

## Hysteroscopy in Libyan women with Recurrent Pregnancy Loss

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### ABSTRACT

**Background:** Hysteroscopy is an efficient procedure of management in many gynecologic conditions. There are few published data on hysteroscopy and recurrent pregnancy loss especially in developing countries.

**Objectives:** To assess hysteroscopic findings in patients with consecutive miscarriages, and to compare the prevalence of uterine abnormalities between women with two and three or more miscarriages.

**Methods:** Three hundred and twenty four women with two or more consecutive miscarriages were enrolled in the study. All participants underwent a diagnostic hysteroscopy. Congenital (arcuate uterus, septate uterus, unicornuate uterus) and acquired uterine abnormalities (intrauterine adhesions, polyp and submucous myoma) were documented. The findings were compared between the groups of women with two miscarriages and women who had three or more miscarriages.

**Results:** Out of a total of 324 women [their mean (SD) of the age and gravidity was 28.3 (6.5) years and 5.1(1.5), respectively] 135 (41.7%) and 189 (58.3%) had two consecutive miscarriages and three or more consecutive miscarriages, respectively. While 194 (59.9%) women had no pathological findings on hysteroscopy, 130 (40.1%) women were found to have uterine anomalies. The congenital anomalies were found in 79 (24.4%) and the acquired were in 51 (15.7%) women. In comparison with women who had three or more miscarriages, women who had two miscarriages had significantly higher number of congenital anomalies, 53/135 (39.2%) vs. 26/189 (13.8%),  $P < 0.001$ . However there was no significant difference in the acquired anomalies between women who had two miscarriages and women who had three or more miscarriages.

**Conclusions:** Patients who had two consecutive miscarriages were found to have a higher prevalence of congenital anatomical abnormalities. Diagnostic hysteroscopy should be carried out after two such miscarriages.

**Keywords:** Hysteroscope, Recurrent Pregnancy Loss, miscarriage, Libya.

**R**ecurrent pregnancy loss (RPL) is traditionally defined as three or more spontaneous, consecutive pregnancy losses before completion of 20 weeks of gestation or the expulsion of a fetus weighing  $<500\text{g}^1$ . Spontaneous miscarriage and RPL occur in 15% and 1-2% of clinically diagnosed pregnancies in women of reproductive age, respectively<sup>2</sup>. Several factors are associated

with RPL such as embryonic/chromosomal abnormalities, maternal anatomic abnormalities (e.g. septate uterus), luteal phase defects, maternal autoimmune diseases, and antiphospholipid syndrome and to a lesser degree infection and hypercoagulable state<sup>3-5</sup>. However, there is an ongoing debate on possible causes of recurrent miscarriages as the exact pathophysiology and the majority of risk factors are not precisely described<sup>4</sup>.

Congenital, or Mullerian anomalies such as septate, bicornuate, didelphic or unicornuate uterus were assumed to cause recurrent pregnancy complications such as late or recurrent early miscarriage, abnormal fetal presentation, intrauterine growth restriction and prematurity<sup>6,7</sup>. Furthermore, a number of acquired uterine anomalies such as fibroids,

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intrauterine adhesions and endometrial polyps were described with varying prevalence in patients with recurrent miscarriages, although their direct influence on miscarriages is not completely understood<sup>8,9</sup>. Likewise intrauterine adhesions (most often seen after sharp curettage) are associated with recurrent miscarriage<sup>10,11</sup>.

Classically, a workup for a cause of RPL is recommended after three miscarriages. Recent findings do not necessarily support this traditional evaluation protocol<sup>12,13</sup>. The evaluation of healthy women after a single loss is not usually recommended, as this is a relatively common/sporadic event. However, the risk of another pregnancy loss after two miscarriages is only slightly lower (24-29%) than that of women with three or more losses (31-33%)<sup>14</sup>. Therefore, it is reasonable to start evaluating the case after two or more consecutive losses especially in elder women (> 35 years) or when the couples have difficulty in conceiving<sup>15</sup>.

The aim of this study was to explore the hysteroscopic findings in patients with recurrent miscarriages.

#### MATERIALS AND METHODS:

A cross sectional study was conducted over a period of four years from July 2009 to June 2013 at Obstetrics and Gynecology departments, Misurata Central Hospital, Misurata Oncology Centre and Iben-Sina Teaching hospital, Libya. Women with two or more consecutive miscarriages with pregnancy losses occurring during the first 20 weeks of gestation were enrolled to the study. According to the criteria of Weiss et al., 2005<sup>16</sup>, a miscarriage was defined as: the spontaneous expulsion of a product of conception; the disappearance of fetal heart activity on ultrasound examinations; or failure of  $\beta$ -hCG to rise in serial measurements. There were no exclusion criteria such as karyotyping abnormalities or positive antiphospholipid antibodies. After signing an informed consent data were collected on patient's age, gravidity, parity and their outcomes and other investigative procedures already performed. The exact gestational age

at the time of miscarriage was recorded for each patient. Then the previous transvaginal ultrasound results were checked if a gestational sac, fetal shadow or heart activity was documented at any time prior to miscarriages.

