Office hysteroscopy in recurrent second trimester abortion

Thesis

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List of Abbreviation

AS	Ashermann syndrome
CJD	Creutzfeldt-Jakob disease
2D U/S	Two dimensional ultrasound
3D U/S	Three dimensional ultrasound
HSG	Hystrosalpingography
IVF	Invitro fertilization
IUA	Intrauterine adhesion
IVIG	Intravenous immunoglobulin
LMWH	Low molecular weight heparin
RSA	Recurrent spontaneous abortion
RM	Recurrent miscarriage
RPL	Recurrent pregnancy loss
SHG	Sonohystrography
TNF	Tumour necrosis factor
UFH	Unfractionated heparin
NAD	No abnormality detected
IUA	Intrauterine adhesions

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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).** A particular form of abortion, which causes great stress to patients and doctors, is the recurrent pregnancy loss (RPL) **(Barranger et al., 2002).**

Recurrent pregnancy loss is defined as three or more consecutive pregnancy losses before the 20th week of gestation **(Sierra & Stephenson, 2006).** The incidence of RPL is (3-5) %. After the second loss, there is already a higher risk of miscarriage complicating the next gestation **(Salim et al., 2003).**

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

The etiology of RPL can be divided according to their therapeutic potential into treatable and currently untreatable causes. 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 **(Ventolini et al., 2004)**.

Among the diagnosed causes of recurrent pregnancy loss, uterine abnormalities were the most frequent (19.5%), followed by immunological Problems (17.1%)**.** 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% **(Sotirio et al., 2008).**

Uterine abnormalities can be either congenital (i.e. Mullerian anomalies) or acquired (e.g. submucous myomas, endometrial polyps and adhesion) **(Salim et al., 2003).** The importance of uterine polyps and leiomyomas in RPL is matter of - debate; they can interfere with fertility, creating a hostile environment to embryo

implantation. It is estimated that about 41% of women with leiomyomata, especially submucous one, could abort **(Salvador et al., 2002).**

Pregnancy losses with uterine congenital abnormalities usually occur later in Pregnancy in the second trimester; however, the presence of a uterine anomaly after repeated early losses deserves consideration of surgical repai**r (Leon and Marc, 2011).**

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**). Hysteroscopy is therefore very accurate in identifying congenital uterine anomalies and is often used to establish a definitive diagnosis after abnormal hysterosalpingography findings **(Homer et al., 2002).**

Rates of pregnancy after hysteroscopic metroplasty in septated uterus, or hysteroscopic lysis of intrauterine adhesions are reported to be high, with an 87% pregnancy rate postoperatively **(Barranger et al., 2002).**

However, the importance of each one on the genesis of the RPL, as well as the severity of the defect necessary to cause the gestation interruption is still controversial **(Salim et al., 2003).**

AIM OF THE WORK

Assessment of incidence and types of uterine defects in patients with recurrent second trimester abortion.

REVIEW OF LITERATURE

Recurrent abortion

Recurrent pregnancy loss is a profound personal tragedy to the couple seeking parenthood and forms a great clinical challenge to their physician. From a clinical point of view, couples are often extremely distressed and look for both an adequate explanation and preventive treatment in the next pregnancy. Genetics, immunology, endoscopy and reproductive physiology have contributed much in understanding and treating the problem of recurrent pregnancy loss **(Kutteh and Pasquarette, 1995).**

NOMENCLATURE:

Recurrent miscarriage,habitual abortion,recurrent spontaneous abortion and recurrent or repetitive pregnancy loss have been used in the literature. However,the phrase "Recurrent pregnany loss"has gained popularity because it avoids the stigmas engaged by-"abortion"and" habitual".The latter terms may imply,to some persons, that free choice was involved in a couple's reproductive history **(Hata Saka,1995)**

DEFINITION:

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 **(WHO, 1977)**.

A preclinical miscarriage is defined as a demise which occurred before 6 weeks of gestation. Clinical miscarriage can be divided into embryonic or fetal: embryonic miscarriage is defined as an embryo with crown rump length of more than or equal to 5 mm; without cardiac activity. A fetal miscarriage is defined as a

fetus of 10-20 weeks size without cardiac activity **(Rai and Regan, 2006; Stephenson and Kutteh, 2007)**.

Recurrent miscarriage should be defined, according to the above definition of miscarriage, as at least three consecutive miscarriages, whereas recurrent pregnancy loss could also include pregnancy losses up to 28 weeks gestation **(Farquharson et al., 2005)**.

However, there is no consensus regarding the definition of recurrent miscarriage and many clinicians define recurrent miscarriage as two or more losses before the fetus has reached viability **(Roman, 1984; Goddijn et al., 2004; Sugiura-Ogasawara et al., 2004)**. 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, 2003)**, but according to American college of obstetricians and gynecologists **(ACOG, 2001)** and the American society for reproductive medicine **(ASRM, 2005)**, the definition is two or three consecutive losses.

Recurring miscarriages are considered when pregnancy is spontaneously interrupted in three consecutive episodes either previously to 20 weeks of gestational age or before the fetus reaches 500 g in weight**(Weiss et al., 2005).** More recently, there has been a tendency to include into this diagnosis those patients with two early spontaneous pregnancy losses, mainly if they occur later than the age of 35 years **(Li et al., 2002).** This new approach prevents delays in recognizing the disease in a more critical age group; however, it can contribute to a higher number of studies and invasive procedures ordered in this population, with no benefits necessarily resulting from the case management **(Stephenson, 1996)**.

