

Adolesanlarda Anormal Uterin Kanamanın Değerlendirilmesi: Tersiyer Merkez Deneyimi

Reyhan Gündüz

ÖZET

Giriş ve Amaç: Anormal uterin kanaması olan adolesanların demografik, ultrasonografik, klinik ve laboratuvar verilerini değerlendirmektir. Anemi derecelerine göre menarajisi olan adolesanları üç gruba ayırıp kanama etiyojisini ve şiddetini belirleyerek literatüre katkı sunmaktır.

Gereç ve Yöntemler: Adolesan dönemde olup menarajisi olan 112 kadının verileri retrospektif olarak incelendi. Hafif menaraji Hemoglobun (Hgb) > 12 g/dl, orta derecede menaraji Hgb 10-12 g/dl ve şiddetli menaraji Hgb ≤ 10 g/dl olarak üç gruba ayrıldı. Veriler bu üç grup arasında karşılaştırıldı.

Bulgular: Çalışmaya dahil edilen adolesanların yaş ortalamaları 17.9±1.5 yıl, Hgb değerleri ortalama olarak 11±3.5 g/dl olarak belirlendi. %59.6'sında (53) hafif anemi, %19.1'inde (17) orta derecede anemi, %21.3'ünde (19) ağır derecede anemi belirlendi. Hgb değerine göre ayırdığımız üç grup arasında demografik ve klinik veriler açısından istatistiksel olarak anlamlı fark bulamadık. İki hastada faktör 8 eksikliği, bir hastada glanzman trombositopenisi ve altı hastada ITP tespit ettik. Gebeliğe bağlı menarajiyi %25 (28) olarak belirledik.

Sonuç: Adolesan dönemde yoğun olarak görülebilen menarajinin değerlendirilmesinde disfonksiyonel uterin kanama dışında sebep olabilecek kanama bozukluklarını ve gebeliği de aklımızda tutup multidisipliner olarak bu durumu yönetmemiz gerekmektedir.

Anahtar kelimeler: Adolesan, anormal uterin kanama, menaraji, kanama bozukluğu, gebelik.

The Evaluation of Abnormal Uterine Bleeding in Adolescents: Tertiary Center Experience

ABSTRACT

Aim: The purpose of the present study was to evaluate demographic, ultrasonographic, clinical, and laboratory data of adolescents who had abnormal uterine bleeding. The study also aimed to contribute to the literature by dividing adolescents who had menorrhagia into three groups based on their degree of anemia and determining the etiology and severity of bleeding.

¹ İletişim Yazarı: ryhn.gunduz@gmail.com

¹ Doç. Dr. Dicle Üniversitesi Tıp Fakültesi 0000-0001-8468-7038.

Material and Methods: The data of 112 women who had menorrhagia during adolescence were retrospectively analyzed. Mild menorrhagia was divided into three groups as Hemoglobin (Hgb) > 12 g/dl, moderate menorrhagia Hgb 10-12 g/dl, and severe menorrhagia Hgb ≤ 10 g/dl. The data were then compared among these three groups.

Results: The mean age of the adolescents included in the study was 17.9 ±1.5 years, and the mean Hgb value was 11 ±3.5 g/dl. Mild anemia was determined in 59.6% (53), moderate anemia in 19.1% (17), and severe anemia in 21.3% (19). No statistically significant differences were detected in demographic and clinical data among the three groups we separated based on Hgb values. Factor 8 deficiency was detected in two patients, Glanzmann Thrombocytopenia in one patient, and ITP in six patients. Pregnancy-related menorrhagia was determined in 25% (28).

Conclusion: In the evaluation of menorrhagia, which might be detected frequently in adolescence, clinicians must keep in mind the bleeding disorders and pregnancy that might cause it, other than dysfunctional uterine bleeding, and manage this condition in a multidisciplinary manner.

Keywords: Adolescent, abnormal uterine bleeding, menorrhagia, bleeding disorder, pregnancy.

