Anatomic Considerations in RPL

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7.1 Introduction

Anatomic defects, both congenital and acquired of the uterus and the cervix, have been implicated in the etiology of recurrent pregnancy loss (RPL). These defects are listed in Table 7.1.

7.2 Congenital Uterine Anomalies

The exact contribution of congenital uterine anomalies to recurrent pregnancy loss (RPL) is not known. The reported prevalence in this population ranges between 1.8 and 37.6% [1]. This variability reflects the differences in the criteria and techniques used for diagnosis and the fact that available studies have included women with two, three, or more miscarriages in both the first and second trimester of pregnancy [2]. Generally, uterine malformations lead to second trimester abortions. Exact mechanism by which anatomic defects are thought to cause miscarriage is unclear, but it is attributed to decreasing effective intrauterine volume and abnormal and defective placentation.

Uterine defects causing RPL in decreasing order of frequency are septate (35%), bicornuate (25%), and arcuate uterus (20%) [3]. Other less common anomalies are didelphys and unicornuate uterus.

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Table 7.1 Anatomic defects associated with recurrent pregnancy loss

Congenital	Acquired
– Septate uterus	– Leiomyoma
– Bicornuate uterus	– Intrauterine adhesions (Asherman's syndrome)
– Arcuate uterus	– Cervical insufficiency
– Unicornuate uterus	
– Didelphys	

7.2.1 Septate Uterus

Septate uterus is by far the most common developmental anomaly (35%) [2] and is associated with poorest pregnancy outcomes [4]. It results from the failure of reabsorption of midline uterine septum between the two mullerian ducts. It could be complete if septum reaches up to internal os or partial if it falls short of internal os.

Poor reproductive outcomes are due to poor septal vascularization impairing placentation, increased amount of muscle tissue in the septum causing uncoordinated uterine contractions, and reduced effective length of uterine cavity.

Although septate uterus is not always associated with poor pregnancy outcomes, its detection in a patient of RPL warrants treatment [3, 5]. Treatment of choice is hysteroscopic septoplasty. It is a relatively safe and easy procedure and is associated with low morbidity. Significantly better reproductive outcomes have been reported with a reduction in RPL from 83 to 33% and an increase in live birth up to 67% [6]. Hysteroscopic septoplasty can be performed with laser, microscissors, or electrosurgical instruments. The septum is incised (rather than excision) just short of myometrium. The portion of the septum which is left retracts over itself. Procedure is considered complete when both the ostia are visualized simultaneously and hysteroscope can be moved freely between the two corneal recesses. Post-procedure, hormone therapy should be given for 2–4 months for endometrial regrowth [6].

7.2.2 Bicornuate Uterus

Bicornuate uterus is the second most common anomaly associated with RPL (25%). The etiology is incomplete fusion of mullerian ducts resulting in a deep fundal cleft and a common lower segment. It may be associated with a single cervix (Bicornuate unicollis) or two cervices (Bicornuate bicollis).

Surgery is generally not necessary until it is associated with RPL and no other etiologies are found. Strassman metroplasty is the procedure of choice for unification of two horns.

Data on reproductive outcomes after surgery with bicornuate uterus is limited. In one study of 22 patients with bicornuate uterus, 88% achieved live birth after Strassman metroplasty [7].

7.2.3   Arcuate Uterus

It is considered as a normal variant and is not associated with poor reproductive outcomes [8].

Other anomalies like uterus didelphys and unicornuate uterus though less common are associated with very poor pregnancy outcomes. Data on surgical treatment is very limited and cases have to be individualized.

7.3   Acquired Defects

7.3.1   Leiomyoma

Leiomyoma as a cause of RPL has always been debated. Several mechanisms have been proposed including:

- Mechanical compression of the fetus by the large fibroid.
- Large submucosal fibroid may cause distension of the uterine cavity.
- Increased contractility of the uterus.

Numerous studies have investigated the role of fibroid in causing pregnancy loss. Interestingly, majority of these studies have been conducted in patients undergoing in vitro fertilization (IVF) for infertility. Spontaneous miscarriage was higher in females having submucosal and intramural fibroids than with no fibroid [9]. No major difference was reported for pregnancy and delivery rate in women with subserosal fibroids [10, 11]. Thus, surgical removal of submucosal and intramural fibroids distorting cavity results in a better pregnancy outcome and live birth rate [11]. If a fibroid is subserosal or intramural and not distorting the uterine cavity, surgical treatment is not of much benefit, though the decision should be individualized for age, parity, site, size, number of fibroids, and other associated sign and symptoms.

