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Differences in bleeding phenotype and provider interventions in postmenarchal adolescents when compared to adult women with bleeding disorders and heavy menstrual bleeding

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Abstract

Introduction—Due to lack of patient/health care provider awareness causing delayed diagnosis, the bleeding phenotype and provider interventions in adolescents with heavy menstrual bleeding (HMB) and bleeding disorders (BD) may be different when compared to adults.

Aim—The aim of this study was to compare/characterize bleeding phenotype and provider interventions in postmenarchal adolescents < 18 years and premenopausal adults ≥ 18 years with HMB and BD.

Methods—Patient demographics, BD, and provider interventions/therapy details for HMB were compared between both age groups enrolled in the Centers for Disease Control and Prevention (CDC) Female Universal Data Collection (UDC) surveillance project in United States hemophilia

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DISCLOSURE

P. Kouides receives honoraria as a member of the advisory board of CSL Behring and serves as a consultant to Baxalta. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

AUTHORS' CONTRIBUTIONS

LS designed the study, contributed to data analysis and interpretation and wrote the manuscript; QZ analysed the data and contributed to data interpretation and manuscript writing; VB contributed to the study design, data analysis and interpretation and manuscript writing; JD, AH and PK contributed to the study design, data interpretation and critically reviewed the manuscript; RK oversaw the study design, data interpretation and critically reviewed the manuscript.

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treatment centres. Cross-sectional descriptive analyses including frequency distributions, summary statistics, bivariate and logistic regression analyses were performed.

Results—Of 269 females (79 adolescents; median age 16 years, interquartile range (IQR) = 2; 190 adults; median age 27 years, IQR = 13) evaluated, BD distribution was similar in both groups. Compared to adolescents, adults more often had family history of bleeding (Adjusted odds ratios [AOR] = 2.6, 1.3–5.6), delay in diagnosis (AOR = 2.5, 1.2–4.9), bleeding with dental procedures (AOR = 2.0, 1.0–4.0), gastrointestinal bleeding (AOR = 4.6, 1.0–21.9), anaemia (AOR = 2.7, 1.4–5.2), utilized desmopressin less often (AOR = 0.4, 0.2–0.8) and underwent gynaecologic procedure/surgery more frequently (AOR = 5.9, 1.3–27.3).

Conclusion—Bleeding phenotypes of adolescents and adults with HMB and BD were different with more frequent bleeding complications, anaemia, gynaecologic procedures/surgeries, less desmopressin use and more delay in diagnosing BD in adults. Longitudinal studies are needed to determine whether improved patient/provider awareness and education will translate to early diagnosis and timely management of BD/HMB in adolescents that may prevent/reduce future haematologic/gynaecologic complications.

Keywords

adolescents; bleeding disorder; bleeding phenotype; females; heavy menstrual bleeding; provider intervention

1 | INTRODUCTION

Bleeding disorders (BD) such as von Willebrand disease (VWD), coagulation factor deficiencies and platelet disorders (PD) are frequently reported in adolescents with heavy menstrual bleeding (HMB).[1,2] Although the overall prevalence rates of BD are comparable in adolescent and adult females with HMB,[3] the bleeding phenotype and provider interventions may be different. Potential differences may include younger age at presentation with symptoms in adolescents. At any age, lack of patient/provider awareness can cause delay in diagnosis and more bleeding complications. Studies of females with diagnosed BD have consistently found that although bleeding symptoms often began during childhood and adolescence, the diagnosis was most often not made until adulthood.[4,5] Such delays in care seeking and BD diagnosis may lead to delay in therapy, education and counselling, and increasing risk for complications among these women during their adult reproductive years. Knowledge about the differences in the phenotype of adolescent vs adult women with BD and HMB and the provider interventions offered may help to formulate future measures for earlier detection and management of BD, thereby minimizing hematologic/gynaecologic complications.

