Hemophilia A Bleeding Frequency and Its Impact on Specific Quality of Life Domains: A Pilot Study

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Background

Hemophilia, a rare bleeding disorder characterized by a deficiency of coagulation factors, significantly impacts the quality of life of those affected. According to the World Blood Disease Registry (WBDR) 2023 data, there are 257,146 individuals with hemophilia worldwide, with hemophilia A (HA) constituting approximately 80% of these cases.[1] In Taiwan, the recorded prevalence of HA as of 2019 was 8.58 cases per 100,000 population, with a total of 992 identified patients.[2, 3] Frequent bleeding episodes are a hallmark of hemophilia and have a profound negative impact on quality of life.[4] To address this, the Haemophilia Quality of Life Assessment project was launched in 1998 to develop and validate a comprehensive assessment tool specifically tailored for children and adolescents with hemophilia. The project culminated in the creation of three validated versions of the Haemo-QOL questionnaire, covering various domains such as physical health, emotional well-being, and self-perception, etc. These questionnaires are designed to measure the quality of life of patients over the past month or week, with higher scores indicating poorer quality of life.[5]

While studies have established a link between frequent bleeding and low quality of life in hemophilia patients, the specific correlations between Haemo-QOL domains and bleeding frequency have been less extensively explored. This study aims to delve deeper into these relationships, providing valuable insights into the multifaceted impact of hemophilia on patients' overall well-being.

Objective

This study aimed to investigate the association between bleeding frequency and individual Haemo-QoL domains in Hemophilia A patients.

Method

Study Setting

The study was conducted at Kaohsiung Medical University Chung-Ho Memorial Hospital (KMUH), a tertiary care teaching hospital in Kaohsiung, Taiwan. Established in 1957, KMUH serves as a leading center for medical treatment, research, and clinical training. Its Hemophilia Center offers comprehensive care for hemophilia patients, making it an ideal setting to investigate the relationship between bleeding frequency and quality of life (QoL) in individuals with Hemophilia A. As a primary referral center for hemophilia care in southern Taiwan, KMUH provides specialized expertise and a unique cohort of patients for this study.

Study Subjects

The study included adult male patients with hemophilia A, aged 18 years or older, who were regularly followed at the hematology outpatient clinic of Kaohsiung Medical University Chung-Ho Memorial Hospital (KMUH) in 2023.

- **Inclusion Criteria**:
  - Confirmed diagnosed with hemophilia A
  - Male
  - Received treatment at KMUH for a minimum of 6 months prior to study enrollment.
- **Exclusion Criteria**:
  - Patients diagnosed with hemophilia B or other bleeding disorders.
  - Individuals unable to complete the study questionnaire due to cognitive or communication limitations.

Study Design

This is a **cross-sectional observational study** that aimed to evaluate the quality of life (QoL), and bleeding episodes in hemophilia A patients. Data was collected through patient-reported outcomes and medical a review of medical records.

Questionnaire and Data Collection

Participants completed the Haemo-QoL, a well-established patient-reported outcome measure designed to assess health-related quality of life (HRQoL) in individuals with hemophilia. The questionnaire encompasses a range of domains (Table 1), with higher scores indicating poorer HRQoL. Bleeding frequency was self-reported by participants using detailed diaries and corroborated by clinical records whenever possible. Supplementary data, including severity, age, weight, etc. were also collected.

Statistical Analysis

Data were analyzed using IBM-SPSS Statistics (version 25). The following statistical methods were employed:

- **Descriptive Statistics:** Descriptive statistics were calculated to summarize the demographic and clinical characteristics of the study subjects. Means and standard deviations (SD) were used for continuous variables, while frequencies and percentages were reported for categorical variables. These results are presented in Table 2.
- **Kendall's Tau-b Correlation:** To assess the association between bleeding frequency and various QoL domains, Kendall's Tau-b correlation analysis was conducted. This non-parametric test is suitable for ordinal data. The correlation coefficients (τ) and p-values are presented in Table 3, with statistical significance set at $p < 0.05$. and $p < 0.001$.
- **Hierarchical Regression Analysis:** A hierarchical regression model was employed to examine the effect of bleeding frequency on the Physical Health domain while controlling for potential confounding variables such as age, weight, medication type, and dosage. The adjusted R-squared indicates the proportion of variance in physical health explained by the included variables.

