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Diagnostic Process of Adolescents with Abnormal Uterine Bleeding in Pediatric Departments: Single Center Results

Anormal Uterin Kanaması Olan Ergenlerin Tanı Süreci: Tek Merkez Sonuçları

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ABSTRACT

Objective: The present study aims to assess patients who applied to our hospital for abnormal uterine bleeding (AUB), and to examine the differences between cases diagnosed with hemostasis disorders and others.

Methods: This study prospectively included 105 patients who presented with AUB between 2021 and 2022. Complete blood count, peripheral blood smear, prothrombin time, activated partial thromboplastin time, fibrinogen level, thrombin time, von Willebrand factor antigen, ristocetin cofactor activity, factor VIII: C activity, flow cytometric analysis of platelet surface glycoproteins (Gp Ib/V/IX and Gp IIb/IIIa), biochemical assessments of iron status and blood group analyses, pelvic ultrasonographic imaging, and endocrine evaluations were conducted on the patients. The other factor tests were also assessed in cases with suspected hemostasis disorders.

Results: The mean age of the 105 patients included in the present study was found to be 15.3 (minimum: 11.3-maximum: 19.3) years. The most common etiology was ovulatory dysfunction in 55% (n=58) cases, followed by hemostasis disorders with 13.3% (n=14) cases, and genitourinary system infections with 9.5% cases. The level of deficiency was found to be mild in all cases with factor deficiency. The mean menarche-to-diagnosis time was determined to be 3.3 years for the patients with hemostasis disorders.

Conclusion: It is important to obtain detailed patient and family history, the menstrual history and physical examination of adolescent patients, and closely follow up on those having AUB for emergencies. Some patients' hemoglobin levels may decrease severely, and their hemodynamics may be impaired.

Keywords: Adolescents, blood disorders, abnormal uterine bleeding

ÖZ

Amaç: Bu çalışmanın amacı, anormal uterin kanama (AUK) nedeniyle hastanemize başvuran hastaları değerlendirmek ve hemostaz bozuklukları tanısı almış olgular ile diğerleri arasındaki farkları incelemektir.

Yöntemler: Bu çalışmaya 2021-2022 yılları arasında AUK ile başvuran 105 hasta prospektif olarak dahil edildi. Tam kan sayımı, periferik kan yayması, protrombin zamanı, aktive parsiyel tromboplastin zamanı, fibrinojen seviyesi, trombin zamanı, von Willebrand faktör antijeni, ristocetin kofaktör aktivitesi, faktör VIII: C aktivitesi, trombosit yüzey glikoproteinlerinin (Gp Ib/V/IX ve Gp IIb/IIIa) akım sitometrik analizi, demir durumunun biyokimyasal değerlendirmeleri ve kan grubu analizleri, pelvik ultrasonografik görüntüleme ve endokrin değerlendirmeleri hastalara yapıldı. Hemostaz bozukluklarından şüphelenilen olgularda diğer faktör testleri de değerlendirildi.

Bulgular: Çalışmaya dahil edilen 105 hastanın yaş ortalaması 15,3 (minimum: 11,3-maksimum: 19,3) yıl olarak bulundu. En sık etiyoloji %55 (n=58) olguda yumurtlama disfonksiyonuydu, bunu %13,3 (n=14) olgu ile hemostaz bozuklukları ve %9,5 olgu ile genitoüriner sistem enfeksiyonları izledi. Faktör eksikliği olan tüm olgularda eksiklik seviyesi hafif bulundu. Hemostaz bozukluğu olan hastalarda ortalama menarş-tanı süresi 3,3 yıl olarak belirlendi.

Sonuç: Ergen hastalarda ayrıntılı hasta ve aile öyküsü, adet öyküsü ve fizik muayene almak ve AUK olanların acil durumlar için yakın takibi önemlidir. Bazı hastaların hemoglobin seviyeleri ciddi şekilde düşebilir ve hemodinamikleri bozulabilir.