There are no published studies comparing the bleeding phenotype and management details in adolescent and adult females with BD and HMB. To address this gap, we analysed females with BD to compare and characterize the bleeding phenotype and provider interventions for HMB in postmenarchal adolescents <18 years in comparison with premenopausal adults >/= 18 years. We hypothesized that the bleeding phenotype and provider interventions of BD are different in adolescents and adults with HMB.

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2 | MATERIALS AND METHODS

The Universal Data Collection (UDC) surveillance project conducted by the Centers for Disease Control and Prevention (CDC) and 135 U.S. federally funded haemophilia treatment centres (HTCs) collected data annually from 1998–2011 on persons with BD to identify and characterize complications. A female data collection module was added to UDC in 2009 and implemented in 23 HTCs to prospectively characterize females with BD, and to monitor bleeding and reproductive complications.[5] The female UDC module collected data on diagnoses, menstrual bleeding, other bleeding symptoms, obstetrical-gynaecological symptoms, treatment and gynaecological/reproductive history. All females with BD aged ≥2 years receiving care at the HTCs were eligible for enrollment. Females with VWD, coagulation factor deficiencies (factor levels <50%) and/or platelet disorders were eligible. HMB was defined as menstrual bleeding requiring protection change at least every 2 hours on heaviest days. This analysis represents cross-sectional data from participants enrolled from September 2009 through September 2011. A registration form completed at baseline consisted of: (i) demographic information and source of referral to HTC, (ii) diagnoses and family history of BD, (iii) history of bleeding symptoms and resulting provider interventions, (iv) treatment history for bleeding problems, (v) history of gynaecological abnormalities and reproductive outcomes, and (vi) history of menopause and menopause-related treatment for bleeding. Primarily registration data are included in this analysis; height and weight were included from the annual form to calculate body mass index (BMI). The protocol was reviewed and approved by institutional review boards at CDC and the individual sites. Menarche was self-reported by the study participants. To minimize recall bias, HMB analyses were restricted to postmenarchal females and excluded self-identified postmenopausal women. There was a delay in diagnosis of a BD if age at diagnosis was greater than the age at first bleed in years; the median difference in years was also calculated.

For this study analysis, we compared the study population of postmenarchal adolescents <18 years old and premenopausal adults >/= 18 years old who had a BD and HMB enrolled in the female UDC project. Patient demographics, diagnoses, bleeding symptoms, provider interventions, medical and surgical treatment for HMB, and treatment of anaemia as listed in Tables 1, 2 and 3, were compared for adolescents and adults.

2.1 | Statistical analysis

The statistical analysis for the study was done in 2 steps. First, in bivariate analysis, differences in patient demographics, diagnoses, bleeding symptoms, provider interventions, medical and surgical treatment for HMB between adolescents and adults groups were examined using Pearson's Chi-squares test of independence for categorical variables and a median test for continuous variables. Count and percentages for categorical variables and median and interquartile ranges (IQR) for continuous variables were calculated because age in the study population was not normally distributed. Clinically important variables or variables with P values ≤.15 in bivariate analysis were used as independent variable candidates to build 2 separate multivariate logistic regression models. A symptom model and a treatment model were each estimated with the dependent variable of adulthood status in

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order to examine the independent associations of bleeding symptoms or treatment for HMB with being adult vs adolescent. To adjust for confounders, race/ethnicity, diagnosis of VWD, anaemia and family history of BD were also included in the models as covariates. The final models included covariates and clinical variables with *P* values <.05. Adjusted odds ratios (AOR) and 95% confidence intervals were computed. All statistical analyses were based on two-sided tests with a significance level of 0.05, and conducted using SAS 9.1.3. (Cary, NC, USA). Cases with missing data for any variable were excluded from the specific analysis.