  - $y = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \beta_4 x_4 + \beta_5 x_5 + \varepsilon$

    y = Haemo - QoL Physical Health Domain Score
    β_0 = Intercept
    x_1 = Age
    x_2 = Weight.
    x_3 = Medication Type
    x_4 = Dosage
    x_5 = Bleeding Frequency

Table 1. Haemo-QoL Domains

Domains	Name of Domains	Brief Descriptions
1	Physical Health	Measures the physical impact of haemophilia, including pain, mobility limitations, and physical function.
2	Feelings	Assesses the emotional burden of living with haemophilia, including anger, worry, and feeling excluded.
3	View of Yourself	Evaluates how haemophilia affects self-perception, including feelings of envy, body image, and the difficulty of managing the condition.
4	Sports and Leisure	Assesses the restrictions on sports, freedom to travel, and the necessity to plan activities in advance.
5	Work and School	Examines the impact of haemophilia on work and school, including attendance, performance, and focus.
6	Dealing with Haemophilia	Evaluates the ability to manage bleeds, recognize symptoms, and feel in control of haemophilia.
7	Treatment	Assesses the treatment-related factors, such as dependence on factor concentrate, physician reliance, and concerns about injections or complications.
8	Future	Assesses the concerns about the future, including fears of worsening health, life plans, and potential disability.
9	Family Planning	Assesses the fears and concerns regarding raising a family, including the ability to have and care for children.
10	Partnership and Sexuality	Addresses the insecurities in relationships and the impact of haemophilia on dating and intimate relationships.

Results

Although a general trend towards lower Haemo-QoL scores (indicating poorer quality of life) was observed across most domains in patients experiencing bleeding during the study period, statistical analysis did not reveal a significant difference between bleeding and no bleeding groups (Figure1). Hierarchical regression analysis, controlling for age, weight, medication type, and dosage, demonstrated a significant between bleeding frequency and the Physical health function of individuals with hemophilia A (Table 4).

Table 2. Characteristics of the Study Subjects

Variables	Bleeding Group (n=9)	No Bleeding Group (n=15)	p-value (t-test)
Age (Mean ± SD)	38.67 ± 9.51	35.53 ± 14.61	0.572
Weight (Mean ± SD)	79.75 ± 10.05	72.68 ± 9.99	0.311
Dose (IU) (Mean ± SD)	4000.00 ± 1511.86	3686.67 ± 1355.95	0.496

Table 3. Kendall's Tau-b Correlation Between Bleeding Frequency and Haemo-QoL Domains

	QD1	QD2	QD3	QD4	QD5	QD6	QD7	QD8	QD9	QD10	Bleeding
QD1	1	0.472**	0.337*	-0.019	0.363*	0.229	0.356*	0.515**	0.212	0.300	0.14
QD2		1	0.560**	0.224	0.519**	0.163	0.543**	0.802**	0.554**	0.653**	0.141
QD3			1	0.153	0.282	0.097	0.510**	0.519**	0.317	0.535**	0.053
QD4				1	0.237	-0.02	0.305*	0.156	0.359*	0.194	-0.066
QD5		*p < 0.05			1	0.151	0.427**	0.455**	0.628**	0.334*	0.239
QD6		**p < 0.001				1	0.158	0.196	0.188	0.259	0.084
QD7							1	0.541**	0.648**	0.437**	0.024
QD8								1	0.494**	0.511**	0.11
QD9									1	0.368*	0.105
QD10										1	0.132
Bleeding											1

(QD: Haemo-QoL domain)

