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RESEARCH

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# Rare bleeding disorders in Egyptian females presented with heavy menstrual bleeding: single-center study

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## Abstract

**Background** Heavy menstrual bleeding is an important health problem in women of reproductive age and is also one of the most common symptoms in women with bleeding disorders. Data about the frequency of rare bleeding disorders are limited, and population-based studies are lacking, so we aimed to determine the frequency of rare bleeding disorders among women presented with heavy menstrual periods that cannot be attributed to obvious problems.

**Methods** Complete blood count and bleeding profiles include activated partial thromboplastin time, prothrombin time, factor VIII activity assay, ristocetin cofactor activity, von Willebrand antigen assay, platelet aggregation tests and other factor assays in 100 out of 300 females presented with unexplained heavy menstrual period, pictorial bleeding assessment chart (PBAC) > 100 as a screening tool for heavy menstrual periods, and or International Society of Thrombosis and Hemostasis-Bleeding Assessment Tool (ISTH-BAT) > 6.

**Results** A total of 300 women with heavy menstrual periods without an obvious explained cause were included in our study. Among them, we found 100 (30%) females with a mean PBAC of 234 ± 147 and mean ISTH-BAT of 9 ± 5 denoting HMB may be due to underlying bleeding disorders. Among them, the most common diagnosis was VWD in 30 (30%). Other disorders were as follows: 28 (28%) cases with clotting factor deficiencies, 24 (24%) cases were found to have platelet dysfunction, and in 18% of our studied cases, we did not find a clear cause of their bleeding disorders (unknown).

**Conclusion** Rare bleeding disorders are not uncommon and require comprehensive hemostatic evaluation as well as simple tools like PBAC and ISTH-BAT questionnaires for the identification of females presented with unexplained HMB.

**Keywords** Rare bleeding disorders, Heavy menstrual bleeding, BPAC score, ISTH-BAT

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## Introduction

Heavy menstrual bleeding (HMB) is often defined as menstrual bleeding consistently lasting > 8 days or a menstruation volume that negatively impacts the patient's marital, social, emotional, or physical well-being [1].

Rare bleeding disorder (RBD) is a term that is commonly used to define deficiencies of coagulation factors like FVIII, FVII, and fibrinogen deficiencies [2] which are better defined as rare factor deficiencies (RFD) while hereditary platelet disorders (platelet dysfunctions and hereditary thrombocytopenia) as well as rare acquired bleeding diseases (acquired hemophilia, acquired Glanzmann) could be added to them within the same term of RBD.

Rare bleeding disorders (RBD) are found in approximately one in five women who present to a gynecologist with heavy menstrual bleeding (HMB) [3].

RBD is characterized by a wide range of symptoms, ranging from mild to severe, and they can differ greatly between illnesses and even within patients with the same disease [4].

Even though HMB had mostly been present since menarche, according to some reports, 28 was the median age of RBD diagnosis, indicating a substantial gap in diagnosis [5]. In women, the average interval between the age at which bleeding began and the age at diagnosis was 6 years longer than in men in a large Dutch study [6]. The fact that standard screening tests for coagulation do not rule out the possibility of a (mild) uncommon coagulation factor deficit could account for a part of the diagnostic delay, also most females presented with HMB were unaware that it is heavy menstrual periods and need laboratory tests.

Women with RBD need particular consideration and care, as in addition to menorrhagia, the risk of hemorrhagic ovary cysts, endometrial hyperplasia, polyps, and fibroids as well as the clinical challenges associated with pregnancy and childbirth as miscarriages, and pregnancy-related hemorrhagic events have been frequently documented in them [7].

Accurate information about the frequency of RBD in women presenting with HMB is vital to increase the early detection of RBD and to give those women a personalized, efficient treatment plan that includes enough supportive care to prevent hemorrhagic episodes. That is why our study aims to determine the frequency of rare bleeding disorders among a cohort of Egyptian women presented with heavy menstrual periods that cannot be attributed to a gynecological problem.