3 | RESULTS

Of 269 postmenarchal and premenopausal females with HMB and BD who formed the study population (Table 1), 79 (29%) were adolescents aged < 18 years, with a median age of 16 years (IQR = 2). One hundred and ninety (70%) were adults aged >/= 18 years, with a median age of 27 years (IQR = 13). Overall, 206 (77%) patients were White (non-Hispanic), 26 (10%) were Hispanic and 20 (7%) were Black (non-Hispanic) and 17 (6%) self-identified as other race/ethnicity. There were more Whites (*P* = .05) and less Hispanics (*P* = .05) in adults when compared to adolescents. Overall, 152 (57%) females reported family history of BD; this was unknown in 44 (16%). Majority of the patients were diagnosed with VWD (n = 223; 83%); other diagnoses included coagulation factor deficiency in 44 (16%) (factor VIII deficiency in 19 (7%), factor IX deficiency in 7 (3%), other coagulation factor deficiencies in 18 [7%]) and PD (platelet function disorders [PFD] and thrombocytopenia) in 11 (4%); 9 (3%) patients had unspecified BD. (Table 1). No statistically significant difference in BD diagnoses was detected between the 2 groups. The majority had a single BD diagnosis (n = 249, 92.6%), few (n = 11, 4.1%) had multiple. The median age at first bleed (any bleed) was 10 years (IQR = 10 years) and the median age at diagnosis of BD was 14 years (IQR = 13 years). The difference between the median age at first bleed in adolescents (9 years; IQR 10) when compared to adults (10.5 years; IQR 10), was not statistically significant (*P* = .46). The median age at diagnosis of BD was 12 (IQR 7) for adolescents vs 16 (IQR 16) for adults (*P* < .0001). Forty-five adolescents (57%) and 138 adults (73%) (*P* = .01) had a delay in diagnosis. The median delay in diagnosis was 8 years overall (range 0.5–32 years), 4 years (range 1–13.5 years) in adolescents, and 10 years (range 0.5–32 years) in adults (*P* = .005). BD were diagnosed in 51% (n = 97) of adult women before age 18, 41% (n = 77) diagnosed after age 18, with the remaining unknown. To ensure that our findings about delayed diagnosis were not due to selection bias, we also compared the delay in diagnosis in adolescents vs adults diagnosed before age 18 years. The delay in diagnosis in adults with age at diagnosis < 18 years was also greater when compared to that in adolescents (median 10 vs 4, IQR 12.5 vs 7 years respectively; *P* = .0021). There was no statistically significant difference in the age at menarche, BMI and anaemia between both groups.

There were differences in the bleeding phenotype of the adults when compared to adolescents (Table 2). On bivariate analysis, adults more often reported bleeding after surgery (*P* = .02), pregnancy/postpartum (*P* < .0001) and gastrointestinal bleeding (*P* = .01); bleeding after dental procedures trended towards significance (*P* = .09). Rate of bleeding per surgery/procedure could not be calculated as data on the total number of surgery/procedures were not collected. Two pregnancies were reported in 2 adolescents vs 279 pregnancies in 108 (56%) adults. Bleeding complications during pregnancy/postpartum were reported by

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53% (57/108) of adults when compared to 100% (2/2) of adolescents. Of the study participants, 15% of adolescents (n = 12) and 6% of adults (n = 12) had HMB as the only bleeding symptom ($P = .02$). Irregular menstrual cycles were reported in 49% (n = 37) and 54% (n = 105) of adolescents and adults respectively ($P = .62$). Medical and surgical management of HMB were compared between the groups (Table 2). A similar proportion of adults and adolescents underwent any therapy for HMB (n = 145; 76% vs n = 59; 75% respectively; $P = .78$) and medical therapy (n = 151; 79% vs n = 63; 80% respectively; $P = 1.0$; some patients received more than 1 medication). On bivariate analysis for HMB management, desmopressin was used more often by adolescents ($P = .01$), and gynaecologic procedure/surgery was performed more often in adults ($P = .02$). No adolescent underwent endometrial ablation, uterine artery embolization or hysterectomy. Antifibrinolytic agents, hormonal therapy, clotting factor products, and blood/plasma products were used similarly in both groups.

