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Isthmocele: An Underrecognized Contributor To Infertility

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Abstract

Isthmocele, also known as a cesarean scar defect or uterine niche, is an increasingly recognized complication of prior cesarean delivery and an underappreciated contributor to infertility and gynecologic morbidity. Although many patients are asymptomatic, isthmocele may present with abnormal uterine bleeding, postmenstrual spotting, chronic pelvic pain, dyspareunia, and secondary infertility, and it may also increase the risk of adverse obstetric outcomes in future pregnancies. The likelihood of isthmocele appears to rise with multiple cesarean deliveries and with surgical and patient-related factors that impair uterine healing, including single-layer closure, obesity, smoking, diabetes, and hypertensive disorders. Diagnosis is typically made with transvaginal ultrasound, while hysteroscopy and magnetic resonance imaging may be useful in selected cases for confirmation or surgical planning. Management should be individualized based on symptom burden, defect size, residual myometrial thickness, and reproductive goals. Medical therapy may provide symptomatic relief in some patients, but surgical repair, particularly laparoscopic repair for larger or deeper defects, may improve fertility outcomes and reduce obstetric risk in appropriately selected patients. Greater clinician awareness of isthmocele is essential to support timely diagnosis, counseling, and treatment in women with prior cesarean delivery who desire future fertility.

Introduction

The global rise in cesarean delivery rates has led to an increasing incidence of the gynecologic complication known as isthmocele, a uterine scar defect. Isthmocele is characterized by a pouch-like defect at the site of a prior cesarean section incision or other uterine surgery, resulting from inadequate healing of the uterine wall. Although often underdiagnosed and asymptomatic, isthmocele has been associated with infertility, abnormal uterine bleeding, chronic pelvic pain, and obstetric complications. **[1]** In women desiring future fertility, isthmocele has been associated with reduced natural conception rates, recurrent implantation failures, and poorer outcomes following assisted reproductive technologies. **[1]** This paper aims to review the etiology, risk factors, clinical presentation, diagnostic modalities, and management options for isthmocele, with a focus on its role in infertility and reproductive outcomes.

Epidemiology

Isthmocele, also referred to as a cesarean scar defect or uterine niche, is an increasingly recognized sequela of cesarean delivery. The true prevalence is difficult to determine because many cases are asymptomatic and remain undiagnosed; however, reported incidence rates in women with prior cesarean section range widely from approximately 20% to 70%. **[1, 2]** Prevalence estimates vary substantially depending on the population studied and the diagnostic modality used, with higher detection rates reported when sonohysterography is employed rather than transvaginal ultrasound alone. **[2]**

Several observational studies have demonstrated that nearly one-third of women with a history of cesarean delivery may have an identifiable isthmocele on imaging, particularly among those presenting with abnormal uterine bleeding or infertility-related symptoms. **[1]** The prevalence appears to increase in parallel with rising global cesarean section rates, suggesting that isthmocele will represent an increasingly common gynecologic and reproductive health issue. **[1-3]** Importantly, detection rates increase with the number of prior cesarean deliveries, with some series reporting isthmocele in the majority of women after multiple cesarean sections.

Risk Factors

Cesarean-Related Factors

The most consistently identified risk factor for isthmocele formation is the number of prior cesarean sections. Increasing cesarean frequency is associated with progressive thinning of the residual myometrium at the isthmic level, predisposing to defect formation. Surgical factors also play a critical role. Vertical uterine incisions are

associated with a higher risk of isthmocele compared with transverse incisions, likely due to greater disruption of myometrial architecture. **[1, 2]**

Uterine closure technique significantly influences healing. Single-layer continuous suturing has been associated with reduced perfusion and increased risk of cesarean scar defects, whereas double-layer closure appears to provide improved myometrial approximation and decreased isthmocele risk. **[1, 2]** The use of long-lasting absorbable suture material has similarly been associated with improved scar integrity. **[1]**

Labor and Delivery Characteristics

Cesarean delivery performed at early cervical dilation (<2 cm) has been associated with a higher incidence of isthmocele compared with cesarean delivery during advanced labor, potentially due to differences in incision location relative to the internal cervical os. **[1]** Emergency cesarean delivery and prolonged labor prior to surgery have also been implicated, likely through impaired uterine perfusion and increased tissue stress. **[2]** Twin pregnancy represents an additional delivery-related risk factor, as increased uterine distension and mechanical load may impair scar healing. **[1]**

