

## Hysteroscopy in the Evaluation of Recurrent Miscarriage

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**Abstract: Objective:** assessment of prevalence and types of uterine defects through hysteroscopy. **Methods:** A consecutive cohort of 100 non-pregnant patients with a history of three or more consecutive unexplained first and second trimester miscarriages before 20 weeks were recruited from clinic. A written informed consent was obtained from all patients before participation. **Results:** 71 % of patients have normal hysteroscopic findings, while 29% of patients showing abnormal findings with 16% congenital anomalies and 13% acquired, the most common anomaly was septate uterus in 11% of patients. **Conclusion:** It appears that hysteroscopy is a most useful tool in the diagnosis of recurrent miscarriage that can be performed safely and efficiently without anesthesia in most cases. The prevalence of uterine anomalies in patients with unexplained recurrent miscarriages is 29%, septate uterus was the most common anomaly and for this reason uterine anomalies should be systematically assessed in patients with previous unexplained recurrent miscarriage.

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**Keywords:** Hysteroscopy, recurrent miscarriage

### 1. Introduction:

The journey from conception to birth is fraught with danger. It has been estimated that (20-30) % of all conceptions fail (*Salmon, 2004*). A particular form of abortion, which causes great stress to patients and doctors, is the recurrent pregnancy loss (RPL) (*Barranger et al., 2002*).

RPL defined as three or more consecutive pregnancy losses before the 20<sup>th</sup> week of gestation (*Sierra and Stephenson, 2006*).

Hysteroscopy offers great assistance for the interpretation of uncertain findings from other diagnostic methods. Furthermore it enables direct visualization of cervical canal, uterine cavity and increase the precision and accuracy in the diagnosis of intrauterine abnormalities (*Ceci et al., 2004*)

#### Uterine Cavity Assessment:

There are few accurate methods investigating uterine cavity (ultrasound, HSG, hysterosonography and magnetic resonance imaging) however the gold standard for uterine cavity assessment is hysteroscopy. (*Barranger et al., 2002*).

Recurrent pregnancy loss (Miscarriage) is the commonest complication of pregnancy. The generally accepted definition stipulates that the fetus or embryo should weigh 500 gm or less, a stage corresponding to a gestational age of 20 weeks, according to the world health organization.

The number of miscarriages has been a debate, according to the Royal college of obstetricians and gynecologists, the definition is three or more consecutive losses (*RCOG guidelines, 2003*), but according to American college of obstetricians and

gynecologists (*ACOG, 2001*), and the American society for reproductive medicine, the definition is two or three consecutive losses.

### 2. Patients and Methods:

This study was carried out in ALazhar Maternity hospital after the approval of the research Ethics Committee, during the period between March 2013 and February 2015. A consecutive cohort of 100 non-pregnant patients with a history of three or more consecutive unexplained first and second trimester miscarriages before 20 weeks were recruited from clinic. A written informed consent was obtained from all patients before participation.

#### Inclusion criteria:

1. Normal transvaginal ultrasound scan.
2. Normal urinalysis.
3. None of the patients is a carrier of Neisseria gonorrhoea, Chlamydia trachomatis or Syphilis as proved by cervical smear.
4. Normal lupus anticoagulant, anticardiolipin antibodies.
5. Normal complete blood count.
6. Normal Sedimentation rate.
7. Normal Progesterone levels in the luteal phase.
8. All the husbands had a spermogram within normal limits.

#### Exclusion criteria:

1. Therapeutic abortion.
2. Patients with proved cause (s) for RPL.
3. Patients with acute or recent pelvic infection.
4. Patients with suspected or confirmed

pregnancy.

5. Patients with uterine cavity pathology previously known to the examiners.

6. Patients were known to be carriers of balanced chromosomal anomalies.

7. Patients had uncontrolled or previously undiagnosed endocrinological diseases such as diabetes or hypothyroidism.

**Methods:**

- All patients will be subjected to.

**I. History taking:**

- Personal history.
- Menstrual cycle regulation.
- Detailed 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:**

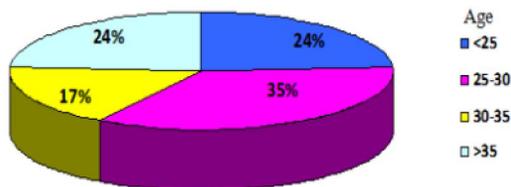
General, Abdominal and pelvic examination.