Anahtar Sözcükler: Ergenler, kan hastalıkları, anormal uterin kanama

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INTRODUCTION

Abnormal uterine bleeding (AUB) is defined as abnormal bleeding from the uterine corpus from the aspects of bleeding duration, volume, frequency, and/or regularity (1). It is one of the urgent gynecological problems that are frequently encountered in adolescence and can cause concern. It was reported that 40% of healthy adolescents have had AUB at some point in their lives (2). AUB can lead to anemia, fatigue, and hemodynamic instability among adolescents, as well as other problems such as absenteeism from school, reduced quality of life, and falling behind in sports activities (3).

The American College of Obstetrics and Gynecology and the American Academy of Pediatrics defined normal menstruation as bleeding that occurs every 21-45 days, lasts less than 7 days, and does not require more than 3 pads or 6 tampons per day (4,5). Heavy menstrual bleeding is defined as bleeding that lasts longer than 7 days and/or blood loss of >80 mL per menstrual cycle, including the need to change pads every one to two hours, the use of two layers of tampons, staining bed or clothing, and the formation of clots larger than 2.5 cm (5,6). The International Federation of Gynecology and Obstetrics (FIGO) classified the causes of AUB into structural and non-structural categories (7). Structural causes include polyp, adenomyosis, leiomyoma, and malignancy (and hyperplasia) (PALM), while non-structural causes include coagulopathy, ovulatory disorders, endometrial, iatrogenic, and not otherwise classified (COEIN).

Structural AUB is seen very rarely in adolescents. The most common cause of AUB is the ovulatory dysfunction originating from the immaturity of the hypothalamic-pituitary-ovarian axis. Almost half of menstrual cycles are anovulatory for the first two years after menarche. The menstrual cycle interval narrows as age advances. In the 3rd year after menarche, the normal menstrual cycle is every 21-34 days, in 60-80% of cases. In addition, endocrinological causes such as thyroid diseases, hyperprolactinemia, hyperandrogenemia/polycystic ovary syndrome (PCOS), and obesity can cause ovulatory dysfunction. Pregnancy must also be considered for its impact and subsequently excluded where necessary. The patient should be examined for endometriosis and vulvovaginitis. The use of drugs, anticoagulants, or depot progesterone should be investigated. Moreover, trauma and foreign bodies are other causes of AUB (8).

Along with ovulatory dysfunction, coagulopathies also play an important role in the etiology of AUB. Previous studies reported that the frequency of underlying coagulopathies ranged between 8 and 62 % (9). It was shown that approximately 19% of adolescents requiring hospitalization due to excessive and prolonged menstrual bleeding (menorrhagia) have a coagulation disorder and more than 50% have a bleeding disorder, such as thrombocytopenia, von Willebrand disease, and leukemia (10). Von Willebrand disease is the most common hereditary bleeding disorder associated with AUB. The frequency of von Willebrand disease was reported to be 65% among women presenting with AUB (11). Factor XI deficiency, Glanzmann's thrombasthenia, and aplastic anemia are also associated with AUB. In 2010, the International Society on Thrombosis and Hemostasis (ISTH) developed a bleeding assessment tool (BAT) for the evaluation of patients with bleeding. Accordingly, ≥3 points were accepted as abnormal in children (12).

In this study, we aimed to assess adolescent patients who applied to our hospital with AUB, and to examine possible etiological factors.

MATERIALS AND METHODS

This study included 105 patients who applied to the pediatric hematology outpatient clinic between 2021 and 2022 for menstrual bleeding lasting longer than seven days, more frequent than a 21-day cycle, and increased blood loss in one cycle. Ethical approval (approval number: 2021/21-268, date: 06.12.2021) was obtained from the Erzurum City Hospital's Ethics Committee. The present study was carried out prospectively.

