

CLINICAL RESEARCH

Red Flag Study: An observational cross-sectional survey looking at bleeding in patients with a bleeding disorder who are lost to follow-up

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Background: Regular follow-up visits and routine care is important for people with a mild bleeding disorder in terms of lowering their risk of complications from untreated bleeds and helping them maintain a healthy lifestyle. However, follow-up visits among this population can sometimes be missed for unclear reasons. **Aim:** The present study aimed to question if lost-to-follow-up patients with a bleeding disorder experience unreported but important bleeding events

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People with mild bleeding disorders who are lost to follow-up may experience bleeding episodes that impact their quality of life. A recent Canadian study suggests education is key to enabling better reporting and management of bleeds among this patient group, and improving their overall health outcomes.

that are not communicated to their haemophilia treatment centre (HTC) and if they could benefit from more frequent clinic visits. **Methods:** A multicentre paper-based cross-sectional survey was sent to people diagnosed with an inherited blood disorder and lost to follow-up for two years or more. Those who met the eligibility criteria received the survey by mail and completed and returned it to their HTC between October 2015 and July 2016. **Results:** Invitation packages were sent to 71 individuals; 14 questionnaires

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returned, with a survey response rate of 19.7%. Of the 14 returned surveys, only 11 participants were eligible who either responded completely or partially to the survey. Quality of life was reported as almost never or never a problem by all but one participant, who limited activities due to bleeding problems. Spontaneous nosebleeds were sometimes, often or always a problem for three participants; one female participant reported issues associated with heavy menstrual bleeding as often or almost always a problem.

Conclusion: We concluded that although the mean annual bleeding self-reported events were relatively low, they cannot be underestimated when keeping in mind the limitations and challenges of accessing data among this population. Our study highlighted the importance of educating this group of patients on their bleeding disorder and engaging them in their own care and health status, which may result in improving their health-related quality of life and overall health outcomes.

Keywords: *mild bleeding disorders, haemophilia, education, follow-up*

Bleeding disorders are a group of conditions that result in abnormal blood coagulation. The inability to form a stable blood clot may result in a life-threatening bleeding condition. People with haemophilia (PwH) may experience bleeding into joints, muscles, or other parts of their bodies ^[1]. Severity levels for haemophilia have generally been defined by baseline factor VIII or factor IX activity: severe <1% of normal, moderate 1% to <5%, and mild 5% to 40%. Clinical signs of moderate or severe cases include readily recognised bleeding occurring spontaneously or as a result of minor trauma during routine physical activity. In contrast, people with mild bleeding disorders, von Willebrand disease (VWD) or platelet function disorders may not necessarily have abnormal or prolonged bleeding problems until they experience serious trauma or have a post-operative bleeding episode ^[2]. All PwH (mild, moderate and severe) and those with other bleeding disorders may also experience bleeds identified as subclinical episodes, which go unrecognised by the patient and it may not be clear that treatment is needed ^[3,4]. If not treated promptly, some bleeds will take longer to stop and will require longer period of time to heal. Therefore, after being diagnosed with a bleeding disorder, it is recommended that patients follow a treatment plan, receive routine care involving at least one clinic visit

per year, maintain a healthy lifestyle, and learn how to lower their risk of complications, as recommended in the World Federation of Hemophilia (WFH) Guidelines for the Management of Hemophilia ^[2].

In reality, many people with a mild bleeding disorder become lost to follow-up. The reasons for this remain unclear, but may be linked to complications of their disorder being infrequent or subclinical so that the disease is minimised, often until a catastrophic injury or post-operative bleed occurs. It is not known whether this patient group also experience known bleeding episodes that are not treated. Our survey aimed to determine if lost-to-follow-up patients with a bleeding disorder are experiencing important bleeding events that are not communicated to their haemophilia treatment centre (HTC) and to evaluate if more frequent clinic visits could benefit this population.