1. INTRODUCTION

Based on the definition of the World Health Organization (WHO), adolescents are individuals between the ages of 10-19. Adolescence is a pubertal transition period accompanied by physiological and psychological changes. It is estimated that 18% of the world's population is in this age group and most of them are in developing countries. A woman's reproductive health is shaped during adolescence. Age at menarche and menstrual pattern are the most important factors determining a woman's health (WHO, 2010; Ravi et al., 2016).

The normal menstrual cycle must be approximately 21-45 days, with menstrual bleeding lasting 2-7 days. Normal blood loss requires 30 mL per cycle or three to six pads or tampons per day. Irregular menstrual cycles occur most frequently physiologically in the first 2-3 years after menarche (ACOG, 2015).

Based on the definition of the American College of Obstetricians and Gynecologists (ACOG), Abnormal Uterine Bleeding (AUB) is characterized by unpredictable timing and variable amounts of menstrual blood flow (ACOG, 2015). Menorrhagia is common among adolescents. The term menorrhagia is defined as bleeding that lasts longer than a week or exceeds 80 mL per cycle and is often defined as increased menstrual blood volume interfering with a woman's daily activities, regardless of how much she bleeds. Based on the International Federation of Gynecology and Obstetrics (FIGO), the term AUB is used to describe "any deviation from normal menstruation or the normal menstrual cycle pattern" (Haamid et al., 2017; Fraser et al., 2011).

Abnormal uterine bleeding affects 3-20% of women of reproductive age with an incidence in adolescents under 18 years of age varying between 8.6% and 37.5% in questionnaire-based population surveys from different countries (Revel-Vilk et al., 2012). However, few data are available on the frequency of AUB in young women over 18 years of age, when

menstruation is no longer anovulatory. In adolescents, AUB is the most common cause of gynecological problems and is a significant source of stress for affected adolescents and their families. Menorrhagia is the most common symptom (Munro et al., 2018). AUB is a public health problem for several reasons. First of all, it is the most common cause of anemia in menstruating women. AUB might also affect physical, emotional, and social well-being and quality of life. It has been reported that AUB might lead to absenteeism from education and thus to a decrease in academic achievement (Fraser et al., 2009).

In adolescents who have symptoms of AUB, pregnancy, sexual trauma, and infection must be reliably excluded, regardless of sexual history. It is also important to remember that pelvic inflammatory disease and ectopic pregnancy might present as AUB and abdominal pain, and after their exclusion, the PALM-COEIN (polyp, adenomyosis, leiomyoma, malignancy, and hyperplasia, coagulopathy, ovulatory dysfunction, endometrial, iatrogenic, and not yet classified) system of AUB might be considered. Structural causes (PALM) are rare in adolescents, accounting for only about 1.3% of AUB in this population. Nonstructural causes (COEIN) are more common in the adolescent population, with ovulatory dysfunction being the most common. Ovulatory dysfunction because of the immature hypothalamic-pituitary-ovarian axis is seen in 95% of adolescents who had AUB (Pecchioli et al., 2017; Hernandez et al., 2020).

The present study aimed to evaluate the demographic, ultrasonographic, clinical, and laboratory data of adolescents who had abnormal uterine bleeding who applied to our clinic, which is a tertiary health center. It also aimed to contribute to the literature by dividing adolescents into 3 based on their degree of anemia and determining the etiology and severity of bleeding in adolescents.

2. METHODS

This retrospective study included 112 women who were in adolescence and applied to the Dicle University Faculty of Medicine, Department of Obstetrics and Gynecology with symptoms of abnormal uterine bleeding between January 2018 and October 2022 with an approval number of 12 and date 07.11.2022 from the ethics committee of Dicle University Faculty of Medicine for the present study.

Adolescents who had menarche were included in the present study. All adolescents included had menorrhagia, that is, heavy menstrual bleeding. Adolescents who had amenorrhea, normal menstrual patterns, or normal menstrual bleeding, and those with an intrauterine device were not included in the study. The age, marital status, gravida, parity, abortion, number of living children, systemic diseases, drug use history, ultrasonography findings, and laboratory values of the adolescents included in the study were obtained by reviewing the hospital information management system archive and patient files.