First of all, detailed anamnesis was obtained from the patients (items questioned are listed in Table 1), and this was done by performing a physical examination. No survey was conducted on quality of life, but some questions were asked about their school life and emotional state in the first assessment (Table 1). The assessments made after the anamnesis and physical examination are summarized in Figure 1. Platelet function tests and PFA-100/200 tests could not be conducted since they were not available.

The patients underwent endocrine evaluation for goiter and hyperandrogenemia, and were examined for vaginal infection. Thyroid function tests and βHCG levels were conducted to exclude pregnancy. Even though structural bleeding is seen very rarely in adolescents, pelvic ultrasonography was performed in all patients to rule out that condition. Patients were also examined for endometrial thickness and PCOS by pelvic ultrasonography. Ovulatory dysfunction was considered in patients if structural disorders and systemic diseases that could lead to vaginal bleeding were excluded. The cut-off values recommended by the World Health Organization were used when grading anemia (6.5-7.9, severe; 8-9.4, moderate; 9.5-10.9, mild; and >12, normal) (13).

The patients were also evaluated by using the ISTH-BAT scoring system.

According to this system:

0 point: Trivial

1 point: Consultation only or changing pads more frequently than every 2 hours or clot sand flooding or Pictorial Blood Assessment Chart Score >100

Table 1. Items evaluated when taking the anamnesis of the patients

Item
Age at presentation
Age at menarche
Bleeding duration and frequency
Additional complaints (vaginal discharge, dysuria, etc.)
Pad changing frequency
Presence of clot formation
Presence of another bleeding problem (post-dental treatment, ecchymosis in any body area, nose bleeding, etc.)
Presence of bleeding problem in family
History of related treatment (iron, tranexamic acid, or hormone)
History of related hospitalization (blood transfusion requirement)
Success in school, school absence, and emotional state

2 points: Time of work/school >2X year or requiring antifibrinolytic agents or hormonal therapy or iron therapy

3 points: Requiring combined with antifibrinolytic agents and hormonal therapy or present since menarche and >12 month

4 points: Acute menorrhagia requiring hospital admission and emergency treatment or blood transfusion or replacement agents or desmopressin. ISTH-BAT score of ≥3 is considered "abnormal" for children under 18 years old.

Patients were grouped by their menstrual bleeding patterns. Those who reported bleeding longer than seven days were considered to have long-term bleeding. Patients who had more than 80 mL of bleeding, needed to change pads every 1-2 hours, used baby/adult diapers, and had blood stains on their clothes or bedding were considered to have heavy menstrual bleeding. Moreover, patients who had bleeding more frequently than 21 days were included in the frequent menstrual bleeding group.

All coagulation factor levels were assessed according to the age reference values for children. The patients, whose factor levels were lower than the reference levels, were evaluated for a second time, but some of them did not attend their follow-up.

Statistical Analysis

"SPSS v.28.0 (IBM Corp., Armonk, NY, USA)" was used for statistical analyses. Descriptive statistics were used to characterize demographics, age at diagnosis, etiology of AUB, and bleeding episodes. Data were expressed as mean ± standard deviation and median (min., max.). Etiologies, hemoglobin measurement on admission, and patient characteristics were compared using the Mann-Whitney test for continuous variables and Pearson's chi-square test for categorical variables. The Kruskal-Wallis test was used when making comparisons between the groups. To compare age between two groups, Student's t-test was used. Correlation analysis was used to measure correlation between hemoglobin and quality of life. Statistical significance was set at $p<0.05$.

RESULTS

The mean age of the 105 patients included in this study was determined to be 14.27±1.86 years. Forty percent (n=42) of the cases were within the first year of menarche, and 60% (n=63) had been menstruating for more than one year. Sixty-six (62.9%), cases had complaints from the onset of menarche. The time since menarche was longer than one year in 12 patients with hemostasis disorders.