Hysteroscopy was performed under general anaesthesia in the proliferative phase of the menstrual cycle. Cervical dilatation was performed (when necessary) to enable the insertion of the hysteroscope. Glycine 1.5% was used as distension medium. Operative hysteroscopy was performed to remove the discovered anomalies. Hysteroscopic findings were documented. Laparoscopy was performed if needed e.g. to differentiate between complete septate and didelphic uterus or between partially septate and bicornuate uterus.

#### Statistics

Data were entered and analyzed in a computer using SPSS for Windows. Chi square/Fisher's exact test was used for comparison of proportion.  $P < 0.05$  was considered significant.

#### RESULTS:

Three hundred and twenty four women were enrolled in the study; their basic characteristics were shown in table 1. Out of these 324 women, 135 (41.7%) and 189 (58.3%) had two consecutive miscarriages and three or more consecutive miscarriages, respectively.

Table (1): Basic characteristics of Libyan women with recurrent pregnancy loss women presented for hysteroscopy.

Variable	Mean (SD)
Age, year	28.3(6.5)
Gravidity	5.1 (1.5)
Number of miscarriage	2.8(0.6)

While 130 (40.1%) women were found to have uterine anomalies, 194 (59.9%) women had no pathological findings on hysteroscopy. These uterine anomalies were congenital in 79 (24.4%) and acquired in 51 (15.7%) women (Figure 1).

In comparison with women who had  $\geq$  three miscarriages, women who had two miscarriages had significantly higher number of congenital anomalies (specially arcuate and septate uteri), 53/135 (39.2%) vs. 26/189 (13.8%),  $P < 0.001$ . However there was no significant difference in the acquired

anomalies between women who had two miscarriages and women who had  $\geq$  three miscarriages (Table 2).

None of the women had complications (cervical tears, false passage, uterine perforation, infection) during/after hysteroscopy.

Table (2): Percent of the anomalies in Libyan women with two miscarriages and women with  $\geq$  three miscarriages

Anomalies	Women with two miscarriages (n=135)	Women with $\geq$ three miscarriages (n=189)	P
Congenital (uterus)	53 (39.2)	26 (13.8)	<0.001
Arcuate	28(20.7)	13(6.9)	<0.001
Sepatate	20(14.8)	10(5.3)	0.004
Bicornuate	5(3.7)	2(1.1)	0.106
Unicornuate	0(0)	1(0.5)	0.397
Acquired	21 (15.1)	30 (15.9)	0.938
Endometrial polyp	8(5.9)	13(6.9)	0.731
Intrauterine adhesions	8(5.9)	10(5.3)	0.966
Fibroid	4(3.0)	5(2.6)	0.863
Polypoid endometrium	1(0.7)	2(1.1)	0.768

