

# Evolving paradigms in the diagnosis and management of premenopausal women with abnormal uterine bleeding

Mine Senem Yılmaz Aksoy<sup>1</sup>, Teymur Bornaun<sup>1</sup>

Department of Obstetrics and Gynecology, University of Health Sciences, İstanbul Bağcılar Training and Research Hospital, İstanbul, Türkiye

## ABSTRACT

Abnormal uterine bleeding (AUB) is a common gynecological complaint among premenopausal women, encompassing a wide range of underlying disorders that complicate diagnosis and management. The evolving paradigms in medical science now incorporate advanced imaging techniques, personalized medicine, and molecular diagnostics to improve the accuracy of diagnoses and the effectiveness of treatment plans. This review examines recent advancements in the diagnostic approach, including the use of transvaginal ultrasonography, hysteroscopy, and biomarker analysis, which have significantly refined the identification of endometrial pathologies. Furthermore, we discuss the shift towards individualized treatment strategies that consider patient-specific factors such as age, reproductive plans, and comorbidities, facilitating tailored therapies. Special attention is given to the role of medical therapies ranging from hormonal treatments to novel non-hormonal drugs, as well as the consideration of minimally invasive surgical options as part of a comprehensive management strategy. By integrating current research findings with clinical practice guidelines, this article aims to provide a synthesized view of the dynamic field of AUB management, proposing a multidisciplinary approach to enhance patient outcomes in premenopausal women.

**Keywords:** Abnormal uterine bleeding, premenopausal women, personalized medicine, molecular diagnostics

Abnormal uterine bleeding (AUB) in premenopausal women represents a significant diagnostic and therapeutic challenge within the field of gynecology. AUB disrupts the normal menstrual cycle, characterized by deviations in the frequency, volume, and duration of menstrual bleeding. This condition is a predominant health concern not only due to its prevalence but also because of its profound impact on a woman's quality of life, encompassing physical discomfort, emotional distress, and social or occupational disruptions [1].

The management of AUB has historically been dic-

tated by a combination of empirical approaches and a limited understanding of its etiology. However, advancements in medical technology and a deepening of our pathophysiological understanding have ushered in an era of more targeted and effective management strategies [2-4]. These advances facilitate a move away from the "one-size-fits-all" approach, toward more personalized medical care, tailored to the unique needs of each patient based on specific diagnostic data [5].

The International Federation of Gynecology and Obstetrics (FIGO) provides a classification system that categorizes AUB into structural and non-structural

**Corresponding author:** Mine Senem Yılmaz Aksoy, MD.,  
Phone: +90 212 440 40 00, E-mail: [dr.senem.yilmaz@gmail.com](mailto:dr.senem.yilmaz@gmail.com)

**How to cite this article:** Yılmaz Aksoy MS, Bornaun T. Evolving paradigms in the diagnosis and management of premenopausal women with abnormal uterine bleeding. Eur Res J. 2024;10(4):41-425. doi: 10.18621/eurj.1478034



This is an open access article distributed under the terms of [Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License](https://creativecommons.org/licenses/by-nc-nd/4.0/)

**Received:** May 3, 2024  
**Accepted:** June 7, 2024  
**Published Online:** June 27, 2024

Copyright © 2024 by Prusa Medical Publishing  
Available at <https://dergipark.org.tr/en/pub/eurj>



causes, known respectively as PALM (Polyps, Adenomyosis, Leiomyomas, Malignancy) and COEIN (Coagulopathies, Ovulatory dysfunctions, Endometrial, Iatrogenic, Not yet classified). This classification system aids clinicians in pinpointing the precise etiology of AUB, thereby guiding appropriate and specific treatment modalities [2, 6].

The diagnostic process for AUB has become increasingly sophisticated, incorporating a range of modalities such as transvaginal ultrasonography, which offers a first-line non-invasive method that can identify structural causes of AUB with high accuracy. Magnetic resonance imaging (MRI) and hysteroscopy serve as additional diagnostic tools that provide detailed anatomic and functional insights, particularly useful in complex cases where initial imaging may not yield definitive results [7-9].

From a therapeutic perspective, the paradigm shift toward medical management has reduced the reliance on invasive surgical procedures. Medications such as tranexamic acid and non-steroidal anti-inflammatory drugs (NSAIDs) effectively manage bleeding and pain associated with AUB [10]. Hormonal therapies, including the use of oral contraceptives and progesterone therapies, not only regulate menstrual cycles but also treat underlying disorders like endometrial hyperplasia. For cases where medical management is insufficient or inappropriate, minimally invasive surgical options such as endometrial ablation or resectoscopic myomectomy are considered, which preserve uterine integrity and offer rapid recovery [11, 12].

Moreover, the role of novel therapies and emerging technologies cannot be overstated. The development of new pharmaceutical agents targeting specific pathways involved in endometrial proliferation and angiogenesis presents a promising horizon for those affected by AUB. Likewise, advancements in surgical technology continue to refine the safety and efficacy of procedures, minimizing their invasiveness and associated risks [5, 13].

The aim of this review is to critically analyze the latest advancements in the diagnosis and management of AUB, reflecting on how these have transformed clinical practices and improved patient outcomes. This article seeks to synthesize current research findings with established clinical guidelines to offer a comprehensive perspective on the most effective strategies for

managing this condition. The review's significance lies in its potential to guide clinicians towards more precise diagnostic techniques and tailored therapeutic interventions, thus ensuring better management of AUB, minimizing invasive procedures, and enhancing the quality of life for affected women.

Despite considerable advancements in medical technology and understanding, many women with AUB still undergo unnecessary invasive procedures due to misdiagnosis or suboptimal management. Addressing this issue, our review highlights the importance of using a systematic approach for diagnosis, based on the FIGO classification system, which categorizes AUB into structural (PALM) and non-structural (COEIN) causes. This classification is crucial for directing specific, cause-based therapeutic strategies which can range from pharmacological treatments to conservative surgical interventions.