Classifying the cases by their menstrual bleeding episodes, it was determined that 50 patients (47.6%) had prolonged bleeding, 35 patients (33.3%) had heavy menstrual bleeding, and 20 patients (19%) had frequent bleeding. The most frequently noted bleeding episodes in patients with hemostasis disorders were prolonged bleeding (Table 2).

In 28.5% (n=30) of the cases, there was a history of bleeding problems other than menstrual bleeding. Sixteen patients had a family history of various bleeding problems. Only one of the patients with hemostasis disorders had a family history, and six patients had additional complaints, such as abnormal bleeding during tooth extraction, easy bruising, and nose bleeding. These complaints did not differ significantly in a statistical manner differ from those in the group without hemostasis disorders.

Using the ISTH-BAT scoring system, 62.9% (n=66) of the cases scored ≤2 points, 17.1% (n=18) 3 points, and 20% (n=21) 4 points. Nine patients with hemostasis disorders had a BAT score of 3-4 points, including 5 cases with von Willebrand disease, 2 cases with factor VII deficiency, 1 case with leukemia, and 1 case diagnosed with Glanzmann thrombasthenia. Examining the cases etiologically, it was found that the most common cause of AUB was ovulatory dysfunction originating from the immaturity of the hypothalamic-pituitary-ovarian axis, in 55% of the cases. In addition, hemostasis disorders were also responsible for AUB in 13.3% of the patients and were responsible for genitourinary system infections in 9.5% (Table 3).

Given the results obtained from pelvic ultrasonography imaging, three cases were diagnosed with PCOS, five cases with hemorrhagic ovarian cysts, and one case with an arcuate uterus.

