Cytogenetic Study for Couples with Repeated Abortion

Thesis

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A1c	Glycosylated hemoglobin
AC	Abnormal child
ACA	Anticardiolipin antibody activity
ACOG	American College of Obstetricians and Gynecologists
APLAs	Antiphospholipid antibodies.
APLs	Antiplatelets
DES	Diethylstilbestrol
FM	Fetal Malformation
ID	Infant death
IPLWG	Inherited pregnancy loss working group
IUFD	Intrauterine fetal death
LAC	Lupus anticoagulant
LDA	low dose aspirin
LPD	Luteal phase defects
LMWH	low molecular weight heparin
ND	Neonatal death.
PCOS	Polycystic ovaries
POC	product of conceptus
PL	Pregnancy loss
PRL	prolactin
RA	Repeated abortion
RCOG	Royal Collage of Obestetricians and Gynaecologist
Rcp	Reciprocal translocation
RM	Recurent miscarriage
Rob	Robertsonian translocation.
RPL	Recurrent pregnancy loss
SAB	Spontaneous abortion
SB	Stillbirth
SLE	Systemic Lupus Erythematosus
Th 1	T- helper cells
TS	Turner syndrome
TSH	Thyroid stimulating hormone
UFH	unfractionated heparin

Introduction

Pregnancy loss is very common, both preclinically and clinically. Many embryo are never implant and are lost even before clinical recognition of pregnancy **(*Wilcox et al., 1988).***

Abortion is defined as the termination of pregnancy before 20 weeks of gestation. Approximately 15% of clinically recognizable pregnancies end in spontaneous abortion ***(Hogge, 2003).***

Miscarriages affect 15% of women, primarly in the first trimester, whilst most are sporadic and non recurrent, there is a subset comprising 2-5% of couples that suffers recurrent miscarriage ***(Clark, 2003).***

Patients are usually classified as having recurrent spontaneous abortion after three or more losses, but sometimes two losses is used as the criterion ***(Warburton , 2000),*** as Some clinician favor changing the definition to two or more consecutive losses ***(Regan, 1991).***

Most textbooks define recurrent pregnancy loss (RPL) as three or more consecutive spontaneous abortions. This definition can be further subdivided into primary (all pregnancies lost) or secondary (after a successful pregnancy). In many clinical situations, the definition is altered to two or more consecutive spontaneous abortions ***(Awad ,2004).*** While the inherited pregnancy loss working group (IPLWG) defines recurrent miscarriage as three or more clinically recognized consecutive or non-consecutive pregnancy losses occurring prior to fetal viability (<24 weeks) ***(Laurino et al., 2005).***

Recurrent miscarriages have a range of possible causes including genetic, anatomic, endocrine, immune, infective,

thrombophilic, and unexplained ***(Kavalier, 2005).***

In approximately 3-6 %of couples with recurrent pregnancy loss, one partner will have a genetically balanced structural chromosome rearrangement. Balanced translocations account for the largest percentage of these karyotypic abnormalities ***(Franssen et al., 2005).***

They can cause pregnancy loss because segregation during meiosis results in gametes with duplication or deficiency of chromosome segments. Other genetically balanced structural chromosome abnormalities, such as chromosome inversions, account for a small percentage of abnormal parental karyotypes among couples with recurrent pregnancy loss. The clinical consequences of such abnormal gametes include repeated abortions, still birth and giving birth to malformed children and severe mental handicap ***(Carp et al., 2004).***

Prenatal diagnosis is therefore must be offered to carrier couples in subsequent pregnancies. No consensus exist between current guidelines for the management of recurrent miscarriage on whether chromosome analysis should be offered after two or three miscarriage ***(Royal collage of obstetrician and Gynacologist, 2003).***

Aim of the work:

The aim of this work is to study the frequency and type of chromosomal aberrations that contribute to the occurrence of repeated abortions in Egypt.

