

**How to Cite:**

Labib, N. S., Mohesen, M. N., SaLem, S. A. mohamed, M. khalil, E., & El Wahed, H. A. A. (2022). Role of hysteroscopy in evaluation of recurrent pregnancy loss. *International Journal of Health Sciences*, 6(S1), 13983–13993. <https://doi.org/10.53730/ijhs.v6nS1.8666>

## **Role of hysteroscopy in evaluation of recurrent pregnancy loss**

**Noha Sayed Labib**

Asistant Lecturer of Obstetrics and Gynecology, Beni-suef University Hospital, Egypt

Corresponding author Email: [nohasayed456@yahoo.com](mailto:nohasayed456@yahoo.com)

**Mohamed Nagy Mohesen**

Lecture of Obstetrics and Gynecology department, Faculty of Medicine, Beni-suef University, Egypt

**Sara Abdallah mohamed SaLem**

Lecture of Obstetrics and Gynecology department, Faculty of Medicine, Beni-suef University, Egypt

**Eman M.khalil**

Lecture of Obstetrics and Gynecology department, Faculty of Medicine, Beni-suef University, Egypt

**Hamada Ashry Abd El Wahed**

Lecture of Obstetrics and Gynecology department, Faculty of Medicine, Beni-suef University, Egypt

**Abstract**--Objective: to detect the uterine abnormalities missed in U/S scan and HSG using hysteroscopy, in females presenting with recurrent pregnancy loss &to study hysteroscopic therapuatic potential to that pathology. Methodology: prospective cohort study, conducted in obstetrics & gynecology department of, Beni-suef University Hospital.on one hundred women with recurrent 1<sup>st</sup> &2<sup>nd</sup> trimester pregnancy loss recruited for hysteroscopy. A rigid fiberoptic 2.7mm, 0 and 30 degrees angled hysteroscopy along with an operative channel for grasping forceps or scissors were used for both diagnostic and operative indications. The findings, and different types of abnormalities, comparison between<or=3 &>3 cosecutive miscarriage as regarding hysteroscopic findings &impact of the procedure on management were recorded. Results: In this study In the normal hysteroscopy group, 24women (29.3%) achieved a successful ongoing pregnancy without additional treatment, 49 (59.8%) had recurrent miscarriages again, and 4(5%) had persistent secondary infertility .In women who needed and had hysteroscopic correction of a SUA, the

number of successful ongoing pregnancies was significantly higher 13 (72.2%) vs (29.3%) in normal group and the number of new abortions significantly was lower than in those who had no pathology 3(16.7%)vs (59.8%) with statistically significance between the 2 groups (p value = 0.002). Conclusion: It is observed that thin adhesions, polyps and small sub mucosal myomas that are not diagnosed by HSG or U/S can be diagnosed by hysteroscopy. And fine synechia were the most common abnormality detected in (7%) of the patients, 72..2% of patients with SUAs achieved a successful ongoing pregnancy following hysteroscopic metroplasty. Hysteroscopy has much to offer in the diagnosis and treatment of SUAs.

**Keywords**---Recurrent pregnancy loss, hysteroscopy, polyp, synechia, submucous myoma.

## Introduction

The journey from conception to birth is fraught with danger. It has been estimated that (50-70%) of all conceptions fail (1). A particular form of abortion, which causes great stress to patients and doctors, is the recurrent pregnancy loss (RPL) (2). RPL was defined as three or more consecutive pregnancy losses before the 20<sup>th</sup> week of gestation (3), but changed now to two or more consecutive pregnancy loss before 20<sup>th</sup> week of gestation. Most investigators agree that both ectopic and molar pregnancies should not be included in the definition (4). The incidence of RPL is 3-5 %. After the second loss, there is already a higher risk of miscarriage complicating the next gestation (5). Whereas inherited and acquired factors have been implicated in the etiology of RPL, most (50–60)% of the cases remain idiopathic (6).

The prevalence of uterine malformation is estimated to be 6.7% in the general population, slightly higher 7.3% in the infertility population, and significantly higher in a population of women with a history of recurrent miscarriages 16% (7). The uterine anomalies can be either congenital (i.e., Mullerian anomalies) or acquired (e.g., submucous myomas, endometrial polyps,adhesion) (5). The management of these abnormalities using hysteroscopy as inspecting device might therefore enhancing the pregnancy either spontaneously or after specialized fertility treatment ,such as intrauterine insemination or in vitro fertilization (8)

Nevertheless, even for experienced gynecologists the hysteroscopy diagnosis of the major uterine cavity abnormalities may be problematic (9). Recently, methodological and technological improvement results that diagnostic and operative hysteroscopy be more cost effective, efficient raising pregnancy rate (8) Recently,a reduction in hysteroscopy cost associated with reduced optical diameters has allowed hystertoscopy to be performed in outpatient basis with no anathesia use , minimal discomfort and optimal acceptance by patients(10).

