


ORIGINAL ARTICLE

Posttraumatic stress disorder and posttraumatic stress symptoms among adults with hemophilia A and B

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Abstract

Background: Persons with hemophilia may encounter various traumatic experiences related to their bleeding disorder throughout their lifetime. Little is known about the clinical impact of disease-related trauma on this population.

Objectives: To explore the prevalence of posttraumatic stress disorder (PTSD) and posttraumatic stress symptoms in adults with hemophilia A and B and characterize the traumatic experiences they report.

Methods: An online survey tool collecting data on participant characteristics and a validated questionnaire containing the PTSD checklist for Diagnostic and Statistical Manual of Mental Disorders 5 were distributed via Research Electronic Data Capture to adults with hemophilia A and B during their annual visit to their hemophilia treatment center. Participants were asked about traumatic experiences specific to their hemophilia prior to self-administering the PTSD checklist for Diagnostic and Statistical Manual of Mental Disorders 5 questionnaire.

Results: Survey responses from 178 individuals across 3 hemophilia treatment centers were included in the analysis, representing a 70% response rate. One hundred one (56.7%) participants identified a hemophilia-related traumatic event, and 21 (11.8%) participants met criteria for a provisional diagnosis of PTSD. Multivariable analysis showed higher odds of a positive PTSD screen in participants with noninfectious (odds ratio [OR], 13.89; 95% CI, 2.23-86.62) and infectious comorbidities (OR, 11.18; 95% CI, 1.34-93.45) and in participants with >1 mental health comorbidity (OR, 10.07; 95% CI, 2.39-42.52). On the contrary, age >46 years (OR, 0.6; 95% CI, 0.01-0.62) and higher education (OR, 0.25; 95% CI, 0.07-0.88) reduced odds of PTSD.

Conclusion: Persons with hemophilia are at risk of developing PTSD and posttraumatic stress symptoms. These data support the need for trauma screening, psychosocial services in the bleeding disorders community, and provision of trauma-informed care by providers.

KEYWORDS

adult, hemophilia, posttraumatic, prevalence, stress disorders

Essentials

- Posttraumatic stress disorder prevalence was identified among adults with hemophilia.
- A validated survey tool was administered online to adults with hemophilia at 3 clinics.
- Criteria for posttraumatic stress disorder were met by 11.8% of participants; 5 themes of trauma emerged in subjective description.
- We recommend trauma screening for patients and trauma-informed care education for providers.

1 | BACKGROUND AND SIGNIFICANCE

There is a growing amount of research focused on posttraumatic stress disorder (PTSD) in individuals who have experienced chronic and acute medical illness. After being exposed to a traumatic event, symptoms of PTSD include intrusive memories, avoidance of reminders of the traumatic event, negative alterations in cognitions and mood, and marked alterations in arousal and reactivity [1]. Persons with hemophilia may be at risk for developing PTSD or posttraumatic stress symptoms (PTSS) as a result of disease-related events throughout their lifetime.

Several factors put the hemophilia community at risk for PTSD and PTSS. Treatment contamination in the 1980s yielded high rates of infectious disease including HIV and hepatitis within the hemophilia population; the repercussions of the HIV/AIDs epidemic had a devastating impact on the hemophilia community. Past studies have shown that health-related quality of life is negatively impacted by specific events related to hemophilia, including hepatitis, disability, acute bleeds, and arthropathy [2,3]. Other research studies illustrate a high prevalence of depression and anxiety among persons with hemophilia [4,5], but little is known about the clinical impact of trauma and disease-specific challenges on this population.

Understanding the breadth of trauma among persons with hemophilia is important because its impact on health outcomes is significant. In other disease groups, studies show that PTSD may lead to reduced adherence to treatment and increased risk for poor overall health outcomes [6–8]. Developing illness-induced PTSD has been shown to increase overall physical disease burden [9]. Additionally, pain is commonly experienced by those with hemophilia; literature suggests that those with chronic pain and comorbid PTSD report more severe pain and poorer quality of life than those with chronic pain alone [10]. Another potentially concerning risk of PTSD is developing substance dependence, as past research shows an association between childhood trauma exposure and development of substance use disorders later in life [11].