Adolescents who were included in the present study were defined as women aged 10–19 years, following the WHO definition. The cases using more than three well-soaked pads or

diapers per day, the presence of blood clots in menstrual bleeding within seven days, or prolonged bleeding for more than seven days with or without excessive bleeding were considered as menorrhagia cases because it is difficult to find a quantitative estimate of menstrual blood loss (Prasad et al., 2016). Participants were classified based on the degree of anemia. Mild menorrhagia was divided into three groups as hemoglobin (Hgb) > 12 g/dl, moderate menorrhagia Hgb 10–12 g/dl, and severe menorrhagia Hgb ≤ 10 g/dl. The data were compared among these three groups.

The SPSS 23 statistical package program was used for statistical analyses. The descriptive data were given by using mean, standard deviation, number, and percentage. The Kolmogrow-Smirnow Test was performed to understand whether the data were normally distributed. The Chi-Square Test was used to evaluate categorical data. The One-Way Anova, which is a parametric test, was used for those that were normally distributed, and the Friedman test, which is a non-parametric test, was performed for those that were not normally distributed. A $p < 0.05$ value was accepted as statistically significant.

3. RESULTS

A total of 112 adolescent women who had menorrhagia were identified during the study period. The mean age of these adolescents was 17.9 ± 1.5 years, mean Hgb values were 11 ± 3.5 g/dl, mean international normalized ratio (INR) values were 0.9 ± 0.3 , 57.1% (64) of the adolescents were married, mean gravida number was 0.9 ± 1.1 , 17% (19) had systemic diseases, and 26.8% (30) were using medications. The demographic and clinical data are given in Table 1.

Among the adolescents included in the study, 59.6% (53) had mild anemia, 19.1% (17) had moderate anemia, and 21.3% (19) had severe anemia (Table 1).

Table 1. The Evaluation of the Demographic and Clinical Data

	Mean±SD
Age (years)	17.9±1.5
Gravida	0.9±1.1
Parity	0.4±0.8
Abortion	0.1±0.4
Live	0.4±0.8
Hemoglobin (g/dl)	11±3.5
Platelets (e3/uL)	273.000±130.000
White blood cell count (e3/uL)	8.7±4.5
International Normalized Ratio (INR)	0.9±0.3

Marital status	Married	n (%) 64 (57.1)
	Single	48 (42.9)
Systemic disease	Yes	19 (17)
	No	93 (83)
Drug use	Yes	30 (26.8)
	No	82 (73.2)
Anemia	Mild	53 (59.6)
	Moderate	17 (19.1)
	Severe	19 (21.3)

Data are given as mean \pm SD (min-max)

When the adolescents were divided into 3 groups as mild, moderate, and severe anemia based on their Hgb values and compared their demographic and clinical data, no significant difference was found between the three groups in terms of the presence of systemic disease, marital status, drug use rates, age, gravida numbers, platelet values and INR values ($p>0.05$) (Table 2).

When the presence of systemic diseases was examined among the three groups, we determined that a total of two adolescents who had factor 8 deficiency were in the severe anemia group, one patient with Glansmann Thrombocytopenia was in the moderate anemia group, three of the 6 adolescents who had immune thrombocytopenia (ITP) had mild anemia, one had moderate anemia and two had severe anemia. Although not statistically significant, it was found that adolescents in the mild anemia group used more drugs (13). The most commonly used drugs were determined to be combined oral contraceptives (7), tranexamic acid (6), and progesterone (6). The number of adolescents using mefenamic acid was three and it was determined that it was used in combination with other drugs. Intrauterine pregnancy was detected in 19.6% (22) of the adolescents included in the present study, ectopic pregnancy in 1.8% (2), and molar pregnancy in 3.6% (4).