Patient-Related Factors

Several maternal characteristics may adversely affect uterine wound healing. Elevated body mass index has been consistently associated with increased isthmocele risk, possibly due to increased intra-abdominal pressure and higher rates of postoperative adhesion formation. **[1, 2]** Metabolic conditions such as gestational diabetes may impair fibroblast activity and tissue perfusion, thereby delaying scar remodeling. **[3]**

Hypertension has been associated with isthmocele development, potentially through compromised uterine blood flow and altered vascular remodeling at the scar site. **[1]** Endometriosis, ectopic pregnancy, and spontaneous abortion have also been correlated with isthmocele, possibly through inflammatory mechanisms or disruption of the uterine isthmus. **[2]**

Anatomical factors such as a retroflexed or retroverted uterus may contribute by altering mechanical forces at the scar site, although data remain inconsistent. **[1]** Lifestyle factors, particularly cigarette smoking, have been associated with impaired uterine scar healing and increased defect formation due to vascular compromise and reduced oxygen delivery to healing tissues. **[1]**

Clinical Manifestations

The clinical presentation of isthmocele is heterogeneous, ranging from asymptomatic incidental findings to significant gynecologic, reproductive, and obstetric morbidity. Many patients remain asymptomatic, contributing to underdiagnosis; however, when symptoms are present, they most commonly involve abnormal uterine bleeding, pelvic pain, and reproductive dysfunction. **[1-3]** Symptom severity appears to correlate with defect size, residual myometrial thickness, and the presence of intracavitary fluid. **[1, 2]**

Abnormal Uterine Bleeding

Abnormal uterine bleeding (AUB), particularly postmenstrual spotting, is the most frequently reported symptom associated with isthmocele. **[1-3]** The defect creates a pouch within the anterior lower uterine segment that can retain menstrual blood, which is subsequently released after menses has concluded. This mechanism explains the characteristic pattern of prolonged or intermittent spotting following otherwise normal menstruation. **[1]** Meta-analytic data demonstrate a significantly increased risk of AUB in women with isthmocele compared with those without cesarean scar defects. **[1]** Chronic inflammation within the niche and impaired uterine contractility may further contribute to prolonged bleeding and irregular menstrual patterns. **[1-3]** Larger defects have been associated with a higher prevalence and severity of bleeding symptoms. **[3]**

Pelvic Pain and Dyspareunia

Pelvic pain, including dysmenorrhea and chronic pelvic discomfort, is another common manifestation. **[1, 2]** Dyspareunia has been frequently reported, likely related to local inflammation, scar tissue irritation, or altered uterine mobility associated with the defect. **[1]** These symptoms may significantly impact quality of life, sexual function, and psychosocial well-being. **[2, 3]**

Reproductive Manifestations

Isthmocele has been associated with secondary infertility, reduced pregnancy rates, and adverse outcomes in assisted reproductive technologies. **[1-3]** Proposed mechanisms include chronic inflammation of the endometrial cavity, accumulation of intracavitary fluid with embryotoxic effects, and mechanical interference with sperm transport or embryo implantation. **[2-3]** Women with isthmocele undergoing in vitro fertilization have demonstrated lower clinical pregnancy and live birth rates compared with women without cesarean scar defects. **[2]**

An increased risk of spontaneous abortion has also been reported, particularly in patients with thin residual myometrium and larger defects, although the strength of this association varies across studies. **[1-3]**

Obstetric and Pregnancy-Related Complications

In subsequent pregnancies, isthmocele may predispose patients to serious obstetric complications. These include cesarean scar pregnancy, abnormal placentation (placenta previa and placenta accreta spectrum), uterine dehiscence, and uterine rupture. **[1-3]** The risk of uterine rupture appears to correlate strongly with residual myometrial thickness, with thinner scars conferring higher risk. **[2, 3]**

Isthmocele may also serve as a site for ectopic implantation, particularly in women with prior uterine surgery, posing a risk for severe hemorrhage and pregnancy loss. **[1, 2]** Given these risks, recognition of isthmocele prior to conception or early in pregnancy is clinically important.

Urinary and Adjacent Organ Symptoms

Although less common, urinary symptoms such as frequency, urgency, or difficulty with bladder emptying have been described, likely due to the anatomical proximity of the bladder to the anterior uterine wall and mass effect from larger defects. **[1]** These manifestations underscore the potential for isthmocele to affect adjacent pelvic structures beyond the reproductive system.

