorsal lithotomy position. The entire treatment was conducted with utmost care to ensure an aseptic approach. After inserting a speculum to view the cervix, it was cleansed with an antiseptic solution, such as povidone-iodine. The anterior lip of the cervix may be stabilized for hysteroscope implantation with the use of a tenaculum.

Hysteroscope Insertion:

A narrow, illuminated tube called a hysteroscope was delicately threaded into the endocervical canal via the external cervical os. To enhance vision, the uterine cavity was enlarged by the introduction of a distention medium, a liquid. A bird's-eye view was captured once inside the uterine cavity. Every part of the uterus, including the sides, top cavity, front, and back, is examined methodically. Photos or video recordings were made of any anomalies that were found. Thoroughly removing the hysteroscope while carefully examining for any residual abnormalities followed the completion of the diagnostic survey and any required procedures, such as biopsies. If an anaesthetic was administered during the procedure, patients should be monitored for a few hours afterwards; otherwise, they can usually return to their regular routines quite quickly.

Primary outcome:

Find out how common uterine defects are and what kinds there are by doing a hysteroscopic examination.

Secondary outcome:

Assess the important predictors of patients with abnormal uterine findings (demographic, laboratory, history and clinical parameters).

Statistical analysis:

Data was collected, reviewed, coded, and entered using IBM SPSS (IBM Corp., 2020). (Armonk, NY: IBM Corp.) SPSS Statistics for Windows 27.0. Mean, standard deviation, and range were used to report parametric data, whereas median and interquartile range were used for non-parametric data. Counts and percentages were used for the qualitative variables. If any cell's anticipated count was below 5, we compared the groups' qualitative data using Chi-square or Fisher's exact testing.

When comparing two groups with quantitative data and parametric distribution, we utilized independent t-tests; when comparing groups with non-parametric distribution, we used Mann-Whitney tests. The optimal cutoff for recurrent abortion was determined using receiver operating characteristic curve (ROC) analysis, which took into account sensitivity, specificity, PPV, NPV, and AUC to differentiate between patients with normal and abnormal hysteroscopy findings. We utilized a margin of error of 5% and a confidence interval of 95%. As a result, the p-value was worthy of note: Indicators of non-significance (NS) include values greater than 0.05, significantness (S) is indicated by values less than 0.05, and highly significantness (HS) is indicated by values less than 0.01.

3. Results

Table 1. Features of the research population's demographics

VARIABLE	Min	Max	Mean	SD
CHRONOLOGICAL AGE (YEARS)	18	45	32	7
MASS (KILOGRAMS)	46	85	66	9
ELEVATION IN METERS	1.49	1.75	1.61	.05
BMI (KG/M ²)	18.3	34.6	25.7	3.5

Min=minimum, Max=maximum, SD=standard deviation.

The mean age of all patients was 32-years median (31), mean weight was 66kg median (67), mean height was 1.61m median (1.61), and mean BMI was 25.7kg/m² median (25.7), (table 1).

Table 2. Parity of the study population.

VARIABLE	FREQUENCY	PERCENT
PARITY		
P0	51	51%
P1	26	26%
P2	13	13%
P3	6	6%
P4	2	2%
P5	2	2%

Most of our patients are nulliparous 51% followed by history of one, two, three, four and five deliveries respectively, (table 2; figure 1).

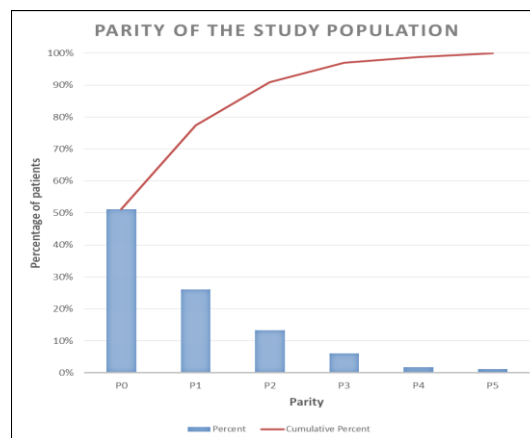


Figure 1. Parity of the study population.

Table 3. The study population's prior abortion frequency.