While the prevalence of illness-induced PTSD, specifically in cancer, cardiovascular disease, and stroke, ranges from 12% to 15% [12], the subjective experience of trauma or the prevalence of PTSD or PTSS among persons with hemophilia has not been evaluated. This study was conducted to better predict risk factors associated with PTSD development in those with hemophilia in order to determine

who might need assessment, intervention, and assistance. Early assessment and intervention may lead to better health outcomes.

A survey-based, cross-sectional study was conducted to screen for specific trauma symptoms and to explore the prevalence of preliminary PTSD diagnoses in adults with hemophilia. Additionally, the subjective description of traumatic experiences identified by participants was characterized to determine experiences unique to hemophilia that are associated with potential development of PTSS or PTSD.

2 | METHODS

2.1 | Participants

Adults aged ≥ 20 years with an established diagnosis of hemophilia A or B were included in this cross-sectional, survey-based study. Potential participants were receiving care at the Boston Hemophilia Treatment Center (Massachusetts), the Mount Sinai Hemophilia Treatment Center (New York), or the M Health Fairview Center for Bleeding and Clotting Disorders (Minnesota) at the time of data collection. The survey was available only in English, so non-English speakers were excluded from participation. The survey was administered between February 2020 and December 2021.

2.2 | Recruitment

Potential participants were informed of the study during their annual comprehensive clinic evaluation at their respective hemophilia treatment center (HTC). If they expressed interest in participation, a survey link was sent electronically, and participants self-administered the survey. The link included a research information sheet and the survey tool. Information containing mental health resources and education on PTSD was also made available. The survey link was password protected with a unique ID to allow appropriate follow-up by the social worker if a participant screened positive for a provisional diagnosis of PTSD. All data collected were based on patient-reported outcomes.

Online consent was obtained at the onset of the survey. Survey responses were collected via Research Electronic Data Capture, a secure, web-based, data collection tool. Participants were given the option to skip questions and were instructed to stop taking the survey

at any point if they were experiencing emotional distress. This study was approved by the institutional review boards at Brigham and Women's Hospital, Icahn School of Medicine at Mount Sinai, and the University of Minnesota.

2.3 | Survey instrument

The tool for this study had 2 components ([Supplementary Material](#)).

2.3.1 | Participant characteristics

The tool was used to collect the following information: age, gender (defined by self-report), employment status, and education attainment. Within this tool, participants were asked to identify specifics of their hemophilia diagnosis, including severity, comorbidities, and past hemophilia-related hospitalizations. Participants were then asked if there had been any particularly stressful episodes or features of their hemophilia that had caused significant distress throughout their life. They were given the opportunity to provide a description of the traumatic experience and estimate when in their life it occurred. Finally, participants were asked whether they had been previously diagnosed with any of the following mental health conditions: anxiety, PTSD, depression, bipolar disorder, or other mood or psychiatric disorders.

2.3.2 | PTSD checklist for Diagnostic and Statistical Manual of Mental Disorders 5

The PTSD checklist for Diagnostic and Statistical Manual of Mental Disorders 5 (DSM-5) (PCL-5) is a validated, 20-item, self-report questionnaire that assesses the 4 DSM-5 symptom clusters (PTSS) of PTSD; it can be used to screen for PTSD symptoms and/or provide a provisional diagnosis of PTSD [13]. Responses on each item are scored using a 5-point Likert scale: "Not at all," "A little bit," "Moderately," "Quite a bit," and "Extremely." The PCL-5 measures DSM-5 symptom cluster severity scores by summing the scores for the items within a given cluster, that is, cluster B/intrusion symptoms (items 1-5), cluster C/avoidance symptoms (items 6-7), cluster D/negative alterations in cognition/mood (items 8-14), and cluster E/arousal or reactivity symptoms (items 15-20).

Using the PCL-5, a provisional PTSD diagnosis can be made in 2 ways. The first way is by summing the total score from all 20 items (range, 0-80) on the questionnaire (method 1). A symptom severity score of 31 to 33 was supported in the literature as the recommended cutoff score for a positive PTSD screen [14]; a cutoff score of 31 was used in this study to maximize sensitivity.