## Patients and methods

### Patients

We conducted a cross-sectional study enrolling a total of 300 Egyptian females referred with unexplained Heavy menstrual bleeding (HMB); all were recruited from the clinics of the clinical hematology unit, Internal Medicine and Gynecology Departments of the Kasr Al-Ainy Teaching Hospital as well as the Egyptian Society of Hemophilia, where they recruited between February 2020 and May 2023. Known causes of gynecological HMB had been ruled out by the patients' gynecologists. Oral contraceptives, intrauterine device (IUD), anticoagulants, or antiplatelets were not received by any of the individuals. Also, any patients with autoimmune or endocrinal disease were excluded. Prior to the start of the study and patient recruitment, each patient provided their informed consent; the study was approved by the local ethical committee of the Faculty of Medicine, Cairo University, MD-12–2021. The study complied with good clinical practice protocols and the ethical rules in the Declaration of Helsinki (as revised in Tokyo 2004).

### Methods

All subjects with unexplained heavy menstrual bleeding were subjected to full history taking (especially bleeding manifestations, drug intake, and family history), assessment of bleeding by using the International Society of Thrombosis and Hemostasis-Bleeding Assessment Tool (ISTH-BAT) questionnaire, and evaluation of menstrual blood loss by using pictorial bleeding assessment chart (PBAC), thorough clinical examination, all females with ISTH-BAT > 6 and PBAC > 100 subjected to laboratory investigations according to our proposed flow diagram (Fig. 1) which included full blood count (CBC) and blood film, and the coagulation tests listed below were carried out within 4 h of blood collection: prothrombin time (PT), activated partial thromboplastin time (aPTT), factor VIII assay, von Willebrand disease (VWD) panel (vWF:Ag and vWF:RCo), and platelet aggregation tests. Plasma 1:1 mixing studies at 0 and after 2 h of incubation were done if prolonged PT and/or aPTT and accordingly other factor assays.

#### *ISTH-BAT questionnaire*

Fourteen categories in the ISTH-BAT are used to evaluate bleeding symptoms retrospectively, and research has demonstrated that the existence of an inherited bleeding disease is linked to a high bleeding score. Each of the 14 variables is scored from 0 to 4 [except for CNS bleeding when the scores are 0, 3, or 4], and from this, a final score is calculated. Abnormal ISTH-BAT scores