VARIABLE	FREQUENCY	PERCENT
FREQUENCY OF PREVIOUS ABORTIONS		
3 abortions	45	45
4 abortions	20	20
5 abortions	12	12
6 abortions	7	7
7 abortions	5	5
8 abortions	4	4
9 abortions	1	1
10 abortions	3	3
≥11 abortions	3	3

The largest proportion of our study population 45% had three miscarriages, (table 3; figure 2).

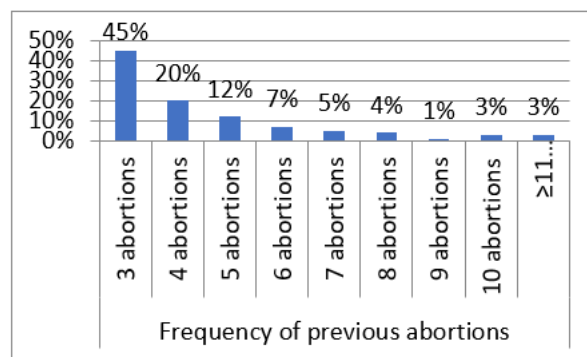


Figure 2. The prevalence of prior abortions among the research participants.

Table 4. Hysteroscopic examination results.

VARIABLE	FREQUENCY	PERCENT
HYSTEROSCOPIC FINDINGS		
Normal	47	47.0%
Uterine septum	20	20.0%
Endometrial polyp(s)	11	11.0%
Submucous fibroid	6	6%
Bicornuate uterus	2	2%
Adhesion(s)	9	9%
Arcuate uterus	2	2%
Cervical polyp	2	2%
Single uterine horn with single tubal ostium	1	1%
ULTIMATE RESULT OF HYSTEROSCOPIC EXAMINATION		
Normal hysteroscopic findings	47	47.0%
Abnormal hysteroscopic findings	53	53.0%

According to this data, there are 47 normal cases (47%) and 53 aberrant cases (53%), (table 4; figure 3).

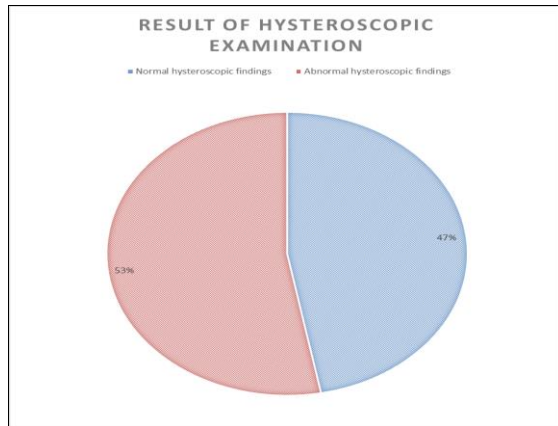


Figure 3. Ultimate result of hysteroscopic examination.

Table 5. Comparing the prevalence of prior abortions and births in women with normal or aberrant hysteroscopic findings

VARIABLE	NORMAL HYSTEROSCOPIC FINDINGS (N=47)			ABNORMAL HYSTEROSCOPIC FINDINGS (N=53)			p-value *
	Median	IQR	Mean rank	Median	IQR	Mean rank	
FREQUENCY OF PREVIOUS DELIVERIES	1	0 to 1	86.4	0	0 to 1	79.1	0.286
FREQUENCY OF PREVIOUS ABORTIONS	3	4 to 5	75.1	4	3 to 6	90.9	0.025

Data are median and interquartile range (IQR).*: Mann-Whitney test

No significant relationship according to frequency of previous deliveries and significant according to frequency of previous abortions, (table 5; figure 4).

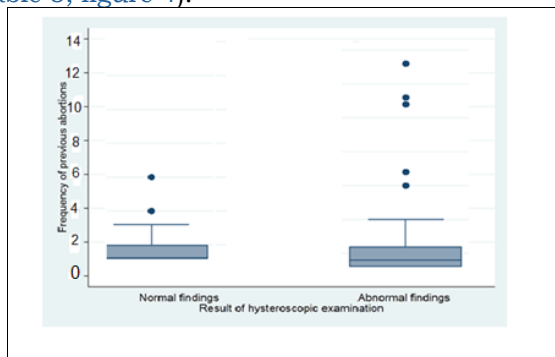


Figure 4. how frequently patients with normal or bad hysteroscopic findings have had abortions in the past. The interquartile range, or box, is the range between the first and third quartiles. The median, or second quartile, is shown by the line inside the box. With outliers and extreme values (rounded markers) excluded, whiskers show the lowest and maximum values.