The second method of scoring is by following the DSM-5 diagnostic rule, which requires that following a traumatic event, the person endorses each PTSD symptom cluster by scoring moderately or above on at least 1 B item, 1 C item, 2 D items, and 2 E items (method 2). In this study, a participant was determined to be experiencing PTSS if they endorsed at least 1 PTSD symptom cluster following this rule. Both methods of scoring were used to assess the prevalence of PTSD.

TABLE 1 Demographic and clinical characteristics of participants.

Characteristic	Values (N = 178)
Age (y), median (IQR)	38 (29-52)
Missing age, n (%)	12 (6.7)
Gender, n (%)	
Male	167 (93.8)
Female	11 (6.2)
Education level, n (%)	
Did not complete high school	2 (1.1)
Completed high school	49 (27.5)
Completed college	81 (45.5)
Master's degree or higher	46 (25.8)
Employment status, n (%)	
Full-time	118 (66.3)
Part-time	10 (5.6)
Student	5 (2.8)
Full-time parent	1 (0.6)
Unemployed (not due to hemophilia)	25 (14.0)
Unemployed (due to hemophilia)	17 (9.6)
Unanswered	2 (1.1)
Diagnosis, n (%)	
Severe A	86 (48.3)
Moderate A	18 (10.1)
Mild A	29 (16.3)
Severe B	21 (11.8)
Moderate B	13 (7.3)
Mild B	10 (5.6)
Unanswered	1 (0.6)
Traumatic event, n (%)	
No	76 (42.7)
Yes	101 (56.7)
Unanswered	1 (0.6)
Prior hemophilia-related hospitalization, n (%)	
No	36 (20.2)
Yes	142 (79.8)

2.4 | Analysis

2.4.1 | Statistical methods

Participants who skipped more than 1 question on the PCL-5 were considered to have incomplete data and were excluded from analysis. Descriptive statistics are provided by number of participants and percentage for categorical variables, separately for those who met

TABLE 2 Sources of reported trauma.

Sources of trauma	Values (N = 101), n (%)
Noninfectious medical event	83 (82.1)
Psychosocial	48 (47.5)
Pain	14 (13.8)
Hepatitis C	11 (10.9)
HIV/AIDS	10 (9.9)
>1 source	53 (52.5)

criteria for a provisional PTSD diagnosis or did not, and for those who met who met clinical criteria for each PTSD symptom cluster. Associations between the PCL-5 score and other variables were investigated using the Wilcoxon sum-rank test or the Kruskal-Wallis test, depending on the number of levels in the variable. Age was categorized as ≤ 34 years, 35 to 46 years, and ≥ 47 years. Comorbidities were categorized by the absence or presence of infectious disease (HIV/AIDS/hepatitis) and noninfectious disease (inhibitor/arthropathy), and based on these, participants were grouped into 4 categories. The Fisher exact test was used to assess the association between the PTSS and hemophilia severity. Odds ratios (ORs) for PTSD were calculated using logistic regression. Multivariable logistic regression models were used to identify features of the participants that were associated with differential odds of a provisional PTSD diagnosis. These models were fit using backward elimination until the model stabilized. All analyses were performed using R 4.0.2 (R Core Team [2023]. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria. <https://www.R-project.org>). The stepwise multivariable model was fit using the *Mass* package; *tidyverse* was used for data manipulation. We report point estimates with 95% CIs, based on logistic regression models.

2.4.2 | Qualitative methods

Participants were asked if there had been any particularly stressful episodes or features of their hemophilia that have caused significant distress throughout their lives. They were given the opportunity to provide a brief narrative of the traumatic experience and recall when in their lives it occurred. Using inductive coding, responses received in this narrative were analyzed for understanding of lived experiences. Sources of trauma emerged as themes, which were then categorized.

Brief narratives were organized in a spreadsheet, and data were read several times and grouped into themes. The themes were further analyzed to identify recurring language, patterns, and opinions and then were organized in a cohesive manner as related to the purpose of the study. Initial review and analysis were independently completed by each HTC social worker, and then outcomes were compared and discussed until a final consensus on descriptive coding was reached and turned into this study's final narrative.

TABLE 3 Characterization of trauma.