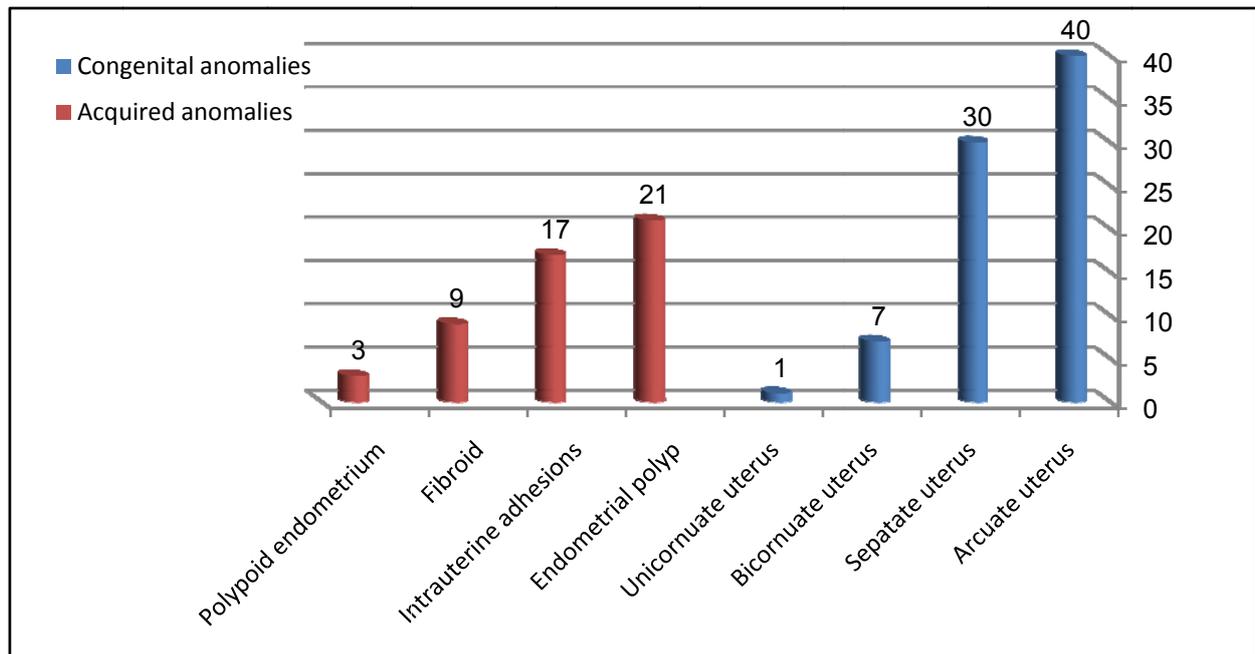


Figure (1): Types and frequency of hysteroscopic findings

**DISCUSSION:**

Uterine abnormalities might have a causal role in infertility and in the recurrent miscarriages whether of the first or second trimester<sup>17,18</sup>. Uterine abnormalities perhaps impair the proper embryo implantation and growth due to poor vascularization<sup>19</sup>.

Previous reports showed that 2-5 % of women with a good obstetric history or those at low risk for complications had uterine anomalies<sup>20,21</sup>. On the other hand around one third of infertile women were reported to have abnormal intrauterine findings<sup>9</sup>. Yet varied rates (6.3 - 67 %) of anomalies were reported in patients with recurrent pregnancy losses

<sup>21,16</sup>. These variations could be explained by the difference in study designs and the variations of anomalies reported in the respective studies <sup>16</sup>.

In the current analysis, women who had two miscarriages had significantly higher number of congenital anomalies, 53/135 (39.2%) vs. 26/189 (13.8%),  $P < 0.001$ . Congenital uterine anomalies were previously reported in 17-25% of patients with recurrent miscarriages<sup>22,23</sup>. Since there was no exclusion criterion in this study, other causes of miscarriages were not analyzed and hence could not be excluded. According to this result, patients who have suffered two miscarriages have more risk of congenital uterine pathology and equal risk of acquired pathology compared to those with three or more miscarriages. The role of arcuate uteri in the development of miscarriages is not that clear and may be controversial. However, the significance of other congenital anomalies for the development of pregnancy complications is well established <sup>16, 24-26</sup>. It was decided to include arcuate uteri in the current analysis as they are generally accepted and described as congenital anomalies in an established classification system (American Society of Reproductive Medicine, 1988).

The question when to investigate recurrent pregnancy loss is also one of cost-benefit. A workup investigation after two pregnancy losses will unnecessarily increase in the number of the investigated women. Women with recurrent pregnancy loss generally have a good prognosis in their subsequent pregnancy. After two miscarriages, 76% of patients can expect a successful subsequent pregnancy outcome <sup>27</sup> and therefore will not benefit from investigation. These findings were contradicted by another study<sup>28</sup>, which found that the miscarriage rate increased substantially from 25 to 45% when comparing women with two or three previous miscarriages respectively. Other researchers confirmed poor prognosis only when the number of subsequent pregnancy losses increased to four<sup>29</sup> and six<sup>30</sup> miscarriages. Diagnostic methods to assess the inner architecture of the uterus include transvaginal

ultrasound, hysterosalpingography (HSG), and hysteroscopy. It is generally accepted that hysteroscopy, possibly in combination with laparoscopy are the most accurate procedures in the diagnosis of congenital uterine anomalies <sup>22</sup>. Hysteroscopy is generally regarded to be essential when intrauterine pathology is suspected on transvaginal ultrasound, HSG <sup>31</sup>. However, even if no anomalies are found with the latter diagnostic tools, subtle intrauterine pathologies may be detected by hysteroscopy in 25-50% of patients <sup>31,32</sup>. Consequently, two-dimensional ultrasound and HSG are considered to be inadequate for diagnostic purpose as they are less accurate<sup>22</sup>. A comparison of sonographic results with hysteroscopic findings was not the aim of the present study. Contrary to transvaginal ultrasound; hysteroscopy offers both a diagnostic and direct therapeutic approach of intrauterine congenital anomalies and acquired anomalies such as adhesions, fibroids and polyps. A therapeutic septum dissection or adhesiolysis may improve the outcome in subsequent pregnancies<sup>33,34</sup>.

#### CONCLUSION:

Hysteroscopy is a simple and efficient tool in the early diagnosis and management of congenital and acquired uterine pathologies that might be causing recurrent pregnancy loss. Patients are advised to have it performed after two miscarriages.

#### Conflict of interest statement:

No actual or potential conflict of interest exists in relation to this article.

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