Table 6. Utilizing the incidence of prior abortions, ROC curve analysis is used to distinguish between patients with normal or abnormal hysteroscopic findings

VARIABLE	VALUE	95% CI
AREA UNDER THE ROC CURVE (AUC)	0.596	0.517 to 0.672
Z STATISTIC	2.272	
P-VALUE (AUC=0.5) *	0.023	
YOUDEN INDEX J	0.1753	

ASSOCIATED CUTOFF CRITERION	≤5	
SENSITIVITY	85.1%	75.8% - 91.8%
SPECIFICITY	32.5%	22.2% - 44.1%
POSITIVE LIKELIHOOD RATIO (+LR)	1.26	1.1 - 1.5
NEGATIVE LIKELIHOOD RATIO (-LR)	0.46	0.3 - 0.8
POSITIVE PREDICTIVE VALUE (+PV)	58.7%	54.4% - 63.0%
NEGATIVE PREDICTIVE VALUE (-PV)	65.8%	51.4% - 77.7%

*: Delong method.

The area under the ROC curve for the frequency of prior abortions was 0.596 (95% CI=0.517 to 0.672, p-value=0.023), suggesting that it had a limited diagnostic value. With a frequency of ≤5 abortions, the optimal cut-off criterion has a sensitivity of 85.1%, specificity of 32.5%, positive predictive value (+PV) of 58.7%, and negative predictive value (-PV) of 65.8%, (table 7; figure 5).

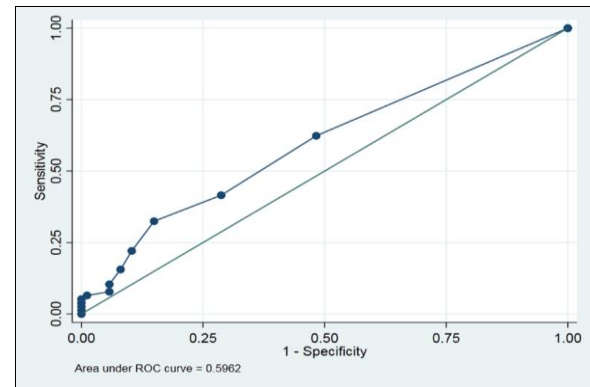


Figure 5. ROC curve for using the frequency of prior abortions to distinguish between patients with normal or abnormal hysteroscopic findings. AUC = 0.596 (95% C = 0.517 to 0.672, p-value = 0.023) is the area under the ROC curve. A sensitivity of 85.1%, specificity of 32.5%, positive predictive value (+PV) of 58.7%, and negative predictive value (-PV) of 65.8% are associated with a frequency of ≤5 abortions.

4. Discussion

Only about seven percent of women overall have a congenital uterine anomaly, whereas about ten to fifteen percent of women with RPL do. Impaired uterine distention or incorrect implantation owing to reduced septal vascularity, elevated inflammation, or diminished sensitivity to steroid hormones can be associated with pregnancy loss.⁶

The endometrial cavity is best assessed by hysteroscopy, which allows direct sight of the endometrium. Hysteroscopy has improved pregnancy outcomes by detecting and treating several congenital and acquired uterine abnormalities.⁷

The average age of the mothers in our study group was 32±7 years, according to our findings. All of this lines up with Souza et al.,⁸ and Bohlmann et al.,⁹ They disagreed with the results that showed it to be 31-39 and 32.95±4.46 respectively Ventolini et al.,¹⁰ and Alobaidy et al.,¹¹ This could be because to social and racial characteristics, since it was 28.1 and 27.9±3.4

respectively.

The average body mass index in this research was 25.7 ± 3.5 . In this case, it coincided with Alobaidy et al.,¹¹ the value was 26.3 ± 2.3 and was in disagreement with Souza et al.,⁸ this could be because our population has a greater obesity rate, which was 23.4 in the past.

The majority of the patients in this study were 51 (or 51% of the total), and their average number of previous deliveries was 1 ± 0.2 .

Results from the following investigations were very similar, Bohlmann et al.,⁹ it was discovered that 54.5% were non-para, and Souza et al.,⁸ The research found that prior deliveries had an average of 0.5 ± 1 .

While Alobaidy et al.,¹¹ discovered conflicting findings with a 68% null success rate, Elsokkary et al.,¹² equally rejected the idea of nulliparity (88%). In Weiss et al.,¹³ it is possible that our patients' diminished understanding of the need for prenatal care is to blame for the much lower mean of 5.08 ± 2.29 compared to previous deliveries.

