Recurrent Pregnancy Loss(RPL)

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RPL defined as 3 or more consecutive pregnancy losses <20 weeks gestation or with a fetal weight<500 grams.

Incidence is approx. 1% of fertile couples.

Primary RPL- Multiple pregnancy losses in a women who has never delivered a live born.

Secondary RPL-Multiple pregnancy losses in a women with prior live birth

Etiology

Three widely accepted causes:

- Parental chromosomal abnormality
- Antiphospholipid antibody syndrome
- Structural uterine abnormalities

Other causes:

- Uncontrolled diabetes mellitus
- Overt hypothyroidism
- Progesteron deficiency by luteal phase defect and PCOS
- Hyperprolactinemia
- Inherited thrombophilia
- Maternal infections e.g. syphilis, toxoplasma
- Unexplained

Parental chromosomal abnormalities

- Accounts 2 to 4% of RPL
- One of the important causes of 1st trimester RPL
- Of abnormalities, reciprocal translocations are most common & followed by robertsonian translocations
- Karyotyping of both couple is considered
- Thorough genetic counseling of couples c abnormal karyotyping is needed
- Couples can be offered in vitro fertilization followed by preimplantation genetic diagnosis

Immunological Factors

- Autoimmune factors(antiphospholipid antibody)
- Antinuclear antibodies(ANA)
- Allo immune (immunity against another person-fetus and father) factor

Antiphospholipid antibody(APLA)syndrome

- One of the major causes of 2nd trimester RPL
- 85-90% miscarriage occurs c untreated APLA
- Fetal death is due to extensive thrombosis and infarction in placental tissue
- Diagnosis done by clinical and laboratory criteria…

Clinical criteria

Obstetric:

i. One or more unexplained deaths of a morphologically normal fetus at or beyond 10weeks
ii. Severe preeclampsia or placental insufficiency necessitating delivery before 34 weeks
iii. Three or more unexplained consecutive spontaneous abortion before 10 weeks

Vascular: one or more episodes of arterial, venous, or small vessel thrombosis in any tissue or organ

Laboratory criteria

i. Presence of lupus anticoagulant
ii. Medium or high serum levels of IgM or IgG anticardiolipin antibodies
iii. Anti beta-2 glycoprotein IgM or IgG antibodies

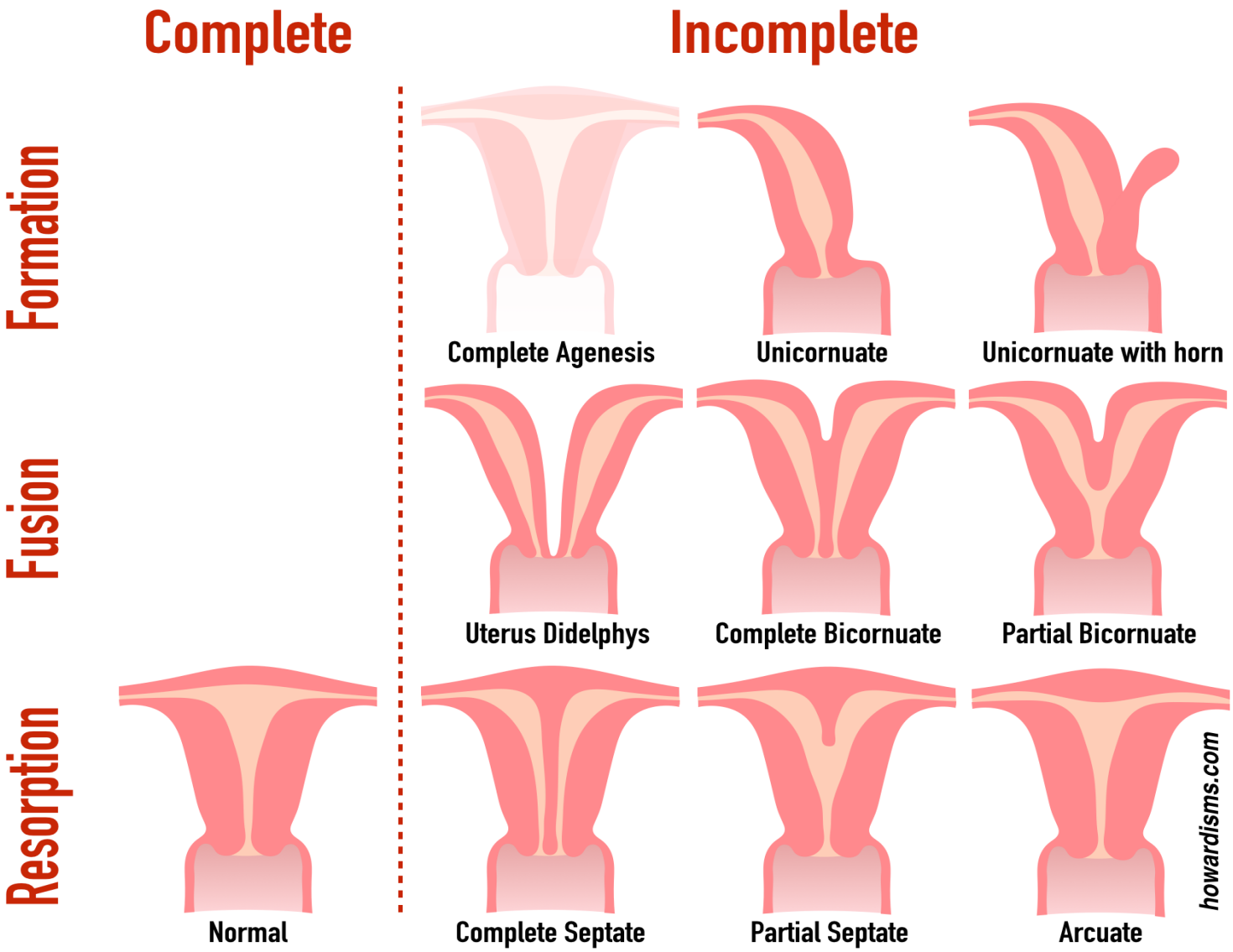
- At least one clinical and one laboratory criteria must be present for diagnosis
- Laboratory tests must be positive on two or more occasions at least 12 weeks apart