On multivariate analysis in the bleeding symptoms model, there was a lower odds of Hispanics (AOR 0.3, 95% CI 0.1–0.7), but higher odds of family history of BD (2.6, 95% CI 1.3–5.6), anaemia (AOR 2.2, 95% CI 1.2–4.2), delay in diagnosis (AOR 2.5, 95% CI 1.2–4.9), bleeding during dental procedures (AOR 2, 95% CI 1–4) and gastrointestinal bleeding (AOR 4.6, 95% CI 1–21.9) among adults when compared to adolescents. In the HMB management model, there was a lower odds of Hispanics (AOR 0.3, 95% CI 0.1–0.9) and desmopressin use (AOR 0.4, 95% CI 0.2–0.8) but a higher odds of having family history of BD (AOR 3, 95% CI 1.5–6.3), anaemia (AOR 2.7, 95% CI 1.4–5.2), delay in diagnosis (AOR 2.4, 95% CI 1.2–4.6) and gynaecologic procedure or surgery (AOR 5.9, 95% CI 1.3–27.3) among adults when compared to adolescents. All results were statistically significant.

4 | DISCUSSION

In females with HMB, adults facing more haemostatic challenges may have greater likelihood of being diagnosed with BD and receiving appropriate management. As anovulatory bleeding due to physiologic immaturity is common in the adolescent, an underlying BD may not be considered by the treating physician as a potential cause of HMB. The bleeding phenotype is different in both age groups as shown in our study, and lack of recognition of bleeding symptoms as due to an underlying BD can lead to increased complications. Our study is the first attempt to compare the bleeding profile, BD diagnoses, medical/surgical/procedural management in adolescents vs adults with HMB. There were more Whites and fewer Hispanics among adults when compared to adolescents, similar to US population patterns.[6] The ethnic distribution between adults and adolescents is comparable to the population of males with haemophilia seen at US HTCs.[7,8] Adults more often had a family history of a BD. The longer time for evaluation to establish BD diagnosis in adults could have resulted in more referrals and evaluation of their family members. No difference was noted between the 2 groups in the type of BD diagnoses and the sub-types of VWD, the most common BD diagnosed in the study population. PD were reported overall in 4% of the patients. This is likely an underrepresentation, as PFD are reportedly a common cause of HMB.[9,10] This may be due to underdiagnosis of PD or lack of management of these patients in HTCs.

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Proportionately, more adolescents presented with HMB as the only bleeding symptom when compared to adults, which was statistically significant ($P = .02$). This is most likely due to the younger aged adolescents not experiencing as many haemostatic challenges as adults. Contrary to the common assumption that irregular cycles are more frequent in adolescents, we found irregular menstrual cycles to be equally prevalent in both groups. The findings in our study underline the delay in diagnosis of BD in females with HMB. Overall, there was a delay in diagnosis of 8 years in our study population. This was more pronounced in adults than in adolescents, which was statistically significant. BD were diagnosed in only 51% (n = 97) of adults before age 18. The delay in diagnosis in adults with age at diagnosis < 18 years was greater than that in adolescents. Delay in diagnosis of BD was also statistically significant on multivariate analysis by both models. We suspect the difference in delay in diagnosis in adults vs adolescents is because of improved earlier diagnosis due to greater awareness in the past decade through national advocacy organizations such as the National Hemophilia Foundation and the Foundation for Women and Girls with Blood Disorders (FWGBD).