With a mean of 5 ± 4 and a range of 3–11 abortions, our patients had a history of past miscarriages, with 45% of patients having had three abortions.

All of these line up with Elsokkary et al.,¹² where prior miscarriages had a mean of 3–5, Bohlmann et al.,⁹ with a mean of (3.74 ± 1.09) , Camuzcuoglu et al.,¹⁴ with a mean of (3.62) , Souza et al.,⁸ with a mean of 3, and Alobaidy et al.,¹¹ with on average 3.2 ± 1.1 ; nevertheless, our study cohort may have a larger number of previous abortions due to late obstetric consultation.

Median (IQR=3) versus 4 (normal hysteroscopy vs. abnormal hysteroscopy), $p=0.025$, indicates that patients with abnormal hysteroscopy findings have a considerably lower number of prior abortions.

Elsokkary et al.,¹² Bohlmann et al.,⁹ and Moiety et al.,¹⁵ Abnormal hysteroscopic findings were detected in 54.5%, 42.9%, and 43.8% of the study population, respectively. Whereas, Souza et al.,⁸ Ventolini et al.,¹⁰ Weiss et al.,¹³ and Camuzcuoglu et al.,¹⁴ discovered varying outcomes, with aberrant hysteroscopic findings observed in 33.3%, 39.1%, 31%, and 70.8% of the patients analyzed, respectively.

Twenty women (20%) in our study had uterine septal defects, making it the most prevalent uterine anomaly in women experiencing recurrent first-trimester abortions. This outcome resembles that of Weiss et al.,¹³ Elsokkary et al.,¹² Moiety et al.,¹⁵ and Bohlmann et al.,⁹, while in Ventolini et al.,¹⁰ and Camuzcuoglu et al.,¹⁴. Most commonly found were adhesions within the uterus.

One possible way that a septate uterus causes

pregnancy loss is by preventing proper blood flow to the septum, which can hinder implantation. Nevertheless, the precise process remains uncertain.¹⁶

Our study population ranked endometrial polyp(s) as the third most common uterine anomaly in 11 cases (11.0%). I concur with this being Al Chami and Saridogan¹⁷ and El-bareg et al.,¹⁸ and disagree with Weiss et al.,¹³ Ventolini et al.,¹⁰ and Souza et al.⁸

Concentrated growths of endometrial glands, stroma, and blood arteries that form endometrial polyps on the uterine mucosa. Around 10% of women in the general population will have uterine polyps.¹⁹ The endometrial receptivity of uteri with polyps may be impaired because polyps change the expression of the HOXA10 and HOXA11 genes, which are known to be indicators of endometrial receptivity.²⁰ The most reliable way to detect endometrial polyps is with a hysteroscopy. In addition, hysteroscopy enables the excision of endometrial abnormalities like polyps and tiny submucous fibroids all at once, making it an ideal therapeutic option.¹⁷

Intrauterine adhesions in our study population were found in 9 cases (9%). This is consistent with Bohlmann et al.,⁹ and Weiss et al.,¹³ where 9.8% and 11% of the samples had adhesions, respectively. Endometritis, curettage, myoma excision, structural uterine defect treatment, or caesarean section are common causes of intrauterine adhesions.²¹

Six instances (6%) in the current study had submucous myomas; Bohlmann et al.,⁹ agree with us on 7.6% of cases, and 5% of cases in El-bareg et al.¹⁸

One of the study's strengths is that it was the first of its kind to examine the use of hysteroscopy to determine the frequency and kind of uterine abnormalities in women who experienced repeated miscarriages at Al-Azhar University Hospital. Care was taken to ensure that all follow-up data were recorded and that only comprehensive information was used for data analysis.

4. Conclusion

Even without an anaesthetic, hysteroscopy is a safe, sensitive, and dependable diagnostic tool that can be done on an outpatient basis. This test has been shown to be the gold standard for assessing the uterine cavity, which allows for the diagnosis and, in some cases, treatment of uterine issues that may be causing repeated miscarriages. The most common uterine anomaly in women who experience repeated miscarriages in the third trimester is a uterine septum.

Disclosure

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Authorship

All authors have a substantial contribution to the article

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Conflicts of interest

There are no conflicts of interest.

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