Trauma characteristic	Positive PTSD screen (N = 21), n (%)	All participants who endorsed traumatic events (N = 101), n (%)
Chronic trauma	19 (90.4)	83 (82.2)
Multiple sources of trauma	12 (57.1)	53 (52.5)
Occurred or began during childhood	13 (62)	59 (58.4)

PTSD, posttraumatic stress disorder.

3 | RESULTS

Of the 253 patients who met eligibility criteria and were asked to participate in this study, 186 patients responded to the survey. The data from 178 participants were included in the analysis. This excludes the 8 participants who skipped more than 1 question on the PCL-5 and were considered to have incomplete PCL-5 data. The final sample represented an overall response rate of 70%. Participants had a median age of 38 (IQR, 29-52) and 167 participants (93.8%) were male. Severity and type of participants' hemophilia varied and included: severe A, 86 (48.3%); moderate A, 18 (10.1%); mild A, 29 (16.3%); severe B, 21 (11.8%); moderate B, 13 (7.3%); mild B, 10 (5.6%); and not identified, 1 (0.6%). Demographic and clinical characteristics of participants are reported in [Table 1](#).

More than half of the participants ($n = 101$, 56.7%) identified a traumatic event related to their hemophilia. The following 5 themes emerged from sources of trauma described: noninfectious medical event(s), psychosocial, pain, hepatitis, and HIV/AIDS. For more than half (52.5%) of the participants who identified a traumatic event, more than 1 theme was represented in their trauma description. Among those who identified a trauma, 83 participants (82.1%) reported trauma related to a noninfectious medical event like a bleed or injury, and 48 participants (47.5%) reported a psychosocial issue like being bullied or missing important events as a source of their hemophilia-related trauma. Other traumatic events were described as pain ($n = 14$, 13.8%), related to hepatitis ($n = 11$, 10.9%), or related to HIV/AIDS ($n = 10$, 9.9%). For the 101 individual descriptions of traumatic events that were collected in this study, 166 sources of trauma were reported overall ([Table 2](#)).

The qualitative data highlight the complexity of trauma for persons with hemophilia in terms of its genesis and duration. Most participants (82.2%) who identified trauma described recurring or chronic traumatic events related to their hemophilia, as opposed to the 17.8% of participants who reported an isolated event in the past. Many (58.4%) participants indicated that their trauma began or occurred during childhood; of these, 83% ($n = 49$) described their trauma as chronic rather than a one-time event. An additional 19 participants did not specify trauma onset or duration but rather made statements such as "my whole life" ([Table 3](#)).

Total scores on the PCL-5 ranged from 0 to 66, with a median of 8. The percentage of all participants who met provisional criteria for PTSD diagnosis was 11.8% ($n = 21$) using either diagnostic method, including 6 (28.6%) participants reporting a prior PTSD diagnosis.

TABLE 4 Number of participants who endorsed each post-traumatic stress symptom (via Diagnostic and Statistical Manual of Mental Disorders 5 rule) by cluster.

Cluster	Values (N = 178), n (%)
Cluster B (intrusion)	57 (32.0)
Cluster C (avoidance)	47 (26.4)
Cluster D (negative cognition/mood)	51 (28.7)
Cluster E (reactivity/hypervigilance)	45 (25.3)

Among those who screened positive for PTSD, 62% reported that their trauma began in childhood, 90.4% described their trauma as recurring or chronic in nature, and 57.1% reported multiple themes of trauma (Table 3).

Approximately one-third (35.4%) of participants endorsed PTSS by reporting a traumatic event and meeting clinical diagnostic criteria for at least 1 PTSD symptom cluster. Cluster B (intrusion) symptoms were endorsed most frequently by participants (Table 4). The Figure shows the percentage of participants who answered moderately or above on each PCL-5 question. Among the PCL-5 questions, participants most frequently endorsed trouble falling asleep or staying asleep due to their traumatic event.

The final multivariable model showed higher odds of a positive PTSD screen in participants with infectious and/or noninfectious comorbidities: infectious comorbidities only (OR, 11.18; 95% CI, 1.34-93.45); noninfectious comorbidities only (OR, 13.89; 95% CI, 2.23-86.62), both noninfectious and infectious medical comorbidities (OR, 85.24; 95% CI, 6.1-1190.91). Reporting more than 1 mental health comorbidity (excluding prior PTSD) also increased the odds of a positive PTSD screen (OR, 10.07; 95% CI, 2.39-42.52). On the contrary, age >46 years (OR, 0.6; 95% CI, 0.01-0.62) and higher education (OR, 0.25; 95% CI, 0.07-0.88) were associated with reduced odds of PTSD (Table 5). As no female study participants screened positive for PTSD, gender was not considered for inclusion in the model.