Not surprisingly, adults more often reported bleeding after surgical procedures, and gastrointestinal bleeding on bivariate analysis, and bleeding with dental procedures was statistically significant and gastrointestinal bleeding trended towards significance on multivariate analysis. Even though pregnancy/postpartum bleeding was more often reported in adults on bivariate analysis, this is likely due to more adults experiencing pregnancy when compared to only 2 adolescents, precluding meaningful comparison and hence this was not included in multivariate analysis. Since iron deficiency is cumulative over time, not surprisingly, anaemia reported more often in adults when compared to adolescents had statistical significance on multivariate analysis. Early diagnosis of BD will enable providers to administer haemostatic prophylaxis during pregnancy/postpartum, procedures and surgeries, and to educate the patient to avoid risk factors, which can further minimize complications. The delay in BD diagnosis in adults may have led to HMB and other bleeding complications, causing anaemia. Although the haemostatic challenges are likely age-dependent, it is possible that if adults had been diagnosed earlier and received appropriate therapy, this could have minimized bleeding complications. A previous study reported similar results of 16-year delay between the first bleeding symptoms and clinical recognition in a comparable age group.[4] A recent study that examined obstetrician-gynaecologists' practices in the evaluation of BD in females with HMB demonstrated that a greater proportion of physicians surveyed would consider BD as underlying cause of HMB for adolescents (77%) in comparison to reproductive-age women (36.4%).[11] Improved provider awareness and earlier diagnosis in adolescents will hopefully translate in the future to appropriate management of BD leading to decrease in bleeding complications in both age groups.

Our study finding of equal utilization of HMB therapy by both groups is reassuring. Although hormonal therapy and antifibrinolytic agents were used equally by both groups, desmopressin was utilized more often by adolescents. Medical therapy, either with hormonal agents and/or haemostatic therapy, is the cornerstone of HMB management in adolescents.[12,13] The choice of therapy may be dictated by the patient's age, menstrual cycle characteristics, patient's acceptance of medication, side effect profile, the need for

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contraception and the family's cultural values and preferences. Desmopressin, a good choice in VWD as well as minor PFD,[14] was more commonly utilized by the adolescents in our study, likely because of the ease of intranasal administration, intake limited to days of menstrual bleeding, to avoid hormonal agents due to its side effect profile/need for continued use and/or parental preference of non-contraceptive therapy. Adults utilized desmopressin less and likely opted for other treatment modalities such as hormonal therapy and surgical interventions, in part due to contraceptive benefits from hormonal therapy, and preference for definitive outcome with surgical interventions. Antifibrinolytic agents can also control HMB with the advantage of medication intake limited to the days of bleeding. Oral tranexamic acid (TXA), reportedly more effective than epsilon aminocaproic acid and intranasal desmopressin,[15] has been used extensively for HMB in Europe and Canada, and is available in the US for adults since its FDA approval in 2009.[16] Up to one-third of adolescents in our study used antifibrinolytics although the package insert for TXA states use for age ≥18 years, as the licensure study excluded younger patients.[17] The recent availability in the US and more research in the future on efficacy and safety in adolescents[18] may bring forth increased utilization of TXA in females with HMB.

We found that, overall, gynaecologic surgery/procedure was performed more often in adults when compared to adolescents. This is perhaps because adults having suffered with HMB for decades are reluctant to be on long-term medical therapy opting instead for gynaecological intervention. It is reassuring to note that no adolescent underwent major surgery/procedure for HMB management such as endometrial ablation, uterine artery embolization or hysterectomy. Medical management is the preferred mode of therapy in adolescents with HMB, with other gynaecologic procedures/surgeries avoided in order to preserve fertility.[12,13]

Our study limitations include the following: this is retrospectively collected, self-reported data based on patient recall which is subject to under-/overestimation of morbidity and lack of accuracy; small sample size which may preclude meaningful comparison of patient subsets; sample bias, as it is not clear how many eligible HTC patients elected to participate in the female UDC project and the HTC patients may not be representative of all patients in the community; lack of a denominator to calculate bleeding rate per procedure in order to correct for the increased prevalence by age, as our data collection did not include number of procedures. There is potential for selection bias; by virtue of receiving care at a HTC, adolescents are more likely to be diagnosed at a younger age. Also, as the data is self-reported, adults with physiologic vs surgical menopause could not be distinguished. The difference in the site of first bleed between the 2 groups was not analysed as part of this study; whether this difference will lead to earlier recognition of BD needs further exploration. As the study data are from 2009 to 2011, this may not accurately reflect current practice in the diagnosis and management of HMB.