Moreover, this article emphasizes the role of new diagnostic tools, including advanced imaging techniques and molecular diagnostics, in enhancing the precision of AUB diagnostics. These technological advancements not only help in identifying the specific types of AUB more accurately but also play a pivotal role in monitoring treatment efficacy and predicting outcomes. The review also delves into the latest therapeutic options, including the increasing use of medical management over surgical interventions. It assesses the efficacy of newer pharmacological agents that target specific pathophysiological pathways involved in AUB, thus offering personalized treatment options that align with the individual patient profiles.

## PATHOPHYSIOLOGY OF ABNORMAL UTERINE BLEEDING

### Understanding the Biological Foundations

Abnormal uterine bleeding (AUB) in premenopausal women encompasses a spectrum of symptoms that deviate from normal menstrual patterns, characterized by irregularity in timing, volume, or duration of menstrual flow. The complexity of AUB stems from the orchestrated processes governed by the hypothalamic-pituitary-ovarian (HPO) axis, which regulates the menstrual cycle through a precise hormonal balance [14, 15]. Disruptions in this system can lead to a range

of menstrual irregularities collectively referred to as AUB.

The menstrual cycle itself is divided into several phases, each marked by specific hormonal activities. The follicular phase begins with the secretion of gonadotropin-releasing hormone (GnRH) from the hypothalamus, which stimulates the anterior pituitary gland to release follicle-stimulating hormone (FSH) and luteinizing hormone (LH) [16]. These hormones promote follicle development and estrogen production from the ovaries. Mid-cycle LH surge triggers ovulation, releasing the egg and initiating the luteal phase, during which the corpus luteum forms and produces progesterone. This hormone is crucial for stabilizing the endometrial lining and preparing it for potential pregnancy. If pregnancy does not occur, progesterone levels fall, leading to the shedding of the endometrial lining as menstruation [17].

Disruptions in any part of this cycle can lead to AUB. These disruptions can be caused by a wide range of factors, including hormonal imbalances, structural abnormalities within the uterus, or systemic medical conditions. To systematically diagnose and manage AUB, the International Federation of Gynecology and Obstetrics (FIGO) has developed a classification system known as PALM-COEIN [18, 19]. This system categorizes the causes of AUB into structural causes (PALM: Polyps, Adenomyosis, Leiomyomas, Malignancy) and non-structural causes (COEIN: Coagulopathies, Ovulatory dysfunctions, Endometrial, Iatrogenic, Not classified). Understanding this classification is crucial for clinicians to direct specific investigations and treatments [20].

## FACTORS INFLUENCING ABNORMAL UTERINE BLEEDING

### Hormonal Influence

Hormones play a pivotal role in the pathophysiology of AUB. An imbalance in estrogen and progesterone levels is a common culprit. In conditions such as polycystic ovary syndrome (PCOS), ovulatory dysfunction can lead to prolonged estrogen exposure without progesterone counterbalance, causing endometrial hyperplasia and irregular bleeding. Similarly, thyroid dysfunctions can disrupt the hormonal balance necessary for regular menstruation, leading to AUB [18, 21].

### Endometrial Environment

At the cellular level, the endometrial environment itself is critical in the development of AUB. Local factors within the uterus, such as the presence of polyps or fibroids, can mechanically disrupt the endometrium, leading to bleeding. Moreover, adenomyosis, where endometrial tissue grows into the uterine muscle, creates a hyper-vascular environment that is prone to bleeding. Angiogenic factors, such as vascular endothelial growth factor (VEGF), are often elevated in these conditions, promoting further vascular instability and bleeding [19].

### Systemic Conditions

Systemic medical conditions also significantly influence menstrual bleeding. Coagulation disorders, such as von Willebrand disease, impair the blood's ability to clot, which can manifest as increased menstrual bleeding or AUB. Liver disease affects the metabolism of hormones such as estrogen and progesterone, leading to hormonal imbalances that can cause AUB. Even medications, particularly anticoagulants or hormone therapies, can induce AUB as a side effect [20, 21].

### Integrative View on AUB

Addressing AUB effectively requires an integrative approach that considers these multifaceted contributions to the pathology. Clinicians must evaluate hormonal levels, assess for structural anomalies via imaging like ultrasound or MRI, and consider systemic medical conditions that could be contributing to the symptoms. This comprehensive approach ensures that treatment strategies are targeted not just to symptom management but to the underlying causes, enhancing the effectiveness of interventions and patient outcomes [22].

In conclusion, the pathophysiology of AUB is complex and influenced by an array of factors including hormonal imbalances, structural abnormalities, and systemic conditions. Understanding these factors is crucial for the effective management of AUB. Employing the FIGO classification system facilitates a structured diagnostic approach, allowing clinicians to tailor interventions accurately and manage AUB effectively, thereby improving the quality of life for affected women [23]. This comprehensive

understanding also underscores the importance of ongoing research and education to continuously refine the approaches to diagnosing and treating this prevalent and impactful health issue.

## DIAGNOSTIC APPROACHES TO ABNORMAL UTERINE BLEEDING

### Clinical Evaluation

The initial approach to diagnosing abnormal uterine bleeding (AUB) involves a thorough clinical evaluation that establishes a comprehensive understanding of the patient's symptoms and medical history. This step is crucial as it guides the subsequent diagnostic pathway and informs potential therapeutic strategies [24-27].

The clinical evaluation begins with a detailed medical history that should cover the duration, frequency, and volume of menstrual bleeding. Clinicians should ask about the regularity of menstrual cycles, the presence of any associated symptoms such as pelvic pain, and the impact of bleeding on daily activities. Medical history should also include inquiries into reproductive history, including pregnancies, childbirth, and any gynecological surgeries or conditions such as fibroids or endometriosis [24].