4 | DISCUSSION

It is well established that persons with hemophilia face complex disease-related challenges throughout their life. This study characterized some of these challenges and identified the prevalence of traumatic events, PTSD, and PTSS among adult persons with hemophilia. Our findings show that most adults with hemophilia can identify a disease-related traumatic event, and more than one-third experience clinically significant trauma symptoms. We report that the prevalence of PTSD among adults with hemophilia (11.8%) is roughly 3 times higher than the rates of PTSD experienced in the general population at any given point in time (3.5%-4.7%) [15,16]. Importantly, a majority of those who screened positive for PTSD did not have an established PTSD diagnosis. This may reflect a general lack of screening in this population, underreporting symptoms due to mental health stigma, or may reflect false positive screens in this study.

Although the association between hemophilia severity and PTSD was not deemed statistically significant within this study sample, it is interesting to note that among those with severe hemophilia A and B, 14% met criteria for a provisional PTSD diagnosis. This statistic is consistent with the prevalence of PTSD previously reported in other studies of cardiovascular disease, stroke, and cancer (12%-25%) [9,12]. Overall, these findings suggest that persons with hemophilia are at risk of experiencing PTSS and developing PTSD related to their disease.

This study found several contributing factors that may lead to the development of PTSD symptoms among persons with hemophilia, most notably related to their complex medical experiences. Participants with infectious and noninfectious medical comorbidities including HIV, hepatitis, arthropathy, and inhibitors had higher odds of screening positive for PTSD than participants without medical comorbidities. Noninfectious medical events specific to hemophilia, such as bleeding and development of joint disease, accounted for the majority (82.1%) of self-reported hemophilia-related traumatic events. Perhaps, the more compelling finding was that 92% of participants who endorsed trauma identified an experience that required some level of medical attention, intervention, or interaction with their medical provider. Because hemophilia requires patients to be dependent on the medical system, medical providers should recognize that patients may be experiencing trauma while under their care, or that their interaction with the healthcare system might be retraumatizing. Participants who reported a previous hemophilia-related hospitalization had a higher average PCL-5 score (10) than those who had not been hospitalized (2). For persons with hemophilia, exposure to medical trauma may contribute to the development of PTSD and PTSS or exacerbate trauma symptoms due to the compounding nature of their disease-related experiences.

The considerable rate of endorsement of PTSS in this sample of adults with hemophilia is not surprising. While intrusion symptoms were endorsed most frequently, all 4 PTSD symptom clusters (intrusion, avoidance, negative mood, and arousal) were experienced by at least 25% of study participants. Evaluating each PTSD symptom cluster (PTSS) severity informs providers about how patients process the psychosocial components of their hemophilia, so that targeted mental health interventions or tailored trauma-informed care techniques can be employed. Since hemophilia requires ongoing monitoring and management of symptoms and there is no clear disease conclusion, the potential exposure to trauma or development of medical comorbidities continues. As a result, PTSS presentation may fluctuate over time.

It is plausible that this study did not adequately capture the full scope of traumatic events among adults with hemophilia, or associated trauma symptoms. A large portion of participants ($n = 51$) scored greater than 0 on the PCL-5 but answered "no" when asked if they experienced trauma related to their hemophilia. The symptoms they endorsed could have been related to hemophilia, to another traumatic event in their life, or to both. If related to hemophilia, actual hemophilia-related trauma symptom burden may be much higher than reported here. Additionally, given that avoidance is a common effect of trauma [17], it is conceivable that patients experiencing symptoms