Nevertheless, this is a first attempt to compare the bleeding phenotype, complications and management of females with HMB and BD, confirming findings of delayed diagnosis and increased bleeding complications in adults when compared to adolescents. Although there has been progress over the last decade,[11] additional efforts are needed to increase awareness and action in recognizing BD in females. These findings, we hope, will kindle further efforts

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to overcome the lack of patient/physician awareness and pave way for future studies to prospectively evaluate the effect of early provider intervention in minimizing complications in this population.

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References

1. James AH. Bleeding disorders in adolescents. Obstet Gynecol Clin North Am. 2009; 36:153–162. [PubMed: 19344853]
2. Venkateswaran L, Dietrich JE. Gynecologic concerns in pubertal females with blood disorders. J Pediatr Adolesc Gynecol. 2013; 26:80–85. [PubMed: 23095526]
3. James AH. Women and bleeding disorders. Haemophilia. 2010; 16(Suppl 5):160–167. [PubMed: 20590876]
4. Kirtava A, Crudder S, Dilley A, et al. Trends in clinical management of women with von Willebrand disease: a survey of 75 women enrolled in haemophilia treatment centres in the United States. Haemophilia. 2004; 10:158–161. [PubMed: 14962204]
5. Byams VR, Kouides PA, Kulkarni R, et al. Surveillance of female patients with inherited bleeding disorders in United States Haemophilia Treatment Centres. Haemophilia. 2011; 17(Suppl 1):6–13. [PubMed: 21692922]
6. Patten, E. The Nation's Latino Population Is Defined by Its Youth. Washington, DC: Pew Research Center; 2016.
7. Monahan PE, Baker JR, Riske B, et al. Physical functioning in boys with haemophilia in the U.S. Am J Prev Med. 2011; 41:S360–S368. [PubMed: 22099359]
8. Mazepa MA, Monahan PE, Baker JR, et al. Men with severe haemophilia in the United States: birth cohort analysis of a large national database. Blood. 2016; 127:3073–3081. [PubMed: 26983851]
9. Philipp CS, Dilley A, Miller CH, et al. Platelet functional defects in women with unexplained menorrhagia. J Thromb Haemost. 2003; 1:477–484. [PubMed: 12871453]
10. Mills HL, Abdel-Baki MS, Teruya J, et al. Platelet function defects in adolescents with heavy menstrual bleeding. Haemophilia. 2014; 20:249–254. [PubMed: 24251971]
11. Byams VR, Anderson BL, Grant AM, et al. Evaluation of bleeding disorders in women with menorrhagia: a survey of obstetrician-gynecologists. Am J Obstet Gynecol. 2012; 207:269.e1–269.e5. [PubMed: 22901979]
12. Sokkary N, Dietrich JE. Management of heavy menstrual bleeding in adolescents. Curr Opin Obstet Gynecol. 2012; 24:275–280. [PubMed: 22729091]
13. Wilkinson JP, Kadir RA. Management of abnormal uterine bleeding in adolescents. J Pediatr Adolesc Gynecol. 2010; 23:S22–S30. [PubMed: 20869283]
14. Leissinger C, Carcao M, Gill JC, et al. Desmopressin (DDAVP) in the management of patients with congenital bleeding disorders. Haemophilia. 2014; 20:158–167. [PubMed: 23937614]
15. Kouides PA, Byams VR, Philipp CS, et al. Multisite management study of menorrhagia with abnormal laboratory haemostasis: a prospective crossover study of intranasal desmopressin and oral tranexamic acid. Br J Haematol. 2009; 145:212–220. [PubMed: 19236375]
16. Lukes AS, Kouides PA, Moore KA. Tranexamic acid: a novel oral formulation for the treatment of heavy menstrual bleeding. Womens Health (Lond). 2011; 7:151–158. [PubMed: 21410342]
17. Lukes AS, Moore KA, Muse KN, et al. Tranexamic acid treatment for heavy menstrual bleeding: a randopmized controlled trial. Obstet Gynecol. 2010; 116:865–875. [PubMed: 20859150]
18. Srivaths LV, Dietrich JE, Yee DL, et al. Oral tranexamic acid versus combined oral contraceptives for adolescent heavy menstrual bleeding. J Pediatr Adolesc Gynecol. 2015; 28:254–257. [PubMed: 26024940]