METHODS

A postal survey was developed by a team of expert haemophilia physicians, clinic directors and haemophilia nurse case managers from two HTCs participating in this study: Children's Hospital of Eastern Ontario (CHEO), Ottawa, Ontario, and Moncton Hospital, Moncton, New Brunswick. Both participating sites obtained local Research Ethics Board approval before starting the study. The survey included questions aimed at evaluating the participants' quality of life, bleeding events, dental, gastrointestinal and urinary problems, sexual activity, energy level, current medications, and menstrual periods for female participants. Participants were asked to rate their experience of different types of bleeding episode since their last appointment at their HTC on a scale from 0 to 4, where 0 was 'never been a problem' and 4 was 'almost always a problem'.

People diagnosed with an inherited blood disorder and lost to follow-up at their HTC for two years or more were screened monthly by their treatment team in order to confirm their eligibility for the study. Our inclusion criteria included patients of any age diagnosed with a clotting factor deficiency 5%–40%, Type 1 von Willebrand disease or platelet function disorder, who had not been seen in their HTC for more than two years. Patients and/or families who could not answer the questionnaire in English or French and those who reported that they had been seen in clinic within the last two years were excluded.

Once eligibility was confirmed, study packages were mailed out to potential participants (or their caregivers).

Study packages included an invitation letter and a paper-based anonymised questionnaire. The invitation letter explained the aim and the outcome of the study as well as the next steps if they decided to participate. A postage-paid return envelope was also provided in the study packages to be used to return the completed questionnaire to the clinic. A reminder letter and a second copy of the questionnaire were sent out to those who had not responded one month later.

RESULTS

Invitation packages were sent to 71 potential participants and questionnaires were completed and returned to the participating sites between October 2015 and July 2016. Fourteen questionnaires were returned, giving a survey response rate of 19.7%. Participants were deemed to be ineligible if they self-reported their last appointment at their HTC as being 'Within the last year' or '1 to less than 2 years ago'. Of the 14 returned surveys, only 11 were eligible and either responded completely or partially to the survey.

Different disease populations represented by the respondents were Type 1 VWD (n=5), platelet function disorder (n=5), and mild haemophilia (n=1). Approximately equal numbers of age range (9–17 years and 30–64 years) were represented (54.5% and 45.5% respectively) including both males (n=5) and females (n=6). The results are summarised in Tables 1 and 2.

Quality of life was reported as never or almost never a problem for any of the respondents, with the exception of one participant who had to limit their activities because of bleeding problems. In addition, one participant reported that they often had a problem with bleeding, with nosebleeds that lasted longer than 10 minutes. Two participants reported spontaneous nose bleeding as sometimes or often being a problem, while it was always a problem for one participant. Managing nosebleeds on their own was sometimes or often a problem for two participants. Dental problems were sometimes a problem for one participant, and for another participant who was having complications with dental work. Energy levels were sometimes a problem in terms of being irritable, feeling tired, having difficulty in concentrating, difficulty sleeping, and feeling sad or depressed. Among female respondents, issues relating to heavy menstrual bleeding, including frequent changing of pads, wearing double pads and saturating clothes, were reported by one participant as often a problem or almost always a problem.

DISCUSSION

Despite sending reminders to potential participants to complete the survey, we believe that some individuals may simply have chosen not to participate, resulting in an overall low response rate for our survey at 19.7%^[5]. Reasons for non-response may relate to the length and sensitive nature of the questionnaire, which has previously been described with unexpectedly low response rates in health-related studies, negatively affecting the sample size and the analysis results^[6]. Previous reports looking at multivariable models, mixing reminders between written emails or text messages and verbal reminders via telephone, have shown that the response rate can be 13% higher than using one technique alone^[7,8].

