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Research Article

Validity of Hysteroscopy in Detection of Uterine Cavity Abnormalities in Women with Recurrent Pregnancy Loss

Abstract

Objective: To explore the validity of hysteroscopy in detection of uterine cavity abnormalities in women with recurrent pregnancy loss.

Patients and Methods: This was a prospective study performed at Ain Shams University Maternity Hospital, over a 3-year period, between Jan 2013 and Jan 2016, and included 200 women who were presented for evaluation of the cause of repeated early pregnancy loss and scheduled for hysteroscopy for assessment of any uterine cavity abnormality. Participant ages ranged from 18 to 35 years. A written informed consent was obtained from all women before participation.

Results: the mean age was 29.5 ± 3.5 , the mean number of previous abortion 4.1 ± 1.1 , the mean number of 1st trimesteric abortion was 2 with range and the mean number of 2nd trimesteric abortion was 2. In this study, 81 % of patients were nullipara. It was also found that hysteroscopic findings were found in 41.5%. Uterine anomalies was present in 14%, including septate uterus and intrauterine adhesion (IUAs) were present in 11 %. Endometrial polyps were present in 3.5%, bicornute uterus in 3.5%, unicornuate uterus in 3.5% while submucous myomas were present in 6.5%. It was found that 17% need hysteroscopic intervention including 7.5% need septectomy 4.5% need adhesiolysis, 2.5% need myomectomy while 2.5% need polypectomy.

Conclusions: Structural uterine abnormalities were detected in nearly 41.1% of patients with recurrent miscarriages, hysteroscopy has much to offer in the diagnosis of uterine cavity abnormalities, for this reason it should be included in assessment of patients with a history of recurrent miscarriage.

Introduction

Recurrent miscarriage is considered when pregnancy is spontaneously interrupted in three consecutive episodes either before 20 weeks of gestation or before the fetus is 500g in weight [1]. Recurrent pregnancy loss has major effect on the psycho-social status of couples. It has been demonstrated that up to 3% of women experience recurrent loss of pregnancy and the cause is idiopathic in approximately 50% of cases [2].

The etiology of recurrent pregnancy loss can be classified according to their therapeutic potential into potentially treatable and currently untreatable etiologies. The potentially treatable causes are structural defects, endocrine abnormalities (luteal phase defect), thrombotic pregnancies (thrombophilia or autoantibodies) and immunological disorders (immunoglobulins and immunization) the currently untreatable cases are genetic abnormalities and idiopathic etiologies [3].

Hysteroscopy offers great help in the interpretation of uncertain findings from other diagnostic modalities. Moreover, it enables direct visualization of cervical canal, uterine cavity and improve the accuracy in the evaluation of intrauterine abnormalities [4].

The uterine anomalies can be either congenital (i.e., mullerian anomalies) or acquired (e.g., submucous myomas, endometrial

polyps and adhesion) [5]. Mullerian anomalies have been found in (8-10%) of women with recurrent pregnancy loss and uterine septum was the most common anomaly. Most of the defects are treatable [6]. Rates of conception after hysteroscopic metroplasty in septate uterus, or hysteroscopic cutting of intra-uterine adhesion are stated to be high with 87% conception rate postoperatively [7].

In this study, the aim was to evaluate the hysteroscopic value in the management of intrauterine lesion in women with recurrent pregnancy loss.

Patients and Methods

This study was performed in Ain Shams Maternity University Hospital after the approval of the Research Ethics Committee, during the period between Jan 2013 to Jan 2015 where 200 non-pregnant women with a history of three or more consecutive unexplained first and second trimester miscarriages before 20 weeks were recruited from recurrent miscarriage clinic. Written informed consent was taken from all women before participation in this study.

Inclusion criteria

1. Recurrent abortions (3 times of abortions) or more.
2. No contraindication for hysteroscopy (recent infection).
3. Normal progesterone levels in the luteal phase

- Investigations are normal while HSG looking abnormal.