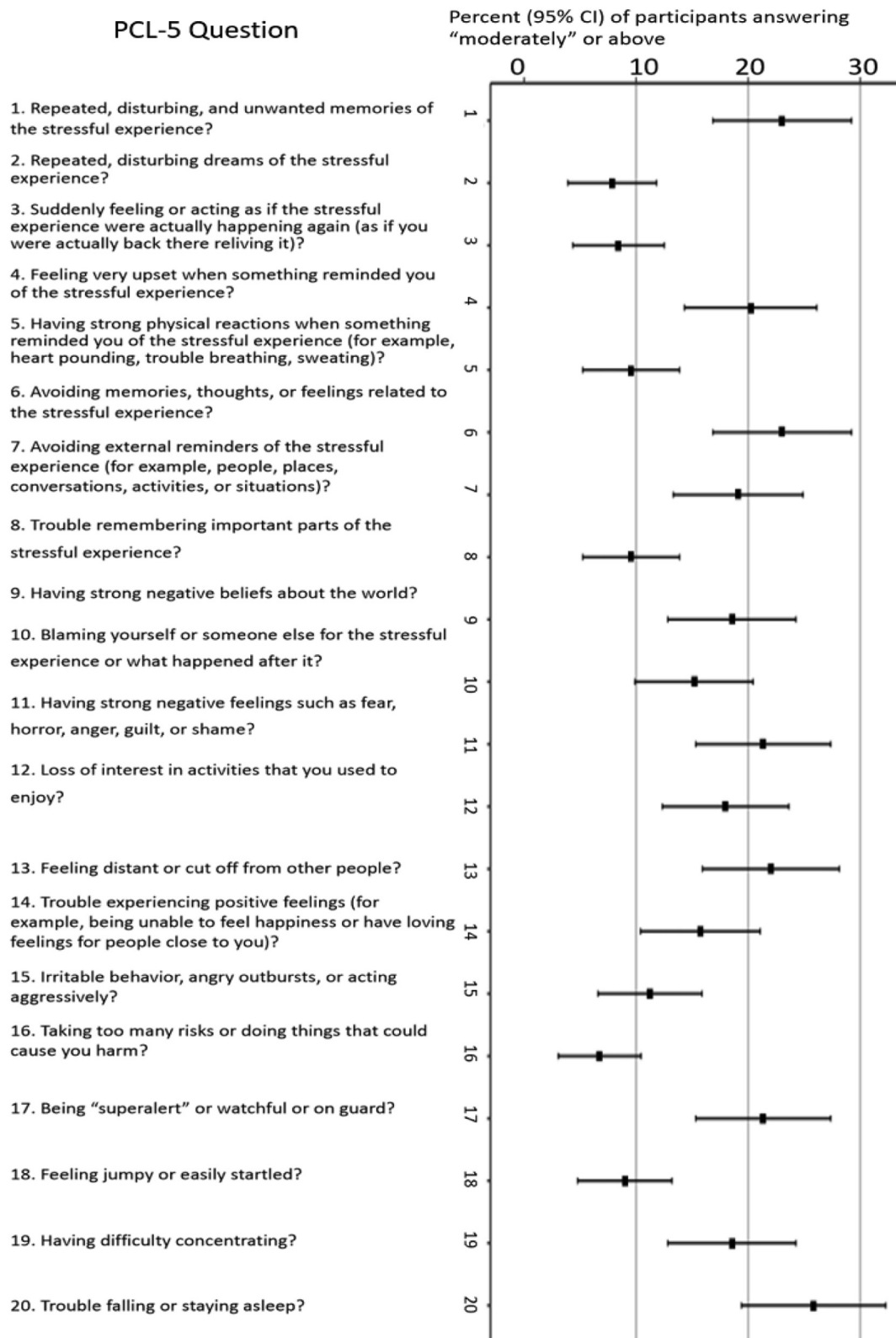


FIGURE Responses to the posttraumatic stress disorder checklist for Diagnostic and Statistical Manual of Mental Disorders 5 (PCL-5) questionnaire. (Note that some PCL-5 questions are abbreviated).

of hemophilia-related trauma missed routine appointments or opted out of taking the survey, which may have contributed to selection bias. Since not all persons with hemophilia have access to HTC, data about

trauma in that subset of this population could not be captured here. With a higher response rate, it is possible that the prevalence of PTSS and PTSD would increase within this population.

TABLE 5 Univariable and multivariable logistic regression models of the associations between demographic and clinical features and post-traumatic stress disorder.