Although the mean annual bleeding self-reported events were relatively low in our study, they should not be underestimated. Accessing data among this patient population is difficult, and it should be acknowledged that even among our small sample, some bleeding events were reported as being sometimes, often or always a problem (e.g. nosebleeds, heavy menstrual bleeding). The gap in knowledge regarding bleed identification, management and reporting is a crucial issue^[9]. Since the threshold above which a patient may seek medical attention is subjective, reporting and interpretation of bleeding is reliant on patient self-assessment. Patients may pay undue attention to overt bleeding episodes, such as nosebleeds, whereas other bleeds may be ignored or go unnoticed^[3,4]. Education is therefore key in ensuring that patients are better equipped to report their bleeding episodes. Current educational strategies and content may be similar, but information received by families is variable depending on the educator. The benefits of empowering patients to participate in their health care cannot be underestimated.

Technology has a key role to play in supporting education and engagement among people with bleeding disorders. For our patient population, tools for patient engagement could include patient portals, such as MyChart (Epic) and MyCBDR (Canadian Bleeding Disorder Registry), which could enable the administration of patient-reported outcome measures (PROM) by sending out electronic surveys. This approach would allow for self-reporting to the HTC between clinic visits and enriches information about clinical and quality of life outcomes while capturing the gaps in patient knowledge. Offering electronic consultations can also allow for a continuous communication between the patient and their HTC.

while avoiding face-to-face consultation ^[10]. In the long term, this could help to maintain ongoing clinic contact and keep people with bleeding disorders engaged in managing their condition, while minimising both patient and health care delivery costs by decreasing the frequency of clinic visits. Web-based patient education may also be a useful tool, by providing digital, comprehensive, evidence-based modules that engage patients of all ages, and their caregivers, through self-directed learning. Incorporating videos in patient's education can increase the understanding of self-managing and decrease the stress associated with learning while adding the consistency factor to the learning materials offered to patients.

Although bleeding problems were mostly reported by study participants as 'never a problem' or 'almost never a problem', nosebleeds and heavy menstrual bleeding were an issue for some, and one participant reported sometimes limiting activities due to bleeding problems. All educational interventions should emphasise the fact that even if bleeds rarely occur, individuals with a bleeding disorder need to register and maintain routine visits to their HTC to receive regular assessment and ensure the identification of any disease-associated complications, such as iron deficiency anaemia, complications that impact on quality of life, and the need for multiple admissions due to post-operative bleeding. It is also important that this patient group is aware of the importance of seeking treatment if bleeding was noticed after significant injury or post-operatively so that bleeding can be treated early and adequately ^[11]. This may be an issue of increasing importance with the existence of an ageing bleeding disorders population who may be more at risk of falls and comorbidities ^[4]. Teaching sessions focusing on how to identify and report signs of minor bleeds with highlights on the consequences of several untreated bleeds can equip patients with the proper knowledge on the importance of seeking treatment. Equal attention should be drawn to different bleeding sites. For example, although some nose and mouth bleeds might visibly be minor, patients should be aware that sometimes it is hard to know the amount of bleeding when the blood is swallowed or flows down the back of the throat. They can also sometimes be hard to stop because it is difficult for a clot to form on a moist surface. Patients should be aware of signs to monitor to serve as a self-assurance tool for them to seeking medical attention.

CONCLUSION

Even though the mean annual bleeding report for people with mild bleeding disorders can be relatively low, it can have a measurable impact on QOL and on their clinical burden ^[3]. As previously reported about this population, financial, insurance and scheduling appointments are barriers, but one of the most important barriers is educational and involves lack of awareness among patients regarding the important signs of bleeding ^[9]. Patients can frequently experience minor bleeding episodes that can have a significant impact if not treated promptly and adequately. Engaging this population in their health management has the potential to normalise their lives, improve their health-related QOL and provide them with a smarter, safer future.

To conclude, while our data provides a snapshot of some events as self-reported by lost to follow-up people with a bleeding disorder, it also shows limitations in accessing data within this population and raises a red flag calling for strategies aimed at engaging this difficult-to-access patient group. This will help to enable a patient-centred care and education for people with mild bleeding disorders that takes into account the sensitivities, feelings, fears, and other issues associated with their condition.