Chapter 1:

Abortion

Definitions:

Spontaneous abortion (SAB) or miscarriage is defined as the involuntary termination of pregnancy before 20 weeks of gestation (dated from the last menstrual period) or spontaneous expulsion of fetus below a fetal weight of 500g ***(Speroff and Fritz, 2005).***

Miscarriage can be further divided into embryonic losses which occure before the ninth gestational week and into fetal losses which occure at or after the 9^{th} to 20^{th} weeks of gestation ***(lee and Siliver, 2000),*** table (1) shows terms used to describe pregnancy loss ***(Petrosa, 2006).***

Table (1): Terms used to describe pregnancy loss ***(Petrosa, 2006).***

Term	Definition
Chemical pregnancy loss	Loss of biochemically evident pregenancy
Early pregnancy loss	Abortion of the first trimester, loss of histologically recognized pregnancy, or a loss based on ultrasonographic findings.
SAB	Pregnancy loss before 20 weeks gestation, as based on last menstrual period
Habitual or recurrent abortion	3 or more consecutive SABs
Stillbirth	Pregnancy loss after 20 weeks' gestation (neonatal loss is the death of a live born fetus)

Recurrent pregnancy loss is usually defined as three or more spontaneous pregnancy losses (not necessarily consecutive) ***(lee et al., 2000)*.**

Recurrent first trimesteric abortion is defined as the occurrence of 3 or more clinically recognized spontaneous losses before 12 weeks from the last menstrual period *(**Wilcox et al., 1988**).*

Incidence

Pregnancy loss is the most commen complication of pregnancy and it is estimated that fetal viability is only achieved in 30% of all human conceptions. 50% of which are lost prior to first missed menses ***(clark, 2003).***

Miscarriage affect 15% of women, primarily in the first trimester, whilst most are sporadic and none-recurrent, there is a subset comprising 2-5 % of couples that suffers recurrent miscarriage ***(clark, 2003).***

Miscarriage risk increases with the number of previous pregnancy losses but rarely exceeds 40-50%. Risk for pregnancy loss also rises with increasing maternal age, moderately after 35 and more rapidly after age 40 ***(Nybo Andersen et al., 2000).***

Etiological factors

Among all factors the only undisputed causes of recurrent

pregnancy loss are genetic factors, anatomic or immunologic ***(Speroff and Fritz, 2005).***

Alloimmunopathology, inherited thrombophilias, endocrinopathies, infections and environmental exposure have been implicated but are not established causes of recurrent abortion ***(Speroff et aI., 2005).***

Even after a comprehensive evaluation recurrent pregnancy loss remains unexplained in well more than half of affected couples ***(Speroff et aI., 2005).*** Table (2) shows commonly reported causes of recurrent pregnancy loss.

Table (2): Commonly reported causes of recurrent pregnancy loss ***(Laurino et al., 2005)***

Commonly reported causes of recurrent pregnancy loss
Endocrine
Uncontrolled diabetes mellitus
Luteal phase deficiency (remains in conclusive, limited to 1st trimester.
Polycystic ovarian syndrome.
Environmental agents
Prolonged exposure to alcohol, smoking, cocain.
Immunologic
Antiphospholipid syndrome
Maternal factors (acquired, inherited, structural)
Uterine anatomic malformations
Myomas
Cervical abnormalities
Chromosomal and single gene disorders
Fetal chromosomal abnormalities
Parental balanced translocation
Alpha thalassemia major
Thrombophilia
X-linked mal lethal conditions

I- Non Genetic factors

1-Anatomic factors

a- Congenital malformation

b- Uterine leiomyomas and polyps

c- Intrauterine adhesions

d- Incompetent internal cervical os

2- Systemic and localized endocrine abnormalities

a- Thyroid disease

b- Diabetes mellitus

c- Hypersecretion of LH

d- Polycystic ovaries

e- High androgen level

f- Hyperprolactinemia

g- Luteal phase defect

h- Primary endometrial defect

3- Immunological factors:

a- Autoimmune mechanism

b- Alloimmune mechanism

4-Infectious causes

5- Lifestyle factors, environmental factors and miscellaneous factors