

Role of Hysteroscopy in Evaluation of Recurrent Pregnancy Loss

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Abstract: The purpose of this study was to the usage of hysteroscopy to assess the prevalence and types of uterine defects in patients with recurrent pregnancy loss. Hysteroscopy was found that 72% of patients have normal hysteroscopy findings, while 28% of patients showing abnormal findings with 16% congenital anomalies and 12% acquired, the most common anomaly was septate uterus in 8% of patients. No statistically significant difference between both groups as regard uterine anomalies. Comparison between recurrent 1st versus 2nd trimester miscarriages as regard age and prior deliveries found that, 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. There was no significant correlations between age prior deliveries and number of miscarriages.

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1. Introduction

Recently methodological and technological improvement results that diagnostic and operative hysteroscopy be more cost effective, efficient raising pregnancy rate (Bosteels, Kasius *et al.*, 2015), safe, and useful in infertile patients (Carneiro, 2014).

When the implantation successfully happened in the uterine cavity by the adhesion between the blastocyst and the endometrium (Quaranta, Erez *et al.*, 2015), human life starts. After one year of trying to get pregnant, infertility is diagnosed. Primary defined if no conception happened before and secondary in previous conception. About 40% of infertile couples due to multiple causes (F., Hacker MD *et al.*, 2010).

It is known that the uterine abnormalities, such as polyps, fibroids, septa or adhesions, may disturb the pregnancy. The uterine anomalies distribution and frequency are similar in patients with two or more consecutive miscarriages and the diagnostic hysteroscopy can be recommended after two miscarriages (B. Seçkin1, E. Sarikaya1 *et al.*, 2012).

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 (Bosteels, Kasius *et al.*, 2013, Bosteels, Kasius *et al.*, 2015). Nevertheless, even for experienced gynecologists the hysteroscopy diagnosis of the major uterine cavity abnormalities may be problematic (Güven, Bakay *et al.*, 2012).

About 70-75% of all conceptions fail (F., Hacker MD *et al.*, 2010), of those that are recognized, 15-20% result in spontaneous abortions (SABs) or ectopic pregnancies (Petrozza, 2012). Unexplained subfertility can be found in 30% to 40% of subfertile couples (Güven, Bakay *et al.*, 2012). Intrauterine adhesions are in 0.3% to 14% of subfertile women (Fatemi, Kasius *et al.*, 2010), uterine septum is present in 1% to 3.6% of women with otherwise unexplained subfertility (Saravelos, Cocksedge *et al.*, 2008).

Recurrent pregnancy loss (RPL) is the most stressful form of abortions for patients and doctors (Carp, Barranger, Gervaise *et al.*, 2002, Jeve and Davies 2014). Petrozza (2012), it is defined as three or more consecutive pregnancy losses before the 20th week of gestation (Sierra and Stephenson, 2006). Most investigators agree that both ectopic and molar pregnancies should not be included in the definition (Petrozza 2012).

The prevalence of uterine malformation is 6.7% in the general population, slightly higher 7.3% in the infertility population, and more in women's with a history of recurrent miscarriages 16% (Bosteels, Weyers *et al.*, 2010).

The significance of uterine polyps and leiomyoma in RPL is unclear; they can interfere with fertility (Bailey, Jaslow *et al.*, 2015), creating a hostile environment to embryo implantation. With about 41% of women having leiomyoma, especially sub mucous one, could abort (Trivedi and Abreo 2009, Desai and Patel 2011)

The aim of work was the usage of hysteroscopy to assess the prevalence and types of uterine defects in patients with recurrent pregnancy loss (RPL).

2. Patients and Methods

This study was carried out in El Sayed Galal University hospital after the approval of the research Ethics Committee,. A consecutive cohort of 50 non-pregnant patients with a history of three or more consecutive unexplained first and second trimester miscarriages before 20 weeks were recruited from recurrent miscarriage clinic. A written informed consent was obtained from all patients before participation.