**II. Office hysteroscopy.**

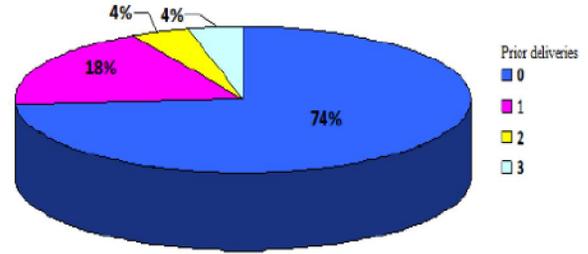
**Statistical analysis:**

- Analysis of data was done by IBM computer using SPSS (statistical package for social science version 12) as follows
- Description of quantitative variables as mean, SD and range
- Description of qualitative variables as number and percentage
  - Chi-square test was used to compare qualitative variables between groups.
  - Fisher exact test was used when one expected cell or more are less than 5.
  - Unpaired t-test was used to compare quantitative variables, in parametric data (SD<50% mean)'.
    - Mann Whitney test was used instead of unpaired t-test in non-parametric data (SD>50%mean).
    - Spearman Correlation co-efficient test was used to rank variables versus each other positively or inversely
      - *P value >0.05 insignificant.*
      - *P<0.05 significant.*
      - P<0.01 highly significant.*

**Results:**



**Fig 1: Distribution of the patients as regard age.**



**Fig 2: Distribution of the patients as regard prior deliveries.**

The current study was conducted in Al azhar University Maternity Hospital during the period between March 2013 and February 2015. A total of 100 women with recurrent unexplained miscarriage were included in the study.

**Table 1: Distribution of the patients as regard general characteristics**

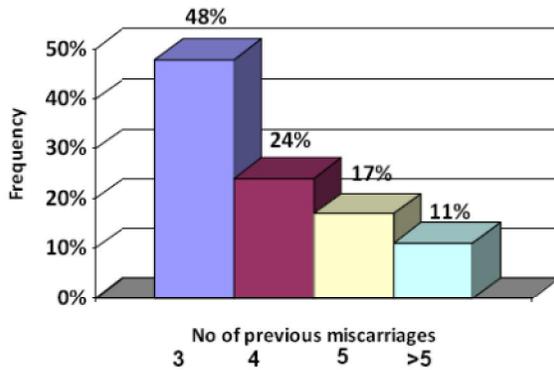
Variables	No	%
<b>Age</b>		
<25	24	24%
25-30	35	35%
30-35	17	17%
>35	24	24%
<b>Mean + SD</b>	30.1+6	18-43
<b>Prior deliveries</b>		
0	74	74%
1	18	18%
2	4	4%
3	4	4%
<b>Mean ± SD</b>	1+0.3	0-3

This table shows that majority of the studied cases 35% aged between (25-30) years, most of the patients were nullipara 74%.

**Table 2: Number of patients with previous miscarriages.**

No of previous miscarriages	No	%
3	48	48
4	24	24
5	17	17
> 5	11	11
<b>Mean + SD</b>	4+1.6	3-12

This table shows that majority of the patients had 3 previous miscarriages 48%.

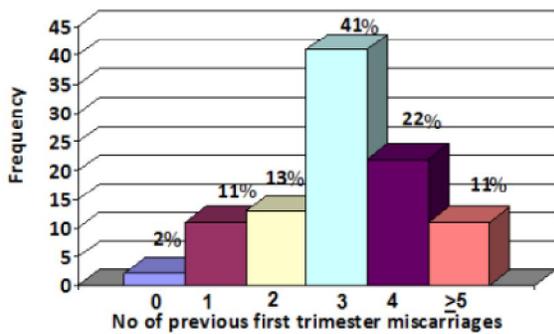


**Fig 3: Distribution of No. of Previous Miscarriages.**

**Table 3: Distribution of No. of previous first trimester miscarriages.**

No. of previous first trimester miscarriages	Frequency
0	2 %
1	11 %
2	13 %
3	41 %
4	22 %
≥ 5	11 %

This table show that 2% had no previous first trimester miscarriage, 11% had single previous first trimester miscarriage, 13% had 2 previous first trimester miscarriages, 41% had 3 previous first trimester miscarriages, 22% had 4 previous first trimester miscarriages, while 11% had ≥ 5 previous first trimester miscarriages.