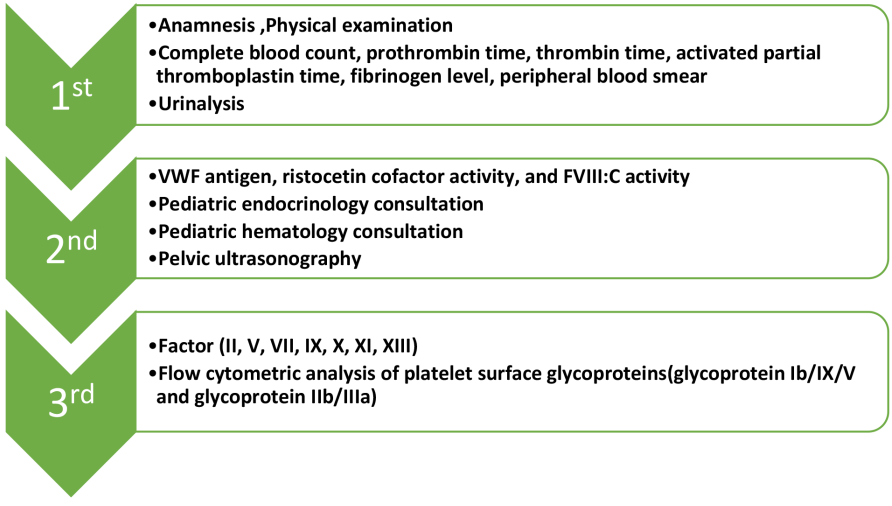

Figure 1. Patients evaluation algorithm

Table 2. Baseline characteristics of patients

	All (n=105)	With hemostasis disorders (n=14)	Without hemostasis disorders (n=91)	p
Age (years) (mean ± SD)	**14.27±1.86**	**15.29±1.89**	**14.1±1.82**	**p=0.02**
Time since menarche				p=0.12
<1 year	**42 (40%)**	**2 (14.3%)**	**40 (43.9%)**	
>1 year	**63 (60%)**	**12 (85.7%)**	**51 (56.1%)**	
Bleeding episodes				p=0.64
Prolonged	**50 (47.6%)**	**8 (57.2%)**	**42 (46.2%)**	
Heavy	**35 (33.3%)**	**3 (21.4%)**	**32 (35.2%)**	
Frequent	**20 (19%)**	**3 (21.4%)**	**17 (18.6%)**	
Other bleeding symptoms	**30 (28.5%)**	**6 (43.8%)**	**24 (26.4%)**	p=0.21
Family history	**16 (15.2%)**	**1 (7.1%)**	**15 (16.5%)**	p=0.69
ISTH-BAT score				p=0.11
≤2	**66 (62.9%)**	**5 (35.7%)**	**61 (67%)**	
3	**18 (17.1%)**	**5 (35.7%)**	**13 (14.3%)**	
4	**21 (20%)**	**4 (28.6%)**	**17 (18.8%)**	
Drug use history				p=0.57
Iron therapy	**22 (20.9%)**	**2 (14.3%)**	**20 (21.9%)**	
Oral contraseptive	**15 (14.3%)**	**3 (21.4%)**	**12 (13%)**	
Both (iron and oral contraceptive)	**4 (3.8%)**		**4 (4.4%)**	
Hemoglobin (g/dL) (median) (min-max)	**12.9 (3.4-15.7)**	**12.5 (3.4-14.4)**	**12.9 (5-15.7)**	p=0.37
Normal (>12)	**73 (69.5%)**	**8 (57.1%)**	**65 (71.4%)**	
Mild (9.5-10.9)	**13 (12.4%)**	**2 (14.3%)**	**11 (12.1%)**	
Moderate (8-9.4)	**6 (5.7%)**	**2 (14.3%)**	**4 (4.4%)**	
Severe (6.5-7.9)	**13 (12.4%)**	**2 (14.3%)**	**11 (12.1%)**	

SD: Standard deviation, ISTH: International Society on Thrombosis and Hemostasis, BAT: Bleeding assessment tool

Table 3. Causes of abnormal uterine bleeding

Cause	n (%)
Endocrinal causes	
Ovulatory dysfunction	58 (55)
Obesity	11 (10.5)
Hemorrhagic ovarian cyst	5 (4.8)
PCOS	3 (2.9)
Hypothyroidism	1 (0.9)
Hyperprolactinemia	1 (0.9)
Hematological causes	
von Willebrand disease	8 (7.6)
Factor VII deficiency	2 (1.9)
Factor XI deficiency	1 (0.9)
Factor V deficiency	1 (0.9)
Glanzmann thrombasthenia	1 (0.9)
Leukemia	1 (0.9)
Genitourinary system infections	10 (9.5)
Structural causes (arcuate uterus)	1 (0.9)
Other (celiac disease)	1 (0.9)

PCOS: Polycystic ovary syndrome

Von Willebrand disease was observed to be the most common hematological cause. The cases of von Willebrand disease were consistent with type-1 von Willebrand disease (vWF: /ratio of >0.6). The patients with other factor deficiencies also had mild deficiencies. Flow cytometric analysis of platelet surface glycoproteins (glycoprotein Ib/IX/V and glycoprotein IIb/IIIa) was conducted in 42 cases. One patient was diagnosed with Glanzmann thrombasthenia, whereas the remaining patients had normal results. Aggregometry tests could not be conducted. No platelet clustering was observed in the peripheral smear assessment of the patient with Glanzmann thrombasthenia.

Among the most common conditions causing ovulatory dysfunction, obesity was observed in 11 patients, PCOS in 3 patients, hypothyroidism in 1 patient, pituitary adenoma in 1 patient, and hyperprolactinemia in 1 patient. In addition, 1 patient had uncontrolled celiac disease.

Overall, the median hemoglobin concentration was 12.9 (3.4-15.7) g/dl. Thirteen (12.4%) patients had decreased hemoglobin levels, requiring a red blood cell transfusion. Eleven patients with severe anemia were not diagnosed with hemostasis disorder (Table 2). Forty-six (46.7%) patients stated that their quality of life was affected. There was a statistically significant correlation between hemoglobin levels and quality of life (correlation coefficient: -0.471). The

number of those whose quality of life was affected increased as the hemoglobin value decreased. Figure 2 illustrates the classification of the cases by hemoglobin levels.

