KURZA, Katarzyna, KOŚCIUSZKO, Zuzanna, SOBIŃSKI, Adam, CZERWONKA, Matylda, PODOLEC, Julianna, CIRAOLO, Silvia, AGNIESZKA KULCZYCKA-ROWICKA, WOJDA, Joanna, LESICZKA-FEDORYJ, Katarzyna and WALCZAK, Anna. Exploring Asherman's Syndrome: Insights from a Comprehensive Literature Review. Quality in Sport. 2025;46:66567. eISSN 2450-3118.
https://doi.org/10.12775/QS.2025.46.66567
https://apcz.umk.pl/QS/article/view/66567

The journal has been awarded 20 points in the parametric evaluation by the Ministry of Higher Education and Science of Poland. This is according to the Annex to the announcement of the Minister of Higher Education and Science dated 05.01.2024, No. 32553. The journal has a Unique Identifier: 201398. Scientific disciplines assigned: Economics and Finance (Field of Social Sciences); Management and Quality Sciences (Field of Social Sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398. Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).
The authors declare that there is no conflict of interest regarding the publication of this paper.
Received: 08.11.2025. Revised: 16.11.2025. Accepted: 16.11.2025. Published: 17.11.2025.

Exploring Asherman's Syndrome: Insights from a Comprehensive Literature Review

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Abstract

Purpose: This review aims to analyze the etiology, diagnosis, and management of Asherman's Syndrome, focusing on advancements in treatment, emerging therapies, and persistent research gaps. Asherman's Syndrome, characterized by intrauterine adhesions, leads to menstrual irregularities, infertility, and recurrent pregnancy loss.

Materials and Methods: A comprehensive review of published studies on Asherman's Syndrome was conducted, examining current diagnostic methods, treatment approaches, and therapeutic outcomes. Key sources included clinical trials, meta-analyses, and reviews from 1894 to 2021.

Results: Endometrial trauma, often from dilation and curettage, is the primary cause of Asherman's Syndrome. Diagnostic tools like three-dimensional ultrasound and hysteroscopy improve detection accuracy. Hysteroscopic adhesiolysis remains the gold standard treatment,

with success rates of 70–85% in mild to moderate cases. Adjunct therapies, such as hormonal treatments and intrauterine devices, reduce adhesion recurrence. Emerging therapies like platelet-rich plasma and stem cell treatments show potential for improving endometrial regeneration and fertility but require further validation.

Conclusions: While advances in hysteroscopy and regenerative medicine have enhanced outcomes for Asherman's Syndrome, severe cases remain challenging due to high recurrence and poor reproductive results. Early diagnosis, multidisciplinary care, and standardized treatment protocols are essential. Further research is needed to validate emerging therapies, refine diagnostic tools, and improve quality of life for affected women.

Keywords: Asherman's Syndrome; intrauterine adhesions; infertility; hysteroscopy; menstrual abnormalities

Introduction

Asherman's Syndrome, or intrauterine adhesion, is a condition marked by the formation of scar tissue within the uterine cavity, leading to partial or total obstruction of the endometrial cavity (1,2). This disorder significantly impacts reproductive health, often causing menstrual disturbances, infertility, and recurrent pregnancy loss (3,4). Originally identified by Heinrich Fritsch in 1894, its comprehensive description by Joseph Asherman in 1948 led to its current name (1).

The primary cause of AS is trauma to the endometrium, often following surgical interventions such as dilation and curettage, particularly after miscarriages or postpartum complications (5,6). Additional risk factors include uterine surgeries (e.g., myomectomy), pelvic infections, and chronic conditions such as tuberculosis and schistosomiasis (7,8). In low-resource settings, unsafe abortions further contribute to the global incidence of Asherman's Syndrome (9,10).

Asherman's Syndrome presents variably, with symptoms depending on the extent of adhesions. Common manifestations include hypomenorrhea, secondary amenorrhea, infertility, and cyclic pelvic pain (3,9). Diagnostic advances, including hysterosalpingography, sonohysterography, and magnetic resonance imaging, have improved the ability to detect intrauterine abnormalities (6,13). However, hysteroscopy remains the gold standard, offering both diagnostic and therapeutic benefits (6,13).