Figure 1. Compare Haemo-QoL Domain Scores between Bleeding vs. Non-bleeding Groups
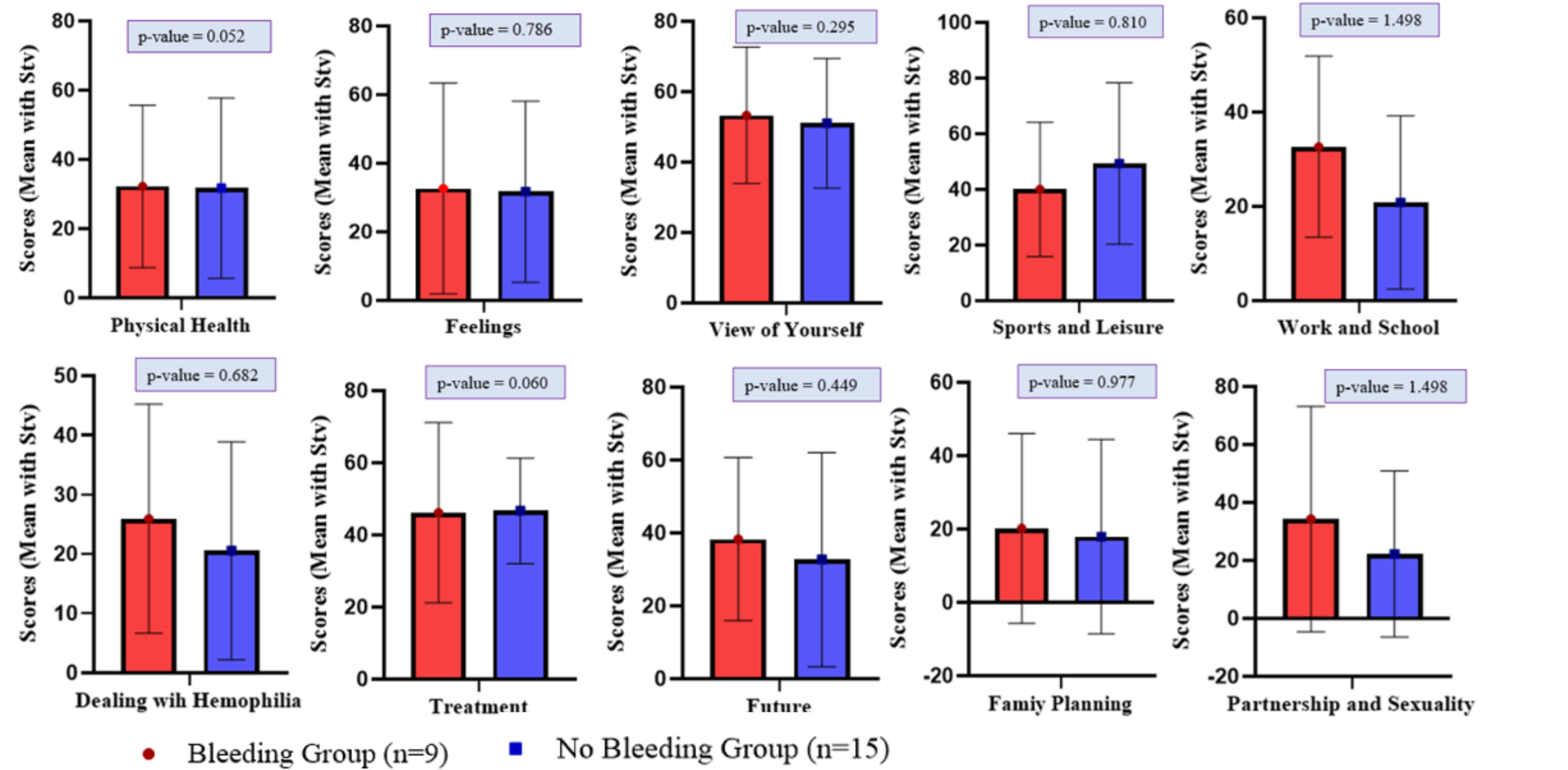

- Bleeding Group (n=9)
- No Bleeding Group (n=15)

Table 4. Hierarchical Regression Analysis Results (Haemo-QOL-Physical Health Domain)

Variables	B	SE	Beta	t-statistic	p-value
Age	-0.526	0.111	-0.403	-4.732	0.001
Weight	-0.977	0.207	-0.602	-4.732	0.001
Medication Type	0.485	0.208	0.334	2.326	0.040
Dosage	0.004	0.002	0.312	2.508	0.029
Bleeding Frequency	0.249	0.0112	0.349	2.231	0.047
Constant	18.123	2.635		6.782	
R²	0.889				
Adjusted R²	0.839				

(B: Hierarchical regression coefficient, SE: Standard error, Beta: Standardized regression coefficient)

Conclusions

This pilot study suggests that bleeding frequency might primarily impact the physical function domain of hemophilia-related quality of life. Future research with larger samples can confirm these findings and explore the influence of bleeding on other QoL aspects. This knowledge can inform the development of targeted interventions that address specific patient needs based on bleeding frequency and its impact on their quality of life.

References:

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