Sample size was calculated using Epi Info® version 6.0, setting the power (β) at 80% and significance level (α) at 0.05. Data from a previous study (**Dendrinios, Grigoriou et al., 2008**), indicated that the prevalence of uterine anomalies was 27% of women with recurrent pregnancy loss. Calculation according to these values produced an average sample size of 100 case.

3. Results

This study was carried out in EL-Sayed Galal Hospital after the approval of the research Ethics Committee. A consecutive cohort of 50 non-pregnant patients with a history of three or more consecutive unexplained first and second trimester miscarriages before 20 weeks will be recruited from recurrent miscarriage clinic. The data was collected, tabulated and analyzed as follows:

The general characteristics of the studied group, the age was ranged from 22-37 years with a mean of 29.48 ± 4.63 years, the most frequent age group was between (25-30) years (36.0%) of the patients. Regarding previous deliveries most of the patients were nullipara 76.0%. The number of previous miscarriages, the miscarriages ranged from 3-10 with mean 4.34 ± 1.87 , the majority of the patients had 3 previous miscarriages 46.0%.

The distribution of studied group regarding the number of previous first trimester miscarriages. It was found that 4.0% had no previous first trimester miscarriage, 12% had single previous first trimester miscarriage, 12% had 2 previous first trimester miscarriages, 38% had 3 previous first trimester miscarriages, 24% had 4 previous first trimester miscarriages, while 10% had ≥ 5 previous first trimester miscarriages.

The distribution of the studied patients regarding the number of previous second trimester miscarriages, it was found that, 62.0% had no previous second trimester miscarriage, 12% had single previous second trimester miscarriage, 8% had 2 previous second trimester miscarriages, 8% had 3 previous second trimester miscarriages, 6% had 4 previous second trimester miscarriages, while 2% had ≥ 5 previous second trimester miscarriage.

Table (1): Distribution of the studied patients regarding hysteroscopy findings.

Finding	No.	%
Normal	36	72.0
Abnormal	14	28.0
Congenital anomaly	8	16.0
▪ Septate uterus	4	8.0
▪ Bicornuate uterus	2	4.0
▪ Unicornuate uterus	2	4.0
Acquired anomaly	6	12.0
▪ Endometrial polyp	1	2.0
▪ Intrauter. Adhesions	3	6.0
▪ Submucousmyoma	2	4.0

Table (1), shows Distribution of the studied patients regarding hysteroscopy findings, it was found that 72% of patients have normal hysteroscopy findings, while 28% of patients showing abnormal findings with 16% congenital anomalies and 12% acquired, the most common anomaly was septate uterus in 8% of patients.

Table (2): Comparison between recurrent 1st versus 2nd trimester miscarriages as regard hysteroscopy findings

Findings	1 st (N=37)		2 nd (N=8)		Fisher exact test p-value
	No.	%	No.	%	
Congenital anomalies					0.75
▪ Septate uterus	2	5.4	1	12.5	
▪ Bicornuate uterus	1	2.7	1	12.5	
▪ Unicornuate uterus	1	2.7	0	0	
Acquired anomalies					0.66
Endometrial polyp	1	2.7	0	0	
Intrauterine adhesions	1	2.7	1	12.5	
Submucousmyoma	0	0.0	0	0	

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

Table (3): Comparison between patients with 3 and >3 consecutive miscarriages as regard hysteroscopy findings

Findings	3 consecutive miscarriages N=23		>3 consecutive miscarriages N=27		Fisher exact test p-value
	No.	%	No.	%	
Congenital anomalies	2	8.7	2	7.4	0.44
▪ Septate uterus	1	4.3	1	3.7	
▪ Bicornuate uterus	0	0.0	2	7.4	
▪ Unicornuate uterus					
Acquired anomalies	1	4.3	0	0.0	0.399
▪ Endometrial polyp	1	4.3	2	7.4	
▪ Intrauterine adhesions	0	0.0	2	7.4	
▪ Submucous polyp					

Table (3), show the comparison between patients with 3 and >3 consecutive miscarriages as regard hysteroscopy findings, it was found 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.