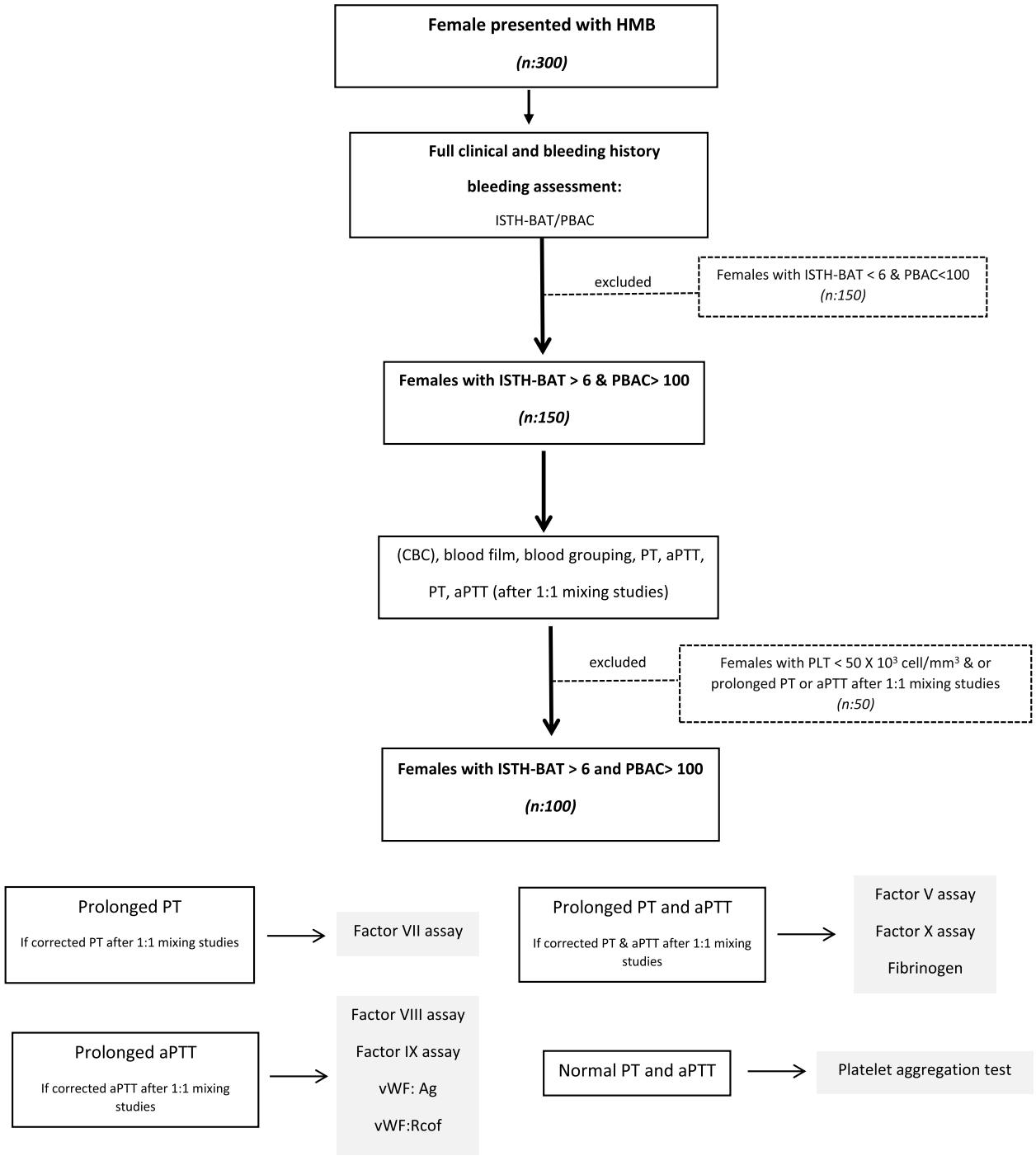


**Fig. 1** Flow diagram of our presented study

have been identified as > 6 in adult females [8]. One of the ISTH-BAT's limitations is that it is insensitive to acquired bleeding disorders which are outside the scope of our study.

***PBAC questionnaire***

## The pictorial blood assessment chart (PBAC) score

This technique keeps track of how many tampons or towels are used and the degree to which they are stained with

blood. Every participant received instructions on how to finish the PBAC score during their subsequent menstrual period. The chart consists of images representing lightly, moderately, and heavily stained sanitary towels (scored as 1, 5, and 20, respectively) and tampons (scored as 1, 5, or 10, respectively); passage of clots (assigned ascending scores from 1 to 5) and episodes of flooding are also recorded. Most women who have been diagnosed with bleeding disorders have confirmed PBAC scores of more than 100 [9].

#### Sample collection

Venous blood samples were collected from females with ISTH-PAT > 6 and PBAC > 100 (2 cc of blood in each EDTA and 3.2% citrated tubes). Within 2–4 h, using a standard technique, all coagulation test samples, including PT, APTT, and other coagulation factors, were centrifuged and the plasma separated. On the same day of collection, CBC and blood film tests were performed using ABX Micros 60 from Horiba, and PT and PTT were carried out using Siemens Reagents Innovin and Pathromtin SL. Factor VIII and VWF ristocetin co-factor activity were tested using the Innovance from Siemens using Sysmex CS2500 equipment. VWF antigen was tested using the Vidas VWF from Biomerieux, and Platelet aggregation tests were carried out from the Hyphen BioMed using Sysmex CS2500 equipment.

#### Statistical analysis

Version 25 of the statistical package SPSS (Statistical Package for the Social Sciences) was used to code and enter the data. For quantitative data, the mean, standard deviation, median, minimum, and maximum were used; for categorical data, the frequency (count) and relative frequency (%) were used to summarize the data. Cross-tabulations were used to show the bivariate association, and when necessary, the Fisher exact or chi-square test was used to compare the proportions. To compare normally distributed quantitative data, one-way ANOVA, post hoc tests, and *T*-independent tests were employed. Pearson correlation was used to compare normally distributed quantitative data. The level of significance was set at a probability (*P*) value < 0.05.