Physical examination is another foundational element of the clinical evaluation and typically includes a pelvic exam. During the pelvic exam, clinicians assess the size and shape of the uterus and ovaries, check for any abnormalities or masses, and evaluate signs of hormonal imbalances such as hirsutism or acne. The examination might also involve a Pap test to check for cervical dysplasia or cancer if the patient is due for screening [23].

Documenting symptoms accurately is vital for diagnosing AUB. The use of symptom diaries, where patients record the days they bleed and note the heaviness of the flow, can provide valuable insights into the pattern of bleeding. This documentation aids in differentiating between various types of AUB and is essential for aligning with the FIGO classification for more targeted investigations [24, 26].

### Advanced Diagnostic Tools

After the initial clinical evaluation, more specific diagnostic tools can be employed to further investigate the causes of AUB. The selection of these tools often

depends on the findings from the clinical evaluation and the suspected underlying causes [26].

### Transvaginal Ultrasound

Transvaginal ultrasound (TVUS) is often the first-line imaging tool due to its non-invasive nature and effectiveness in evaluating pelvic structures. TVUS can provide detailed images of the uterus, endometrium, and ovaries, allowing for the identification of structural causes of AUB such as polyps, fibroids, and adenomyosis. It can also assess the thickness and texture of the endometrium, which is crucial for diagnosing endometrial hyperplasia or other intrauterine abnormalities. The major strengths of TVUS include its accessibility, cost-effectiveness, and detailed visualization of pelvic anatomy. However, its limitations lie in its operator dependency and less effectiveness in patients with a high body mass index or those with extensive pelvic scarring [23, 25].

### Magnetic Resonance Imaging (MRI)

MRI is used selectively for diagnosing AUB, particularly when TVUS results are inconclusive or when more detailed imaging of the uterine myometrium is necessary. MRI is highly sensitive and specific for diagnosing adenomyosis and distinguishing it from other uterine pathologies like fibroids. Its multiplanar imaging capability provides a comprehensive view of the pelvic anatomy without radiation exposure. However, MRI is more expensive, less available, and requires more time for both performing the scan and interpreting the results compared to TVUS [26].

### Hysteroscopy

Hysteroscopy is an invasive procedure that allows direct visualization of the uterine cavity and is used when there is a need to assess intrauterine pathologies that might not be adequately visualized by imaging studies alone. It is particularly useful for diagnosing and sometimes treating uterine polyps, submucosal fibroids, and focal areas of endometrial hyperplasia. Hysteroscopy provides the advantage of direct visualization and the ability to perform therapeutic interventions simultaneously, such as polypectomy or biopsy. Its limitations include the need for anesthesia, the risks associated with invasive procedures, and its dependency on the skill and experience of the operator [27].



## The Role of Laboratory Tests

Laboratory tests play a complementary role in the diagnosis of AUB. Blood tests, hormonal panels, and biopsy procedures are critical, especially when non-structural causes of AUB are suspected [28-30].

### Blood Tests

Complete blood count (CBC) can detect anemia, which may result from chronic heavy menstrual bleeding. Coagulation profiles (PT, aPTT) are essential if a bleeding disorder is suspected. Thyroid function tests are also recommended as hypothyroidism or hyperthyroidism can cause menstrual irregularities [30].

### Hormonal Panels

Hormonal assessments include measuring levels of estrogen, progesterone, LH, FSH, and prolactin, particularly when endocrine disorders or ovulatory dysfunctions are suspected. These tests help in understanding the hormonal milieu that may be contributing to AUB [31].

### Endometrial Biopsy

An endometrial biopsy is indicated if there is a suspicion of endometrial hyperplasia or cancer, especially in women over the age of 35 or those with risk factors such as obesity or PCOS. This procedure involves sampling the endometrial tissue and is typically performed if the endometrial thickness on ultrasound is greater than the normal limits for the patient's age and reproductive status [24, 30].

In summary, the diagnostic approach to AUB involves a multi-faceted strategy incorporating clinical evaluation, advanced imaging, and laboratory testing. Each diagnostic tool or procedure provides unique and complementary insights, which collectively contribute to a comprehensive understanding of the etiology of AUB. This rigorous diagnostic process is essential for developing an effective and individualized management plan for women suffering from AUB, ultimately aiming to improve their quality of life and reproductive health outcomes.

## MANAGEMENT OF ABNORMAL UTERINE BLEEDING

### First-line Medical Therapies

The medical management of abnormal uterine bleed-

ing (AUB) aims to alleviate symptoms, improve quality of life, and address underlying pathologies. First-line therapies include nonsteroidal anti-inflammatory drugs (NSAIDs), tranexamic acid, oral contraceptives (OCs), and hormonal intrauterine devices (IUDs), each offering unique mechanisms of action and benefits.

### NSAIDs

NSAIDs inhibit prostaglandin synthesis, thereby reducing menstrual blood flow and alleviating associated pain. These drugs are particularly effective in women with dysmenorrhea or heavy menstrual bleeding. By inhibiting prostaglandin production, NSAIDs not only reduce menstrual flow but also mitigate associated symptoms such as pelvic discomfort and cramping. Commonly used NSAIDs include ibuprofen, naproxen, and mefenamic acid. While generally well-tolerated, NSAIDs may cause gastrointestinal irritation or renal impairment, necessitating caution in patients with preexisting gastrointestinal disorders or renal insufficiency [28].

### Tranexamic Acid

Tranexamic acid is an antifibrinolytic agent that promotes blood clotting by inhibiting the breakdown of fibrin, thereby reducing menstrual blood loss. It is highly effective in reducing the volume and duration of menstrual bleeding, particularly in women with menorrhagia or bleeding disorders. Tranexamic acid is typically administered orally and can be initiated at the onset of menstruation or upon the onset of heavy bleeding. While generally safe, caution is advised in patients with a history of thromboembolic events or those at risk of thrombosis [29].