7.3.2   Intrauterine Adhesions (Asherman's Syndrome)

Asherman syndrome usually causes infertility and menstrual problems but rarely can be associated with recurrent miscarriages. This is attributed to the decrease in functional intrauterine volume because of fibrotic bands. Common causes for intrauterine adhesions are vigorous postpartum curettage, endometrial tuberculosis, schistosomiasis, or other uterine surgery. It has been estimated that there is a 25% risk of developing Asherman's syndrome if dilatation and curettage is performed 1–4 weeks after delivery, 30.9% after missed abortion, and 6.4% after incomplete miscarriage [12–15].

March et al. [16] classified intrauterine adhesions as mild, moderate, and severe on hysteroscopy:

1. Mild: Less than three-fourth of the uterine cavity is involved. Adhesions are thin and flimsy. The fundus and the ostial areas are either minimally or not involved.
2. Moderate: One-fourth to three-fourths of the uterine cavity is involved. Adhesions are present but there is no agglutination of the walls. Fundus and ostial areas are only partially occluded.
3. Severe: More than three-fourths of the uterine cavity is involved. Thick bands and agglutination of the uterine walls are present. Ostial areas and the upper cavity are occluded.

Hysteroscopy is the mainstay in the diagnosis of intrauterine adhesions. Treatment includes hysteroscopic resection of the intrauterine adhesions and preventing regrowth of the fibrous tissue by supporting the endometrium with hormones.

7.3.3   Cervical Insufficiency

ACOG defines cervical incompetence as "inability of the uterine cervix to retain the pregnancy in second trimester in the absence of clinical contractions or labor or both." Cervical insufficiency affects 1% of pregnant females [17]. With cervical cerclage, improvement in pregnancy outcome has been reported. Studies have reported that improvement in pregnancy outcome occurred, with 68–78% of patients having term vaginal delivery after placement of cervical stitch [18, 19].

Causes of cervical insufficiency could be congenital or acquired (Table 7.2).

Diagnosis can be made either on the basis of history, examination findings, or investigations.

7.3.3.1 History-Based Diagnosis
- History of repeated second trimester losses associated with short painless labor and premature preterm rupture of membranes (PPROM)
- History of progressive early deliveries in subsequent pregnancies

Table 7.2 Causes of cervical insufficiency

Congenital causes	Acquired causes
(a) Connective tissue disorders (Marfan's syndrome, Ehlers-Danlos syndrome (b) Uterine malformations like unicornuate, bicornuate, or didelphys uterus	(a) Forceful or repeated dilatation and curettage (b) Cone biopsy (c) Unrepaired cervical tears (d) Instrumental delivery in a partially dilated cervix (e) Surgical procedure like Fothergill's operation, Duhrssen's incision

7.3.3.2 Examination
- Dilatation of the internal os with protruding membranes on per speculum examination
- Digital palpation—shortening of the length of the cervix
- Ultrasonographic assessment of the cervical length

7.3.3.3 Investigations
Inter-conceptional period:

- Passage of hegar dilator no.8 beyond the internal os without resistance and pain and absence of the snap upon withdrawal of the dilator
- Shirodkar's test—passage of uterine sound without resistance or pain

Various other tests using balloon of Foley's catheter have been postulated, but none of these can conclusively make or refute the diagnosis of incompetent cervix in nonpregnant state and should not be used [20].

During pregnancy:

Cervical length in general population is relatively stable after midtrimester. This fact may be helpful in serial evaluation of the cervical length for predicting preterm labor. Transvaginal sonography (TVS) is the most accurate method of measurement of cervical length, and transabdominal scan should not preferably be used for assessment of the cervix length [20]. Technique for USG measurement should be standardized so as to reduce the observational errors. Criteria proposed by Kagan are widely accepted and used [21].

Criteria for assessment of cervical length by TVS are:

- Patient's bladder must be empty.
- A longitudinal view of cervix should be obtained.
- The cervical canal and surrounding cervical mucosa should be identified.
- Pressure on the cervix should be minimal (as it elongates the cervical canal).
- Magnify the image, so that cervix should occupy 50–75% of the screen.
- The cervical length should be measured between the external and internal os.

With TVS, 25 mm length corresponds to tenth percentile and is suggested as the cut-off limit at 24-week period of gestation. Chances of preterm labor increase by sixfold if cervical length is <25 mm at 24 weeks [22, 23].

7.3.3.4 Management
As per RCOG guidelines, previous terminology of prophylactic, elective, or emergency cervical cerclage can be ambiguous [2]. Nomenclature based on indication is recommended and should be used.

- History-indicated cerclage
- Ultrasound-indicated cerclage
- Rescue cerclage

History-indicated cerclage: Women with three or more previous preterm births and/or second trimester losses are the candidates for cervical cerclage under this heading. It should not be routinely offered to women with two or fewer previous preterm births and/or second trimester losses.

