

Collagen at the Core: Understanding Spontaneous Uterine Rupture in Unscarred Uteri

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Background

Uterine rupture is a rare but life-threatening obstetric emergency with significant maternal and foetal morbidity. While most cases occur in women with a prior uterine scar, it can also affect unscarred uteri, requiring high clinical vigilance. A U.S. national study found an incidence of 1.8 per 10,000 deliveries in unscarred uteri, with multiple pregnancy, chorioamnionitis, multiparity, and advanced maternal age as key risk factors. Although these are well-established, the role of connective tissue abnormalities, particularly involving collagen, has received less attention. Collagen, a key structural protein in the uterine extracellular matrix, provides strength, elasticity, and tensile integrity, and its synthesis is shaped by genetic, environmental, nutritional, and racial factors. Clinical signs such as striae or skin laxity may signal increased rupture risk. We conducted a literature review on collagen abnormalities in spontaneous rupture of unscarred uteri, focusing on genetic, nutritional, and racial influences on collagen integrity and uterine strength.

Methodology

A systematic review was conducted using PubMed, Embase, and Cochrane Library. Keywords included “uterine rupture,” “unscarred uterus,” “collagen,” and “connective tissue disorders.” Studies reporting spontaneous rupture without prior uterine surgery and potential collagen abnormalities were included. Key themes and knowledge gaps were identified.

References:
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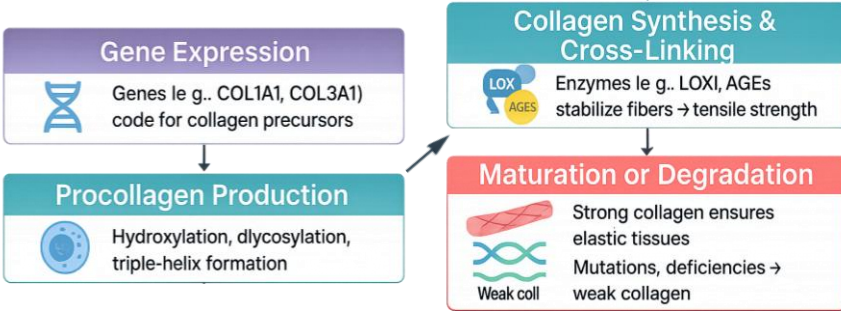
Results

Collagen cross-linking, essential for uterine strength and elasticity, is regulated by lysyl oxidase (LOX) and advanced glycation end-products (AGEs). Disruption of these pathways impairs tissue integrity, contributing to complications such as fibroids, preterm birth, and implantation failure (Kurt et al., 2023). A systematic review of six studies (412 pregnancies) identified that women with vascular Ehlers-Danlos syndrome (vEDS) are at high risk of uterine rupture, leading to recommendations for elective caesarean at 37 weeks to prevent expulsive trauma (MacCarrick et al., 2014). Similar risks were reported in Loeys-Dietz syndrome (TGF- β mutations) and Osteogenesis Imperfecta, where altered collagen expression and myometrial weakness were documented (Andreani et al., 2016). Environmental exposure to propylparaben – a common cosmetic preservative – disrupted uterine collagen architecture in animal models (Arshee et al., 2025). Nutritional factors such as vitamin C and dietary collagen were shown to enhance synthesis and support uterine tissue resilience.

Disorder	Gene Affected	Effect on Collagen	Uterine Rupture Risk
EDS (vEDS)	COL3A1	↓ Type III collagen	High
Loeys-Dietz	TGF-B	↑ Fragility	Moderate-High
Osteogenesis Imperfecta	COL1A1/2	↓ Type I	Moderate



Collagen Metabolism



Conclusion

Genetic, environmental, nutritional, and racial factors may impact collagen quality and uterine strength. Further research is needed to clarify these influences and identify those at risk of rupture. Understanding the underlying mechanisms could enable targeted treatments and improve diagnosis, risk assessment, and outcomes.