None of the patients with factor deficiencies required factor therapy. The patients, who were found to be obese, were treated and followed up for obesity. The treatments applied to the cases are summarized in Figure 3.

Before admission to our outpatient clinic, 15 patients (14.3%) had a history of oral contraceptive use, 22 (21%) had a history of iron therapy, and 4 (3.8%) had a history of both. The frequency of bleeding diathesis was not increased in these patients. None of the patients used any drugs that could cause hemostasis disorders.

DISCUSSION

AUB has significant implications in adolescence since it causes a decrease in quality of life, an increased tendency to depression, and severe anemia that can be life-threatening. In addition, school absenteeism increases among adolescents with AUB, which results in a decrease in school success (3,14-18). It raises concern among both adolescents and their parents. Therefore, providing appropriate medical treatment and psychological support is very important when adolescents present at the hospital due to AUB. In the present study, it was observed that school absences are high in these patients, and their emotional state is not good.

It is important to obtain a detailed menstrual history of adolescent AUB cases and investigate the presence of other bleeding problems, including easy bruising, nose bleeding, and post-surgical bleeding, which may indicate hemostasis disorders in those presenting with heavy bleeding, as well as the history of bleeding in the family (19). Given the detailed anamneses obtained in this study, there was a history of other bleeding disorders in 30 cases and a family history in 16 cases, for these cases. However, no statistically significant difference was found between patients with and without hemostasis disorders. This might be because of the few cases of hemostasis disorders.

Anovulatory bleeding is often seen in the first two years after menarche. In cases involving hemostasis disorders in this study, the time since menarche was longer than one year (mean: 3.3 years), and their complaints had been present since menarche. The patients generally complained of prolonged bleeding. Complications increase when patients cannot be diagnosed promptly.

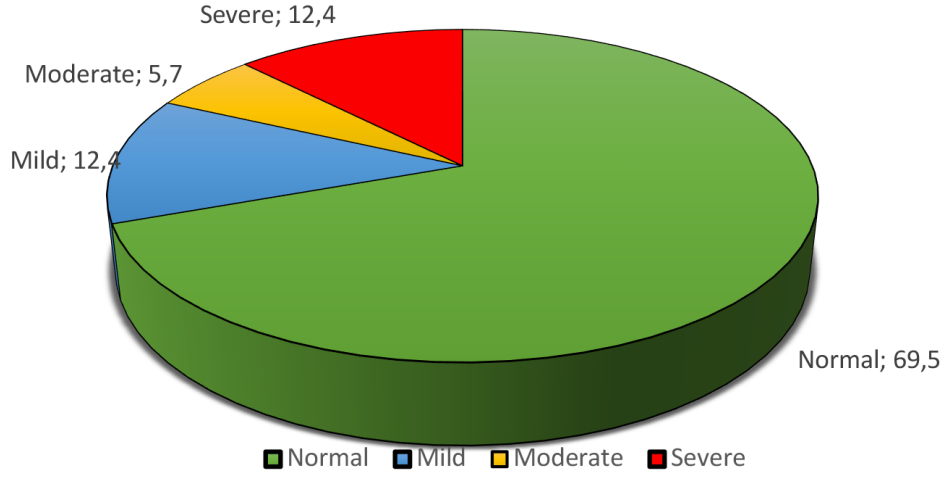

Figure 2. Classification of the cases according to anemia levels.