#### Sample size calculation

It was done using the frequency of bleeding disorders in women with abnormal vaginal bleeding. In the screening of bleeding disorders in adolescents and young women with menorrhagia, 20% of patients with menorrhagia were discovered to have bleeding disorders [3]. The sample size needed for the research study was calculated using G*Power (a free-to-use software used to calculate statistical power and sample size). The calculation of sample size was 300 cases with paired samples to achieve a power of 85% and a level of significance of 5% (two-sided).

## Results

Overall, 300 women with a history of HMB without an obvious explained gynecological or endocrinal cause were included in our study. Among them, we found 100 (30%) females with PBAC > 100 and/or ISTH-PAT > 6 denoting HMB may be due to underlying bleeding disorders. They were subjected to more detailed laboratory studies for rare bleeding disorders after the exclusion of 50 females suspected to have acquired causes of bleeding like immune thrombocytopenia, acquired hemophilia, or antiphospholipid antibodies.

#### Patients' characteristics

The 100 females had age ranges of 14–45 years with a mean age of 26 ± 9 years. Their PBAC score ranges from 100 to 950 with a mean of 234 ± 147. Their ISTH-BAT score ranges from 4 to 22, with a mean of 9 ± 5, VWD was the most often identified diagnosis among the 100 HMB women with suspected bleeding disorders and was found in 30 (30%) cases. Other disorders were found as follows: 28 (28%) cases with clotting factor deficiencies, 24 (24%) cases were found to have platelet dysfunction, and in 18% of our studied cases, we did not find a clear cause of their bleeding disorders (unknown) by our available investigations in the study; 33% (33/100) of our studied cases were found to have a family history of bleeding tendencies most of them were found to have VWD (13/33), while no family history found in cases of an unclear cause of bleeding. Our patients' characteristics are shown in Table 1.

#### Bleeding characteristics

Regarding the PBAC score, the highest mean score was found to be 385.33 ± 289.15 in patients diagnosed with FVII deficiency. In contrast, the lowest mean score was found to be 139.67 ± 18.62 in patients with unknown cause of bleeding disorders; also, regarding the ISTH-BAT score, the highest mean score was found to be 13.67 ± 4.163 in patients diagnosed with platelet dysfunctions. At the same time, the lowest mean score was found to be 4.50 ± 0.78 also among patients with unknown bleeding disorders.

Regarding bleeding manifestations among the studied group, the most frequent manifestation apart from HMB was found to be easy bruising in 80% of our studied cases; surprisingly, 20% of them had a history of postpartum bleeding, and 3% of them had a history of intraabdominal bleeding. The most frequent bleeding symptom in patients with VWD was epistaxis 22/30, in patients with

**Table 1** Characteristics of studied females with HMB PBAC > 100 and/or ISTH-PAT > 6

| Parameter[a] (*n* = 100) | Subcategory | Frequency |
|---|---|---|
| **Cases discovered to have a detectable RBD[b]** | No | **18** |
| | Yes | **82** |
| **Family history of abnormal bleeding** | No | **67** |
| | Yes | **33** |
| **Bleeding manifestations** | Epistaxis | **59** |
| | Bleeding per gum | **64** |
| | Easy bruising (cutaneous) | **80** |
| | Hematuria | **5** |
| | GIT bleeding | **25** |
| | Prolonged bleeding after cut | **36** |
| | Bleeding after surgery | **3** |
| | Post-partum hemorrhage | **20** |
| | Deep hematoma | **3** |
| | Intraabdominal bleeding | **3** |
| **Subtypes of discovered RBDs** | **Unknown RBD[b]** | **18** |
| | **VWD** | **30** |
| | Type 1 | **23** |
| | Type 2 | **6** |
| | Type 3 | **1** |
| | **Clotting factors disorders** | **28** |
| | FVII deficiency | **9** |
| | FVIII deficiency | **12** |
| | FIX deficiency | **2** |
| | FV deficiency | **5** |
| | **Platelet dysfunctions** | **24** |
| | Glanzmann thrombasthenia | **20** |
| | Bernard-Soulier syndrome | **4** |