## Patients and Methods

A consecutive cohort study was carried out in Beni suef university hospital after the approval of the research Ethics Committee on 100 non-pregnant patients with a history of two or more consecutive unexplained first and second trimester miscarriages before 20 weeks recruited from our outpatient clinic. A written informed consent was obtained from all patients before participation.

**Sample size estimation:** Sample size was calculated using EpiInfo® version 6.0, setting the power ( $\beta$ ) at 80% and significance level ( $\alpha$ ) at 0.05. Data from a previous study (11), indicated that the prevalence of uterine abnormalities was up to 27% of women with recurrent pregnancy loss. Calculation according to these values produced an average sample size of 100 cases.

**Inclusion criteria:** Normal transvaginal ultrasound scan, normal hormonal profile, normal urine analysis, normal lupus anticoagulant, anticardiolipin antibodies, normal complete blood count, normal Progesterone levels in the luteal phase, normal & non conclusive HSG result and all the husbands had a semen analysis within normal limits.

**Exclusion criteria:** Therapeutic abortion, patients with proved cause (s) for RPL, patients with acute or recent pelvic infection, patients with suspected or confirmed pregnancy, patients with uterine cavity pathology previously known to the examiners and patients were known to be carriers of balanced chromosomal anomalies. Patients had uncontrolled or previously undiagnosed endocrinological diseases such as diabetes or hypothyroidism.

## Methods

All patients were subjected to:

**History: Personal history:** name, age and occupation. **Menstrual history:** with special emphasis on date of last menstrual period to exclude pregnancy and regularity of the cycle & change of pattern. **Present history** regarding the patient's complaint with emphasis on presence of any symptoms denoting pelvic infection, and presence of vaginal bleeding. **Obstetric history:** with emphasis on the number of spontaneous abortion (causes, gestational age if possibly). **Surgical intervention:** (evacuation and curettage) and the occurrence of postoperative complication.

**Physical Examination including: General examination:** including pulse, temperature and blood pressure, with emphasis on presence of pallor, cyanosis and jaundice. **Abdominal examination:** with emphasis on presence of ascites, and presence of scars of previous operation. **Gynecological examination:** including inspection of external genitalia, digital examination including per vaginal and bimanual examination to detect the size of the uterus, its position, mobility, any cervical masses, any adnexal masses, speculum examination and rectal examination if necessary

**Hysteroscopy: Anesthesia:** general anesthesia was used.

**Procedure: Instrumentation:** Fiberoptic light, Hysteroscopic equipment telescope: rigid, 30 ° angles, the sheath have a 3-5-mm outer diameter, **Camera, Monitor.**

Speculum, a tenaculum and a sound were made ready to be used when needed. We carried out hysteroscopic removal of polyps, adhesions, and myomas and correction of the septate uterus in all patients affected, using wire loops under direct visualization. No surgery was performed in women with Arcuate uterus.

After that, the scope was removed and patient was recovered from anaesthesia. Finally the evaluation and the data that had been found were written in details by the surgeon. Any complication in the form of pain, bleeding, vasovagal attack and perforation, were registered in the patient sheet. All patients with adhesions had an intrauterine device inserted to prevent recurrence and they received conjugated equine oestrogens (0.625 mg daily for four months) for endometrial support. We follow up patients of normal & abnormal hysteroscopic findings following hysteroscopy and compare between both groups as regard successful ongoing pregnancy rates & abortion rates after hysteroscopy to assess its therapeutic potential to the pathology.

**1ryOut come:** Assessment of the prevalence and types of uterine defects missed by other methods in patients with recurrent miscarriage using hysteroscopy

**2ryOut come:** follow up of the patients following hysteroscopy till 25 wk of gestation & comparison between normal & SUA groups as regard successful ongoing pregnancy rate & abortion rate to assess the impact of ttt on successful ongoing pregnancy

**N.B.** we use the American Fertility Society/American Society for Reproductive Medicine classification of intrauterine adhesions.

