Recurrent Miscarriage (1st Trimester)

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*Introduction

*Miscarriage is the term used for pregnancy loss up to 24 weeks of gestation .

*The WHO has defined spontaneous abortion as expulsion of an embryo or fetus weighing 500 g or less , corresponding to about 20 to 22 weeks gestation.

*Early pregnancy loss is the most common complication of human gestation. Sporadic miscarriage is very common ,and 25% of all women become pregnant will experience one or more pregnancy losses.

*Between 1-2% of all couples will experience recurrent miscarriage ,defined as the loss of three or more consecutive pregnancies.

*Approximately 80% to 90% of women with a single spontaneous abortion will deliver a viable live infant in the next pregnancy.

*After a second pregnancy loss, couples naturally want to know the risk of another loss &what they can do to ensure a successful pregnancy .

Etiology..

*Determining the cause of recurrent miscarriage can be extremely problematic.

*The main causes of recurrent first trimester miscarriage includes:

1-Implantation factor..
2-Genetic problem...
3-Uterine anatomy problems..
4-PCO associated with hypersecretion of LH..
5-Primary antiphospholipid syndrome PAPS..
6-Unexplained...

1)Implantation factors:

*Implantation is a complex & finely programmed process , involving many interactions within & between maternal & fetal cell populations.

*Polypeptide factors called cytokines possibly exerting a positive effect on implantation. The endometrium is an active producer of cytokines, which may be required for both blastocyt attachment & maternal recognition of pregnancy & communication with the embryo.

*A cytokines defect can lead to implantation failure, but the exact mechanism for this has not yet been established.

*Most cases due to this factor are unrecognized & occurs before or during the next expected menses.

2) Genetic factors:

*A helpful statistic is that 45% of first trimester losses have an abnormal karyotype. The most common genetic abnormality is Trisomy. As well as Trisomy 21,or downs syndrome, Trisomy 16, 22, &15 are common also.

*From other hand, recurrent miscarriage may result from two different situations producing chromosomal abnormality:

1-Structural aberration as:

- Translocation: (occurs when two chromosomes break & rejoin again in wrong combination .It involve chromosomes 21/14, 21/22, 21/21),

  50% of all unbalanced translocations arise do novo during gametogenesis.

- Inversion: in one of the parent. (inverted chromosome is one in which apportion of the genes has been re-arranged in a reverse order).

2- Recurrence of numerical abnormalities in the miscarriage, (triploidy, tetraploidy & polyploidy)

3)Uterine anatomy problems:

*Congenital structural abnormalities such as bicornuat uterus & septate uterus are believed to cause about 5% of recurrent miscarriage.

*The anomalies vary from uterus didelphys to septate uteri & include intrauterine fibroids.

*Usually recurrent miscarriage occurs in 1st trimester with septate uterus & in 2nd trimester with bicornuat uterus.

*A uterine septum can be defined as: central fusion anomaly of the uterus that extends along, at least, half the length of the uterine cavity. The septum can extend down to the level of the external os.

*From the published data, the normal population incidence of intrauterine septum is likely to be approximately 2.7%.

*The possible causes of recurrent fetal loss includes: poor implantation site on the septum &/or disordered blood supply of the implantation of that site.

N.B. Heinonen (1994) in a retrospective 10-year data collection period ,found similar pregnancy rates in patients with & without uterine anomalies ,except for a small group with subseptate uteri.

4) PCO with hyper secretion of LH.

*Patients with PCOD appear to have an increased risk of spontaneous abortion. This has been attributed to elevated levels of LH.

*Mechanism includes:

1-It is known that the midcycle LH surge causes resumption of meiosis in the preovulatory oocyte by antagonizing the action of meiosis inhibition factors MIF (factor responsible for holding the oocyte in the diplotene stage of the first meiotic division until just before ovulation).

It has been suggested that raised follicular phase LH concentration may cause premature resumption of meiosis in the oocyte .This has led to the concept of ovulation of physiologically aged oocyte that either cannot be fertilized or if fertilized lead to the production of an abnormal embryo that is lost in early pregnancy.