*n* number, % percentage, *PBAC* pictorial bleeding assessment chart, *ISTH-PAT* International Society of Thrombosis and Hemostasis, *HMB* heavy menstrual bleeding, *RBD* rare bleeding disorder, *GIT* gastrointestinal tract, *vWD* von Willebrand disease, *F* clotting factor

[a] Among 300 patients with HMB, only 100 had high PBAC > 100 and/or ISTH-BAT > 6 and were investigated for RBDs

[b] Undetectable cause of bleeding (no obvious endocrinal, gynecological, autoimmune or acquired cause of bleeding)

clotting factor deficiencies was bleeding gum 17/24, and in patients with platelet dysfunction was easy bruising 21/24.

### Laboratory findings

Regarding laboratory data of our studied cases which are summarized in Table 2, the mean hemoglobin was 9.8 ± 1.2 g/dl, and no one among our studied cases had normal hemoglobin, the mean platelet count was $285 \pm 88 \times 10^3$ cell/mm$^3$, and only one patient had thrombocytopenia with platelet count of $90 \times 10^3$ cell/mm$^3$ who discovered to have BSS; the mean PT was 14.8 ± 8 s, but its mean in factor VII deficiency cases was 29.55 ± 13.69 s while the mean PTT was 41.5 ± 20 s and its mean in VWD cases was 42.8 ± 8.4 s; in hemophilia A cases, it was 43.87 ± 7.37 s, and in hemophilia B cases, it was 46 ± 4 s. Fifty-three percent of our studied cases had normal PT and PTT, and five cases had both PT and PTT prolonged which were discovered to have FV deficiency. No one of our cases had abnormal fibrinogen. All cases of clotting factor deficiencies were either mild or moderate deficiencies except one case with severe factor VII deficiency.

## Discussion

### Heavy menstrual periods and rare bleeding disorders

Menorrhagia is a common health problem in adolescents and adult females with considerable implications on their health-related quality of life (HRQoL) as well as their educational, physical, and social performance [10, 11]. Accurate information about the geographical frequency of RBD in women presenting with HMB is still an unmet need to provide those women with an effective and individualized treatment plan that is why our study aimed to determine the frequency of rare bleeding disorders among a cohort of Egyptian women presented with heavy menstrual periods that could be attributed to a bleeding

