

*Research Article***Characteristics and management of heavy menstrual bleeding in girls with bleeding tendency**

Attia Mohamed\* and Hams A. Attalla\*\*

\* Department of Obstetrics and Gynecology, Faculty of Medicine, Al-Azhar University, Cairo, Egypt.

\*\* Department of Pediatrics, Faculty of Medicine, Helwan University, Helwan, Cairo, Egypt.

**Abstract**

**Background:** Among adolescent with heavy menstrual bleeding (HMB), there is a considerable number of adolescent who have bleeding tendency or bleeding disorders. This study aimed to discuss the pattern of menstruation and the management of the HMB in girls with bleeding disorders. **Methods:** In this retrospective study, we included girls aged 9-18 years old who had established bleeding tendency due to bleeding disorders in our pediatric hematology clinic. These girls were referred to the pediatrics gynecology clinic to reviews their pattern of menstruation and the treatment of their HMB. **Results:** Among 58 girls reviewed, 51 were included in our analysis, 34 of them were already had menarche. Among these post-menarcheal girls, 16 girls revealed HMB at menarche. The menstruation of girls with bleeding disorder related to defect in von Willebr and factor lasted more than seven days. The hormonal therapy was the first line of treatment of HMB; however, 50.9% of them failed the first line of treatment. Therefore, the second line of treatment, combined hormonal and non-hormonal therapy, was started for them. **Conclusion:** The risk of HMB after menarche is increased in young girls with bleeding disorders. Premenstrual counseling with pediatrics gynecologist and hematologist is recommended for young girls with bleeding disorders to discuss the pattern of menstrual bleeding and the possible treatment of the heady bleeding.

**Keywords:** Bleeding disorder, Patterns of menstruation, Heavy menstrual bleeding

**Introduction**

After menarche, many young girls experience heavy menstrual bleeding (HMB). This is mostly due to delay in the development of hypothalamic-pituitary-ovarian axis. Taking the bleeding disorders and tendency to bleed in consideration, a large fraction of young girls, ranging from 7% to 62%, with HMB was reported to have bleeding diseases<sup>1-3</sup>. According to these young girls with established bleeding disorders, the time of menarche is a potentially challenging time and could be characterized by HMB, defect in the social activities, bad conduction in the school, and worse effect on the quality of life<sup>4</sup>.

The management of HMB in young girls with bleeding disorders is a challenging process. Many girls experience using hormonal therapy, some add to this hormonal therapy other non-hormonal modalities. However, the literature has no guidelines regarding the optimum management plan for treating HMB in young girls with bleeding diforders<sup>5,6</sup>. Therefore, this study aimed to outline the characteristics and modalities of menstruation in young girls with

bleeding disorders. Furthermore, it aims to investigate the treatment option to overcome the HMB in these patients.

**Methods**

We included young girls aged from 9 to 18 years who already registered and known to have one of the bleeding disorders who used to come to our pediatric hematology clinic and pediatric gynecology clinic.

The study participants and their representatives agreed and signed the informed consent after explaining the study and its objectives. Therefore, this study was conducted under the declaration of Helsinki. The institutional review board revised and approved the study protocol.

**Data collection**

From each included girl, demographic data, including age, age at menarche, age of starting HMB, body mass index, type of bleeding disease, and family history of bleeding disorders were collected. Furthermore, the status of menarche, the pattern of menstruation, the treatment HMB, and the side effects of that

treatment were also collected for analysis. Data regarding HMB were mostly depending on the subject self-reporting without ranking or scales. The bleeding diseases were categorized mainly into four categories; diseases associated with platelets dysfunction, diseases associated with defect in clotting factors (including factors VII, VIII, IX, X, and XIII), von Willebrand disease with its types, and diseases associated with defect in fibrinolytic pathway.

The used hormonal therapy for HMB included combined estrogen and progesterone contraceptive pills, oral progesterone alone, depot medroxyprogesterone acetate, and contraceptive patches. The nonhormonal therapy included desmopressin, factor infusion, and antifibrinolytics therapy (including aminocaproic acid and tranexamic acid). The combined treatment included any combination between both hormonal and non-hormonal therapy.