	PTSD = No (N = 157) n (%)	PTSD = Yes (N = 21) n (%)	Univariable model Odds ratio (95% CI)	Multivariable model Odds ratio (95% CI)
Age				
20-34 y (reference)	56 (35.7)	7 (33.3)	1	1
35-46 y	40 (25.5)	8 (38.1)	1.6 (0.54-4.77)	0.56 (0.1-3.32)
46+ y	51 (32.5)	4 (19)	0.63 (0.17-2.27)	0.06 (0.01-0.62)
Missing	10 (6.4)	2 (9.5)		
Gender				
Male (reference)	146 (93)	21 (100)	1	
Female	11 (7)	0 (0)	Cannot compute	
Education				
High school (reference)	40 (25.5)	11 (52.4)	1	1
College or above	117 (74.5)	10 (47.6)	0.31 (0.12-0.79)	0.25 (0.07-0.88)
Employment				
Employed (reference)	116 (73.9)	12 (57.1)	1	
Unemployed	41 (26.1)	9 (42.9)	2.12 (0.83-5.4)	
Prior hemophilia-related hospitalization				
Yes (reference)	121 (77.1)	21 (100)	1	
No	36 (22.9)	0 (0)	Cannot compute	
Comorbidities				
Neither (reference)	83 (52.9)	4 (19)	1	1
Infectious comorbidities only	37 (23.6)	6 (28.6)	3.36 (0.9-12.64)	11.18 (1.34-93.45)
Noninfectious comorbidities only	19 (12.1)	6 (28.6)	6.55 (1.68-25.52)	13.89 (2.23-86.62)
Both infectious and noninfectious comorbidities	18 (11.5)	5 (23.8)	5.76 (1.41-23.61)	85.24 (6.1-1190.91)
Number of prior mental health comorbidities				
0 (reference)	123 (78.3)	7 (33.3)	1	1
1	18 (11.5)	5 (23.8)	4.88 (1.4-17.03)	2.58 (0.54-12.34)
>1	16 (10.2)	9 (42.9)	9.88 (3.24-30.19)	10.07 (2.39-42.52)
Severity of hemophilia				
Mild/moderate (reference) ^a	64 (41.0)	6 (28.6)	1	1
Severe ^a	92 (58.6)	15 (71.4)	1.77 (0.65-4.79)	0.29 (0.0-1.24)

PTSD, posttraumatic stress disorder.

^aSeverity was not reported for 1 participant, who is thus excluded from the table.

Multivariable analysis showed that, in addition to the clinical comorbidities that were associated with increased odds of PTSD development, demographic features such as older age and having some college education were associated with reduced odds of developing PTSD as a result of hemophilia. These data expose the vulnerability of younger and less educated adults to the development of PTSD, particularly those with medical or mental health comorbidities.

The lack of association between PTSD symptomatology and hemophilia severity in the univariate setting was unexpected given the health management requirements of severe disease. One explanation

is that those with mild disease interface with the medical system less often and may be less equipped to navigate the medical challenges of hemophilia, thus creating a more stressful or traumatic situation if a medical issue arises. Some adults with mild or moderate hemophilia are diagnosed later in life following an accident, bleeding event, major surgery, or medical intervention (ie, wisdom teeth removal). This can lead to a reshaping of identity as a person living with a chronic illness. Receiving a diagnosis later in life has the potential to be uniquely traumatizing, as opposed to receiving a diagnosis in childhood, where identity formation occurs alongside the hemophilia diagnosis.

The diagnosis of PTSD is discerning in that it acknowledges the impact of potentially life-threatening or life-altering experiences that persons with hemophilia face in a comprehensive way. It lays out a framework in which intrusion symptoms, hyperarousal symptoms, cognitive symptoms, and avoidance symptoms may be pathologized and contextualized beyond looking at quality of life, depression, and anxiety alone. This study shows that the nature of trauma for persons with hemophilia is complex, multilayered, and often recurring. Among those who screened positive for PTSD, most reported that their hemophilia-related trauma began in childhood, and more than half reported multiple sources of trauma. When a trauma occurred during childhood, it was likely for the participant to re-experience trauma over time. Nearly half of the participants who identified a traumatic event reported that their trauma was related to a psychosocial stressor, highlighting the social and emotional impact of hemophilia.