Ultrasound-indicated cerclage: Women with history of one or more spontaneous midtrimester losses or preterm birth and who are undergoing ultrasound surveillance of cervical length should be offered cerclage, if cervix is 25 mm or less at or before 24 weeks of gestation. Cervical length screening is generally started at about 14 weeks in patients who are at high risk. There is no consensus on optimal timing or frequency of serial evaluation of cervical length. Repeat measurements should be at suitable intervals to minimize the observational errors with minimum interval being at least 1 week [20].

Timing of cerclage: Commonly performed around 12–14-week period of gestation for women with history-based diagnosis.

Procedure: Surgery of choice is cervical cerclage, which can be performed either by transvaginal route or by transabdominal route.

Prerequisites for surgery: Apart from routine antenatal investigations, first trimester ultrasound, screening to rule out congenital malformation, endocervical and high vaginal swab, and urine culture and sensitivity should be done.

7.3.3.5 Transvaginal Cerclage Operation

McDonald's Stitch
A purse-string suture using Mersilk or nylon is applied as high as possible at the cervicovaginal junction, below bladder. Four to five bites are taken and the knot is tied posteriorly. Stitch is removed after 37 completed weeks or when the patient goes into labor.

Shirodkar Stitch
In this procedure, the suture is placed at the level of internal os after retraction of the bladder. In the original technique, fascia lata was used for the stitch.

Steps of Shirodkar procedure:

- Transverse incision of about 2–3 cm is made on anterior vaginal wall at the cervicovaginal junction.
- Bladder is pushed up, well above the internal os.
- The cervix is pulled upward and an incision of about 2 cm is made on posterior vaginal wall at or above the internal os.
- A 5 mm Mersilene tape on a curved atraumatic needle is passed posteroanteriorly through the paracervical tissue and brought out through the anterior incision and then again anteroposteriorly so that knot ends up posteriorly avoiding the bladder.
- After the knot is tied, the band and the knot are anchored with the help of permanent stitch such as Mersilk or Prolene.

- Anterior and posterior incisions are closed with chromic catgut or any other absorbable suture.

  Advantage

- It is high up, close to internal os, and most part of the suture is buried.

  Disadvantages

- More chances of bleeding
- Difficult removal

7.3.3.6 Abdominal Cerclage

Indications
- Previous failed vaginal cerclage
- Extremely scarred or lacerated cervix due to previous surgeries like extensive cone biopsy or amputation
- Absent or hypoplastic cervix with history suggestive of cervical insufficiency

Procedure
- Abdomen is opened via transverse or vertical incision.
- Bladder flap is incised transversely till the level of internal cervical os.
- Mersilene tape is passed through the avascular space between the ascending and descending branches of uterine arteries.
- Tape is anchored to the uterine surface with the help of permanent sutures.
- Care should be taken not to twist the tape.

7.3.3.7 Laparoscopic Approach
Procedure is similar to transabdominal cerclage except that the procedure is done laparoscopically.

It has the added benefit of reduced blood loss, less postoperative pain, less adhesions, decreased hospital stay, and early recovery. The disadvantages of the procedure are high chances of ureteric injury and subsequent delivery is by cesarean section only.

7.3.3.8 Complications of Cerclage Operation
1. Infection
2. Hemorrhage
3. Preterm premature rupture of membranes
4. Cervical stenosis
5. Cervical dystocia and uterine rupture may also occur if there is delay in removal of stitch

7.4 Evidence-Based Management of Anatomic Abnormality in RPL

7.4.1 ASRM Committee Opinion

Congenital uterine abnormalities are generally associated with second trimester pregnancy losses and other pregnancy-related complications like preterm labor, malpresentation, and high chances of cesarean section. Role of uterine abnormalities in first trimester recurrent pregnancy loss is controversial, but assessment of uterine cavity is recommended.

The management of RPL patients with intrauterine synechiae and fibroid and polyp is debatable, and surgical correction of significant uterine defects should be considered.

7.4.2 RCOG Guidelines

The women with recurrent first trimester loss and one or more second trimester loss should be investigated by pelvic ultrasound for any possible uterine abnormality and if any abnormality is suspected, further investigations like hysteroscopy, laparoscopy, or 3D ultrasound should be done for confirmation. However, there is no conclusive evidence for supporting the benefits of surgical correction of the uterine abnormalities in improving pregnancy outcome.

Cervical cerclage is associated with potential risk of surgery and stimulation of uterine contractions. Therefore it should be considered in carefully selected cases.

Key Points
- Congenital uterine abnormalities are usually associated with second trimester pregnancy losses.
- In cases of recurrent second trimester losses assessment of uterine cavity should be done.
- Cerclage should be applied in carefully selected cases i.e. when indicated by history, ultrasound and emergent cases.

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