Exclusion criteria

- Women with known etiology of recurrent pregnancy loss.
- Women with suspected or confirmed pregnancy.
- Women with acute or recent pelvic infection.
- Women were known to be carries of balanced chromosomal anomalies.
- Women have uncontrolled or previously undiagnosed hormonal defect such as diabetes or hypothyroidis.
- Women with antiphospholipid antibodies.

Methods

After taking informed written consent the recruited women were subjected to careful detailed history and physical examination including general, abdominal and pelvic examination.

Office hysteroscopy

Hysteroscopy was done in the early proliferative phase using normal saline as distention medium. Light was provided by a light source. The patient was placed in dorsal lithotomy position and cleaning the vulva and vagina by antiseptic solution was performed.

Technique

The patient was asked to empty her bladder. After thorough explanation of the procedure, the patient was positioned in the lithotomy position. The thighs should be at a 90 degree angle to the pelvis in order to create enough space for the surgeon to manipulate the hysteroscope. The patient perineum should be just past the edge of the Table. Normal saline was used for uterine distension connected to the inflow channel on the sheath with intravenous tubing. A vaginal wash with saline solution was performed without placing speculum. Before the hysteroscope and sheath insertion into the external os, the sheath was flushed to remove the air. The tip of the hysteroscope was positioned in the introitus, the labia being slightly separated with fingers. The vagina was distended with saline. The scope was driven to the posterior fornix to readily visualize the portio and slowly backwards to identify the external cervical os. When this became visible, the scope was carefully moved forward to the internal os and then the uterine cavity with least possible trauma. The uterine cavity was systematically explored by rotating the fore-oblique scope in order to discover any abnormality in the uterus and/or the right and left tubal ostia. At this stage it is crucial to avoid lateral movements to reduce patient discomfort. After that, the scope was removed and the patient was kept in the supine position for a few minutes to avoid vasovagal attack. Any pathologic lesion was recorded in patient sheet (e.g. Adhesion, septum, uterine polype, submucus fibroids and cervical competence was assessed too). Minor interventions were performed immediately while major once were performed later under anesthesia.

Statistical methods

Data were analyzed using IBM® SPSS® Statistics version 22

(IBM® Corp., Armonk, NY, USA) and XLSTAT™ version 2014.5.03 (Addinsoft™, NY, USA). Normally distributed numerical variables were presented as mean (SD) and intergroup differences were compared using the unpaired *t* test. Skewed numerical variables and discrete variables were presented as median (interquartile range) and between-group comparisons were done using the Mann-Whitney test. Categorical variables were presented as number (%) and intergroup differences were compared using the chi-squared test with Yates’ continuity correction or Fisher’s exact test, when appropriate. Ordinal data were compared using the chi-squared test for trend. A two-sided p-value <0.05 was considered statistically significant.

Results

This current study was conducted in Ain Shams University Maternity Hospital during the period between Jan 2013 to Jan 2016 a total of 200 women with history of recurrent miscarriage were included in the study (Tables 1-3).

Discussion

Repeated pregnancy loss (RPL) is known as three or more consecutive spontaneous miscarriages before the 20th week of

Table 1: The clinic-demographic criteria of women under study.

	Group I (150)
Age	29.5 ± 3.5
Menarche age	10.1 ± 4.2
Body mass index (kg/m2)	28.1 ± 2.4
Previous gravidity	5.3 ± 0.2
Previous abortions	4.1 ± 1.1
1 st trimesteric abortions	2
2 nd trimesteric abortions	2
Nullipara	81%
Multipara	19%
Education	
≤High school	92
>High school	58
Occupation	
House wife	110
Employed/business Woman	40

* Analysis using independent student’s t-test. NS = non-significant, S = significant.

Table 2: Hysteroscopic findings in the whole study population.

Variable	Value
Normal	117 (58.5%)
Abnormal hysteroscopy	83 (41.5%)
Specific abnormalities detected with hysteroscopy	
Septum	28 (14.0%)
Adhesions	22 (11.0%)
Submucous myoma	13 (6.5%)
Endometrial polyp	7 (3.5%)
Bicornuate uterus	7 (3.5%)
Unicornuate uterus	6 (3%)

Table 3: The Rate of performing hysteroscopy-assisted interventions in the whole study population (200 women).