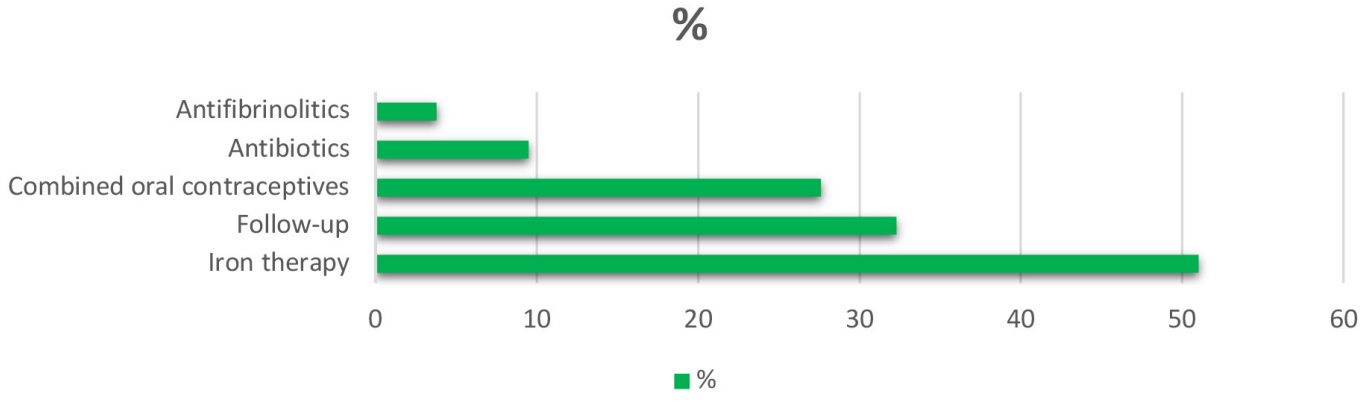

Figure 3. Treatments administered to the participating patients.

The FIGO classification was used for the evaluation of patients with AUB. Structural causes are less common among adolescents than adults. Anovulatory cycles originating from the immaturity of the hypothalamic-pituitary-ovarian axis in adolescents are the most common cause of AUB, but they are mainly considered when other diagnoses are excluded. On the other hand, PCOS and obesity can also lead to anovulatory cycles (20). Coagulopathies are the second-most frequent cause of AUB (21-26). In the present study, the most common etiological cause of AUB was anovulatory cycles, followed by mild factor deficiencies. Although platelet dysfunction is also common in cases of AUB (27-29), this diagnosis could not be made in the present study since this evaluation cannot be performed in our hospital. This can be considered a limitation of the present study.

The most common bleeding disorder in adolescents presenting with AUB is von Willebrand disease (30). Factor V, VII, and XI deficiencies were found in the patients with other factor deficiencies who were involved in this study. However, considering the difficult transportation conditions and the low education level in the geographical region where this study was carried out, it was not possible to follow up on these patients. The ISTH-BAT score is expected to be high in patients with coagulation problems (31). Most (n=9) of the participating patients with hemostasis disorders also had a high ISTH-BAT score. This scoring system can be used for distinguishing patients with bleeding susceptibility.

Performing routine pelvic ultrasonography on adolescent cases presenting with AUB remains controversial (32). However, although these conditions are not common among adolescents, pelvic ultrasonography is also important for detecting structural anomalies, endometrial thickness, and the presence of PCOS. Some hematological and solid tumor cases might have abnormal bleeding (33-37). None of the cases examined in this study had a diagnosis of solid tumors, but imaging can still be important. Patients with PCOS, hemorrhagic ovarian cysts, and structural anomalies might be diagnosed upon their admission to the hospital with the complaint of AUB (38). Eight of the patients participating in this study were diagnosed with PCOS, arcuate uterus, or hemorrhagic cysts, using ultrasonographic imaging.

Hematological malignancies might be present with AUB at the time of diagnosis, due to thrombocytopenia and coagulation disorders. Nebgen et al. (39) retrospectively evaluated 10,682 adult women with hematological malignancies and reported that the primary complaint was AUB in 38 cases at the time of admission. In the present study, one of the patients was diagnosed with acute myeloid leukemia.