Table 2. Comparison of Demographic and Clinical Data Among the Three Groups

	Mild Anemia n = 53 Mean±SD	Moderate Anemia n = 17 Mean±SD	Severe Anemia n= 19 Mean±SD	p
Age (years)	18.1± 1.5	17.7 ± 2.1	17.8± 1.4	0.652
Gravida	1.0± 1.2	1.1± 1.2	0.4± 1.0	0.126
Parity	0.4± 0.7	0.4± 0.6	0.4± 1.0	0.942
Abortion	0.2± 0.5	0.2± 0.5	0.0± 0.0	0.126
Live	0.4± 0.7	0.4± 0.6	0.4± 0.1	0.973
Hemoglobin (g/dl)	13.2± 1.1	10.8± 0.5	7.9± 1.2	0.571
Platelets (e3/uL)	278.000± 72.368	306.588± 146.706	303.278± 176.408	0.974
White blood cell count (e3/uL)	9.1± 3.2	9.3± 4.6	9.3± 5.7	0.230
International Normalized Ratio (INR)	0.9± 0.2	1.02± 0.09	1.05± 0.08	
n=	n	n	n	
Marital status	Married	10	7	0.086
	Single	18	12	
Systemic disease	Yes	6	6	0.076
	No	47	13	
Medicine usage	Yes	13	7	0.205
	No	40	12	

The data are given as Mean ± SD

The data are given as number, p<0.05 statistically significant

4. DISCUSSION

It is already known that the adolescent population is high and menstrual disorders are frequently seen during this period. This age group requires attention because AUB is more common in adolescents and negatively affects the quality of life. This disorder is not reported enough in adolescents. With this study, the purpose was to contribute to the

literature by determining the etiology and severity of menorrhagia seen in adolescents. When we examined our data, we found that 59.6% of the adolescents included in the present study had mild anemia, 57.1 % were married, 25% were pregnant, 17% had systemic diseases, and among the systemic diseases, two adolescents had factor 8 deficiency, six adolescents had ITP, and one adolescent had Glanzmann Thrombocytopenia.

In a retrospective study that aimed to investigate the differences in diagnosis and treatment in 79 adolescents who had and did not have menorrhagia, adolescents known to have bleeding disorders were not included in the study. Adolescents were divided into 2 based on their Hgb values and it was reported that the group with Hgb below 10 was significantly older. However, aside from that, no significant differences were detected between the two groups in terms of the presence of hematological diseases unknown to the patients, anovulation, polycystic ovary syndrome, and uterine structural anomalies. They found the frequency of MTHFR mutation in girls with a history of thrombosis to be 50%, but since this condition did not increase the risk of bleeding or thrombosis, they did not recommend routine evaluation (Kızılcan Çetin et al., 2023). In another study, 111 unmarried adolescents who had menstrual disorders were evaluated. Pregnant women were excluded from the study. It was reported that the most common disorder in adolescence was menorrhagia, with a rate of 33.3% (37). Patients with menorrhagia were divided into three groups based on their Hgb values. Moderate anemia was detected in 40.5% (15) adolescents, severe anemia in 37.8% (14) adolescents, and mild anemia in 21.6% (8) adolescents. The most common etiology of menorrhagia was dysfunctional uterine bleeding in 67.5% (25). ITP was found as a bleeding disorder in only one patient (2.7%) (Prasad et al., 2016). In another retrospective study that evaluated 258 adolescents who applied to the emergency department of a tertiary hospital because of menorrhagia, the data of the adolescents who were admitted and discharged were evaluated (only 17% of the adolescents who applied were admitted). As a result of their study, they reported that most of the adolescents who applied to the emergency department were not anemic and did not receive any treatment (Rosen et al., 2020). In the present study, in which 112 adolescents who had menorrhagia were included, both those with bleeding disorders and pregnant women were included. We detected Factor 8 deficiency in two patients, Glanzmann Thrombocytopenia in 1 patient, and ITP in 6 patients. Pregnancy was detected in 25% (28) of the adolescents who had menorrhagia. When the patients were divided into 3 groups based on their Hgb values, it was found that 59.6% had mild anemia and 21.3% had severe anemia. We determined that there was no difference between the 3 groups in terms of systemic disease, drug use, and marital status. Unlike other studies in the literature, pregnant women were also included in the present study. Since we found the pregnancy rate to be 25% with adolescent menorrhagia in our data, we must exclude pregnancy in the etiology, regardless of sexual history, when evaluating women presenting with adolescent menorrhagia. We recommend that we establish an adolescent clinic to provide counseling to adolescents and provide detailed information about sexuality and adolescent gynecology. In the present study, we observed that most of the adolescents who had menorrhagia