Structural uterine anomalies

Acquired:

i. Uterine synechiae (Asherman syndrome)- due to destruction of large areas of endometrium followed by uterine curettage, hysterescopic surgeries, uterine compression sutures, tuberculosis etc
ii. Submocousal Leiomyoma- at or near implantation site
iii. Cervical insufficiency- due to cervical tears, cervical surgeries, previous cervical dilatation by untrained person

Congenital: Mullerian duct anomalies like-



Diagnosis

HISTORY

- Advanced age(Maternal- Trisomy 13,18,21,47XXY, 47XXX; Paternal- Autosomal dominant)
- Thorough medical, surgical, obstetric and family history taken
- Previous type and gestational period of miscarriage, any histology or karyotype report should be documented

Diagnosis

Physical examination

- Look for pallor, galactorrhoea, thyroid swelling
- Distribution of body hair
- Per abdomen-any mass, scar of previous surgery, free fluid and hernial sites
- Per speculam -rule out vaginal septum, double cervix; if any vaginal infection, swab taken for culture sensitivity
- Per vagina-to assess absence of uterus or size of uterus, consistency of cervix to rule out mullerian anomaly

Diagnosis

Investigation:

Baseline tests:

i. CBC
ii. FBS,PPBS(c 75 gram of glucose),HbA1C
iii. Thyroid profile
iv. ABO & Rh typing

Diagnosis

Special tests:

i. Fasting serum insulin
ii. Lupus anticoagulant, anticardiolipin antibodies, anti beta-2 glycoprotein
iii. Hormone profile(FSH, LH, Prolactine)
iv. Karyotype of couple
v. Ultrasonography of pelvis
vi. Hysterosalpingography
vii. Hysteroscopy
viii. MRI pelvis rarely-to detect cervix and uterine anomaly

Management

Treatment plan is made by specific etiology:

Parental genetic abnormalities:

- Modern treatment of balanced translocation is PGD(preimplantation genetic diagnosis) c in vitro fertilization
- Antenatal genetic tests include –NIPT, chorionic villus sampling, amniocentesis

Preimplantation Genetic Testing

Two separate categories:

A. Preimplantation genetic screening-

- To identify aneuploidy in embryos to improve pregnancy success rate in certain patients populations
- Patients with no identified defect or disease

B. Preimplantation genetic diagnosis-

- To prevent the birth of affected children from parents with a known genetic abnormality

- Three techniques namely polar body analysis, blastomere biopsy and trophectoderm biopsy are widely used for both categories.
- Genetic counselling is always given

Thyroid dysfunction

- Hypothyroidism-levothyroxin
- Hyperthyroidism-propylthiouracil, carbimazole,methimazole
- Monitoing done by serum TSH,FT4, anti TPO every 6weeks
- In overt cases advice of endocrinologist taken

Diabetes mellitus

- Lifestyle modification
- Weight reduction
- Metformin (500 to 2000mg/day)
- Insulin
- Sometimes patients need admission for glucose monitoing
- In overt cases advice of endocrinologist taken

Luteal phase defect:

i. Natural micronized progesterone (100 to 400mg/day, by per vaginal/oral)
ii. Low dose FSH

Polycystic ovarian disease:

i. Lifestyle modification
ii. Metformine
iii. Laparoscopic diathermy/drilling to ovaries in selected resistant cases