## Results

This prospective cohort study was carried out in Beni suef university hospital after the approval of the research Ethics Committee on 100 non pregnant patients with a history of two or more consecutive unexplained first and second trimester miscarriages before 20 weeks recruited from our outpatient clinic.

Table (1): Number of patients with previous miscarriage

No of previous miscarriages	No(%)	Mean ±SD
2	41(41%)	Range(2-12)
3	30(30%)	
4	12(12%)	
5	10(10%)	
>5	7(7%)	

Majority of the patients had 2 previous miscarriages 41%. Table (1)

Table (2): Distribution of No. of previous first trimester miscarriages

No. of previous first trimester miscarriages	Frequency
0	4 %
1	14 %
2	26 %
3	28 %
4	19 %
>5	9 %

4% had no previous first trimester miscarriage, 14% had single previous first trimester miscarriage, 26% had 2 previous first trimester miscarriages, 28% had 3 previous first trimester miscarriages, 19% had 4 previous first trimester miscarriages, while 9% had  $\geq 5$  previous first trimester miscarriages. Table (2)

Table (3): Distribution of No. of previous second trimester miscarriages

No. of previous second trimester miscarriages	Frequency
0	62 %
1	13 %
2	12 %
3	5 %
4	5 %
>5	3 %

62% had no previous second trimester miscarriage, 13% had single previous second trimester miscarriage, 12% had 2 previous second trimester miscarriages, 5% had 3 previous second trimester miscarriages, 5% had 4 previous second trimester miscarriages, while 3% had  $\geq 5$  previous second trimester miscarriage. Table (3)

Table (4): Comparison between recurrent 1<sup>st</sup> versus 2<sup>nd</sup> trimester miscarriages as regard hysteroscopy findings

Findings	1 <sup>st</sup>	2 <sup>nd</sup>		p-value
Congenital anomalies			Chi square ( $\chi^2$ ) test x2(5, N=18) = 10.4	0.034*
▪ subSeptate uterus	0	1(20%)		
▪ Arcuate uterus	0	2(40%)		
Acquired anomalies				
▪ smallEndometrial polyp	5 (38.4%)	0		
▪ Intrauterine adhesions	6 (46.2%)	1(20%)		
▪ Submucous myoma	2 (15.4%)	1 (20%)		

There was a statistically significant difference between both groups as regard hysteroscopic results by using Chi square ( $\chi^2$ ) test. Table (4)

Table (5): Hysteroscopy Findings

Finding	No.( %)
Normal	82(82%)
Abnormal	18(18%)
Congenital anomaly	3(3%)
subSeptate uterus	1(1%)
Arcuate uterus	2(2%)
Acquired anomaly	15(15%)
Endometrial polyp	5(5%)
Intra uterine. Adhesions	7(7%)
Submucous myoma	3(3%)

82% of patients have normal hysteroscopy findings, while 18% of patients showing SUAs with 3% congenital anomalies and 15 % acquired, the most common anomaly was fine IUAs in 7 % of patients & Endometrial polyp in 5% of patients. Table (5)

Table (6): Comparison between normal &amp; abnormal groups as regard successful ongoing pregnancy and abortion rates after follow up

		FOLLOW.UP				Total	P-Value
		Successful Ongoing Pregnancy	Abortion	Loss follow-up	2ry infertility		
Normal group	Count	24	49	5	4	82	0.002
	%	29.3%	59.8%	6.1%	4.9%	100%	
SUAs Group	Count	13	3	0	2	18	
	%	72.2%	16.7%	0	11.1%	100%	

There was a statistically significant difference between normal & SUAs groups as regard Successful Ongoing Pregnancy & Abortion rates. Table (6)

## Discussion

Recurrent pregnancy loss (RPL) is the most stressful form of abortions for patients and doctors, (12). Petrozza (4), it is defined as two or more consecutive pregnancy losses before the 20th week of gestation. Most (the definition (12) The basic work-up has included a HSG to evaluate the uterine cavity and tubal patency. However, HSG does not allow for simultaneous correction of uterine pathology. Moreover HSG may miss 35% of uterine abnormalities. The high false-negative rate, the low-positive predictive value, and the inability to treat abnormal findings concurrently with the diagnosis have limited the use of HSG to assess the endometrial cavity (13). Sonohysterography (SHG) has been proposed as better diagnostic test of the uterine cavity. However, it also suffers from a sensitivity and specificity inferior to that of hysteroscopy in most studies.

