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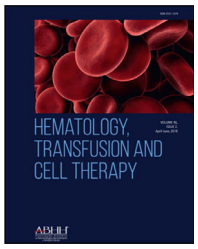

Letter to the Editor

Pediatric standardized bleeding assessment tool for screening bleeding disorder in school-age children

Dear Editor,

Mild bleeding disorders are underreported due to their minor signs and symptoms. A national survey of bleeding disorders in Thailand demonstrated that almost all of the patients were diagnosed with hemophilia (91.4%).[1] In addition, the small ratio of health care providers to the population, 1:6,000 in remote areas of Thailand,[2] may contribute to the low number of diagnosed patients. In children, both the Pediatric Bleeding Questionnaire (PBQ) and the International Society on Thrombosis and Hemostasis Bleeding Assessment Tool (ISTH-BAT) have been used successfully to screen bleeding disorders in patients presenting with bleeding problems at hospitals.[3–7] In 2017, a Thai pediatric BAT was developed by translating the questionnaires and the PBQ and ISTH-BAT scoring systems into Thai (Supplementary file). The median (SD) scores in normal Thai children for the PBQ and the ISTH systems were 0 (−1 to 5) and 0 (0 to 5), respectively. From the PBQ and ISTH-BAT scoring systems, a score ≥3, regardless of sex, suggested the presence of a bleeding disorder.[8] However, the application of these tools to the general population is still lacking. Therefore, this study aimed to demonstrate the benefits of Thai pediatric BAT in identifying undiagnosed bleeding disorders in school-age children.

This cross-sectional study, from July 2017 to January 2018, included student subjects from two high schools. These schools were part of the Department of Pediatrics' Ramathibodi School Health Program. After receiving informed consent from the subjects and their parents, the study team arranged a visit day to perform the study. This study was approved by the Ramathibodi Research Ethics Board (ID 04-60-15).

Thai pediatric BAT was simplified by creating a box checklist front page of 13 bleeding symptoms: epistaxis, cutaneous, minor wound, oral cavity, gastrointestinal, hematuria, tooth extraction, surgery, menorrhagia, postpartum, muscle, joint, and central nervous system. The subjects were asked to choose their bleeding symptom(s) and answer the detailed questions on the relevant page of the questionnaire given behind individual checklists. A pictorial blood loss assessment chart was inserted to depict heavy menstrual bleeding.[9] Groups of 5–6 subjects were formed with one pediatrician per group. Before commencing the questionnaires, the pediatrician thoroughly explained all questions to the group. Bleeding information from questionnaires was scored using the PBQ and ISTH-BAT scoring systems. All subjects with a score ≥3 for either of the systems, according to the cut-off score of Thai children, further consented to visit the hematology clinic for blood testing. The Thai pediatric BAT was also reapplied with parents to confirm bleeding history if symptom(s) occurred in early childhood. Laboratory testing included complete blood count, bleeding time, platelet function analysis-100, activated partial thromboplastin time (APTT), prothrombin time (PT), thrombin time (TT), von Willebrand factor antigen (VWF:Ag), ristocetin cofactor activity (VWF:RCo), platelet aggregation test, fibrinogen level, and factor VIII activity. The criteria for VWD diagnosis referred to the recent updated guidelines.[10]

In total, 309 subjects, including 126 males and 183 females, were enrolled. The mean (SD) age was 15.2 (0.5) years. The median (range) of the Thai pediatric BAT scores was 0 (-2 to 5) according to the PBQ scoring system and 0 (0 to 5) according to the ISTH scoring system (Table 1). Eight subjects (1 male and 7 females) had Thai pediatric BAT scores ≥3; among them, the most common bleeding symptoms were oral bleeding, menorrhagia, and epistaxis. Bleeding scores of two subjects were changed according to additional information from their parents; however, their scores remained in the ≥3 scoring range (Table 2). Platelet counts, platelet morphology, APTT, PT, and TT of all subjects were normal. Two subjects were diagnosed with VWD. Subject 5 was diagnosed with VWD type 1 based on low VWF:Ag and VWF:RCo levels, at 35.5% and 32%, respectively. Subject 1 was diagnosed with VWD type 2A based on a low VWF:RCo to VWF:Ag ratio of 0.32 and was later confirmed by a VWF multimeric study. To verify the low probability of bleeding disorders in subjects with scores <3, sixteen subjects with a score of 2 were offered similar laboratory investigations, and fourteen accepted

Table 1 – Characteristic of students from two schools.

Parameter	School A	School B	Total
Number	189	120	309
Male [(number (%)]	68 (36.0)	58 (48.3)	126
Female [(number (%)]	121 (64.0)	62 (51.7)	183
Mean age (SD)	15 (0.4)	15 (0.6)	15 (0.5)
Thai Pediatric-BAT			
Median PBQ scoring key (range)	0 [(-2)-4]	0 [(-1)-5]	0 [(-2)-5]
Median ISTH scoring key (range)	0 [0-3]	0 [0-5]	0 [0-5]
Students with Thai Pediatric-BAT ≥ 3 [(number (%)]	4 (2.1)	4 (3.3)	8 (2.6)
Students with confirmed bleeding disorder [(number (%)]	1 (0.5)	1 (0.8)	2 (0.6)

BAT, bleeding assessment tool; *ISTH*, International Society of Thrombosis and Hemostasis; *PBQ*, Pediatric bleeding questionnaire

the offer. Their laboratory results were normal. Therefore, the prevalence of bleeding disorders in this study was 0.65% (2/309).