Various studies aimed to demonstrate that hypothyroidism can cause delayed puberty and anovulatory cycles (40-43). However, it was observed that the incidence of hypothyroidism does not increase in cases with AUB (44,45). Hypothyroidism was found in only 1 patient participating in this study.

In a study carried out on adults, hyperprolactinemia was found in 17 of 105 patients with AUB (46). In the present study, the prolactin levels of the patients were within the normal range. Only one patient was followed up in the endocrinology department due to hyperprolactinemia and pituitary adenoma, and her prolactin level was normal.

The frequency of AUB in celiac disease is known to be higher when compared to healthy individuals, but the cause of this situation has not yet been clarified. It was considered that this might be due to the dysfunction of the hypothalamic-pituitary-ovarian axis (47). One of the cases involved in this study was monitored for a diagnosis of celiac disease, but it was determined that she did not comply with the recommended diet.

Since one of the most important complications of AUB is anemia, the complete blood count and iron parameters should be evaluated first while examining the patients with this complaint (48-50). Patients may present to the emergency department with severe anemia and encounter life-threatening situations. Therefore, cases with suspected anovulatory cycles should also be followed up closely. In a study carried out by Cooke et al. (49) the mean hemoglobin level of patients who applied to the emergency department with AUB was found to be 7.4 g/dL, which indicates severe anemia. Thirteen of the 105 patients involved in the present study had severe anemia that required a red blood cell transfusion. It was observed that the quality of life was worse for patients with anemia. Twenty-seven of the 73 cases with mild anemia had a history of using iron supplements and/or oral contraceptives before admission to our hospital. It was thought that these patients could have presented with more severe anemia without the use of such medications. It is important to obtain a detailed history of menstruation in adolescents presenting with anemia.

AUB treatment is based on stopping bleeding, relieving patient's concerns, maintaining the menstrual cycle, and treating anemia. Combined oral contraceptives, antifibrinolytics, iron replacement, and antibiotics (when necessary) are the most frequently used options. Iron replacement was started in more than half of our patients; oral contraceptives were started in approximately 30%. Red blood cell replacement was performed in severe anemia cases. The possibility of anovulatory bleeding was considered; and patients without anemia or heavy bleeding were followed up. In addition, antifibrinolytic therapy was administered to those who had factor deficiencies but did not require factor replacement.

CONCLUSION

Menstruation is a physiological event that develops under the influence of many factors. Many adolescents may not be willing to discuss their menstrual history for various reasons. Sufficient time should be allocated for these patients, and they should be followed up closely. It is important to obtain detailed patient's history, family history, menstrual history, and physical examination of adolescent patients. Cases with a history of hemostasis disorders should be referred to a hematology outpatient clinic. The patient's follow-up period and the timing of detailed examinations may vary between individuals. The majority of cases had abnormal bleeding in the anovulatory cycle; therefore, further examinations are unnecessary. However, as seen in the present study, anovulatory bleeding might reach life-threatening levels by causing severe anemia. To avoid unnecessary tests, the diagnosis process should be conducted step by step. Illustrating blood loss patterns in cases using pictured blood loss schemas might provide more objective results. If it is within the first year after menarche, if there is a bleeding history in the family, or if the bleeding reaches the level requiring hormone or iron

therapy, then further tests may be required. Even if they are rare, these malignancies should not be ignored.

Ethics

Ethics Committee Approval: Ethical approval (Approval number: 2021/21-268, date: 06.12.2021) was obtained from the Erzurum City Hospital's Ethics Committee.

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.T., Concept: A.T., Design: A.T., E.D., Supervision: A.T., Resources: A.T., Material: A.T., Data Collection or Processing: A.T., A.Ö., E.D., Analysis or Interpretation: A.T., Literature Search: A.T., Writing: A.T., A.Ö., Critical Review: A.T.

Conflict of Interest: No conflict of interest was declared by the authors.

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