Pathophysiology and Risk Factors

The pathogenesis of Asherman's Syndrome primarily involves the disruption of the basal layer of the endometrium, leading to abnormal wound healing and subsequent fibrosis (7). Damage to this regenerative layer impairs its ability to restore the endometrial lining, resulting in the formation of scar tissue that obliterates the uterine cavity (8,10).

In low-resource settings, where healthcare access is limited, the incidence of Asherman's Syndrome is often driven by septic abortions or repeated uterine evacuations (9,11). It is estimated that over 30% of women who undergo multiple uterine evacuations for retained products of conception develop intrauterine adhesions of varying severity (12). Additionally, emerging research highlights a genetic predisposition to aberrant wound healing in Asherman's Syndrome, implicating molecular pathways such as transforming growth factor-beta (TGF-β) and vascular endothelial growth factor (VEGF) signaling (13,14).

Table 1: Risk Factors for Asherman's Syndrome

Risk Factor	Examples	Notes	References
Trauma to Endometrium	dilation and curettage, uterine surgeries	Most common cause	(5,6,10)
Infections	Pelvic inflammatory disease, tuberculosis	More prevalent in low-resource settings	(7,8,9)
Unsafe Abortions	Non-sterile procedures	Significant global health concern	(9,10)
Genetic Predisposition	Abnormal TGF-β and VEGF signaling pathways	Potentially modifiable with future therapies	(13,14)

Advances in Diagnostic Techniques

Accurate diagnosis of Asherman's Syndrome relies on a combination of clinical evaluation and imaging techniques. Traditional diagnostic tools like hysterosalpingography provide an overview of the uterine cavity but often lack the resolution needed for detailed assessments (6).

Hysteroscopy

Hysteroscopy is regarded as the diagnostic gold standard due to its ability to directly visualize intrauterine adhesions (7). It also facilitates simultaneous therapeutic intervention via adhesiolysis. Modern hysteroscopic techniques allow clinicians to classify adhesions based on severity and extent, using guidelines established by organizations such as the American Society for Reproductive Medicine (7,14).

Three-Dimensional Ultrasound

Three-dimensional ultrasound is gaining recognition as a non-invasive alternative to hysteroscopy. This modality provides detailed images of the uterine cavity and correlates well with hysteroscopic findings, particularly in cases involving mild to moderate adhesions (17).

Magnetic Resonance Imaging (MRI)

MRI is occasionally employed in complex cases where extensive fibrosis or coexisting pathology is suspected (19). While less commonly used in routine practice, its high-resolution imaging capabilities can be invaluable in delineating severe intrauterine abnormalities (19).

Biochemical and Molecular Diagnostics

Recent advancements in the field of biochemical and molecular diagnostics offer promising tools for the early detection of Asherman's Syndrome (16,20). Analysis of endometrial secretions for biomarkers such as cytokines, growth factors, and extracellular matrix proteins may help identify early-stage disease before clinical symptoms become evident (15,16). Genetic testing is also being explored to identify individuals at heightened risk for developing Asherman's Syndrome due to predispositions in wound-healing pathways (16,20).

Table 2: Diagnostic Techniques for Asherman's Syndrome

Technique	Description	Advantages	Limitations	References
Hysteroscopy	Direct visualization of adhesions	High accuracy; therapeutic potential	Invasive; requires anesthesia	(7,14)

Three-Dimensional Ultrasound	Provides detailed imaging of the uterine cavity	Widely available; non-invasive	Limited sensitivity for severe adhesions	(17)
Magnetic Resonance Imaging (MRI)	High-resolution imaging for complex cases	Useful in severe fibrosis or coexisting pathology	Expensive; not widely available	(19)
Biochemical Diagnostics	Biomarker analysis of endometrial secretions	Early-stage detection possible	Lacks established clinical applications	(15,16,20)

Treatment Strategies

Hysteroscopic Adhesiolysis

Hysteroscopic adhesiolysis remains the cornerstone of Asherman's Syndrome treatment, with the primary goal of restoring uterine cavity integrity (14). The procedure involves the mechanical disruption of adhesions under direct visualization, using tools such as scissors, lasers, or electrosurgical devices (14).

The success of hysteroscopic adhesiolysis depends on several factors:

- Operator expertise: Experienced surgeons are better equipped to achieve optimal outcomes while minimizing complications (15).
- Extent of adhesions: Mild and moderate adhesions respond well to treatment, with success rates ranging from 70% to 85%. However, severe cases often pose challenges due to extensive fibrosis and poor endometrial regeneration (12).
- Postoperative care: Adjunctive therapies are crucial in preventing adhesion recurrence (16).