APLA -Therapeutic option

Antiaggregants: Low dose aspirin-

- oral 60 to 80 mg daily
- Started as soon as pregnancy confirmed
- Stopped at 36 weeks or one week prior to delivery

Anticoagulants: A. Unfractionated heparin-

- 5000 to 10000u, S.C.,12hourly
- Started after USG confirmation of intrauterine viable pregnancy
- Stopped 12 hour prior to delivery and restarted 6 hours after delivery, at least 6 weeks of postpartum period

Anticoagulants:

B. LMWH(Low molecular weight heparin) -

- Enoxaperin, 40mg, S.C., once daily
- Dalteperin,5000 u, S.C., once daily
- Started after USG confirmation of intrauterine viable pregnancy
- Stopped 12 hour prior to delivery and restarted 6 hours after delivery, at least 6 weeks of postpartum period
- Changeover to warfarin from heparin is more conventional because of oral route in postpartum period

APLA -other treatment options

- Corticosteroids, IV immunoglobuline as immunosuppressive agents
- Plasmapheresis
- Statins

Treatment of uterine anomalies

Asherman syndrome:

- Hysterescopic synechiolysis

Uterine fibroids:

- Myomectomy in selected cases by laparotomy or laparoscopy

Uterine anomaly :

- Resection of septum hysteroscopically or on laparotomy
- Metroplasty (Strassman) for bicornuate uterus

Cervical insufficiency

- Characterized by painless cervical dilatation in second trimester followed by prolapse and ballooning of membranes into vagina and expulsion of immature fetus
- This sequences repeats in future pregnancy
- Previous forceful dilatation, conization, cautarization, tears of cervix ,congenital weakness of cervix are the important etiology
- Diagnosis-

i. History of 2nd trimester recurrent pregnancy loss

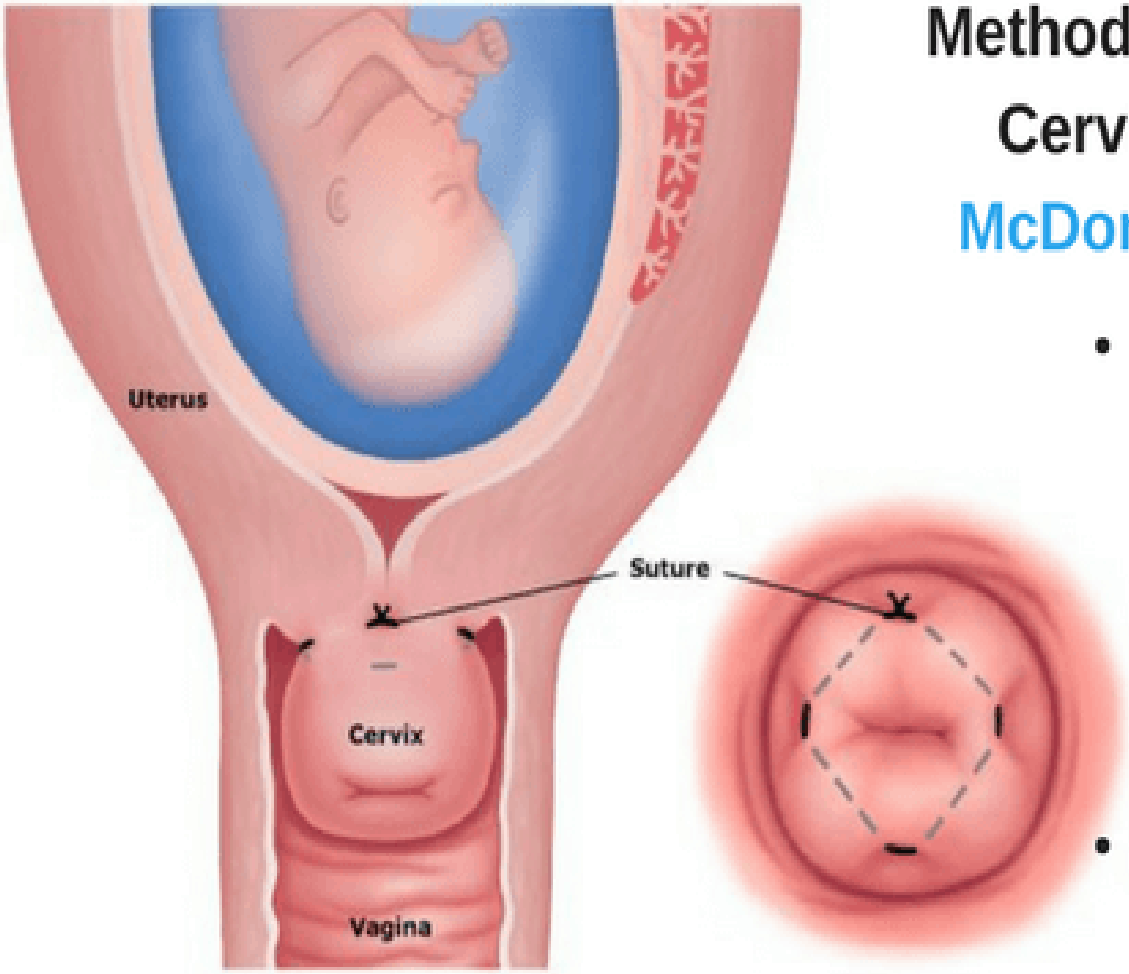
ii. Cervical length <25mm and or diameter of internal os >8mm by TVS

iii. In non pregnant women passes of no. 8 Hegar's dilator through internal os without resistance