This study is the first to demonstrate the use of Thai pediatric BAT for screening bleeding disorders in school-age children. The selected age group was able to report their bleeding symptom(s).[6] The prevalence of VWD in the present report (0.65%) was lower than that in a previous report in healthy Thai blood donors (0.96%).[11] This lower prevalence may be due to subjects with bleeding symptoms in the present study compared with healthy blood donor subjects in the previous study. A community-based screening of bleeding disorders was previously reported using a door-to-door survey by trained workers. A set of screening questions about family history of bleeding and six bleeding symptoms was initially used. Subjects who reported any abnormal bleeding symptoms underwent ISTH-BAT. A total of 33% of the screened subjects were suspected to have bleeding disorders. After blood testing, the results demonstrated an overall prevalence of bleeding disorders of 0.022%.[12] The lower bleeding disorder prevalence could have resulted from unreported milder bleeding symptoms at the time of screening. Therefore, our study demonstrates the potential use of the Thai pediatric BAT as a screening tool in the general population. In addition, the benefits of screening were: (1) an increase in the number of subjects diagnosed with mild bleeding disorders; (2) counseling provision given to diagnosed subjects on the prevention of bleeding; and (3) management of bleeding symptoms, for example, hypermenorrhea and epistaxis using tranexamic acid or desmopressin.

Nonetheless, our study had several limitations. First, the Thai pediatric BAT, designed for health care personnel, required explanation of each bleeding symptom before subjects selected the answers; second, our laboratory testing panel was unable to exclude unique bleeding disorders, such as FXIII deficiency or hyperfibrinolysis. Therefore, further investigation should be considered in patients who are still suspected of having bleeding disorders.

Table 2 – Characteristics of subjects with Thai pediatric BAT ≥3.

Subject	Gender	Age (yrs)	Symptom	The Thai Pediatric-BAT		BT (2–7 min)	PFA-100		Coagulogram (APTT, PT, TT)	Fibrinogen (mg/dL)	VWF: Ag (%)	VWF: RCo (%)	FVIII: C (%)	Platelet aggregation test	Diagnosis
				PBQ ($1^{st}/2^{nd}$)	ISTH ($1^{st}/2^{nd}$)		COL/EPI (<135 sec)	COL/ADP (<130.5 sec)							
1	F	15.3	Oral, ecchymosis	3/3	1/1	N/A	225	163	Normal	306	59.9	19.1	122	Normal	VWD type 2A
2	F	15.3	Epistaxis	3/3	3/3	5	185	233	Normal	251	81.8	61.2	99	Normal	Normal
3	F	15.3	Epistaxis, oral, menorrhagia	3/3	3/3	6.5	N/A	N/A	Normal	306	70	63.7	101	Normal	Normal
4	F	15.7	Epistaxis, oral, menorrhagia	7/3	6/2	4	147	100	Normal	436	146.3	127.4	142	Normal	Normal
5	F	15.9	Epistaxis, oral, menorrhagia	5/5	5/5	5.5	104	81	Normal	222	35.5	32.2	126	Normal	VWD type 1
6	F	15.4	Oral and dental	4/4	4/4	4.5	N/A	N/A	Normal	313	96.8	79.5	139	Normal	Normal
7	M	16.0	Oral and dental	3/4	3/4	5	66	59	Normal	219	166.5	94	220	Normal	Normal
8	F	15.8	Oral and dental	2/2	3/3	2.5	124	117	Normal	276	102.7	100	114	Normal	Normal

APTT, activated partial thromboplastin time; *BT*, bleeding time; *COL/ADP*, collagen/adenosine diphosphate; *COL/EPI*, collagen/epinephrine; *F*, female; *FVIII:C*, factor VIII clotting activity; *ISTH*, International Society on Thrombosis and Hemostasis; *M*, male; *min*, minute; *N/A*, not available; *PBQ*, Pediatric Bleeding Questionnaire; *PFA*, platelet function analysis; *PT*, partial thromboplastin time; *sec*, second; *TT*, thrombin time; *VWD*, von Willebrand disease; *VWF:Ag*, von Willebrand factor antigen; *VWF:RCo*, von Willebrand ristocetin cofactor activity; *yrs*, years.

Note:

1. 1^{st} is the score of subjects from the first screening at school, and 2^{nd} is the score at the hematology clinic with additional information from parents.
2. The laboratory methods of the present study were as follows: platelet function analysis-100 (Sysmex, Kobe, Japan), von Willebrand factor antigen (enzyme-linked immunosorbent assay; ELISA), ristocetin cofactor activity (platelet agglutination, Chrono-Log, Pennsylvania, USA), platelet aggregation test (light transmission Agg, RAM Helena, Texas, USA), and fibrinogen level and factor VIII activity (clotting method, CS-2500 Sysmex, Kobe, Japan).

In summary, screening for bleeding disorders using a Thai pediatric BAT was able to diagnose bleeding disorders, with a VWD prevalence of 0.65%.

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Conflicts of interest

The authors declare no conflicts of interest.

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Supplementary materials

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