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Association of Adenomyosis with Recurrent Miscarriage

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Editorial letter

Authors

AboTaleb Saremi[1,2 *]

1- Sarem Gynecology, Obstetrics and Infertility Research Center, Sarem Women's Hospital, Iran University of Medical Science (IUMS), Tehran, Iran.
2- Sarem Cell Research Center (SCRC), Sarem Women's Hospital, Tehran, Iran.

Corresponding Authors:
AboTaleb Saremi; Sarem Fertility & Infertility Research Center (SAFIR), Sarem Women's Hospital, Iran University of Medical Sciences (IUMS), Tehran, Iran.
Address: Sarem Women Hospital, Basij Square, Phase 3, Ekbatan Town, Tehran, Iran. Postal code: 1396956111, Phone: +98 (21) 44670888, Fax: +98 (21) 44670432.

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Editorial

Introduction: Adenomyosis is the presence of endometrial glands and stroma within the myometrium. The exact pathogenesis of adenomyosis remains unclear, but several theories have been proposed. Common mechanisms include the invasion of the endometrium into the myometrium and the formation of adenomyotic foci from Müllerian remnants. Clinically, adenomyosis typically presents with heavy menstrual bleeding, dysmenorrhea, and diffuse uterine enlargement. However, definitive diagnosis requires histopathological examination, with adenomyosis findings present in 20–30% of hysterectomy specimens. Since a definitive diagnosis necessitates surgical tissue sampling, the exact prevalence of adenomyosis in the general population remains undetermined [1] …

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Adenomyosis is the presence of endometrial glands and stroma within the myometrium. The exact pathogenesis of adenomyosis remains unclear, but several theories have been proposed. Common mechanisms include the invasion of the endometrium into the myometrium and the formation of adenomyotic foci from Müllerian remnants. Clinically, adenomyosis typically presents with heavy menstrual bleeding, dysmenorrhea, and diffuse uterine enlargement. However, definitive diagnosis requires histopathological examination, with adenomyosis findings present in 20–30% of hysterectomy specimens. Since a definitive diagnosis necessitates surgical tissue sampling, the exact prevalence of adenomyosis in the general population remains undetermined [1].

Previous studies suggest that adenomyosis is more prevalent in nulliparous women and increases with age [2,3]. However, these findings may be biased due to diagnostic challenges associated with adenomyosis. Firstly, histopathological examination remains the gold standard for diagnosis, and older women are more likely to undergo surgery. In contrast, less invasive diagnostic tools, such as ultrasound, magnetic resonance imaging (MRI), and hysteroscopy, are preferred for younger women, offering the advantage of concurrent biopsy or treatment [4,5]. Secondly, the clinical manifestations of adenomyosis overlap with other gynecological conditions, such as endometriosis or fibroids, making differential diagnosis challenging. Lastly, no consensus exists regarding ultrasonographic diagnostic criteria for adenomyosis. Consequently, the prevalence of adenomyosis in younger women may be underestimated.

Some studies suggest a causal relationship between adenomyosis and infertility [6,7]. Several reports have highlighted the adverse effects of adenomyosis on assisted reproductive technology (ART) outcomes [8–10]. However, a recent study indicated that while adenomyosis does not impair embryo implantation, it significantly increases miscarriage rates following IVF with egg donation cycles [11].

Recurrent miscarriage (RM) is defined as two or more clinically documented pregnancy losses confirmed by ultrasound or histopathological examination. Possible causes of RM include uterine anomalies, immunological, genetic, endocrine, infectious, environmental, and thrombophilic factors. However, up to 50% of RM cases remain unexplained. Recently, Puente et al. screened a cohort of RM patients for adenomyosis and reported that over one-third of them had the condition. This suggests a possible causal link between adenomyosis and RM, warranting further observational studies [1].

Emerging evidence indicates a strong association between adenomyosis and adverse pregnancy outcomes, particularly RM. Given its significant implications for fertility and pregnancy success, understanding the underlying mechanisms of adenomyosis-related pregnancy loss and developing effective diagnostic and therapeutic strategies are essential.

Recent studies have identified several pathophysiological pathways through which adenomyosis may contribute to pregnancy loss. First, the condition is associated with a chronic inflammatory response in the myometrium, leading to elevated levels of pro-inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α). This inflammatory environment may create a hostile uterine milieu, disrupting embryo implantation and placental development [12]. Additionally, adenomyosis is linked to increased uterine contractility and structural alterations, which may impair fetal growth and heighten the risk of miscarriage [13].

Furthermore, vascular dysfunction and reduced endometrial receptivity play a crucial role in pregnancy failure among women with adenomyosis. Studies have shown that the expression of key implantation markers, such as leukemia inhibitory factor (LIF) and HOXA10, is altered in adenomyotic uteri, indicating impaired endometrial receptivity [14]. Moreover, abnormal angiogenesis, characterized by increased vascular endothelial growth factor (VEGF) expression, may lead to placental insufficiency and early pregnancy loss [15].

Despite these findings, diagnosing adenomyosis in women with RM remains challenging due to symptom overlap with other uterine disorders. Advances in imaging techniques, particularly high-resolution transvaginal ultrasound and MRI, have improved noninvasive detection of adenomyosis [16]. However, a standardized diagnostic criterion for reproductive-aged women is still lacking.

From a therapeutic perspective, the management of adenomyosis in RM patients remains incompletely defined. Current treatment options include hormonal therapies such as gonadotropin-releasing hormone (GnRH) agonists and dienogest, which aim to reduce inflammatory and excessive contractile responses. Emerging evidence suggests that surgical interventions, such as adenomyomectomy, may improve pregnancy outcomes in select cases [12]. Additionally, adjunctive treatments like low-dose aspirin and heparin have been proposed to address vascular defects and implantation failures in these patients [17].

With growing awareness of adenomyosis as a contributor to RM, larger studies are needed to refine diagnostic criteria, clarify underlying mechanisms, and optimize therapeutic strategies. Identifying at-risk individuals and implementing targeted interventions could improve pregnancy outcomes and enhance the reproductive prospects of women affected by this condition.

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