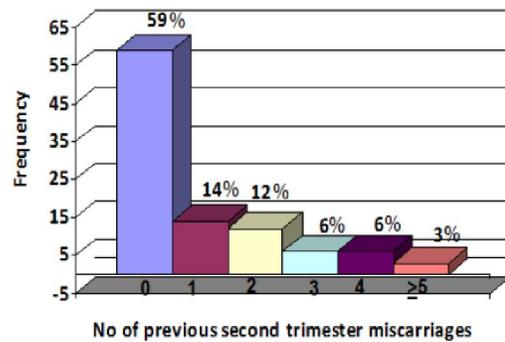
**Fig 4: Distribution of No. of Previous First Trimester Miscarriages.**

Table 4 shows that, 59% had no previous second trimester miscarriage, 14% had single previous second

trimester miscarriage, 12% had 2 previous second trimester miscarriages, 6% had 3 previous second trimester miscarriages, 6% had 4 previous second trimester miscarriages, while 3% had ≥ 5 previous second trimester miscarriages.

**Table 4: Distribution of No. of previous second trimester miscarriages.**

No. of previous second trimester miscarriages	Frequency
0	59 %
1	14 %
2	12 %
3	6 %
4	6 %
≥ 5	3 %

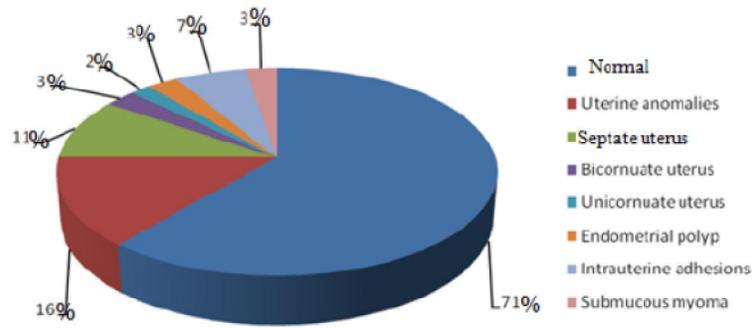


**Fig 5: Bar-Chart showing Distribution of No. of Previous Second Trimester Miscarriages.**

**Table 5: Hysteroscopic Findings.**

Finding	No.	%
<b>Normal</b>	71	71%
<b>Abnormal</b>	29	29%
<b>Congenital anomaly</b>	16	16%
Septate uterus	11	11%
Bicornuate uterus	3	3%
Unicornuate uterus	2	2%
<b>Acquired anomaly</b>	13	13%
Endometrial polyp	3	3%
Intrauter. Adhesions	7	7%
Submucous myoma	3	3%

This table shows that 71 % of patients have normal hysteroscopic findings, while 29% of patients showing abnormal findings with 16% congenital anomalies and 13% acquired, the most common anomaly was septate uterus in 11% of patients.



**Fig 6: Pie-Chart showing distribution of hysteroscopic findings.**

**Table 6: Comparison between recurrent 1<sup>st</sup> versus 2<sup>nd</sup> trimester miscarriages as regard hysteroscopic findings.**

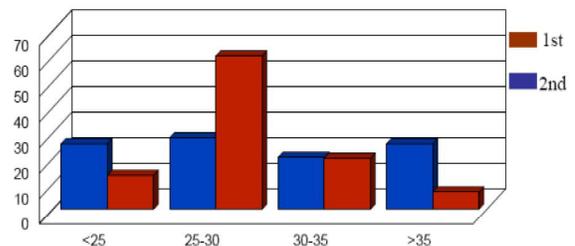
Findings	1 <sup>st</sup> N=74	2 <sup>nd</sup> N=15	X <sup>2</sup>	P
<b>Congenital anomalies</b>				
• Septate uterus	6(8.1%)	2(13.3%)	0.15	>0.05 NS
• Bicornuate uterus	2(2.7%)	1(6.7%)		
• Unicornuate uterus	1(1.4%)	0		
<b>Acquired anomalies</b>				
• Endometrial polyp	2(2.8%)	0	Fisher	>0.05 NS
• Intrauterine adhesions	3(4.1%)	2(66.7%)		
• Submucous myoma	2(2.8%)	1(6.7%)		

This table shows that no statistically significant difference between both groups as regard uterine anomalies. By using Fisher exact test.

**Table 7: Comparison between recurrent 1<sup>st</sup> versus 2<sup>nd</sup> trimester miscarriages as regard age and prior deliveries.**

Variables	1 <sup>st</sup> N=74	2 <sup>nd</sup> N=15	X <sup>2</sup>	P
<b>Age</b>				
• <25	19(25.7%)	2(13.3%)	6	<0.05 S
• 25-30	21(28.4%)	9(60%)		
• 30-35	15(20.3%)	3(20%)		
• >35	19(25.7%)	1(6.7%)		
<b>Prior deliveries</b>				
• 0	52(70.3%)	12(80%)	1.5	>0.05 NS
• 1	15(20.3%)	3(20%)		
• 2	4(5.4%)	0		
• 3	3(4.1%)	0		

This table shows patients with recurrent first trimester miscarriages are older than patients with recurrent second trimester miscarriages with statistically significant difference by using chi-square test. No significant difference as regard prior deliveries.