### **Statistical analysis**

The statistical analysis was conducted on SPSS platform version 23. The categorical data were expressed as number and percentages, while the continuous data were expressed as mean and standard deviation, when the normality achieved, or median and range, when the normality could not be achieved. The four groups of bleeding disorders were compared as regard the prevalence of HMB, the pattern of menstruation, the length of menstruation, and the treatment of HMB using either chi-square test or Fisher's exact test. Furthermore, the four groups were compared to each other as regard the age of menarche onset using ANOVA F-test. The level of significance was set up when the P-value is less than 0.05.

### **Results**

Among the 58 young girls identified, seven girls were excluding due to the lack of sufficient information in their reports. Finally, 51 young girls were included in the analysis. Among them, the von Willebrand disease was present in 28 (54.9%) girls, while the clotting factor defect was present in 14 (27.5%) girls. Furthermore, the platelets dysfunction was present in seven (13.7%) and the defect in the fibrinolytic pathway was present in two (9.3%) girls.

The menarche had occurred to 34 (66.7%) young girl, while 17 (33.3%) girls did not reach the menarche. The menarche age was  $12.3 \pm 1.2$  years. There was no difference between the four groups as regard the menarcheal age ( $P=0.923$ ). Among the 34 post-menarcheal young girls, 16 (47%) girls reported HMB at the menarche. Despite the absence of significant association between the four groups of bleeding disease regarding the presence of HMB at menarche ( $P=0.795$ ), the percentage of HMB at menarche (60%) in girls with platelets dysfunction was higher than other diseases (Table 1).

Interestingly, menses lasting for more than 7 days were present significantly in young girls with von Willebrand disease as compared other bleeding diseases ( $P=0.019$ ). However, there was no significant association between the four groups regarding the presence of irregular menstruation (Table 2).

Among the post-menarcheal girls, only 27.5% had discussed the treatment options for HMB before the menarche in our clinic ( $P < 0.001$ ). The hormonal treatment was prescribed for two patients (22%), while the non-hormonal therapy was prescribed for four patients (44%). Around 33% of the patients did not discuss the treatment options, but instead they were advised to seek for medical help if they experience any disturbance in their menstruation.

The initial therapy of HMB failed in 16 (53.3%) young girls who had both bleeding disease and HMB. Most of the initial therapy (66.7%) was single therapy (either hormonal or non-hormonal). Among this single therapy, the combined estrogen and progesterone contraceptive pills was the most one (50%) (Table 3). Furthermore, the hormonal treatment was most likely to be prescribed for young girls with bleeding diseases due to platelets dysfunction ( $P=0.041$ ).

Having the young girls who failed the initial therapy, a combination between both hormonal and non-hormonal therapy was prescribed in most of them, 12 patient among the 16 patients, (75%) (Table 4). Among these 12 girls, the combined therapy was successful in 10 girls, and two girls were hospitalized due to the severe bleeding.

**Table 1: comparison between the four types of bleeding disorders regarding the heavy menstrual bleeding at menarche.**

Bleeding Disorder	Pre-menarcheal (n=17)	Post-menarcheal (n=34)	Heavy Menstrual Bleeding at Menarche (n=16)
Von Willebrand Disease	45.5%	59.4%	48.8%
Clotting Factor Deficiencies	36.4%	23.2%	37.5%
Platelet Function Disorders	15.2%	13.0%	60.1 %
Fibrinolytic Pathway Defects	3.0%	4.3%	33.3%
<b>No significant difference between groups. (Fisher's Exact Test p=0.795)</b>			

**Table 2: Comparison between the four types of bleeding disorders as regard the duration of menstruation and the irregularity of menstruation.**