4. Discussion

Recurrent pregnancy loss (RPL) generally refers to the occurrence of three or more consecutive losses of clinically recognized pregnancies prior to the 20th week of gestation; RPL is seen in 3–5% of women. (Li *et al.*, 2002). Fifteen twenty percentage of all human pregnancies usually terminate in clinically recognized abortion. The incidence of total human embryonic loss is estimated to be much higher—as high as 31–70%. Chromosomal abnormalities account for 2–10% of clinically recognized RPL and are easily identifiable through genetic amniocentesis and karyotyping. A woman's reproductive history is the most relevant predictive factor for current pregnancy Outcomes.

The etiology of RPL includes genetic abnormalities, immunologic disorders, thrombotic pregnancies, endocrine dysfunction, anatomical defects of the uterus, and idiopathic causes [13]. They can be divided according to their therapeutic potential into treatable and currently untreatable causes [3]. The treatable causes are structural uterine defects, endocrine dysfunction (luteal phase deficiency), thrombotic pregnancies (thrombophilias or autoantibodies), and immunologic disorders (immunoglobulins and immunization). The currently untreatable causes are genetic abnormalities and idiopathic etiologies.

The purpose of this study was to the usage of hysteroscopy to assess the prevalence and types of uterine defects in patients with recurrent pregnancy loss.

This study was carried out in EL-Sayed Galal Hospital after the approval of the research Ethics Committee. A consecutive cohort of 50 non-pregnant patients with a history of three or more consecutive unexplained first and second trimester miscarriages before 20 weeks were recruited from recurrent miscarriage clinic. A written informed consent will be obtained from all patients before participation.

Regarding the general characteristics of the studied group, the age was ranged from 22-37 years with a mean of 29.48±4.63 years, the most frequent age group was between (25-30) years (36.0%) of the patients. Regarding previous deliveries most of the patients were nullipara 76.0%. The number of previous miscarriages ranged from 3-10 with mean 4.34±1.87, the majority of the patients had 3 previous miscarriages 46.0%.

Comparison between patients with 3 and >3 consecutive miscarriages as regard hysteroscopy findings found 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. Regarding correlation between age and prior deliveries versus number of miscarriages, found that there was no significant correlations between age prior deliveries and number of miscarriages.

In study of Ventolini, et al., (2004), which comprised a large family practice population, most of the patients with a history of RPL did not have SUD. Among the patients with RPL related to SUD, the presence of intrauterine adhesions was the most prevalent diagnosis. The therapeutic efficacy for patients with RPL secondary to SUD has been shown to be good in different studies.

The rate of successful pregnancies after the operative hysteroscopy and medical treatment of the SUD in the study approached 78%, as compared to the successful pregnancy rate of only 28.6% in patients with RPL but no uterine anatomical defects ($p < 0.5$).

The two groups were comparable and there was no statistical difference in terms of age, race, parity, or weight. If they could identify the patients with SUD as the cause of RPL and selectively exclude other identifiable causes, we could suggest that in a population like ours (large family medicine practice) the chances of achieving a successful pregnancy are close to 78%.

Studies have sought to analyze if the traditional definition for repeated miscarriage, considering three consecutive episodes, should be reviewed; however, findings are still incipient¹⁻⁵. Our study is in accordance with previous studies demonstrating that although there is a high incidence of anatomical changes in the population of patients with repeated miscarriages^{1,3,19}, there is no difference in incidence of findings regarding patients with two miscarriages compared with those with three or more events.

Jaslow et al., by evaluating a large series of repeated miscarriage cases demonstrated immune changes were similarly distributed, regardless the number of miscarriages. This set of findings indicates the assessment of patients with repeated miscarriages can be reviewed, by trying to identify the patients earlier and in a more particular way. Over the last years, hysteroscopy has been shown as an excellent diagnostic and therapeutic tool in gynecology.