**Fig 7: Comparison between recurrent 1<sup>st</sup> versus 2<sup>nd</sup> trimester miscarriages as regard age and prior deliveries.**

**Table 8: Comparison between patients with 3 versus > 3 consecutive miscarriages as regard age and prior deliveries.**

Variables	3 consecutive miscarriages N=48	>3 consecutive miscarriages N=52	X <sup>2</sup>	P
<b>Age</b>				
• <25	15(31.5%)	9(17.3%)	3.5	>0.05 NS
• 25-30	13(27.1%)	22(42.3%)		
• 30-35	9(18.8%)	8(15.4%)		
• >35	11(22.9%)	13(25%)		
<b>Prior deliveries</b>				
• 0	37(77.1%)	37(71.2%)	1.1	>0.05 NS
• 1	8(16.7%)	10(19.2%)		
• 2	2(4.2%)	2(3.8%)		
• 3	1(2.1%)	3(5.8%)		

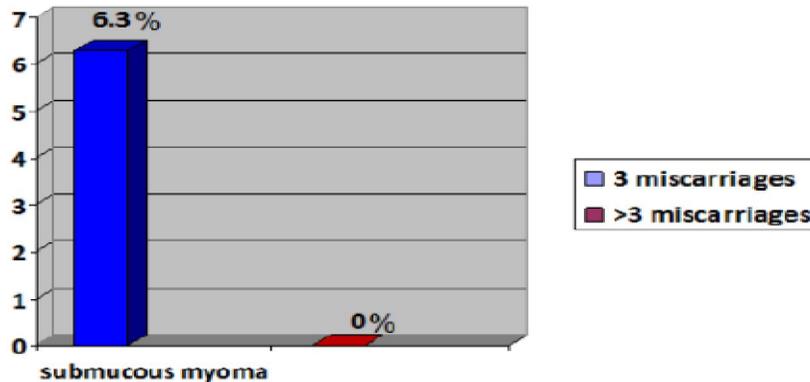
This table shows no statistically significant difference between both groups as regard age and prior deliveries by using chi-square test.

**Table 9: Comparison between patients with 3 and > 3 consecutive miscarriages as regard hysteroscopic findings.**

Findings	3 consecutive miscarriages N=48	>3 consecutive miscarriages N=52	X <sup>2</sup>	P
<b>Congenital anomalies</b>				
• Septate uterus	3(6.3%)	8(15.4%)	1.7	>0.05 NS
• Bicornuate uterus	2(4.1%)	1(19.2%)		
• Unicornuate uterus	1(2%)	1(19.2%)		
<b>Acquired anomalies</b>				
• Endometrial polyp	2(4.2%)	1(2%)	Fisher	>0.05 NS >0.05 NS <0.05 S
• Intrauterine adhesions	3(6.3%)	4(7.7%)		
• Submucous polyp	3(6.3%)	0		

This table shows that sub mucous myoma associated with patients with 3 consecutive miscarriages with significant difference by using

Fisher exact test. No statistically significant difference as regard other anomalies.



**Fig 8: Comparison between patients with 3 and > 3 consecutive miscarriages as regard sub mucous myoma.**

**Table 10: Correlation between age and prior deliveries versus number of miscarriages.**

Variables	No. of miscarriages		First trimester		Second trimester	
	R	P	R	P	R	P
<b>Age</b>	0.15	>0.05	0.22	>0.05	0.16	>0.05
<b>Parity</b>	0.09	>0.05	0.13	>0.05	0.19	>0.05

This table shows no significant correlations between age prior deliveries and number of miscarriages by using correlation co-efficient test.

#### Discussion:

Recent data on recurrent miscarriage (RM) is discussed in the framework of the selection failure hypothesis which states, 'Recurrent miscarriage is the result of failure of the prevention of 'poor quality embryos implanting, allowing embryos that are destined to fail to implant and present clinically as recurrent miscarriage (*Quenby et al., 2002*).

Recurrent miscarriage is a failure of nature's quality control. The assumption that RM results from the maternal rejection of normal fetuses is challenged and evidence reviewed regarding the contribution of abnormal embryos and endometrial receptivity. Further research is needed to understand the mechanisms of maternal tract-embryo interaction and move towards improved management of recurrent pregnancy loss (*Quenby et al., 2002*).

Uterine abnormalities are estimated to play a causal role in a substantial number of couples seeking treatment for recurrent miscarriages (*Michael et al., 2010*).

