

Post-pregnancy loss hysteroscopy as a method for early diagnosis of congenital and acquired intrauterine causes

Thesis

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List of Abbreviations

aCL	: Anticardiolipin antibody .
ACOG	: American college of obstetrician and gynecology.
ASRM	: American society for reproductive medicine.
AUC	: Area under the curve.
CCD	: Charge-coupled device.
CO2	: Carbon dioxide.
DES	: Diethylstilbestrol .
DM	: Diabetes mellitus.
GRIN	: Grade index lens system.
ISTH	: International Society of Thrombosis and Haemostasis .
IUAs	: Intrauterine adhesions.
IUD	: Intrauterine device.
NICE	: National Institute for Health and Clinical Excellence.
PCOS	: Polycystic ovary syndrome.
PID	: Pelvic inflammatory disease.
RCOG	: Royal College of obstetrician and gynecology.
RPL	: Recurrent pregnancy loss.
SLE	: Systemic lupus erythematosus.
TORCH	: Toxoplasma, rubella, CMV, Herpes simplex.
TVUS	: Transvaginal ultrasonography.

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Introduction

The journey from conception to birth is fraught with danger. It has been estimated that (50-70%) of all conceptions fail (*Salmon, 2004*).

Miscarriage is the most common complication of pregnancy. It rarely causes serious health problems (*Trinder et al., 2006*), but it can adversely affect women's social & psychological wellbeing.

Miscarriage is defined as the spontaneous loss of pregnancy before the fetus reaches viability. The term therefore includes all pregnancy losses from the time of conception until 24 weeks of gestation. It should be noted that advances in neonatal care have resulted in a small number of babies surviving before 24 weeks of gestation (*RCOG, 2011*).

A particular form of abortion, which causes great stress to patients and doctors, is the recurrent miscarriage (*Barranger et al., 2002*). Although the pathophysiology remains unknown in almost 50% of cases, structural uterine abnormalities, chromosomal anomalies and maternal thrombophilia have been directly associated with recurrent miscarriage (*RCOG, 2008 and Jauniaux et al., 2006*).

Whereas inherited and acquired (infections, smoking, etc.) factors have been implicated in the etiology of recurrent miscarriage most (50-60) % of the cases remain idiopathic (*Pandey et al., 2005; Carp et al., 2006; Sierra and Stephenson, 2006*).

The etiology of recurrent miscarriage can be divided into first & second trimester miscarriage; according to their therapeutic potential can be divided into treatable and untreatable causes (*Ventolini et al., 2004*). The majority of first-trimester miscarriages are attributable to chromosomal

abnormalities, parental structural chromosomal abnormality, maternal medical conditions such as Diabetes Miletus, maternal uterine anomalies, luteal phase defect (**Regan and Rai, 2000**).

The majority of second-trimester miscarriages causes are infection (chorioamnionitis or maternal systemic infection), cervical weakness, structural uterine abnormalities and thrombophilia. Genetic causes may still play a role in second-trimester miscarriage where a genetic abnormality is involved (15% of cases) which tends to be one that is occasionally seen in term deliveries (trisomies 13, 18 and 21, monosomy x and sex chromosome polsomes) or that involves a gene mutation or deletion (**Simpson, 2007**).

Causes such as structural uterine defects, endocrine dysfunction (luteal phase deficiency), thrombotic pregnancies (thrombophilia or auto antibodies), poorly controlled diabetes, immunologic disorders (immunoglobulin and immunization) and thyroid disease are less common, although potential treatable. The currently untreatable causes are genetic abnormalities and idiopathic etiologies (**Ventolini et al., 2004**).

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% (**Sotirios et al., 2008**). The uterine anomalies can be either congenital (i.e., Mullerian fusion defects) or acquired (e.g., submucous myomas, endometrial polyps, adhesion) (**Salim et al., 2003**).

The importance of uterine polyps and leiomyomas in recurrent miscarriage is a matter of debate; they can interfere with fertility, creating a hostile environment to embryo implantation. It is estimated that about 41% of women with

liomyomata, especially submucous one, could abort (**Salvador et al., 2002**).

Mullerian fusion defects have been found in (8-10) % of women with recurrent miscarriage, uterine septum was the most common anomaly. Many of the defects are amenable to therapy (**Homer et al., 2002**).

Transvaginal ultrasonography (TVUS) provides valuable information in the evaluation of a wide range of gynecological disorders including; uterine and adnexal masses, inflammatory processes and neoplasm. Typical features of benign masses are reproducible even with moderately experienced examiners. It is also useful in assessing non gynecological pelvic conditions such as; masses in the urinary bladder, urinary incontinence and non gynecological pelvic masses (**Guerriero et al., 2009**).

Hysteroscopy is the direct visual examination of the cervical canal and the interior of the uterus using thin, lighted and flexible tube called hysteroscope inserted through the vagina, offers great assistance for the interpretation of uncertain findings from other diagnostic methods and increase the precision and accuracy in the diagnosis of the intrauterine abnormalities (**Ceci et al., 2004**). Hystroscopic findings can be applied toward both diagnosis and therapy in a variety of cases (**Serden et al., 2000**) & (**Isaacson and Keith et al., 2002**).