Bleeding Disorder	Menses Length > 7 days <sup>a</sup> n=26	Irregular Menses <sup>b</sup> N=16
Von Willebrand Disease	63.3%	31.6%
Clotting Factor Deficiencies	23.1%	25.0%
Platelet Function Disorders	33.3%	60%
Fibrinolytic Pathway Defects	0%	0%
<sup>a</sup> Fisher's Exact Test, p=0.019		
<sup>b</sup> Fisher's Exact Test, p=0.63		

**Table 3: comparison between the four types of bleeding disorders as regard the type of initial treatment (hormonal, non-hormonal, and combined)**

Bleeding Disorder	Non-Hormonal	Hormonal	Combination
Von Willebrand Disease	19.4%	47.2%	33.3%
Clotting Factor Deficiencies	38.5%	15.4%	46.2%
Platelet dysfunction	12.5%	87.5%	0%
Fibrinolytic Pathway Defects	33.3%	33.3%	33.3%
<b>P=0.041</b>			

**Table 4: comparison between the four types of bleeding disorders regarding the second line of treatment (hormonal, non-hormonal, and combined)**

Bleeding Disorder	Non-Hormonal	Hormonal	Combination
Von Willebrand Disease	4.5%	18.2%	77.3%
Clotting Factor Deficiencies	0%	0%	100%
Platelet dysfunction	0%	40.0%	60.0%
Fibrinolytic Pathway Defects	0%	0%	110%
<b>P=0.72</b>			

### Discussion

There was a knowledge gap regarding the characteristics of menstruation and presence of menstrual bleeding in young girls who have bleeding disorders and the subsequent management of such bleeding. The previous literature focused on proving the association between HMB in young girls and bleeding disorders. This study focused on illustrating the patterns of menstruation and prevalence of HMB in addition to discussing the treatment options for such bleeding in young girls with bleeding disorders.

There was no difference between the age of menarche in our girls and the age of menarche in the general population. Furthermore, the menarcheal age did not differ among the four groups of bleeding disorders. Despite the absence of difference between the four groups regarding the prevalence of HMB, young girls with von Willebrand disease were associated with increase the duration of menstruation more than seven days. However, there was no difference between the four groups as regard the irregularity of menstruation. This may be due to the small sample size. Therefore, more large-sample sized studies are recommended in the future as these results may be turned into significance.

Surprisingly, our study showed that majority of young girls with bleeding disorders did not discuss the dealing with menstrual bleeding or have a plan for that; however, about half of our post-menarcheal girls reported HMB at menarche. The prevalence of HMB among women with bleeding disorders ranged from 10% to 98% according to the type of the

bleeding disorder<sup>7</sup>. Furthermore, the literature revealed that young girls with bleeding disorders are prone to develop hemorrhagic ovarian cysts<sup>7,8</sup>.

Menarche is very stressful time for young girls with bleeding diseases. However, the literature agreed that these patients should go to the gynecologist from 13 to 15 years old with their family to discuss the menstruation issues and to be offered the pre-menstruation counseling regarding the HMB and its treatment<sup>3,9,10</sup>.

Many of girls in our study started single therapy for HMB; however, a large fraction of them failed this initial therapy and therefore, shifted to combined therapy on it most of them succeeded to stop the bleeding. Therefore, we recommend starting to treat young girls who had bleeding disorders and HMB with combined treatment of both hormonal and non-hormonal therapy.

The absence of randomized trials that discuss the efficacy of treatment options for HMB in young girls with bleeding disorders in addition to the small sample size in our studies hinder us to test the efficacy of each treatment modality for each specific type of bleeding disorders. Therefore, large sample sized clinical trials are needed to fulfil this gap.

In nutshell, young girls with bleeding disorders should seek for consultation regarding the patterns of menstruation and the possibility of HMB, and the treatment options with gynecologist and pediatric hematologist before, the menarche. Young girls with von Willebrand disease are most likely to have prolonged

menstruation. Combined hormonal and non-hormonal therapy is recommended for girls with HMB and known to have bleeding disorder. Further, large-sample sized studies are needed to bring guidelines regarding the patterns of menstrual bleeding and the treatment of HMB.

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