Infertility and Isthmocele

The presence of an isthmocele is associated with impaired fertility, with reported infertility rates ranging from 4% to 19%. **[1]** Multiple mechanisms have been proposed to explain the relationship between isthmocele and infertility. Chronic inflammation plays a central role, leading to sperm damage and reduced sperm motility. **[1]** Inflammatory processes also promote the secretion of pro-inflammatory cytokines, creating a hostile uterine environment that negatively affects embryo implantation, maintenance of pregnancy, and may contribute to adhesion formation. **[1]** In addition, chronic inflammation can impair myometrial healing, resulting in fibrotic yet structurally weak scar tissue. **[1]**

Isthmocele may also lead to the accumulation of fluid and mucus within the uterine cavity, further altering the intrauterine environment and compromising sperm survival and embryo implantation. The collection of blood within the defect can exert cytotoxic effects on the embryo due to excess iron released during hemoglobin degradation. **[1]** Furthermore, isthmocele has been associated with impaired endometrial receptivity and alterations in the uterine microbiota, both of which may adversely affect implantation. **[1]** In some cases, the defect may also create a physical barrier that obstructs sperm migration. **[1]**

Collectively, these mechanisms contribute to poorer outcomes in assisted reproductive technologies, including recurrent implantation failure and lower clinical pregnancy rates in women with isthmocele. **[1]**

Diagnosis

Various diagnostic modalities can be used to identify an isthmocele. Transvaginal ultrasound is the first-line modality and the most commonly recommended diagnostic tool. **[1]** Ultrasonographic features of an isthmocele include an anechoic or hypoechoic pouch-like defect at the site of a prior cesarean section scar, with an indentation depth greater than 2 mm. **[1, 3]** Isthmocele morphology may be classified as simple, simple with a single branch, or complex, characterized by multiple branches. **[1]**

Magnetic resonance imaging (MRI) may be utilized in complex cases or for preoperative surgical planning, as it provides a detailed assessment of the defect, including residual myometrial thickness, as well as the depth and width of the isthmocele. **[1, 3]** Hysterosalpingography can also demonstrate an isthmocele through contrast pooling at the scar site; however, it is not recommended as a primary diagnostic modality and is typically identified incidentally during an infertility evaluation. **[1, 3]**

Hysteroscopy is considered the gold standard for direct visualization of an isthmocele and may be combined with simultaneous surgical treatment in appropriately selected patients with smaller defects. **[1, 3]** Hysteroscopic findings may include hypervascularized areas, active bleeding from the niche, associated polyps, or endometriotic lesions. **[1]** However, this modality is limited in its ability to assess residual myometrial thickness. **[1]**

Management

Management of isthmocele depends on symptom severity and its impact on fertility. In asymptomatic patients with minimal or no effect on fertility, expectant management with clinical monitoring is appropriate. **[1]** In some cases, isthmocele may spontaneously resolve over time. **[1]**

Medical management may be used to alleviate symptoms associated with isthmocele. Combined oral contraceptive pills can reduce abnormal uterine bleeding, stabilize the uterine lining, and regulate the menstrual cycle by preventing excessive endometrial thickening that may exacerbate symptoms. **[1]** Gonadotropin-releasing hormone (GnRH) analogues may be utilized to temporarily suppress ovarian activity, resulting in reduced estrogen synthesis and ovulation suppression. **[1]** This approach can be particularly useful when more intensive hormonal control is required to manage abnormal bleeding and stabilize the endometrium. **[1]** Progesterone-releasing intrauterine devices (IUDs) may also be inserted to mitigate abnormal bleeding and menstrual irregularities by thinning the endometrium and reducing endometrial hypertrophy. **[1]** Treatment with GnRH agonists has additionally been associated with improvement in pelvic pain, dysmenorrhea, and dyspareunia, particularly in patients with concomitant endometriosis. **[1]**

Surgical management is indicated when symptoms are significant, negatively impact quality of life, or interfere with fertility. Hysteroscopic repair is the treatment of choice for small to moderate defects in patients with adequate residual myometrial thickness (greater than 2.5 mm). **[1, 4]** This procedure involves resection of the superior and inferior margins of the defect with ablation of the isthmocele cavity. **[1, 4]** Advantages include its minimally invasive nature and short recovery time; however, this approach does not restore myometrial thickness. **[1, 4]**