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Table 1. Results for questions relating to quality of life, bleeding, dental, GI and urinary problems

SECTION	QUESTION	NEVER A PROBLEM	ALMOST NEVER A PROBLEM	SOMETIMES A PROBLEM	OFTEN A PROBLEM	ALMOST ALWAYS A PROBLEM	NO RESPONSE (NR)	NOT APPLICABLE (NA)
Quality of life	I have felt unwell because of my bleeding disorder	9	2	0	0	0	0	0
	I have missed work or school because of bleeding problems	9	2	0	0	0	0	0
	I have missed 2 or more days of work/school per month because of bleeding problems	11	0	0	0	0	0	0
	I limit my activities because of bleeding problems	10	0	1	0	0	0	0
Bleeding problems	I have visited the emergency department for bleeding problems	9	2	0	0	0	0	0
	I have visited my doctor for bleeding problems	9	2	0	0	0	0	0
	I have nosebleeds that last longer than 10 minutes	9	1	0	1	0	0	0
	I can manage nosebleeds on my own	3	0	1	1	5	1	0
	I need to have treatment with medication for nosebleeds	7	0	0	0	0	4	0
	I have spontaneous nosebleeds	5	0	2	2	1	1	0
	If so, how often	0	0	0	1	1	4	5
Dental problems	I have bleeding around my teeth and gums	7	3	1	0	0	0	0
	I have prolonged bleeding from biting my mouth and tongue	9	2	0	0	0	0	0
	I have bleeding complications with dental work	10	0	1	0	0	0	0
GI and urinary problems	I have bleeding from my rectum	10	1	0	0	0	0	0
	I have vomited blood	11	0	0	0	0	0	0
	I have had vomit that looked like coffee grounds	11	0	0	0	0	0	0
	I have had unexplained stomach pain	10	1	0	0	0	0	0
	I have had bleeding after a colonoscopy	11	0	0	0	0	0	0
	I have had blood in my urine	11	0	0	0	0	0	0
	If so, how often	0	0	0	0	0	0	11

Table 2. Results for female specific questions, and questions on sexual activity, energy levels and medications

SECTION	QUESTION	NEVER A PROBLEM	ALMOST NEVER A PROBLEM	SOMETIMES A PROBLEM	OFTEN A PROBLEM	ALMOST ALWAYS A PROBLEM	NO RESPONSE (NR)	NOT APPLICABLE (NA)
For female patients (N=6)	My periods last longer than 7 days	1	1	0	0	0	5	4
	My periods are less than 28 days apart	1	0	0	0	1	5	4
	I pass clots during my period	1	1	0	0	0	5	4
	I have to change pads every 2 hours or less because of bleeding	1	0	0	0	1	5	4
	I have to change pads/tampons at night	1	0	0	0	1	5	4
	I have to wear double pads	1	0	0	1	0	5	4
	I saturate my clothes	1	0	0	1	0	5	4
	I have had bleeding after sexual activity	1	0	1	0	0	4	5
Sexual activity								
Energy levels	I feel frequently tired or fatigued	1	3	3	1	0	2	1
	I have difficulty concentrating	2	3	2	1	0	2	1
	Family and friends describe me as irritable	3	2	3	0	0	2	1
	I eat a vegetarian diet	8	0	0	0	0	2	1
	I have difficulty sleeping	2	2	2	0	2	2	1
	I have felt the need to take iron supplements	5	2	0	1	0	2	1
	I have felt sad or depressed	2	1	3	1	1	2	1
	I have cancelled plans because of lack of energy	6	1	1	0	0	2	1
Current medications	Please list your current medications including any herbal products or medications without a prescription	1	0	0	0	0	6	0
	Medications listed	Laxaday (laxative), APO Paroxetine, APO Lorazepam, Dixilant (60mg) QD, Rosuvastatin (10mg) QD, Ramipril (2.5mg) QD, Zopidone (7.5mg) QD, Sertraline (50mg) QD and Lorazepam (1mg) BID when needed, high blood pressure meds						