Variable	Value
Interventional hysteroscopy	34 (17.0 %)
Specific hysteroscopy-assisted procedures	
Septectomy	15 (7.5%)
Adhesiolysis	9 (4.5%)
Myomectomy	5 (2.5%)
Polypectomy	5 (2.5%)

gestation [8]. RPL is the outcome of failure of the poor quality embryos to implant and present clinically as recurrent miscarriage [9]. The incidence of recurrent miscarriage is (3-5)%, after the second loss, there is already a higher risk of miscarriage complicating the next gestation [5].

Women with a history of one miscarriage carry a 24% risk of miscarriage in the next pregnancy, while women with a history of 2 miscarriages carry a 26% risk and those with history of previous 3 miscarriages carry a 32% risk of recurrence and thus women who had miscarried two or more consecutive pregnancies deserve an evaluation to look for the cause, which sometimes can be treated [10,11].

Uterine abnormalities are estimated to play a pivotal role in a substantial number of couples seeking treatment for recurrent miscarriages [12]. Their described patho-physiological mechanism is that they prevent proper embryo implantation and development due to poor vascularization with subsequent infertility or miscarriage [13]. This study aimed to assess the prevalence and types of uterine defects in patients with recurrent miscarriage through hysteroscopy. Two hundred nonpregnant patients with a history of three or more spontaneous consecutive 1st and 2nd trimester pregnancy losses before 20 weeks were recruited from recurrent miscarriage clinic. In the present study the mean maternal age was 29.5 ± 3.5 years these results were consistent with other studies [3,14,15], who found that the mean maternal age was 28.1, 30.8 ± 6.2 , 32 ± 5 years respectively. On the other hand Dendrin *et al.* (2008) found that mean maternal age was older 40.5 ± 5.2 years, this may be attributed to late age of marriage in their population [1].

In this study the mean number of previous abortion was 4.1 ± 1.1 , the mean number of first trimesteric abortion was 2, and the mean number of second trimesteric abortion was 2. In the current study 81% of patients were nullipara, this was agree with Weiss *et al.* (2005) who reported the mean number of prior deliveries was 5.08 ± 2.29 [14].

Anatomical uterine defects including Mullerian anomalies, adhesion and fibroids, are frequently found in women with recurrent miscarriage whether of the first or second trimester [16]. In the present study, it was found that 117 of women (58.5%) had a normal hysteroscopic findings and 83 of patients (41.5%) had abnormal hysteroscopic findings. These results are in agreement with those of Ventolini *et al.* 2004 [3], a prospective cohort study included 23 patients with recurrent pregnancy losses underwent diagnostic hysteroscopy and 60.9% had normal hysteroscopic finding and 39.1%

had abnormal hysteroscopic finding also Weiss *et al.* 2005 found that 70% of patients had normal hysteroscopic finding and 30% had abnormal hysteroscopic finding [14].

Bakas *et al.* [17] examined 217 patients by hysteroscopy before IVF and found 69 (31.8) had identified intrauterine lesions. Another study was conducted by Dendrin *et al.* 2008, on 48 patients and found that 52% had normal hysteroscopic finding and 48% had abnormal findings [1]. The reported rate of abnormalities for women with recurrent pregnancy losses varies from 6.3% to 67% with most studies showing more than 25% anomalies. This discrepancy for the incidence of abnormalities among women with recurrent miscarriages represent differences in study design and in the types of abnormalities detected [5].

In the current study septate uterus was the most common uterine anomaly affecting 14% of the patients which was confirmed by HSG or 3DU/S. This result is similar to that reported by Weiss *et al.* (2005) who found septate uterus in 13% of the patient with recurrent abortion [14].

3DU/S has been used in diagnosis of septate uterus [18,19]. However, hysteroscopy remains the gold standard for diagnosing the septate uterus [2]. The septate uterus, according to medical literature, is the most common congenital uterine defect, accounting for 50 - 80% of the müllerian defects. It is also the anomaly with the worst reproductive prognosis, with abortion rates varying from 67 to 87% [20].