### Oral Contraceptives (OCs)

Oral contraceptives are commonly prescribed as first-line therapy for AUB due to their ability to regulate menstrual cycles and reduce menstrual bleeding. Combined oral contraceptives containing both estrogen and progestin suppress ovulation, stabilize the endometrium, and reduce menstrual flow. They also offer additional benefits such as contraception and relief from menstrual-related symptoms such as dysmenorrhea and premenstrual syndrome. Progestin-only pills or continuous-cycle regimens may be preferred in women with contraindications to es-

trogen or those seeking non-contraceptive benefits of OCs. Potential side effects of OCs include nausea, breast tenderness, and breakthrough bleeding, although these typically resolve with continued use [30].

### *Hormonal Intrauterine Devices (IUDs)*

Hormonal IUDs, such as levonorgestrel-releasing intrauterine systems (LNG-IUDs), offer an effective and long-term solution for managing AUB. These devices release progestin locally into the uterine cavity, resulting in endometrial suppression, reduced menstrual flow, and amenorrhea in some cases. LNG-IUDs are particularly suitable for women with heavy menstrual bleeding, as they offer a non-systemic hormonal approach with minimal side effects. Additionally, LNG-IUDs provide long-acting contraception, making them a convenient option for women seeking dual benefits of contraception and menstrual regulation. Insertion of an LNG-IUD is a minor procedure typically performed in an office setting, with potential side effects including irregular bleeding, cramping, and expulsion [31].

### **New Pharmacological Treatments**

In addition to traditional first-line therapies, emerging pharmacological treatments offer promising avenues for the management of AUB by targeting specific pathophysiological pathways.

### *Gonadotropin-Releasing Hormone (GnRH) Agonists*

GnRH agonists suppress the pituitary-ovarian axis, resulting in hypoestrogenism and amenorrhea. These agents are particularly useful in the management of AUB associated with estrogen-dependent conditions such as uterine fibroids or endometriosis. While highly effective in reducing menstrual bleeding and alleviating symptoms, GnRH agonists are associated with menopausal-like side effects such as hot flashes, vaginal dryness, and bone loss. Consequently, they are typically used as short-term therapy or as pre-operative adjuncts to reduce uterine size and vascularity before definitive surgical management [32].

### *Selective Progesterone Receptor Modulators (SPRMs)*

SPRMs are a novel class of drugs that selectively target progesterone receptors in the endometrium, exerting both agonistic and antagonistic effects. By modulating progesterone signaling, SPRMs offer

therapeutic benefits in conditions such as uterine fibroids and endometriosis, where aberrant progesterone action contributes to AUB. Drugs such as ulipristal acetate have demonstrated efficacy in reducing fibroid size, alleviating symptoms, and improving menstrual bleeding patterns. While generally well-tolerated, SPRMs may cause side effects such as headaches, hot flashes, and gastrointestinal disturbances [33].

The medical management of abnormal uterine bleeding encompasses a range of therapeutic options tailored to individual patient needs and preferences. First-line therapies such as NSAIDs, tranexamic acid, oral contraceptives, and hormonal IUDs offer effective symptom relief and menstrual regulation for many women with AUB. Emerging pharmacological treatments, including GnRH agonists and selective progesterone receptor modulators, present promising alternatives for women with refractory AUB or those seeking non-hormonal options. By offering a diverse array of therapeutic modalities, clinicians can effectively address the complex needs of women with AUB, improving their quality of life and reproductive health outcomes [31, 32].

### **Surgical and Minimally Invasive Interventions**

#### *Indications for Surgery*

While medical management is often effective for many cases of abnormal uterine bleeding (AUB), there are situations where surgical intervention becomes necessary. Indications for surgery vary depending on the underlying cause of AUB, the severity of symptoms, and the patient's reproductive goals [4, 7]. One common indication for surgery is the presence of structural abnormalities such as large fibroids, polyps, or adenomyosis that do not respond to medical therapies. These conditions can cause significant symptoms such as heavy menstrual bleeding, pelvic pain, and reproductive issues, warranting surgical intervention to alleviate symptoms and improve quality of life. Additionally, women with AUB associated with endometrial hyperplasia or malignancy may require surgical procedures for diagnostic and therapeutic purposes [21].

Several surgical interventions are available for managing AUB, each with its own effectiveness and associated risks. Hysterectomy, the surgical removal of the uterus, is considered the definitive treatment for many cases of AUB, particularly in women who have completed childbearing or who have failed other treat-

ments. While hysterectomy offers a permanent solution to AUB, it is a major surgical procedure associated with risks such as infection, bleeding, and complications related to anesthesia [34].

For women who wish to preserve their fertility or avoid the risks of hysterectomy, less invasive surgical options may be considered. Endometrial ablation is a minimally invasive procedure that destroys the endometrial lining of the uterus, reducing or eliminating menstrual bleeding. This procedure is suitable for women with AUB due to benign causes such as fibroids or adenomyosis who desire symptom relief without compromising fertility. However, endometrial ablation is not suitable for women with endometrial hyperplasia or malignancy [35, 36].

### *Minimally Invasive Techniques*

In addition to endometrial ablation, other minimally invasive techniques are available for managing AUB, each with its own advantages and considerations. Myomectomy, the surgical removal of uterine fibroids, is an option for women with AUB caused by fibroids who wish to preserve their fertility. This procedure can be performed via laparotomy, laparoscopy, or hysteroscopy, depending on the size and location of the fibroids. While myomectomy can improve symptoms and preserve fertility, it is associated with risks such as bleeding, infection, and fibroid recurrence [1, 37].

Uterine artery embolization (UAE) is another minimally invasive option for managing AUB due to fibroids. During UAE, tiny particles are injected into the blood vessels supplying the fibroids, causing them to shrink and reduce menstrual bleeding. UAE is suitable for women who wish to avoid surgery or preserve their fertility, as it does not involve the removal of uterine tissue. However, UAE is associated with risks such as pelvic pain, post-embolization syndrome, and the potential for complications related to fibroid expulsion [15].