The diagnosis and management of these abnormalities using hysteroscopy as inspecting device might therefore enhancing the pregnancy either spontaneously or after specialized fertility treatment, such as intrauterine insemination or in vitro fertilization (8). The American Society for Reproductive Medicine (ASRM) confirmed that hysteroscopy is the diagnostic and treatable method for the intrauterine disorders (8). This study aimed to assess the prevalence and types of uterine defects missed by other diagnostic methods in patients with recurrent miscarriage using hysteroscopy on 100 non-pregnant patients with a history of two or more consecutive unexplained first and second trimester miscarriages before 20 weeks were recruited from our clinic.

In the current study the mean maternal age was  $30.24 \pm 5.8$  years, most of the patient (36%) between (25-30) years, this result is consistent with other studies of Guimarães Filho, Mattar et al. (14) who found that mean maternal age was 28.1,  $30.8 \pm 6.2$ ,  $32 \pm 5$  years respectively. On the other hand, Dendrinou, Grigoriou et al. (11) found that mean maternal age older  $40.5 \pm 5.2$  years, this may be attributed to late age of marriage in their population.

In the present study the mean number of previous miscarriages was  $1.1 \pm 1.2$ , this result was in consistent with Weiss, Shalev et al. (15) who reported that the mean number of previous miscarriages was  $3.83 \pm 1.47$  this may due to they consider patients with 3 or more consecutive miscarriage. In the present study the mean number of prior deliveries was  $0.4 \pm 0.75$ , most of the patients were nullipara (71%), this was disagree with Weiss, Shalev et al. (15) who reported the mean number of prior deliveries was  $5.08 \pm 2.29$ , this may be attributed to decreased awareness of antenatal care & late obstetric consultation in our patients.

In this study it was found that most of the patients (56%) had  $\geq 3$  previous first trimester miscarriages while 13% of the patients had  $\geq 3$  previous second trimester miscarriages, these results are in agreement with Weiss, Shalev et al. (15) who found that 15% of the patients had  $\geq 3$  previous second trimester miscarriages. In the current study (71%) of the patients  $< \text{or} = 3$  previous miscarriages, 12% had 4 previous miscarriages, 10% had 5 previous miscarriages, while 7% had more than 5 previous miscarriages, these results similar to Guimarães Filho, Mattar et al. (14) who found that most of the patients (71.7%) had 3 previous miscarriages, 20% had 4 previous miscarriages, 6.7% had 5 previous miscarriages, 1.7% had  $> 5$  miscarriages. However the higher number of previous miscarriage in our population may be attributed to late obstetric consultation.

On the other hand abnormal hysteroscopic findings were found in 18% of patients and congenital uterine anomalies were present in 3% and acquired uterine anomalies in 15%, these results were in consistent to Weiss, Shalev et al. (15) who found that congenital uterine anomalies were present in 19%, acquired uterine anomalies was present in 11%. In contrast Dendrinou, Grigoriou et al. (11) found that most of the patients (31%) had acquired uterine anomalies. From the above data the uterine abnormalities associated with recurrent miscarriages in our study are mostly acquired in origin.

According to medical literature the prevalence of Uterine anomalies among patients with RPL vary from 15 to 27% (16). The reported rate of anomalies for

patients with recurrent miscarriages varies from 6.3 to 67%, with most studies showing more than 25% anomalies. This wide discrepancy for the rate of anomalies among patients with recurrent pregnancy losses represents differences in study design and in the types of anomalies reported (5). Results could also be influenced by the characteristics of the population: age of the population, hormonal status, ethnic factor, and the indications for hysteroscopy.

In our study, 15 patients (15%) were found to have uterine cavity changes as detected by hysteroscope, with 3 of them having congenital anomalies (2 cases of arcuate uterus and 1 case of septate uterus) and 15 having acquired anomalies (2 cases of small submucous myoma, 5 cases of small polyps and 7 cases of mild intrauterine synechia) similar to Dendrinios et al in (11) who studied 48 women with more than three consecutive pregnancy losses which occurred prior to the 20th week and hysteroscopy was performed on all of them. 25 women (52%) had normal hysteroscopic findings. The remaining 23 women (48%) presented structural uterine anomalies (SUA): 9 patients had intrauterine adhesions, 4 patients had polyps, 2 patients had sub mucous myomas and 8 patients had congenital structural anomalies (5 cases of septate uterus and 3 cases of bicornuate uterus)