(59.6%) had mild anemia and applied to our tertiary hospital. We need to question why these adolescents and their families believe that their bleeding is severe enough to require them to come to a tertiary hospital. We believe that this situation might be because of either a lack of education on the part of the adolescents and their families or a lack of evaluation by primary healthcare institutions on this issue. We believe that we might find a solution to this situation by conducting public education and screening programs.

If bleeding is cyclical but heavy in terms of volume or duration, the etiology might be coagulopathy. The literature suggests that bleeding disorders are the second most common cause of menorrhagia in the adolescent population, after anovulation (Kabra and Fisher, 2020). A retrospective study was conducted to investigate bleeding disorders in 50 adolescents who had menorrhagia. In this study, bleeding disorders were detected in 22% (n = 11) of the patients. Five patients were reported to have von Willebrand disease, two patients to have ITP, one patient to have Bernard Soulier syndrome, one patient to have Glanzmann thrombocytopenia, one patient to have aplastic anemia, and one patient to have factor X deficiency (Karaman et al., 2016). In a case report evaluating three adolescents who had gynecological complaints and Glanzmann Thrombocytopenia, it was reported that two adolescents had menorrhagia, and severe anemia, and were treated conservatively. As a result of their study, it was reported that patients with Glanzmann thrombocytopenia might present with life-threatening spontaneous bleeding episodes (Vaidya and More, 2018). In the present study, we identified two adolescents who had factor 8 deficiency, one with Glanzmann thrombocytopenia, and six with ITP. If a bleeding disorder is suspected in adolescents who have menorrhagia, we recommend multidisciplinary management with pediatric hematologists to accurately and completely evaluate this age group.

In adolescents, severe bleeding requires treatment. Since the adolescent group is in a transition period and because of their age, these patients apply to both pediatricians and gynecologists. In a prospective study including 17 adolescents who had heavy menstrual bleeding, the success of oral tranexamic acid and combined oral contraceptives in reducing bleeding was compared. It was reported that oral tranexamic acid was as effective as combined oral contraceptives in treatment (Srivaths et al., 2015). In the present study, it was found that combined oral contraceptives, tranexamic acid, and progesterone treatment were used more. It was determined that those using mefenamic acid used this treatment in combination with other drugs. In the literature review, it was seen that there was no standard treatment in the management of adolescent menorrhagia.

The limitation of the present study was that it had a retrospective design and some data were missing because patient data were accessed through the registration system. Its advantage was that it was conducted in a tertiary hospital where multidisciplinary evaluation was possible and the number of patients was high.

5. CONCLUSION

In the evaluation of menorrhagia, which might be detected frequently in adolescence, we need to keep in mind bleeding disorders and pregnancy that might cause menorrhagia, other than dysfunctional uterine bleeding and manage this condition in a multidisciplinary manner.

Statement on Research and Publication Ethics

Throughout the entire process of preparing this article, the research and publication ethics principles of the Manisa Celal Bayar University Institute of Health Sciences Journal have been followed.

Authors' Contribution Rates to the Article

The entire article was written by Reyhan Gündüz.

Declaration of Interest

The author has no conflict of interest with any person or organization.