**Table 2** Parametric data of studied females with HMB suspected to have bleeding disorders[a]

| Parameter[a] ($n=100$) | | Mean ± SD | Range | Parameter | Subcategory | Mean ± SD |
|---|---|---|---|---|---|---|
| **Age (years)** | | 26 ± 9 | 16–45 | **Hb%** (RV, 11.5–14 g/dl) | | **9.8 ± 1.2** |
| | | | | **PLT** (RV, 150–450 × 103 cell/mm$^3$) | | **285 ± 88** |
| **ISTH-BAT score Abnormal if > 6 in adult female** | **All studied cases[a]** | 9 ± 5 | 4–22 | **PT** (RV, 11–14.5 s) | | **14.8 ± 8** |
| | **VWD** | 10.21 ± 5.466 | 4–22 | **aPTT (s)** (RV, 26–40) | | **41.5 ± 20** |
| | **Hemophilia A** | 7.13 ± 2.800 | 5–13 | **vWF: Ag** (RV, 50–150%) | VWD | **29.003 ± 25.825** |
| | **Hemophilia B** | 6.50 ± 2.121 | 5–8 | | Unknown causes | **93.588 ± 17.052** |
| | **FVII deficiency** | 9.67 ± 4.664 | 4–18 | **vWF: RCo** (RV, 70–120%) | VWD | **24.927 ± 22.694** |
| | **FV deficiency** | 11.00 ± 4.848 | 6–19 | | Unknown causes | **116.611 ± 43.564** |
| | **Platelet dysfunction** | 13.67 ± 4.163 | 4–21 | **FVIII assays** (RV, 70–150%) | Hemophilia A | **32 ± 17** |
| | **Unknown causes[b]** | 4.50 ± 0.786 | 4–6 | | VWD | **35 ± 29** |
| **PBAC score If > 100 means HMB** | **All studied cases[a]** | 234 ± 147 | 100–950 | | Unknown causes | |
| | **VWD** | 247.50 ± 156.085 | 120–550 | **FIX assays** (RV, 78–184%) | Hemophilia B | **56 ± 1** |
| | **Hemophilia A** | 206.38 ± 62.976 | 130–315 | **FVII assays** (RV, 50–150%) | Factor VII deficiency | **22 ± 18** |
| | **Hemophilia B** | 272.50 ± 152.028 | 165–380 | **FV assays** (RV, 62–140%) | Factor V deficiency | **7 ± 7** |
| | **FVII deficiency** | 358.33 ± 289.154 | 105–950 | **ADP for PLT aggregation** (RV, 63–89%) | Platelet dysfunction | **31.33 ± 20** |
| | **FV deficiency** | 300.60 ± 163.812 | 170–565 | | Unknown causes | **78 ± 8** |
| | **Platelet dysfunction** | 306.00 ± 78.505 | 228–385 | **Ristocetin for PLT aggregation** (RV, 68–106%) | Platelet dysfunction | **62.125 ± 26.27** |
| | **Unknown causes[b]** | 139.67 ± 18.620 | 107–165 | | Unknown causes | **82 ± 9** |

*n* number, % percentage, *PBAC* pictorial blood loss assessment chart, *ISTH-BAT* International Society on Thrombosis and Hemostasis-Bleeding Assessment Tool, *HMB* heavy menstrual bleeding, *RBD* rare bleeding disorder, *VWD* von Willebrand disease, *F* clotting factor, *NR* normal reference, *SD* standard deviation, *RV* reference value, *s* seconds, *PLT* platelet

[a] Among 300 patients with HMB, only 100 had high PBAC > 100 and/or ISTH-BAT > 6 and were investigated for RBDs

[b] Undetectable cause of bleeding (no obvious endocrinal, gynecological, autoimmune or acquired cause of bleeding)

disorder. In the current study, 300 women with a history of HMB without an obvious explained gynecological, endocrinal, or autoimmune cause were included. Among them, we deeply investigated rare bleeding disorders in 100 (30%) females who were found to have PBAC > 100 (denoting HMB) and/or ISTH-BAT > 6 (denoting underlying bleeding disorder).

We used PBAC as a simple reliable tool to assess HMB as self-perception of menstrual loss is unreliable. PBAC as an assessment tool when used as a diagnostic test to estimate a blood loss of more than 80 ml per menses, a score of ≥ 100 gave a reported sensitivity and specificity of 86 and 89%, respectively [12].

In the general population, bleeding disorders affect 1–2% of people. However, about 20% of adolescent girls who come in for an assessment of heavy menstrual bleeding and 33% of adolescent girls who are hospitalized for heavy menstrual bleeding have bleeding disorders, as stated by the American College of Obstetricians and Gynecologists Committee opinion [13].

### Frequency of rare bleeding disorders among women with HMB

In different reports, the frequency of adolescents with HMB has been observed to have bleeding disorders between 8 and 62% [14]. In our study, we found that 30% of our cases with HMB might be due to rare bleeding disorders based on abnormal PBAC and or ISTH-BAT. Similar results were found in the Middle East region; in a Turkish study by Karaman et al., they found that bleeding disorders were detected in 22% (11/50) of adolescents presented with unexplained HMB [15]. Also, in another Saudi study by Bakr et al., 30.8% (8/26 who finished the investigations) of university students had a bleeding tendency or hemostatic abnormalities as their final diagnosis, while more than half of the sample population's underlying causes of heavy menses had a local uterine issue [16], while an American study by Diaz et al. identified a hemostatic abnormality in 53% (69/131) of young girls with HMB. Of these, low von Willebrand factor activity was a risk factor for bleeding in 32% of cases, and underlying bleeding disorders affected 21% of cases [17]. The actual frequency of bleeding disorders in females with HMB is unknown due to the lack of prospective studies with objective menstrual flow assessment, standardized hemostatic testing, and standardized laboratory definitions of von Willebrand disease and platelet function tests. Also, the discrepancy between our results and others could be attributed to the differences in the ethnic origins or age