Their assumed pathophysiological mechanism is that they impair proper embryo implantation and growth due to poor vascularization with subsequent infertility or miscarriage (*Brown et al., 2000*).

In the present study the mean maternal age was 30.1+6 years, most of the patient (35%) between (25-30) years, this result is consistent with other studies of *Ventolini et al., (2004); Weiss et al., (2005) and Guimarães Filho et al., (2006)* who found that mean maternal age was 28.1, 30.8 ± 6.2, 32 ± 5 years respectively. On the other hand *Dendrinis et al., (2008)* found that mean maternal age older 40.5+5.2 years, this may be attributed to late age of marriage in their population.

In this study the mean number of previous miscarriages was 4 ± 1.6, this result was consistent with *Weiss et al., (2005)* who reported that the mean number of previous miscarriages was 3.83 ± 1.47.

In the present study the mean number of prior deliveries was 1 ± 0.3, most of the patients were nullipara, this was disagree with *Weiss et al., (2005)* who reported the mean number of prior deliveries was 5.08 ± 2.29, this may be attributed to decreased awareness of antenatal care in our patients.

In the current study most of the patients (48%) had 3 previous miscarriages, 24% had 4 previous miscarriages, 17% had 5 previous miscarriages, while 11% had more than 5 previous miscarriages, these results similar to *Guimarães Filho et al., (2006)* 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. In this study it was found that most of the patients (74%) had ≥3 previous first trimester miscarriages while 15% of the patients had ≥3 previous second trimester miscarriages, these results are in agreement with *Weiss et al., (2005)* who found that 16% of the patients had ≥3 previous second trimester miscarriages.

Anatomical uterine defects, including Mullerian anomalies, adhesions and fibroids, are frequently found in women with recurrent miscarriage whether of the first or second trimester (*Propst and Hill, 2000*).

In the current study, normal hysteroscopic findings were the most common findings in (71%) of the patients, these results are consistent with *Weiss et al., (2005)* who reported that 70% of the patients had normal hysteroscopic findings, on the other hand *Guimarães Filho et al., (2006) and Dendrinis et al., (2008)* found normal findings in 58.3%, 52% respectively.

In this study it was found that abnormal hysteroscopic findings were found in 29% of patients and congenital uterine anomalies were present in 16% and acquired uterine anomalies in 13%, these results were similar to *Weiss et al., (2005)* who found that congenital uterine anomalies were present in 19%, acquired uterine anomalies was present in 11%. In contrast, *Dendrinis et al., (2008)* found that 31% of the patients had acquired uterine anomalies.

From the above data the most important uterine abnormalities associated with recurrent miscarriages are congenital in origin.

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 (*Salim et al., 2003*).

In the current study septate uterus was the most common uterine anomaly affecting 11% of the patients which was confirmed by laparoscopy.

This result similar to *Weiss et al., (2005)* who found septate uterus in 13% of the patient, on the other hand this result was disagreed with *Dendrinios et al., (2008)* who found intrauterine adhesions was the most common anomaly affecting 19% of the patients.

The septate uterus, according to medical literature, is the most common congenital uterine anomaly, representing 50 to 80% of the müllerian alterations. It is also the anomaly with the worst reproductive prognosis, with abortion levels varying from 67 to 87% (*Alborzi et al., 2002*).

In our study intra uterine adhesions were the most common acquired uterine anomalies in 7% of the patients.

In this study sub mucous myoma was present in 3% of the patients and endometrial polyp in 3%.

In the current study there was no statistical significant difference between patients with recurrent first and second trimester miscarriages as regard uterine anomalies or number of prior deliveries, these in agreement with *Dendrinios et al., (2008)* and *Weiss et al., (2005)*.

In this study the patients with recurrent first trimester miscarriages are older than patients with recurrent second trimester miscarriages, this result was disagree with *Weiss et al., (2005)* who found that no significant difference between the two groups. However they compared patients with two consecutive miscarriages versus patients with three consecutive miscarriages.

In the present study there were no statistical significant difference between patients with 3 and >3 consecutive miscarriages as regard age and prior deliveries, on the other hand there was association between patients with 3 consecutive miscarriages with presence of sub mucous myoma.

In the current study there were no significant correlations between age, prior deliveries and number of miscarriages.

#### **Recommendations:**

Further studies with large numbers and long term follow up of the patients are recommended. Because uterine anomalies are the most treatable causes of recurrent miscarriage, further studies are recommended for assessment of the role of hysteroscopic surgical correction of uterine anomalies on pregnancy outcome.

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