Patient selection is crucial when considering minimally invasive interventions for AUB. Factors such as age, reproductive goals, the size and location of uterine abnormalities, and overall health should be carefully assessed to determine the most appropriate treatment option for each individual patient. Additionally, thorough preoperative counseling should be provided to ensure that patients understand the benefits, risks, and expected outcomes of the chosen interven-

tion [2-8].

Surgical and minimally invasive interventions play a crucial role in the management of abnormal uterine bleeding, particularly in cases where medical therapies are ineffective or contraindicated. Indications for surgery vary depending on the underlying cause of AUB and the patient's individual circumstances. While hysterectomy remains a definitive treatment option for many cases of AUB, less invasive techniques such as endometrial ablation, myomectomy, and uterine artery embolization offer alternatives for women who wish to preserve their fertility or avoid major surgery. By carefully evaluating patient needs and selecting the most appropriate intervention, clinicians can effectively manage AUB and improve the quality of life for affected women [31-35].

## **EMERGING TECHNOLOGIES AND FUTURE DIRECTIONS**

### **Innovative Diagnostics and Therapies**

Advancements in technology are revolutionizing the diagnosis and treatment of abnormal uterine bleeding (AUB), offering new insights and approaches to improve patient outcomes. Cutting-edge research is exploring innovative diagnostics and therapies that harness the power of artificial intelligence (AI), gene therapy, and other novel technologies [32].

### **Artificial Intelligence in Diagnostics**

One promising area of research is the use of AI in ultrasound analysis for the diagnosis of AUB. AI algorithms trained on large datasets of ultrasound images can automate the detection of structural abnormalities such as fibroids, polyps, and adenomyosis with high accuracy and efficiency [33, 34]. These AI-driven tools have the potential to streamline the diagnostic process, reduce interobserver variability, and improve diagnostic accuracy, particularly in cases where subtle abnormalities may be overlooked by human observers. By enhancing the speed and accuracy of ultrasound analysis, AI technologies hold promise for earlier detection and intervention in women with AUB, leading to improved patient outcomes and reduced healthcare costs [38].

### **Gene Therapy Approaches**

Another area of exploration in AUB research is the

development of gene therapy approaches to target the underlying molecular mechanisms driving abnormal uterine bleeding. Gene therapy holds the potential to correct genetic abnormalities, modulate hormone signaling pathways, and promote tissue regeneration within the uterine cavity [39, 40]. For example, researchers are investigating gene editing techniques such as CRISPR-Cas9 to selectively modify genes associated with endometrial dysfunction or abnormal bleeding patterns. By targeting specific molecular pathways implicated in AUB, gene therapy approaches aim to provide personalized and targeted treatments with minimal side effects, paving the way for more effective and tailored interventions in the future [41].

### **Integrating Patient-centered Care in AUB Management**

Personalized medicine is increasingly shaping the future of AUB treatment, with a focus on integrating patient preferences, values, and lifestyle adjustments into management plans. Patient-centered care emphasizes the importance of involving patients as active participants in their healthcare decisions, tailoring treatments to their individual needs and preferences, and considering the impact of AUB on their quality of life [20].

### **Tailored Treatment Plans**

In the era of personalized medicine, treatment plans for AUB are becoming increasingly tailored to the unique characteristics and preferences of each patient. Clinicians consider factors such as age, reproductive goals, comorbidities, and patient preferences when selecting treatment options, ensuring that interventions align with the patient's values and priorities. Shared decision-making between patients and healthcare providers is central to this approach, empowering patients to actively participate in their care and make informed choices about their treatment options [1, 7, 11].

### **Lifestyle Modifications**

In addition to medical and surgical interventions, lifestyle modifications play an important role in the management of AUB. Patients may be advised to make dietary changes, incorporate regular exercise into their routine, manage stress levels, and optimize their overall health to support hormonal balance and menstrual regularity. Integrating lifestyle modifica-

tions into AUB management plans can complement medical therapies, improve treatment outcomes, and enhance the overall well-being of patients [42].

The future of AUB diagnosis and treatment is shaped by innovative technologies, personalized medicine, and a patient-centered approach to care. Advancements in AI-driven diagnostics and gene therapy hold promise for earlier detection, targeted interventions, and improved outcomes for women with AUB. By integrating patient preferences, values, and lifestyle adjustments into management plans, clinicians can provide more personalized and effective care that addresses the unique needs of each individual patient. As research continues to advance and technology evolves, the landscape of AUB management will continue to evolve, offering new opportunities to optimize patient care and improve quality of life.

## **CHALLENGES AND CONSIDERATIONS IN ABNORMAL UTERINE BLEEDING MANAGEMENT**

### **Managing AUB in Diverse Populations**

Treating AUB poses unique challenges across different demographic groups, requiring clinicians to consider a range of factors such as age, reproductive intentions, and co-existing medical conditions [37, 41].

### **Age-related Considerations**

Age plays a significant role in AUB management, as the etiology and optimal treatment approach may vary depending on the patient's reproductive stage. Adolescents experiencing AUB may have underlying hormonal imbalances or anatomical abnormalities, necessitating thorough evaluation and tailored interventions. In contrast, perimenopausal and postmenopausal women may present with AUB due to endometrial pathology or hormonal fluctuations, requiring different diagnostic and therapeutic strategies. Additionally, older women may have comorbidities that impact treatment decisions, highlighting the importance of a multidisciplinary approach to care [42].

### **Reproductive Intentions**

The reproductive intentions of women with AUB influence treatment decisions, particularly regarding fertility preservation and contraceptive needs. For women desiring future pregnancies, interventions such



as myomectomy or fertility-sparing endometrial ablation may be considered to address underlying causes of AUB while preserving reproductive potential [43, 44]. Conversely, women who have completed child-bearing may opt for definitive treatments such as hysterectomy to alleviate symptoms and minimize the risk of recurrence. Clinicians must engage in shared decision-making with patients to align treatment plans with their reproductive goals and preferences [45].