Over the past decades, hysteroscopy is the gold standard for evaluation of the endometrial cavity lesions such as congenital and acquired uterine anomalies which can be treated hysteroscopically, resulting in improved pregnancy outcome (**Demirol et al., 2004**), so becomes an important diagnostic and therapeutic tool for patients with intrauterine anomalies.

Hysteroscopic myomectomy currently represents the standard minimally invasive surgical procedure for treating submucous fibroids and reproductive issues being the most common indications in case of recurrent miscarriage (***Di Spiezio et al., 2008***).

Hysteroscopic resection of the septum in septate uterus improves pregnancy outcome in women with recurrent miscarriages (***Valli et al., 2004***). Also increases successful pregnancy rates from 3–20% to 70–90% (***Alborzi and dehbashi, 2002***).

Hysteroscopy, with the development and miniaturization of equipment, is currently simple, outpatient cost-effective exploration and it is considered the gold standard for diagnosis of intrauterine lesions.

In this study we utilized conventional transvaginal ultrasonography and hysteroscopy for the detection of congenital and acquired uterine anomalies.

Aim of the Work

To assess efficacy of post - abortion hysteroscopy for detection of congenital and acquired intrauterine anomalies.

Miscarriage

Pregnancy loss is defined as the spontaneous loss of pregnancy before the fetus reaches viability. The term therefore includes all pregnancy losses from the time of conception until 24 weeks of gestation. Occurring in 12 - 30% of clinical pregnancies (**Tien and Tan, 2007**). Unrecognized biochemical pregnancies are included (**RCOG, 2011**).

Recurrent pregnancy loss (RPL) is defined as the loss of consecutive spontaneous three or more first-trimester miscarriages, or one or more second-trimester miscarriages (**RCOG, 2011**).

Some experts consider two consecutive pregnancy losses are sufficient for the diagnosis of RPL because the recurrence rate and risk factors are similar to that after three losses (**Branch et al., 2010**).

The couples with RPL can be divided into subgroups according to their reproductive history:

Primary (no successful pregnancies), secondary (series of miscarriages after a live birth) and tertiary (three non-consecutive miscarriages), they should be considered as separate entities representing probably different pathophysiological mechanisms leading to pregnancy loss. Immunological factors have been suggested to play a greater role in secondary RPL, especially after the first-born son (**Christiansen et al., 2004; Nielsen, 2011**). Non-immunological risk factors, e.g., factor V Leiden mutation, tend to be associated mainly with primary RPL (**Wramsby et al., 2000**).

In comparison to the baseline risk of pregnancy loss in the general obstetric population of between 12 – 30%, the risk

of pregnancy loss in women who have never had a pregnancy loss or primigravida, is low at 4 – 5% (**Tien and Tan, 2007**).

Women with a history of one, two, three and four miscarriages, the risks are significantly increased in the next pregnancy are 19%, 24%, 30% and 40%, respectively (**Tien and Tan, 2007**).

The occurrence of recurrent pregnancy loss has been estimated 1–3% of couples attempting to bear children (**Branch et al., 2010**). While fetal chromosomal abnormalities are responsible for 70% of sporadic pregnancy loss (**Menasha et al., 2005**).

Unexplained RPL is a stressful condition for a couple and supportive care is currently the only assistance that can be offered. Still, early recognition of a potential risk to miscarriage and systematic monitoring has beneficial effect in increasing live birth rates in RPL couples (**Branch et al., 2010; Tang and Quenby, 2010; Musters et al., 2011**).

There are no specific criteria to start investigation after pregnancy loss. The general approach to a patient with recurrent pregnancy loss is to start investigation after three or more miscarriages. However, there has been a tendency to start investigation after two miscarriages (**Weiss et al., 2005**).

Causes and risk factors of pregnancy loss:

1-Anatomic Causes:

- **Congenital :**
- Mullerian system abnormalities
- Diethylstilbestrol exposure
- Incompetent cervix

Acquired

- Incompetent cervix

- Synechiae
- Leiomyomas
- Adenomyomas
- Uterine polyps (*Saravelos and Cocksedge 2010.*)

2-Genetic Causes :

- Chromosomal abnormalities
- Non-chromosomal abnormalities

3-Immunological Causes :

- Autoimmune causes
- Alloimmune causes (*Porter and Scott 2000.*)

4-Infectious Causes :

- Bacteria, Viruses, Parasites, Fungal (*Ford and Schust 2009.*)

5-Endocrinal Causes:

- Diabetes mellitus
- Luteal phase deficiency
- Polycystic ovarian syndrome
- Thyroid disorder (*Arredondo and Noble 2006*)

6-Hematologic Disorders:

- Thrombophilia (*Robertson et al. 2006*)

7-Environmental :

- Smoking
- Excessive alcohol consumption
- Caffeine (*Vibeke 2003*)

1-Anatomical factors:

Anatomic uterine defects are known to cause obstetric complications, including recurrent pregnancy loss, preterm labor, and malpresentation, although many women with such