group of the studied populations, as well as the methodology or timing of laboratory screening.

#### The most frequent RBD among females with HMB

Among our studied cases, the most common diagnosis found was VWD (30%) (most of them were VWD type 1 (23/30) followed by Glanzman thrombasthenia (20%) which is consistent with data from the literature; as VWD was the most commonly seen bleeding disorder in adolescent girls with menorrhagia, Karaman et al. found that VWD was observed in 45.4% in their study [15]; also, Bakr et al. found that 5/8 females were having VWD or low level of vWF panel among their sample population [16]. It is observed that the frequency of VWD in US-based studies has been lower than that in European studies as described in a meta-analysis by Shankar et al. Von Willebrand disease was identified in 131 of the 988 HMB women who participated in the 11 studies; the disease's prevalence varied between 5 and 24% in the individual studies [18]; according to certain publications, platelet dysfunctions were more frequently seen in women who had menorrhagia than VWD, for example, Vo et al., found that 46% of 105 studied females with HMB had a primary qualitative platelet disorder and attributed this higher frequency to due to a lack of systemic evaluation for qualitative platelet function defects in other studies, especially electron microscopy [19].

Of the 100 studied cases suspected to have an underlying bleeding disorder, we did not find a clear diagnosis in 18 cases which could be due to many factors; diagnosis of VWD varies due to several factors, including age, ethnicity, blood groupings, inflammatory mediators, endocrine hormones, and stress factors which can have an impact on plasma levels in VWF [20]. Also, sophisticated and sensitive techniques are needed for the laboratory assessment of a bleeding patient to quantify the platelet aggregations, as well as a thorough coagulation profile that includes fibrinolytic factors was needed and was not included in our study that is why those patients should be retested as they may have mild deficiencies to avoid any complications with surgical challenges.

#### ISTH-BAT and PBAC scores as assessment tools for RBD

The mean PBAC score denoting HMB in our study was 234 ± 147, and the higher score was found in cases discovered to have factor VII deficiency while the lower score > 100 was found in cases with unknown causes for their bleeding. In a retrospective analysis of adult females ($n = 199$) evaluated because of HMB, a PBAC score of > 100 showed 91% sensitivity for identifying patients with coagulation problems, 100% specificity, 100% positive predictive value, and 85.5% negative predictive value [9]. In the same study by Halimeh et al., they discovered that the HMB group had a higher median PBAC score (266) than the control group (60) with the highest median PBAC of 320 in women with thrombocytopenia followed by 297 in FXIII deficiency [9]. Not all our studied cases with PBAC > 100 had abnormal ISTH-BAT scores as the range of it was 4–22, and the highest mean was found in patients with platelet dysfunction and the lowest mean was found in patients with the undetectable cause of HMB. We have to point out that the initial focus of ISTH-BAT validation was on individuals suffering from VWD [21], although few RBD patients have been assessed using it; furthermore, it is well established that ISTH-BAT has little diagnostic utility for individuals with mild bleeding disorders [22]. A large Dutch nationwide cross-sectional study by Saes et al. included 263 known cases with congenital coagulation factor deficiency; the BAT scores for each RBD varied significantly; however, patients with FV and FXIII deficits had the highest median scores and for FII and FX deficiencies; there was a significant association identified between the baseline coagulation factor activity level and the ISTH BAT score [23] which was not assessed in our study.

It was surprising to see that 33% of the individuals in our study had a family history of bleeding tendencies but had not previously received an RBD diagnosis or investigation. Furthermore, the higher mean age at diagnosis in our study population indicates a substantial gap in RBD diagnosis.