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TABLE 1

Patient characteristics in female adolescents vs adults with HMB N (%)

	Total (N = 269)[a]	Adolescent (Postmenarchal) <18 y, N = 79	Adult ≥18 y, N = 190	*P* Value
Age (years)				
Median (IQR)	22 (15)	16 (2)	27 (13)	<.0001
Race/Ethnicity: N (%)				
White (non-Hispanic)	206 (77)	53 (67)	153 (81)	.05
Black (non-Hispanic)	20 (7)	6 (8)	14 (7)	
Hispanic	26 (10)	13 (16)	13 (7)	
Other	17 (6)	7 (9)	10 (5)	
Family history of BD: N (%)				
Yes	152 (57)	35 (44)	117 (62)	.06
No	72 (27)	28 (35)	44 (23)	
Unknown	44 (16)	16 (20)	28 (15)	
Diagnosis: N (%)				
VWD	223 (83)	69/(87)	154 (81)	.21
Coagulation factor deficiency	44 (16)	11 (14)	33 (17)	.59
Platelet disorder	11 (4)	2 (3)	9 (5)	.66
Unspecified	9 (3)	2 (3)	7 (4)	
VWD type: N (%)				
Type 1	188 (84)	60 (76)	128 (67)	.36
Type 2	14 (6)	5 (6)	9 (5)	
Type 3	8 (4)	2 (3)	6 (3)	
Unknown	13 (6)	2 (3)	11 (6)	
Age diagnosed with BD: N (%)				
<18 y old	168 (62)	71 (90)	97 (51)	<.0001
≥18 y old	77 (29)	–	77 (41)	
Unknown age	24 (9)	8 (10)	16 (8)	
Median, IQR	14 (13)	12 (7)	16 (16)	<.0001
Age at first bleed in years				
Median, IQR	10 (10)	9 (10)	10.5 (10)	.46
Delay in diagnosis of BD				

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	Total (N = 269)[a]	**Adolescent (Postmenarchal) <18 y, N = 79**	**Adult ≥18 y, N = 190**	***P* Value**
No	86 (32)	34 (43)	52 (27)	.01
Yes	183 (68)	45 (57)	138 (73)	
Delay in diagnosis of BD in years[b]				
Median, IQR	8 (12)	4 (7)	10 (12)	.005
Age at menarche in years				
Median, IQR	12 (2)	12 (2)	12 (2)	.13
BMI: N (%)				
Normal weight or less	79 (48)	28 (56)	51 (45)	.41
Overweight	39 (23)	10 (20)	29 (25)	
Obese	46 (28)	12 (24)	34 (30)	
Anaemia: N (%)				
No	112 (42)	39 (49)	73 (38)	.14
Yes	144 (54)	36 (46)	108 (57)	
Unknown	12 (4)	3 (4)	9 (5)	

VWD, von Willebrand disease; BD, Bleeding Disorder; HMB, Heavy menstrual bleeding; IQR, interquartile; BD, Bleeding disorder; VWD, von Willebrand Disease.

[a]Due to missing values, the total n may be variable in demographic and clinical characteristics.

[b]Delay in diagnosis of BD was defined as the difference between the age at diagnosis and the age at first bleed in years.