### Co-existing Medical Conditions

Managing AUB in patients with co-existing medical conditions presents additional complexities, as underlying health issues may impact treatment options and outcomes. Women with conditions such as obesity, diabetes, thyroid disorders, or bleeding disorders may require tailored approaches to AUB management to optimize safety and efficacy. Furthermore, medications used to manage chronic conditions may interact with AUB therapies, necessitating careful consideration and coordination of care to minimize adverse effects and drug interactions [42].

### Quality of Life and Psychosocial Aspects

The impact of AUB extends beyond physical symptoms, significantly affecting quality of life and psychosocial well-being. Heavy menstrual bleeding, pain, and unpredictable bleeding patterns can impair daily activities, work productivity, social interactions, and intimate relationships, leading to emotional distress and reduced quality of life. Women with AUB may experience anxiety, depression, social isolation, and impaired self-esteem, highlighting the importance of holistic care that addresses psychosocial needs alongside medical management [7, 39].

### Supportive Care and Counseling

Supportive care and counseling are integral components of AUB management, providing emotional support, education, and coping strategies to help women navigate the challenges of living with AUB. Clinicians should create a supportive and non-judgmental environment where patients feel comfortable discussing their symptoms, concerns, and treatment preferences. Patient education about the etiology of AUB, available treatment options, and expected outcomes empowers women to make informed decisions and actively participate in their care. Additionally,

counseling on lifestyle modifications, stress management techniques, and self-care practices can enhance resilience and improve overall well-being [41, 42].

Managing AUB requires a comprehensive and individualized approach that considers the diverse needs and circumstances of affected women. Clinicians must navigate challenges related to age, reproductive intentions, and co-existing medical conditions while prioritizing patient-centered care and psychosocial support. By addressing these challenges and considerations in AUB management, clinicians can optimize treatment outcomes, improve quality of life, and enhance the overall well-being of women affected by this common and impactful condition.

## CONCLUSIONS

The field of gynecology has witnessed substantial progress in the management of abnormal uterine bleeding (AUB) among premenopausal women. This progression has moved from a conventional, broad-spectrum approach towards a highly sophisticated, individualized methodology. Developments in diagnostic technologies, notably transvaginal ultrasonography, magnetic resonance imaging (MRI), and hysteroscopy, combined with advances in molecular diagnostics, have revolutionized our diagnostic capabilities. Such enhancements in diagnostic accuracy are critical as they provide a foundation for developing personalized therapeutic interventions that are intricately aligned with the unique pathophysiological conditions of each patient.

The systematic application of the International Federation of Gynecology and Obstetrics (FIGO) classification system has been pivotal. It serves as a structured framework that assists clinicians in pinpointing the specific etiologies of AUB, thereby facilitating the implementation of targeted medical and surgical interventions. This nuanced understanding allows for a shift towards primarily medical management, utilizing hormonal therapies and cutting-edge pharmacological agents. This approach reflects a paradigm shift focused on reducing the dependence on invasive surgical procedures and enhancing overall patient outcomes.

Ongoing advancements in technology and the integration of personalized medicine principles are continually refining management strategies for AUB. These include an emphasis on minimally invasive sur-

gical techniques when necessary and a focus on patient-centered care. The field stands on the cusp of further transformative developments with the anticipated integration of artificial intelligence in diagnostic processes and gene therapy in treatment protocols. These innovations promise to further elevate the precision of diagnostics and the effectiveness of treatments.

However, the management of AUB still presents significant challenges, particularly when addressing the needs of diverse populations that may have different reproductive intentions and coexist with various medical conditions. An effective management strategy requires a comprehensive multidisciplinary approach that encompasses not only advanced diagnostic and therapeutic techniques but also a strong emphasis on patient education and psychosocial support. This approach ensures that all aspects of a patient's health and well-being are considered, making the management of AUB more holistic and patient-focused.

Moreover, the quality of life implications for women suffering from AUB cannot be overstated. The physical, emotional, and social burdens of this condition necessitate that therapeutic approaches not only address the physiological aspects of the disease but also the psychological and social impacts. Supportive care, encompassing counseling and lifestyle advice, plays a critical role in this context, providing patients with the tools needed to manage their condition effectively.

As we continue to advance in our understanding and capabilities, the integration of these new technologies and methodologies into everyday clinical practice remains essential. Doing so not only optimizes therapeutic outcomes but also significantly enhances the quality of life for women affected by AUB. This ongoing evolution in the field underscores the critical need for continuous research, innovation, and education in gynecology to keep pace with emerging technologies and changing patient needs. The future of AUB management looks promising, with the potential to offer more precise, effective, and less invasive options for women worldwide.

#### *Authors' Contribution*

Study Conception: TB, MSYA; Study Design: TB, MSYA; Supervision: TB; Funding: N/A; Materials:

N/A; Data Collection and/or Processing: TB, MSYA; Statistical Analysis and/or Data Interpretation: TB, MSYA; Literature Review: TB, MSYA; Manuscript Preparation: TB, MSYA and Critical Review: TB, MSYA.

#### *Conflict of interest*

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

#### *Financing*

The authors disclosed that they did not receive any grant during conduction or writing of this study.