Categorizing and describing traumatic experiences and PTSS among persons with hemophilia help explain the emotional burden patients face because of their disease. The impact of trauma has been well documented in the literature, showing that it can lead to reduced adherence to treatment and increased risk for poor overall health outcomes [6–8,18,19]. Without regular treatment and follow-up, persons with hemophilia are at risk of disease-related complications and potential development of clinical trauma symptoms as a result. An awareness of the type of medical events that could evoke distressing symptoms in persons with hemophilia could increase provider confidence in providing appropriate trauma-informed care. Our findings support the need for improvements in education regarding the nature of trauma among the hemophilia population and trauma prevention strategies for all members of the multidisciplinary healthcare team. Trauma-informed care has the potential to improve patient engagement, treatment adherence, and health outcomes for persons with hemophilia.

This study had several limitations. First, the PCL-5 has been used to measure psychological sequelae with good internal consistency, test-retest reliability, and validity [13], but asks only about single, past traumatic events. This study demonstrated that the nature of the psychological impact of trauma among persons with hemophilia can be both chronic and complex. This survey tool may incorrectly pathologize normal responses to illness as PTSD.

Pain is commonly reported among those with hemophilia, and the literature suggests the interdependence of pain and PTSD symptoms [10,20–22]. Pain as a source of trauma for persons with hemophilia may be underrepresented in this study. A relatively small percentage (19%) of those who met provisional criteria for PTSD stated that pain was a source of trauma; this number may have increased if we asked specifically about pain within the identified traumatic event or how the participant experiences pain. Even though events such as bleeding, surgeries, and hemorrhages could conceivably be painful, if the participant did not cite pain specifically in their trauma description, inductive coding excluded the opportunity for clarification.

Additionally, this study relied on participant self-report regarding both hemophilia diagnosis and mental health diagnosis. Symptoms were assessed at a single point in time and, therefore, are subject to recall bias. Routine or repeat screening could increase understanding

as symptoms may wax and wane over time. Also, since most data were collected during the global COVID-19 pandemic, it is unknown how much COVID-19 impacted the response rate or symptom burden. Finally, race or ethnicity was not queried for in this study. The absence of this information could potentially affect the generalizability of our findings to a broader cross-section of persons with hemophilia and prevents us from determining whether a patient's racial or ethnic background is associated with the development of PTSD in the setting of hemophilia.

This study was limited to the diagnosis of hemophilia A and hemophilia B in adults. For a more comprehensive understanding of what trauma looks like within the broader bleeding disorders population, this research could be expanded to other diagnoses or age groups.

5 | CONCLUSIONS

In conclusion, our research findings suggest that adults with hemophilia are at higher risk than the general population of developing PTSS or PTSD as a result of their disease-related burden, and the nature of their traumatic experiences has now been described. These data support the need for psychosocial services in the bleeding disorders community and improvements in hemostatic therapies. With a more comprehensive understanding of the pervasiveness of trauma symptoms among persons with hemophilia and the experiences they identify as traumatic, better mental health treatment modalities and screening tools may be developed and employed in HTC and beyond.

FUNDING

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ETHICS STATEMENT

This study was approved by the institutional review boards at Brigham and Women's Hospital, Icahn School of Medicine at Mount Sinai, and the University of Minnesota. Online consent was obtained at the onset of the survey. Participants were given the option to skip questions and were instructed to stop taking the survey at any point if they were experiencing emotional distress.

AUTHOR CONTRIBUTIONS

A.S. created the concept and design. A.S., K.B., A.K.W., H.S.P., and A.P. developed the methods. A.S., K.B., A.K.W., and A.P. conducted the research. A.S., K.B., A.K.W., S.R., D.N., and A.P. analyzed the data. A.S., K.B., A.K.W., and A.P., wrote the manuscript. All authors edited and approved the manuscript.

RELATIONSHIP DISCLOSURE

A.P. reports research support from Shire/Takeda and Genentech/Hoffman LaRoche; participation on advisory boards for Genentech, Shire/Takeda, Sigilon, and UniQure; and consulting for Aspa, I-mAb,

and Sunovion. D.N. reports stock ownership in Madrigal Pharmaceuticals.

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SUPPLEMENTARY MATERIAL

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