Carlos, et al., (2011) have found a high prevalence of acquired anatomical abnormalities, particularly intrauterine adhesions. This fact is likely associated with these patients having usually undergone uterine emptying procedures. Uterine curettage is known to produce intrauterine adhesions^{20,21}. Although the intrauterine manual vacuum aspiration procedure is increasingly prevalent here in Porto Alegre, a large number of patients still undergo standard uterine curettage procedures²⁰. In our study, a correlation between hysteroscopy anomalies and number of miscarriages was present ($r = 0.31$); thus, we can assume there is an association between anatomical changes and increased miscarriage incidence. Unfortunately, the correlation is not sustained in cases of intrauterine adhesions ($r = 0.11$).

Carlos, et al., (2011) study has several points to be highlighted. We could show a homogeneous series of repeated miscarriage cases. The data collect was appropriate, controlling the methodology employed to carry out the tests and interexaminer variability. As our practice is a reference center in endoscopy, with studies being performed for various indications, the examiners were unaware of the test indication as it was performed; however, the patient's obstetric and surgical history was informed, preventing the examiner's total blinding.

Moreover, endoscopy availability likely allowed uterine anomalies which otherwise could go undetected or be diagnosed later to be diagnosed earlier. Another noticeable point in our study was a higher number of patients with more than three miscarriages over the group with only two miscarriages¹⁶. Hysterosalpingography has a high false-positive and false-negative rates as a disadvantage, in addition to being a more painful test for most patients.

Elsokkary, et al., (2017) assess the hysteroscopic value in the management of intrauterine lesion in women with recurrent pregnancy loss. This study was done on 200 nonpregnant women with a history of three or more consecutive unexplained first and second trimester miscarriages before 20 weeks were recruited from recurrent miscarriage clinic. A written informed consent was obtained from all women before participation. They found that, the mean age was 30.5(5.7), the mean number of previous abortion 3(3–5) the mean number of the first trimesteric abortion was 2 with range (2–2) the mean number of second trimesteric abortion was 2 with range (1–2). In this study, 88% of patients were nullipara. It was also found that hysteroscopic findings were found in 58.5%. Uterine anomalies was present in 21%, including septate uterus and intrauterine adhesion (IUAs) were present in 12.5%. Endometrial polyps were present in 8.5%, bicornute uterus in 4.5%, unicornuate uterus in 4.5% while submucousmyomas were present in 7.5%. It was found that 48.5% need hysteroscopic intervention including 21% need septectomy 12.5% need adhesiolysis, 6.5% need myomectomy while 8.5% need polypectomy. The study found that no statistically significant difference between patients with normal hysteroscopic finding and patients with abnormal hysteroscopic finding as regard age, time of previous abortion and number of previous abortion. But there was statistically significant difference as regard number of previous delivery and abnormal HSG.

5. Conclusions

We concluded that: hysteroscopy is a useful tool in the diagnosis and treatment of the causes of recurrent miscarriage that can be performed safely without anesthesia in most cases. Women after two spontaneous miscarriages can be advised that hysteroscopy will reveal congenital. Many of the anomalies detected are amenable to therapy and may improve subsequent pregnancy outcome. The decision to begin an investigation after two miscarriages should be individualized. Since the majority of women, after two miscarriages, will have a successful subsequent pregnancy outcome, many will choose to defer an investigation. Others will want to begin an

investigation after two miscarriages because of the stress and frustration associated with aborting rather than 'wait for a third miscarriage'. These patients should not be denied the option of hysteroscopy after discussion of the risks and benefits and informed consent is provided. Our study supports the option of performing a hysteroscopy after two miscarriages since the likelihood of finding a congenital or acquired anomaly is the same as after three or more miscarriages.

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