Laparoscopic isthmocele repair, with or without robotic assistance, is preferred for large or deep defects or in cases of thin residual myometrium. **[1, 4]** This technique involves excision of the scar

defect followed by a two-layer myometrial closure. **[1, 4]** Advantages include restoration of uterine anatomy and myometrial thickness, improved fertility outcomes, and reduced obstetric risks, though it is associated with longer operative times and recovery. **[1, 4]** Fertility restoration has been reported in up to 73% of patients following laparoscopic repair, with a reduced time to conception. **[1, 4]**

Cesarean delivery is recommended for all future pregnancies following isthmocele repair. In patients who conceive prior to surgical correction, elective cesarean delivery before 38 weeks' gestation is advised to minimize the risk of uterine rupture. **[1]** For patients with successful isthmocele repair and uncomplicated pregnancies, cesarean delivery is typically scheduled at 39 weeks' gestation. **[1]** Reported recurrence rates following laparoscopic repair with subsequent cesarean delivery range from approximately 4–16%. **[5]** Although there are no published data specifically reporting recurrence rates after hysteroscopic repair, research has shown that approximately 80% of patients experience complete relief from symptoms, including uterine bleeding and chronic suprapubic pelvic pain, 7% experience partial improvement, and 13% report no change following hysteroscopic repair. **[5]**

Conclusion

Isthmocele is an increasingly prevalent gynecologic condition that parallels the rising global rates of cesarean delivery and represents an important, yet often underrecognized, contributor to gynecologic morbidity and impaired fertility. Although many cases remain asymptomatic, isthmocele can significantly affect reproductive outcomes, menstrual patterns, pelvic pain, and obstetric safety, particularly in women desiring future fertility. Growing evidence supports a multifactorial pathophysiology involving chronic inflammation, impaired myometrial healing, intracavitary fluid accumulation, and mechanical disruption of normal reproductive processes. **[1]**

Accurate diagnosis relies on appropriate imaging modalities, with transvaginal ultrasound serving as the first-line tool and hysteroscopy providing definitive visualization in selected cases. Management should be individualized and guided by symptom severity, defect characteristics, residual myometrial thickness, and reproductive goals. While medical therapy may offer symptomatic relief, surgical repair, particularly laparoscopic repair, has demonstrated improved fertility outcomes and reduced obstetric risk in appropriately selected patients. **[1, 3, 5]**

As cesarean delivery rates continue to rise, increased awareness of isthmocele among clinicians is essential to facilitate timely diagnosis and intervention. Early recognition and individualized treatment of isthmocele may significantly improve reproductive outcomes and long-term gynecologic health in affected women.

Key Points

- Isthmocele is a common but often underdiagnosed complication of prior cesarean delivery.
- Typical symptoms include postmenstrual spotting, abnormal uterine bleeding, pelvic pain, and secondary infertility.
- Risk increases with multiple cesarean deliveries, single-layer closure, and factors that impair wound healing.
- Transvaginal ultrasound is the first-line diagnostic tool; hysteroscopy confirms diagnosis and may allow treatment.
- Management depends on symptoms, residual myometrial thickness, and fertility goals, with surgical repair improving outcomes in selected patients.
- Early recognition may reduce infertility and serious obstetric complications in future pregnancies.

Needs Assessment

Cesarean delivery rates continue to rise globally, increasing the prevalence of long-term uterine scar complications such as isthmocele (cesarean scar defect). Although imaging studies suggest that up to 20% to 70% of women with prior cesarean delivery may have a detectable defect, many clinicians remain unfamiliar with its clinical significance. As a result, isthmocele is frequently underrecognized in patients presenting with postmenstrual spotting, abnormal uterine bleeding, chronic pelvic pain, or secondary infertility.

Delayed or missed diagnosis can lead to prolonged symptoms, unnecessary infertility treatments, and preventable obstetric complications in future pregnancies, including cesarean scar pregnancy, abnormal placentation, uterine dehiscence, and uterine rupture. Variability in cesarean surgical technique and limited awareness of risk factors further contribute to inconsistent counseling and management. In addition, clinicians may be uncertain about when to pursue imaging, how to interpret residual myometrial thickness, and how to select between medical and surgical treatment options.

There is a clear educational gap regarding the pathophysiology, clinical presentation, diagnostic evaluation, and evidence-based management of isthmocele. Increased clinician awareness and improved understanding of individualized treatment strategies are necessary to optimize reproductive outcomes, reduce gynecologic morbidity, and enhance obstetric safety in women with prior cesarean delivery.

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