Cervical insufficiency

- Cervical cerclage is the treatment of choice
- Performed in between 12-14weeks(as usual timing of cervical insufficiency is 16-24weeks)
- By this time, the fetus is large enough to detect anomaly by USG
- Following operation are most commonly performed-

McDonald’s cerclage



Methods/Techniques of Cervical Cerclage:

McDonald's Cerclage

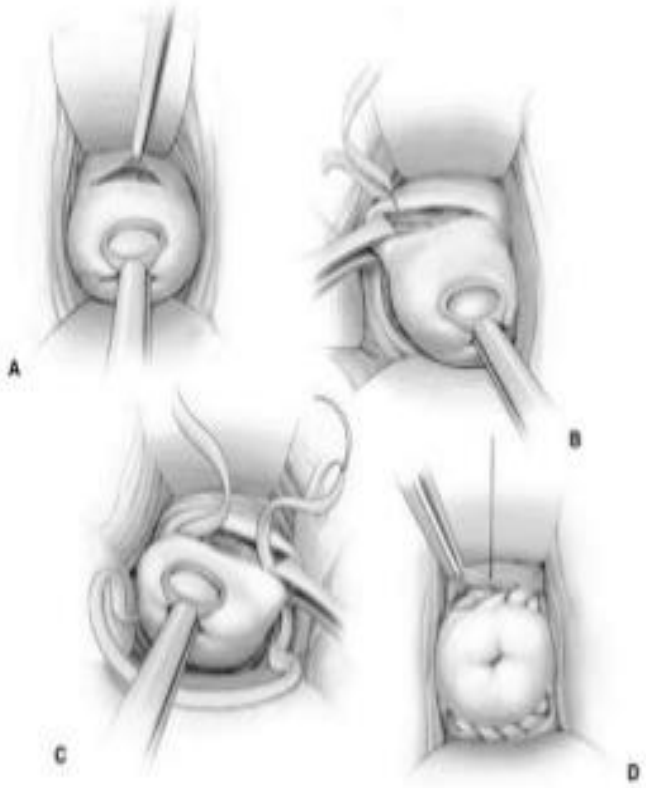
- In this method medically designed thread and needle are used, the internal os is stitched together like the mouth of a closed purse or pouch.
- Internal os is the junction of uterus and cervix.

{ MediFee.com }

Modified Shirodkar's cerclage

Shirodkar Procedure

- Original idea was to leave stitch in situ and opt for caesarean section
- Modified Shirodkar: the delivery does not necessarily have to be by cesarean, nor the suture left intact.
- Success rates 80%



Trans abdominal cerclage

- Also known as Benson and Durfy cerclage
- Performed when there is inaccessible cervix, repeated failure of vaginal approach, congenital short cervix
- The stitches are placed at the level of internal os via pfannenstein incision.
- Disadvantages-always need cesarean delivery

Rescue cerclage

- Salvage measure in case of premature cervical dilatation c exposed fetal membranes in vagina
- Cerclage may delay delivery by 5weeks as compared to expectant management
- Usually done if cervical dilatation <4cm

Suture material

Non absorbable sutures like-

- Mersilene tape
- Black silk
- Nylon
- Ethibond tape
- Monofilament

Contraindication

- Recent past or active vaginal bleeding
- Uterine contraction
- Chorioamnionitis , other vaginal infection
- Already cervix dilatation >4cm
- Fetal compromise

Complication

Early-

- Slipping/cutting of the stitch through cervix
- Rupture of membrane
- Miscarriage
- Premature labor

Late-

- Cervical dystocia, necrosis
- Chronic vaginal discharge

Post operative care

- Sedation
- Tocolysis (Isoxsuprine or Ritodrine 10 mg 8 hourly, for 5 to 7 days) starting a day before operation
- Progesterone supplementation
- Antibiotics coverage
- Bed rest for about 48 hours and then slowly ambulated

Advice on discharge

- Usual antenatal advice and fetal monitoring
- Avoid coitus
- Avoid rough journey
- To report if there is vaginal bleeding/lower abdominal pain

Removal of stitch

At 37 completed weeks or earlier if labor pain start or features of miscarriage appear

Thank you