Adjunct Therapies

Post-surgical interventions focus on promoting endometrial healing and minimizing the risk of adhesion reformation.

1. Hormonal Therapy: High-dose estrogen therapy stimulates endometrial proliferation, creating a more conducive environment for regeneration (16).

2. Mechanical Barriers: Intrauterine balloons, stents, or gel-based barriers are used to keep the uterine walls separated during the healing phase (13).

Regenerative Medicine

Innovative regenerative therapies, such as PRP and stem cell treatments, are emerging as promising options for patients with refractory Asherman's Syndrome.

- Platelet-Rich Plasma: it is rich in growth factors that enhance tissue repair, angiogenesis, and cellular proliferation (8,12). Studies have demonstrated its efficacy in increasing endometrial thickness and improving pregnancy outcomes (8,12). Clinical trials continue to explore its long-term benefits.
- Stem Cells: Mesenchymal stem cells, derived from sources such as bone marrow and menstrual blood, have shown potential in regenerating endometrial tissue (9,17). Ongoing research aims to establish standardized protocols for their clinical application (9,17).

Table 3: Adjunctive Therapies

Therapy	Mechanism	Applications	Challenges	References
Hormonal Therapy	Promotes endometrial proliferation	Prevents adhesion recurrence	Limited efficacy in severe cases	(16)
Mechanical Barriers	Separates uterine walls	Effective adjunct after surgery	Requires careful monitoring	(13)
Platelet-Rich Plasma (PRP)	Enhances tissue repair through growth factors	Promising results in refractory AS	Long-term efficacy still under study	(8,12)
Stem Cell Therapy	Regenerates endometrial tissue	Emerging option for severe cases	Experimental; expensive	(9,17)

Minimally Invasive and Robotic Surgery

Recent advances in minimally invasive and robotic surgical techniques have further refined the management of Asherman's Syndrome. These approaches offer enhanced precision, reduced

recovery times, and lower rates of adhesion recurrence (17,18). Robotic hysteroscopic systems, equipped with advanced imaging and instrumentation, enable better visualization and manipulation of delicate uterine structures (17,18).

Future Directions

Research into Asherman's Syndrome continues to uncover novel approaches to its prevention, diagnosis, and treatment. Potential areas for future exploration include:

1. Development of Biomarkers: Identifying specific molecular markers for early Asherman's Syndrome detection could transform diagnostic capabilities (15).
2. Personalized Medicine: Tailoring treatment strategies based on individual genetic and molecular profiles may optimize outcomes (15).
3. Innovative Materials: The development of bioengineered materials for use as intrauterine barriers or scaffolds may enhance endometrial regeneration (15).
4. Longitudinal Studies: Long-term studies assessing the outcomes of emerging therapies, such as PRP and stem cells, are needed to validate their efficacy and safety (15).

Table 4: Research Directions

Research Area	Focus	Potential Impact	References
Biomarkers	Molecular tools for early detection	Improves diagnostic accuracy	(15,20)
Personalized Medicine	Genetic and molecular profiling	Optimized patient outcomes	(15)
Bioengineered Materials	Intrauterine scaffolds for endometrial regeneration	Enhanced healing in severe AS cases	(15)
Regenerative Therapies	PRP and stem cell treatments	Expands treatment options	(9,17)

Conclusion

Despite significant advancements in understanding and managing Asherman's Syndrome, challenges remain, particularly in cases involving severe adhesions. Hysteroscopic

adhesiolysis, complemented by adjunctive therapies, remains the mainstay of treatment, while emerging regenerative approaches like PRP and stem cells offer new hope. Multidisciplinary collaboration and continued research are essential to address the complexities of this condition, ensuring better outcomes for women worldwide.

As the field continues to evolve, the integration of innovative diagnostic tools, advanced surgical techniques, and personalized care models will be crucial in improving the lives of patients with Asherman's Syndrome. Advocacy for improved access to reproductive healthcare and the empowerment of affected women must also remain central to global health efforts.

Disclosure:

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All authors have read and agreed with the published version of the manuscript. Funding Statement: The study did not receive special funding. Conflict of Interest Statement: There is no conflict of interest.

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