Repeated miscarriages can occur due to a set of factors, such as: genetic, endocrine, immune diseases, coagulation system disorders or anatomical factors**(Li et al., 2002).** Immune changes were more prevalently found in patients with

repeated miscarriages, and the frequency of findings was similar when patients with two miscarriages were compared with those with three or more miscarriages **(Jaslow et al., 2010).**

The definition variation from three consecutive losses to two consecutive losses made an increase in the scale of the problem from 1% to 5% of all couples trying to conceive. It is part of a range of reproductive disorders sharing a common underlying cause **(Greenwood and Jauniaux, 2002)**.

Recurrent abortion must be distinguished from sporadic spontaneous abortion that are nonconsecutive pregnancy losses occurring randomly during a woman's reproductive year **(ACOG, 2001).**

INCIDENCE:

Preclinical or very early pregnancy loss as it is sometimes referred to, is seen in 31% of patients **(Wilcox et al., 1988)**. This entity is diagnosed by performing serum beta HCG assays in the late luteal phase prior to the onset of the next cycle. This accounts for the reduced fecundity of the human female to 30-40% observed in IVF cycles. This also explains the biochemical pregnancies encountered after assisted reproductive techniques **(Farquharson et al., 2005)**.

About 15% of couples lose one recognized pregnancy and 2% lose two. The theoretical risk of three or more losses is only 0.34% **(Carson and Branch, 2001; Kiwi, 2006)**.

Women with a history of one miscarriage carry a 24% risk of miscarriage in the next pregnancy, while women with a history of previous 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 **(Carson and Branch, 2001; Kiwi, 2006)**.

AETIOLOGY

Miscarriages can occur for many reasons, not all of which can be identified. Some of these causes include genetic, uterine or hormonal abnormalities, reproductive tract infections, and tissue rejection. Up to 15% of pregnancy losses in the second trimester may be due to uterine malformation, growths in the uterus (fibroids), or cervical problems. These conditions may also contribute to premature birth. **(Stephenson et al., 2002)**

Second trimester pregnancy loss is uncommon, but it should be regarded as an important event in a woman's obstetric history. Fetal abnormalities, including chromosomal problems, and maternal anatomic factors, immunologic factors, infection, and thrombophilia should be considered; however, a cause-and-effect relationship may be difficult to establish. A thorough history and physical examination should include inquiries about previous pregnancy loss. Laboratory tests may identify treatable etiologies. Although there is limited evidence that specific interventions improve outcomes, management of contributing maternal factors (e.g., smoking, substance abuse) is essential. Preventive measures, including vaccination and folic acid supplementation, are recommended regardless of risk. Management of associated chromosomal factors requires consultation with a genetic counselor or obstetrician. The family physician can play an important role in helping the patient and her family copes with the emotional aspects of pregnancy loss. **(Palter, 2005).**

Pregnancy loss during the second trimester (i.e., 13 to 27 weeks' gestation) is rare and often is not distinguished from first trimester pregnancy loss **(Flint and Gibb, 1996).**

However, a true second trimester loss should be considered a unique entity, and an appropriate evaluation is indicated. Pregnancy loss is considered a miscarriage when it occurs before 20 weeks' gestation; after this time it is

considered a stillbirth. Nevertheless, there is considerable overlap between these definitions, and definitions vary by state **(ACOG, 1996 and Petilt, 1987).**

Rates of pregnancy loss decrease as the pregnancy progresses. Overall, about 10-20 % of all recognized pregnancies and 30-40 % of all conceptions end in pregnancy loss **(Wang et al., 2003).**

Miscarriage that occurs at 13 to 14 weeks' gestation usually reflects a pregnancy loss that happened one to two weeks earlier. Approximately 1-5 % of pregnancies are lost at 13 to 19 weeks' gestation, whereas stillbirth occurs in 0.3 % of pregnancies at 20 to 27 weeks' gestation, a rate similar to that of third trimester stillbirth **(Simpson et al., 1987)**.

Etiologies of Second Trimester Pregnancy Loss

Conditions associated with second trimester pregnancy loss overlap those of the first and third trimesters to a certain extent, but some are characteristic of second trimester losses **(Flint and Gibb, 1996).**

I- CHROMOSOMAL ABNORMALITIES

In addition to their role in first trimester miscarriage, chromosomal abnormalities also cause pregnancy loss in the second trimester. About 24 % of pregnancy losses in the second trimester are caused by chromosomal abnormalities, and about 12 % of late second trimester losses are attributed to this cause **(Warburton et al., 1986).**

Chromosomal abnormalities found in second trimester losses are similar to those found in live births; the most common are trisomies 13, 18, and 21, monosomy X (i.e., Turner syndrome), and sex chromosome polysomies. Genetic factors including chromosomal disorders, single gene defects, and multifactorial

factors account for 3.5-5 % of the causes of recurrent miscarriage **(Egozcue et al., 2000)**.

Fetal aneuploidy is the most important cause of miscarriage before 10 weeks gestation **(Jacobs and Hassold, 1987)**.

At least 50- 60 % of all miscarriages are associated with cytogenetic abnormalities, the most frequent being trisomy followed by polyploidy and monosomy X **(Stephenson et al., 2002)**.

Most human aneuploidies arise from errors in the first meiotic division of the oocyte, which is initiated prenatally and is not complete until ovulation. An increased rate of sperm chromosome abnormality has been reported in couples with recurrent miscarriage **(Giorlandino et al., 1998)** but only 7 % of fetal trisomies have been shown to arise from paternal meiotic errors **(Robinson et al., 1999)**.

II- FETAL AND MATERNAL ANATOMIC FACTORS

Anatomic uterine defects are known to cause obstetric complications, including recurrent pregnancy loss, preterm labor and malpresentation, although many women with such defects may have uncomplicated pregnancies. Most commonly, the complications result from impaired vascularization and fetal growth restriction **(Bricker and Farquharson, 2000)**

A-Congenital mullerian abnormalities:

Will be discussed later.