## REFERENCES

1. Dubil EA, Tian C, Wang G, et al. Racial disparities in molecular subtypes of endometrial cancer. *Gynecol Oncol.* 2018;149(1):106-116. doi: 10.1016/j.ygyno.2017.12.009.
2. Colombo N, Creutzberg C, Amant F, et al; ESMO-ESGO-ESTRO Endometrial Consensus Conference Working Group. ESMO-ESGO-ESTRO Consensus Conference on Endometrial Cancer: diagnosis, treatment and follow-up. *Ann Oncol.* 2016;27(1):16-41. doi: 10.1093/annonc/mdv484.
3. Renehan AG, Zwahlen M, Egger M. Adiposity and cancer risk: new mechanistic insights from epidemiology. *Nat Rev Cancer.* 2015;15(8):484-498. doi: 10.1038/nrc3967.
4. Dashti SG, Chau R, Ouakrim DA, et al. Female Hormonal Factors and the Risk of Endometrial Cancer in Lynch Syndrome. *JAMA.* 2015;314(1):61-71. doi: 10.1001/jama.2015.6789.
5. Naqvi A, MacKintosh ML, Derbyshire AE, Tsakiroglou AM, Walker TDJ, McVey RJ, et al. The impact of obesity and bariatric surgery on the immune microenvironment of the endometrium. *Int J Obes (Lond).* 2022;46(3):605-612. doi: 10.1038/s41366-021-01027-6.
6. Munro MG, Critchley HOD, Fraser IS; FIGO Menstrual Disorders Committee. The two FIGO systems for normal and abnormal uterine bleeding symptoms and classification of causes of abnormal uterine bleeding in the reproductive years: 2018 revisions. *Int J Gynaecol Obstet.* 2018;143(3):393-408. doi: 10.1002/ijgo.12666. Epub 2018 Oct 10. Erratum in: *Int J Gynaecol Obstet.* 2019;144(2):237. doi: 10.1002/ijgo.12709.
7. Bignardi T, Van den Bosch T, Condous G. Abnormal uterine and post-menopausal bleeding in the acute gynaecology unit. *Best Pract Res Clin Obstet Gynaecol.* 2009;23(5):595-607. doi: 10.1016/j.bpobgyn.2009.05.001.
8. Duska LR, Garrett A, Rueda BR, Haas J, Chang Y, Fuller AF. Endometrial Cancer in Women 40 Years Old or Younger. *Gynecol Oncol.* 2001;83(2):388-393. doi: 10.1006/gyno.2001.6434.
9. Singh S, Best C, Dunn S, Leyland N, Wolfman WL. No. 292-Abnormal Uterine Bleeding in Pre-Menopausal Women. *J Obstet Gynaecol Can.* 2018;40(5):e391-e415. doi: 10.1016/j.jogc.2018.03.007.