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TABLE 2

Bivariate analysis of bleeding phenotype and HMB management in female adolescents vs adults with HMB, N (%)

Bleeding phenotype	Total (N = 269)	<18 y (N = 79)	≥18 y (N = 190)	*P* value[a]
More than 1 nosebleed per year lasting 10 min or longer	131 (49)	35 (45)	96 (51)	.42
Oral mucosal bleeding lasting 10 min or longer	77 (29)	25 (32)	52 (28)	.55
Bleeding during or after dental procedures of concern to health care provider	104 (40)	23 (31)	81 (43)	.09
Bleeding from minor cuts lasting 5 min or longer	165 (62)	43 (55)	122 (65)	.17
Bruises larger than a quarter size occurring at least once a month without trauma	173 (65)	47 (60)	126 (67)	.33
Bleeding after surgery of concern to health care provider	96 (36)	19 (25)	77 (41)	.02
Bleeding with pregnancy/postpartum of concern to health care provider	59 (23)	2 (3)	57 (31)	<.0001
Joint bleeding	45 (17)	13 (17)	32 (17)	1.00
Muscle bleeding	22 (8)	3 (4)	19 (10)	.14
Central nervous system bleeding	6 (2)	1 (1)	5 (3)	.67
Gastrointestinal bleeding	26 (10)	2 (3)	24 (13)	.01
Heavy menstrual bleeding management				
Antifibrinolytics (Epsilon aminocaproic acid, Tranexamic acid [TXA])	78 (29)	25 (32)	53 (28)	.56
Desmopressin (DDAVP, Stimate)	102 (38)	39 (49)	63 (33)	.02
Hormonal therapy[b]	158 (59)	46 (58)	112 (59)	1.00
Gynaecologic procedure/surgery[c]	33 (12)	3 (4)	30 (16)	.01
Clotting factor products	17 (6)	6 (8)	11 (6)	.59
Blood or plasma products (packed red blood cell, plasma, cryoprecipitate), platelet transfusion, and other therapies	17 (6)	4 (5)	13 (7)	.78

[a] *P* value was calculated using Pearson's Chi-squares test.

[b] Therapy includes oral contraceptives, levonorgestrel intra-uterine device (LNg IUD), other hormonal contraceptives (patch, ring, implants, injections).

[c] Dilatation and curettage, endometrial ablation, uterine artery embolization, hysterectomy, other gynaecological surgery.

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TABLE 3

Multivariate analysis of bleeding phenotype and HMB management in female adolescents vs adults with heavy menstrual bleeding

Patient characteristics	a. Bleeding symptom model AOR (95%)[a]	b. Heavy menstrual bleeding management model AOR (95%)[a]
Race/Ethnicity (vs White)		
Black (non-Hispanic)	1.2 (0.2–6.4)	1.3 (0.3–6.2)
Hispanic	0.3 (0.1–0.7)	0.3 (0.1–0.9)
Other	0.6 (0.2–2.2)	0.7 (0.2–2.2)
Family history of BD (vs No)		
Yes	2.6 (1.3–5.6)	3.0 (1.5–6.3)
Unknown	1.0 (0.4–2.5)	1.3 (0.5–3.2)
Delay in diagnosis of BD (vs No)	2.5 (1.2–4.9)	2.4 (1.2–4.6)
VWD (Yes vs No)	0.3 (0.1–1.3)	0.4 (0.1–1.5)
Anaemia (Yes vs No)		
Yes	2.2 (1.2–4.2)	2.7 (1.4–5.2)
Unknown	2.3 (0.3–15.3)	2.6 (0.4–16.4)
Bleeding during or after dental procedures of concern to health care provider	2.0 (1.0–4.0)	–
Gastrointestinal bleeding (Yes vs No)	4.6 (1.0–21.9)	–
Desmopressin (Yes vs no)	–	0.4 (0.2–0.8)
Gynaecologic procedure/surgery (Yes vs No)	–	5.9 (1.3–27.3)

[a]AOR: Adjusted odds ratio was calculated using multiple logistic regression.