REFERENCES

- ACOG Committee Opinion No. 651. (2015). Menstruation in girls and adolescents: Using the menstrual cycle as a vital sign. *Obstet Gynecol*, 126(6), e143–6. <https://doi.org/10.1097/AOG.0000000000001215>.
- Fraser, IS., Critchley, HOD., Broder, M., Munro, MG. (2011). The FIGO recommendations on terminologies and definitions for normal and abnormal uterine bleeding. *Semin Reprod Med*, 29, 383-90.
- Fraser, IS., Langham, S., Uhl-Hochgraeber, K. (2009). Health-related quality of life and economic burden of abnormal uterine bleeding. *Expert Review of Obstetrics & Gynecology*, 4, 179-89.
- Haamid, F., Sass, AE., Dietrich, JE. (2017). Heavy menstrual bleeding in adolescents. *J Pediatr Adolesc Gynecol*, 30, 335-40.
- Hernandez, A., Dietrich, JE. (2020). Abnormal Uterine Bleeding in the Adolescent. *Obstet Gynecol*, 135, 615–21.
- Kabra, R., Fisher, M. (2022). Abnormal uterine bleeding in adolescents. *Curr Probl Pediatr Adolesc Health Care*, 52, 101185.
- Karaman, K., Ceylan, N., Karaman, E., Akbayram, S., Akbayram, HT., Kaba, S., et al. (2016). Evaluation of the Hemostatic Disorders in Adolescent Girls with Menorrhagia: Experiences from a Tertiary Referral Hospital. *Indian J Hematol Blood Transfus*, 32(3), 356–61.
- Kızılcın Çetin, S., Aycan, Z., Özsu, E., Şıklar, Z., Ceran, A., Erişen Karaca, S., et al. (2023). Evaluation of Abnormal Uterine Bleeding in Adolescents: Single Center Experience. *J Clin Res Pediatr Endocrinol*, 15(3), 230-37.
- Menstruation in girls and adolescents: using the menstrual cycle as a vital sign. Committee Opinion No. 651. American College of Obstetricians and Gynecologists. (2015). *Obstet Gynecol*, 126, e143–6.
- Munro, MG., Critchley, HOD., Fraser, IS., FIGO Menstrual Disorders Committee. (2018). 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*, 143, 393–408.
- Pecchioli, Y., Oyewumi, L., Allen, LM., Kives, S. (2017). The utility of routine ultrasound in the diagnosis and management of adolescents with abnormal uterine bleeding. *J Pediatr Adolesc Gynecol*, 30, 239–42.
- Prasad, DB., Jagannath, P., Bora, BMK. (2016). Evaluation of Menorrhagia in Adolescent Girls: A Clinical Study Sch. *J. App. Med. Sci*, 4(6F), 2307-11.

- Ravi, R., Shah, P., Palani, G., Edward, S., Sathiyasekaran, BWC. (2016). Prevalence of Menstrual Problems among Adolescent School Girls in Rural Tamil Nadu. *J Pediatr Adolesc Gynecol*, 29, 571-576.
- Revel-Vilk, S., Paltiel, O., Lipschuetz, M., Ilan, U., Hyam, E., Shai, E., Varon, D., et al. (2012). Underdiagnosed menorrhagia in adolescents is associated with underdiagnosed anemia. *J Pediatr*, 160, 468–72.
- Rosen, MW., Weyand, AC., Pennesi, CM., Stoffers, VL., Bourdillon, CM., George, JS., et al. (2020). Adolescents Presenting to the Emergency Department with Heavy Menstrual Bleeding. *J Pediatr Adolesc Gynecol*, 33, 139-43.
- Srivaths, LV., Dietrich, JE., Yee, DL., Sangi-Haghpeykar, H., Mahoney, D. (2015). Oral Tranexamic Acid versus Combined Oral Contraceptives for Adolescent Heavy Menstrual Bleeding: A Pilot Study. *J Pediatr Adolesc Gynecol*, 28, 254-57.
- Vaidya, AA., More, VS. (2018). A case series on Glanzmann thrombasthenia in adolescent girls with puberty menorrhagia. *International Journal of Clinical Obstetrics and Gynaecology*, 2(1), 4-6.
- World Health Organization: Women's health. (2010). Available: <http://www.who.int/mediacentre/factsheets/fs334/en>. Accessed July 1.