All cases had anemia due to iron deficiency anemia and HMB as expected, the restoration of hematological parameters in those women with HMB has been found to have significant implications for general health and well-being by improving HRQoL [24].

Easy bruising (cutaneous bleeding) was the most frequent bleeding manifestation (80%) in our patients with HMB; 87.5% of our patients with platelet disorders reported having easy bruising. While most patients with VWD reported epistaxis and patients with clotting factor deficiencies reported bleeding gum. It is well known that even in patients with the same disorders, RBD patients' clinical symptoms differ greatly from one disorder to the other. It is well known that mucocutaneous bleeding, including HMB, epistaxis, and gum bleeding, is a hallmark of VWD, the most prevalent inherited bleeding disorder [25]. Furthermore, it was noted that 20% of patients with RFD had mucocutaneous or surgically related bleeding while heterozygous individuals commonly do not manifest a bleeding tendency [4].

To our knowledge, at the present time, by reviewing the literature, there are similar publications in the region like Turkey and KSA but no similar published research on the Egyptian population with this sample size, and our publication may encourage the initiation of a large

national registry for rare bleeding disorders, our limitation was the lack of using sensitive laboratory techniques to quantify the platelets aggregations, as well as a thorough coagulation profile that includes fibrinolytic factors for example.

For women with bleeding disorders, accurate diagnosis is essential to receiving the right medical attention. Also, both access to high-quality laboratory assays and an accurate assessment of bleeding symptoms are crucial.

HMB not only significantly increases morbidity but also harms those patients' health-related quality of life. Timely intervention with hormones, hemostatic medications, and prophylactic treatment with factor concentrates are made possible by early diagnosis of RBD, thereby improving outcomes. The goal is to diagnose these patients before menarche to facilitate adequate counseling and enable the application of the best preventative and therapeutic measures. When a woman presents with HMB, it is advised that general practitioners and gynecologists inquire about any past bleeding symptoms and a family history of bleeding manifestations as well as apply simple tools to assess bleeding. Furthermore, screening a patient's family members could help with an early diagnosis.

## Conclusion

Our results demonstrate that unexplained heavy menstrual bleeding (HMB) might be the presenting manifestations of hereditary bleeding disorders as we found that 30% of our cases with HMB might be due to rare bleeding disorders, our recommendation is to screen for inherited bleeding disorders in young women with heavy menstrual bleeding by simple tools like PBAC and ISTH-BAT questionnaires as they are helpful and applicable for early diagnosis cases with rare bleeding disorders.

**Abbreviations**

| | |
|---|---|
| aPTT | Activated partial thromboplastin time |
| BAT | Bleeding Assessment Tool |
| CBC | Complete blood count |
| EDTA | Ethylene diamine tetra acetic acid |
| F | Coagulation factor |
| FV | Factor 5 |
| FVII | Factor 7 |
| FVIII | Factor 8 |
| HMB | Heavy menstrual bleeding |
| HRQoL | Health-related quality of life |
| ISTH | International Society of Thrombosis and Hemostasis |
| PBAC | Pictorial bleeding assessment chart |
| PT | Prothrombin time |
| RBD | Rare bleeding disorders |
| RFD | Rare factor deficiencies |
| VWD | Von Willebrand disease |
| vWF:Ag | Von Willebrand factor antigen |
| vWF:RCo | Ristocetin cofactor activity |

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**Authors' contributions**
The idea of the research is done by Prof. Dr. AA and Prof. Dr. MTE. Data collection is done by all authors. Meticulous laboratory work was done under the supervision of Dr. ND and written by Dr. DE and Dr. MF. All work is revised by all authors with an equal contribution.

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**Availability of data and materials**
All data generated or analyzed during this study are included in this published article.

## Declarations

**Ethics approval and consent to participate.**
Approved by the local ethical committee of the Internal Medicine Department, Faculty of Medicine, Cairo University.

**Consent for publication**
Not applicable.

**Competing interests**
The authors declare that they have no competing interests.

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