Intrauterine adhesions found in 10% to 15% of subfertile patient ([17 FINA DISCUSSION.docx - ENREF 28](#)) usually resulting from endometritis, curettage, intrauterine surgery to remove myomas or to correct structural defect of the uterus, and caesarean section. An abortion can occur as a consequence of a reduction in the endometrial surface to embryo implantation, or due to uterine expansion difficulties (18)

Myomas are usually asymptomatic during gestation, however, there is evidence suggesting a connection with a higher risk of infertility, spontaneous abortion and preterm labor. It is estimated that about 41% of women with myomas, especially submucous ones, could abort (19). In the current study sub septate uterus was the less common uterine anomaly affecting only 1% of the patients. This result is similar to Weiss, Shalev et al. (15) who found septate uterus in 13% of the patients, on the other hand this result was agreed with Salim, Regan et al. (5), Dendrinios, Grigoriou et al. (11) who found intrauterine adhesions was the most common anomaly affecting 19% of the patients, 26% risk of reproductive loss (4)

However, the importance of uterine abnormalities on the genesis of the recurrent miscarriage, as well as the severity of the defect necessary to cause the gestation interruption is still controversial (5). In the current study there was no statistical significant difference between patients with recurrent first and second trimester miscarriages as regard Age, this result was agreed with Weiss, Shalev et al. (15) who found that no significant difference between the two groups. Also there was no statistical significant difference between patients with recurrent first and second trimester miscarriages as regard number of prior deliveries, these in agreement with (11).

But there was statistical significant difference between patients with recurrent first and second trimester miscarriages as regard uterine abnormalities acquired more with 1<sup>st</sup> trimester while congenital more with 2<sup>nd</sup> trimester (p value=0.034).

In the current study, the anatomical changes were detected in 8 (11.2%) out of 71(71%) patients with three or less miscarriages compared with 10(34.4%) out of 29 (29%) patients with more than three consecutive miscarriages with statistically significant difference ( $p$  value =0.003). These results are in disagreement with previous studies Weiss et al., (15), Dendrinos et al., (11) demonstrating that although there was a high incidence of anatomical changes in the population of patients with repeated miscarriages, there was no differences in the incidence of findings regarding patients with three miscarriages compared with those with more than three miscarriage.

After follow up of the patients of normal & abnormal hysteroscopic findings following hysteroscopy, we found 13 women achieved a successful ongoing pregnancy (72.2%) and three women miscarried again (16.7%) & (11%) had 2ry infertility. In the SUA group in agreement with Dendrinos et al., (11) in which 8 women achieved a successful ongoing pregnancy (78%) and five women miscarried again (22%) In the SUA group. Venturoli et al., (20) also achieved a 52% pregnancy rate after hysteroscopic metroplasty in a trial including 141 women with infertility problems and HA.

In the normal hysteroscopy group, twenty four women (29.3%) achieved a successful ongoing pregnancy without additional treatment, 49(59.8%) had recurrent miscarriages, and four (5%) had persistent secondary infertility. The rate of successful, ongoing pregnancies in patients with SUAs was 72.2% in our study, as compared to 29.3% in patients with HA but no SUA with statistically significant difference ( $p$  value =0.002). The rate of new abortions in patients with SUAs was 16.7% in our study, as compared to 59.8% in patients with no SUA with statistically significant difference ( $p$  value =0.002).

Dendrinos et al., (11) also found that women who needed and had hysteroscopic correction of a SUA, the number of successful ongoing pregnancies was significantly higher ( $p$   $\frac{1}{4}$  0.0004) and the number of new abortions significantly lower ( $p$   $\frac{1}{4}$  0.0006) than in those who had no pathology. Finally this study showed that thin adhesions, polyps and small sub mucosal myomas, small septum that are not diagnosed by HSG or U/S can be diagnosed by hysteroscopy. Women tolerance, safety, and feasibility of simultaneous operative correction make the proposed hysteroscopy an ideal and routine procedure in order to diagnose and to treat missed intrauterine abnormalities, in cases with recurrent pregnancy loss.

## **Conclusion**

It appears that hysteroscopy is useful tool in the diagnosis of uterine causes of recurrent miscarriage that may be missed by hysterosalpingography or ultrasonography and also useful tool for management that can be performed safely and efficiently in most cases.

**Conflict of interest:** no conflicts of interest.

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