10. Longacre T, Atkins K, Kempson R, Hendrickson M. The uterine corpus. In: Sternberg's Diagnostic Surgical Pathology. Lippincott Williams & Wilkins, 2005: pp. 2184-2277.
11. Anastasiadis PG, Skaphida PG, Koutlaki NG, Galazios GC, Tsikouras PN, Liberis VA. Descriptive epidemiology of endometrial hyperplasia in patients with abnormal uterine bleeding. *Eur J Gynaecol Oncol.* 2000;21(2):131-134.
12. Liu Z, Doan QV, Blumenthal P, Dubois RW. A Systematic Review Evaluating Health-Related Quality of Life, Work Impairment, and Health-Care Costs and Utilization in Abnormal Uterine Bleeding. *Value Health.* 2007;10(3):183-194. doi: 10.1111/j.1524-4733.2007.00168.x.
13. Munro MG, Critchley HOD, Broder MS, Fraser IS. FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age. *Int J Gynecol Obstet.* 2011;113(1):3-13. doi: 10.1016/j.ijgo.2010.11.011.
14. Jain V, Munro MG, Critchley HOD. Contemporary evaluation of women and girls with abnormal uterine bleeding: FIGO Systems 1 and 2. *Int J Gynecol Obstet.* 2023;162(S2):29-42. doi: 10.1002/ijgo.14946.
15. Harlow SD, Lin X, Ho MJ. Analysis of menstrual diary data across the reproductive life span applicability of the bipartite model approach and the importance of within-woman variance. *J Clin Epidemiol.* 2000;53(7):722-733. doi: 10.1016/S0895-4356(99)00202-4.
16. Whitaker L, Critchley HOD. Abnormal uterine bleeding. *Best Pract Res Clin Obstet Gynaecol.* 2016;34:54-65. doi: 10.1016/j.bpobgyn.2015.11.012.
17. Clark TJ, Stevenson H. Endometrial Polyps and Abnormal Uterine Bleeding (AUB-P): What is the relationship, how are they diagnosed and how are they treated? *Best Pract Res Clin Obstet Gynaecol.* 2017;40:89-104. doi: 10.1016/j.bpobgyn.2016.09.005.
18. Nijkang NP, Anderson L, Markham R, Manconi F. Endometrial polyps: Pathogenesis, sequelae and treatment. *SAGE Open Med.* 2019;7:205031211984824. doi: 10.1177/2050312119848247.
19. Salim S, Won H, Nesbitt-Hawes E, Campbell N, Abbott J. Diagnosis and Management of Endometrial Polyps: A Critical Review of the Literature. *J Minim Invasive Gynecol.* 2011;18(5):569-581. doi: 10.1016/j.jmig.2011.05.018.
20. Lee SC, Kaunitz AM, Sanchez-Ramos L, Rhatigan RM. The Oncogenic Potential of Endometrial Polyps. *Obstet Gynecol.* 2010;116(5):1197-1205. doi: 10.1097/AOG.0b013e3181f74864.
21. Ferrazzi E, Zupi E, Leone FP, et al. How often are endometrial polyps malignant in asymptomatic postmenopausal women? A multicenter study. *Am J Obstet Gynecol.* 2009;200(3):235.e1-6. doi: 10.1016/j.ajog.2008.09.876.
22. Nappi L, Indraccolo U, Di Spiezio Sardo A, et al. Are diabetes, hypertension, and obesity independent risk factors for endometrial polyps? *J Minim Invasive Gynecol.* 2009;16(2):157-162. doi: 10.1016/j.jmig.2008.11.004.
23. Golan A, Sagiv R, Berar M, Ginath S, Glezerman M. Bipolar Electrical Energy in Physiologic Solution-A Revolution in Operative Hysteroscopy. *J Am Assoc Gynecol Laparosc.* 2001;8(2):252-258. doi: 10.1016/S1074-3804(05)60586-5.
24. Kim KR, Peng R, Ro JY, Robboy SJ. A Diagnostically Useful Histopathologic Feature of Endometrial Polyp. *Am J Surg Pathol.* 2004;28(8):1057-1062. doi: 10.1097/01.pas.0000128659.73944.f3.
25. Liu X, Shen M, Qi Q, Zhang H, Guo SW. Corroborating evidence for platelet-induced epithelial-mesenchymal transition and fibroblast-to-myofibroblast transdifferentiation in the development of adenomyosis. *Hum Reprod.* 2016;31(4):734-749. doi: 10.1093/humrep/dew018.
26. Shikata K, Ninomiya T, Kiyohara Y. Diabetes mellitus and cancer risk: Review of the epidemiological evidence. *Cancer Sci.* 2013;104(1):9-14. doi: 10.1111/cas.12043.
27. Esposito K, Chiodini P, Capuano A, Bellastella G, Maiorino MI, Giugliano D. Metabolic syndrome and endometrial cancer: a meta-analysis. *Endocrine.* 2014;45(1):28-36. doi: 10.1007/s12020-013-9973-3.
28. Dueholm M, Lundorf E, Hansen ES, Ledertoug S, Olesen F. Evaluation of the uterine cavity with magnetic resonance imaging, transvaginal sonography, hysterosonographic examination, and diagnostic hysteroscopy. *Fertil Steril.* 2001;76(2):350-357. doi: 10.1016/S0015-0282(01)01900-8.
29. Breitkopf DM, Frederickson RA, Snyder RR. Detection of Benign Endometrial Masses by Endometrial Stripe Measurement in Premenopausal Women. *Obstet Gynecol.* 2004;104(1):120-125. doi: 10.1097/01.AOG.0000130065.49187.c8.
30. Batzer FR. Abnormal uterine bleeding: Imaging techniques for evaluation of the uterine cavity and endometrium before minimally invasive surgery—the case for transvaginal ultrasonography. *J Minim Invasive Gynecol.* 2007;14(1):9-11. doi: 10.1016/j.jmig.2006.08.012.
31. Maheux-Lacroix S, Li F, Laberge PY, Abbott J. Imaging for Polyps and Leiomyomas in Women With Abnormal Uterine Bleeding. *Obstet Gynecol.* 2016;128(6):1425-1436. doi: 10.1097/AOG.0000000000001776.
32. Dueholm M, Lundorf E, Hansen ES, Ledertoug S, Olesen F. Accuracy of magnetic resonance imaging and transvaginal ultrasonography in the diagnosis, mapping, and measurement of uterine myomas. *Am J Obstet Gynecol.* 2002;186(3):409-415. doi: 10.1067/mob.2002.121725.
33. Khalaf K, Terrin M, Jovani M, et al. A comprehensive guide to artificial intelligence in endoscopic ultrasound. *J Clin Med.* 2023;12(11):3757. doi: 10.3390/jcm12113757.
34. Horgan R, Nehme L, Abuhamad A. Artificial intelligence in obstetric ultrasound: A scoping review. *Prenat Diagn.* 2023;43(9):1176-1219. doi: 10.1002/pd.6268.
35. Dijkhuizen FP, Mol BW, Brölmann HA, Heintz AP. The accuracy of endometrial sampling in the diagnosis of patients with endometrial carcinoma and hyperplasia: a meta-analysis. *Cancer.* 2000;89(8):1765-1772.
36. Salazar CA, Isaacson KB. Office Operative Hysteroscopy: An Update. *J Minim Invasive Gynecol.* 2018;25(2):199-208. doi: 10.1016/j.jmig.2017.08.009.
37. Zaino RJ, Carinelli SG, Ellenson LH. Tumours of the uterine corpus: epithelial tumours and precursors. In: Kurman RJ, Carcangiu ML, Herrington S, eds. WHO Classification of Tumours of Female Reproductive Organs. 4th ed. IARC; 2014: pp. 125-134.
38. Huang EC, Crum CP, Hornstein MD. Evaluation of the Cyclic Endometrium and Benign Endometrial Disorders. In: Diagnostic Gynecologic and Obstetric Pathology. 3rd ed. Elsevier; 2018: pp. 471-523.
39. Lacey JV Jr, Chia VM, Rush BB, et al. Incidence rates of en-

- ometrial hyperplasia, endometrial cancer and hysterectomy from 1980 to 2003 within a large prepaid health plan. *Int J Cancer*. 2012;131(8):1921-1929. doi: 10.1002/ijc.27457.
40. WHO. Female Genital Tumours WHO Classification of Tumours. 5th ed.; 2020.
41. Kurman RJ, Kaminski PF, Norris HJ. The behavior of endometrial hyperplasia. A long-term study of "untreated" hyperplasia in 170 patients. *Cancer*. 1985;56(2):403-412. doi:10.1002/1097-0142(19850715)56:2<403::AID-CNCR2820560233>3.0.CO;2-X.
42. Makker V, MacKay H, Ray-Coquard I, et al. Endometrial cancer. *Nat Rev Dis Primers*. 2021;7(1):88. doi: 10.1038/s41572-021-00324-8.
43. Lacey JV Jr, Sherman ME, Rush BB, et al. Absolute risk of endometrial carcinoma during 20-year follow-up among women with endometrial hyperplasia. *J Clin Oncol*. 2010;28(5):788-792. doi: 10.1200/JCO.2009.24.1315.
44. Baak JP, Mutter GL, Robboy S, et al. The molecular genetics and morphometry-based endometrial intraepithelial neoplasia classification system predicts disease progression in endometrial hyperplasia more accurately than the 1994 World Health Organization classification system. *Cancer*. 2005;103(11):2304-2312. doi: 10.1002/cncr.21058.
45. Joshi A, Ellenson LH. PI3K/PTEN/AKT Genetic Mouse Models of Endometrial Carcinoma. *Adv Exp Med Biol*. 2017;943:261-273. doi: 10.1007/978-3-319-43139-0\_9.