2-An endometrial defect, leading to suboptimal implantation ,may be responsible for pregnancy failure. This is supported by the finding that LH receptors are present in the endometrium & by the observation that women with PCO have altered synthesis of endometrial prostaglandins, (play a key role in normal implantation).

5)Primary antiphospholipid syndrome PAPS:

*Recurrent early miscarriage is one of the common obstetric manifestation of antiphospholipid antibody syndrome.
*Three types of APL are of clinical relevance : lupus anticoagulant LA, anticardiolipin antibodies ACL & biologically false-positive serologic results of syphilis FR-SRS.

*The presence of APL has been linked to several medical conditions including: pregnancy loss, arterial & venous thromboses ,autoimmune thrombocytopenia & autoimmune hemolytic anemia .

*Rai et al (1995) reported that 15% of recurrent miscarriage have persistently positive tests for LA or ACL & can therefore be diagnosed as having PAPS.

6)Un-explained causes:

*In about 50% of cases that suffer from recurrent miscarriage no definite cause could be documented. A psychological problems was blamed.

*Recurrent spontaneous abortion are associated with deficiency in vasodilatory prostacyclin &/or dominance of vasoconstrictory thromboxan → uterine ischaemia → miscarriage , IUGR, IUFD.

**Management:

*Recurrent miscarriage is best managed in a specialist center. The main point of management is how can discover the main cause of recurrent miscarriage.

*A good history must be taken includes: present ,past , family, obstetrical, medical & surgical histories .

*The finding of structural chromosomal abnormalities from parental karyotyping provides the most likely cause of recurrent miscarriage & is also the starting point for familial chromosomal analysis.

*Ultrasonography & HSG play a role in diagnosis of anatomical abnormalities.

*All women with a history of recurrent miscarriage should be screened for both LA & ACA.

*In cases of PCO with raised LH, signs & symptoms of PCOD, ultrasonography to confirm the diagnosis of PCO, FSH & LH screen levels during early, late follicular & premenstrual phase of cycle .

*In some centers Doppler study of uterine artery weekly can be done to early diagnosis of uterine ischemia.

**Treatment :

1) **Genetic counseling:** the presence of parental chromosome abnormalities is always an indication for prenatal chromosomes studies in the next pregnancy.

*If karyotypes are normal a cytogenetic study should be done if the next pregnancy again ends as miscarriage .

*If a Trisomy compatible with life is observed , prenatal diagnosis is indicated in the next pregnancy.

2) **Anatomical uterine abnormalities :**

*Myomectomy to improve the uterine cavity anatomical shape.

*The benefit of surgical correction of uterine septum is doughtful. Van Iddekinge & Hofmeyr described successful pregnancies in 78% of patient treated by Strassmann metroplasty for uterine septa.

3) **PCOS with increased LH :**

*The use of LH-RH analogue at least 5 days prior to ovulation &induction of ovulation with pure FSH definitely improve the live birth rate.

4) **PAPS** :

*A varity of treatments including Steroids , Low dose Aspirin & Heparin have been used in order to improve the live birth rate of women with APA.

*Rai et al reported randomized study comparing the efficacy of aspirin 75mg/day vs that of aspirin in combination with low dose heparin (5000 iu sc 12-hours) in improving the live birth rate of women with recurrent miscarriage associated with APA. Treatment with aspirin alone resulted in a live birth rate of 42% but this was significantly improved to 71% among those treated with aspirin plus heparin.

5)Unexplained recurrent miscarriage :

*The following protocol is advisable from the beginning of pregnancy :

-Tocolytic drugs..(Ritodrine, Salbutamol).

Low dose aspirin. -

Supportive progesterone therapy during the first trimester. -

-Solcoseryl injection im 4ml every other day during the first trimester with monitoring of uterine artery pulsitility index PI to increase the dose if required.

-Dealing with emotional consequences.

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