In the current study intrauterine adhesions were the most common acquired uterine anomalies seen in 11% of the patients. Intrauterine synechiae usually resulting from endometritis, curettage, intrauterine surgeries or metroplasty, 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 [21].

Retrospective case series study by Fernandez *et al.* 2000 [22], included 23 women who had Asherman syndrome. The women's mean age was 34 years (± 5.8 years) when treatment for adhesions began. All women initially had adhesions classified as severe with total amenorrhea. At the conclusion of treatment more than 80% of women had either no adhesions at all or very mild adhesion and the overall pregnancy rate was 40.9%. There were nine pregnancies and six term infants (27.2%). All of these pregnancies were spontaneous. The mean time to pregnancy was 10.5 months (± 4.7 months).

In this study submucous myoma was present in 6.5% of the patients and endometrial polyp in 3.5%. Myomas are usually asymptomatic during gestation, however, there is evidence suggesting a connection with a higher risk of subinfertility, spontaneous miscarriages and preterm labor. It is estimated that about 41% of women with myomas, especially submucous ones, could abort [23].

The importance of uterine polyps and myomas in the genesis of abortion is widely discussed. The presence of one of them into the uterine cavity can interfere with implantation and creating a hostile environment to embryo implantation [24]. Klatsky *et al.* 2008 [25], examined the published relationship between uterine myomas and poor reproductive outcomes. Submucosal myomas had the strongest

link with lower ongoing pregnancy rates (odds ratio 0.5; 95% confidence interval, 0.3-0.8) due to decreased embryo implantation. They concluded that, despite the relatively small number of women under study, there is strong evidence favouring hysteroscopic myomectomy in women before undergoing ART.

Submucous fibroids interfere with fertility and should be removed in infertile patients, regardless of the size or symptoms [2,26].

In experienced hands, hysteroscopic myomectomy is minimally invasive, safe and effective [27]. The search for randomized controlled trials (RCT) on the treatment of submucous in fibroid infertile women reported one article. In this prospective randomized matched control trial, 215 women with unexplained infertility and with ultrasonographically detected submucous fibroids were enrolled. Women in the study group had a better possibility of conception after hysteroscopic myomectomy with relative risk of 2.1 (95% confidence interval, 1.5-2.9). No significant difference in conception rates was observed according to fibroid size, number, and location in both groups [28].

In the current study 5 of patients had fibroid resection. According to ASRM 2008 [29], hysteroscopic myomectomy is indicated for intracavitary myomas and submucous myoma having at least 50% of their volume within the uterine cavity. Stamatellos et al. 2008 [30], evaluated 83 women who met the following criteria age under 35 years, from 3 to 8 months of menstrual disorders (metrorrhagia, menometrorrhagia or menorrhagia) and 3 to 18 months of follow up after hysteroscopic polypectomy the result was pregnancy in 61.4% and delivery in 59.2% at term, these rates increased after the procedure.

Published observational studies conducted by Bosteels et al. 2013 [26], found an increased pregnancy rates after the hysteroscopic polypectomy, removal of submucous fibroids, uterine septum or intrauterine adhesions, which can be found in 10% to 15% of women seeking fertility. In our study there is no significant difference between patients with 1st and 2nd trimesteric miscarriage this result was agree with Weiss et al., 2005 [14], who found that no significant difference between two groups. In the present study there was no statistical significant difference between patients with 3 and more than 3 consecutive miscarriages as regard age and prior deliveries, and number of miscarriages. On the other hand Knudsen et al. 1991 [31], published that miscarriage rate increased substantially up to 45% in women with three previous miscarriages. Quenby and Farquharson 1993 [32], found that a poor prognosis was to be expected only when the number of subsequent pregnancy losses increased to four and six miscarriages [33].

Conclusions

In summary, this study demonstrates that it appears 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. The prevalence of uterine anomalies in patients with recurrent miscarriages is 41.5%, septate uterus is the most common anomaly and for this reason uterine anomalies should be systematically assessed in patients with recurrent miscarriage.

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